IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF NEW YORK

IN RE: MDL-1596

ZYPREXA PRODUCTS

LIABILITY LITIGATION

THIS DOCUMENT RELATES TO:

ALL CASES

C O N F I D E N T I A L

- - -

July 27, 2006

- - -

Videotape deposition of

CHARLES BEASLEY, JR., M.D.

VOLUME 2

- - -

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about the meeting in Atlanta with the endocrinology outside consultants, do you recall that?
A. That's correct.
Q. And there was mention in that one e-mail with respect to the fact that those individuals had advised Lilly to look at continuous-type analysis of the Zyprexa data; do you recall that?
A. That's correct.
Q. Did Lilly take that advice?
A. To my understanding, yes. There were a number of activities undertaken during the fall and into the winter with medical supervision by, again, Dr. Cavazzoni involvement of interim statistical resources, I believe, Dr. Sowell was, probably, involved to some extent.
And then there were two separate outside consultants that were involved in analyses, Dr. David Allison, actually, earlier in the year, and then later Dr. John Buse.
Q. And to the best of your

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knowledge, Dr. Beasley, has Lilly continued with the project of the continuous-type analysis of the Zyprexa data with respect to blood glucose?
A. I'm not familiar with the specifics of subsequent analysis, but Lilly has certainly continued a number of projects and analyses in this area. It continues to be, obviously, an important area that is continuing to be studied and evaluated.
Q. You were asked, Dr. Beasley, about your change of responsibilities in moving over to a role regarding Cialis. Do you recall those questions?
A. Yes, I do.
Q. And do you have an understanding of what happened? That is, why you moved over to begin work on Cialis?
A. Yes. The medical director who had been responsible for the compound left the company, going to another company, and the molecule had had its submissions so it was in a critical regulatory phase of its development. And I was felt to have

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particular expertise in working both in the U.S., in Europe, and in Japan on the process of consulting with regulatory bodies around the submissions.
Q. All right.
A. So, it was a very good fit.
Q. Now you were asked some questions about what is marked as Plaintiff's Exhibit 1349, and in particular about Page 6 of that exhibit. I want to put that in front of you. That's the exhibit that shows the number of patients at that time in the Zyprexa clinical trials and the duration of exposure with respect to those patients. Do you recall those questions?
A. Yes, I do.
Q. And let me just ask. This is the exhibit that shows the number of Zyprexa patients that got, for example, more than one dose of the drug, exposure to the drug more than a month, then those who had exposure to the drug more than six months, and those who had exposure more than a year. Do you recall questions about that?

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A. That's correct.
Q. Now, Dr. Beasley, was safety data gathered from all of the patients in each of those groups?
A. Safety data was obtained for all individuals who were exposed to the drug.
Q. Are there recognized international standards, Dr. Beasley, with respect to the duration of exposure in drug studies like the clinical trials performed on Zyprexa?
A. There are. There are what are referred to as the CIOMS guidelines that are generally used and recognized by most regulatory agencies. And these, these are the guidelines that sort of dictate or indicate how many patients should be treated for how long before a new drug application can be submitted.
Q. Now with respect to Zyprexa, and again, referring, specifically, to the international guidelines for the duration of exposure for patients in the clinical trials, what can you tell us about how the Zyprexa

clinical trials matched up with those guidelines?

A. Well, the guidelines suggest the number of patients that should be treated for one or more doses, and that is 1500, and for one or more doses with olanzapine or Zyprexa it was 3,139.

The guidelines, actually, recommend a range for six months or greater, and this is 300 to 600. And the number with olanzapine was 876. And the guidelines for one year is 100. And the number of Zyprexa olanzapine patients was 301.

MR. SEE: Just one moment, Dr. Beasley. We're just looking for an additional document.

MR. ALLEN: If I have a copy I'll give it to you.

MR. SEE: I think Michael has one right here.

MR. ALLEN: All right.

MR. SEE: Thanks a lot.

QUESTIONS BY MR. SEE:

THE WITNESS: Should I, are

we finished with this document?

MR. SEE: I think we're finished with that one, Dr. Beasley, thanks.

QUESTIONS BY MR. SEE:

Q. Now I want to ask you about the, what's marked as Plaintiff's Exhibit 1605, and particularly Page 11 of that exhibit.

If you'll recall that's the exhibit that refers to study HGAJ and particularly the nonfasting glucose levels at any time. Do you recall those questions?

A. That's correct.

Q. Now you were, specifically, asked with respect to the Zyprexa patients about the percentage of patients who had a high glucose reading at any time during that study. Do you remember that?

A. Yes, I do.

Q. And that percent is what?

A. That is 2.6 percent.

Q. All right. Now, there's another value there for Zyprexa patients; is

that correct?

A. Yes, there is.

Q. All right. Now, what was not asked of you, and I want to ask of you, is there a value for the Zyprexa patients in that study for moving from normal or high glucose to a low glucose level?

A. Yes, there is.

Q. Now you were already asked about that but I want to ask you about it. What percentage of Zyprexa patients does that show?

A. That is 7.7 percent.

Q. So does that mean that 7.7 percent of Zyprexa patients?

MR. SEE: Strike that. Let me ask it in another way.

QUESTIONS BY MR. SEE:

Q. With respect to the 7.7 percent for Zyprexa patients, can you tell us what does that signify?

A. Well, that signifies the number of individuals who at some time during up to six weeks of treatment with values

being measured weekly had what was defined as a hypoglycemic value, a abnormally low value of glucose.

Q. Now can you make a comparison between the number of Zyprexa patients that went to low glucose as compared to the percentage that went to high glucose?

A. Well, it was 2.6 percent that went to high and 7.7 percent that went to low. That's the percent for low, or the lows are, probably, about 2.8 times as many patients as went to high.

Q. All right. And with that percentage of Zyprexa patients going to a low glucose level what does that tell us, if anything, about the significance of that, quote, at any time glucose measurement?

A. Well, that would suggest that it's very difficult to interpret these data as particularly meaningful. As I was suggesting, this is one analysis that we would take into consideration with the analysis of end point data, similar data at end point, and then mean change data. Which

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800 and was close to being in diabetic ketoacidosis.

Q. Now, what did that experience teach you, if anything, about the issue of patients with schizophrenia and medical problems like blood glucose as a future doctor and psychiatrist?

A. Well, I think there are two aspects of this with respect to what you've asked me. I always had an interest in general medicine outside psychiatry. Felt like psychiatrists had to be first good physicians. And this patient underscored that with respect to basic common medical diseases, such as diabetes. It was also a very rewarding thing in terms of saving this patient's life.

Q. Dr. Beasley, did you receive any particular national honor or recognition during your medical school career?

A. Well, I graduated with high distinction and departmental honors in pharmacology, psychiatry, neurology, and during my senior year I was named American

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Medical Association Rock-Schleyster scholar, which was a national scholarship. I don't recall the number that were awarded. There was a small number.

Q. You told us, I think, you went on for residency training in psychiatry?

A. That's correct.

Q. Remind us where that was?

A. My internship part of the program was at Yale and my last three years of residency were at the University of Cincinnati.

Q. Now there have been questions during your deposition about clinical studies and controlled clinical trials on potential new drugs. Do you recall questions like that?

A. That's correct.

Q. Did you have any experience in your residency program and training with respect to clinical trials of potential new drugs for psychiatric illnesses?

A. I was, actually, asked to take on a part-time job outside my residency

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by university faculty who were conducting clinical research on new drugs as a co-investigator.

Q. Let me ask you the same question I asked about medical school. Did you have any particular national honor or recognition during your psychiatric residency program?

A. I was, during my senior year, I was named a Laughlin Fellow.

Q. What does that mean?

A. Which is a fellowship to attend and participate in the activities of the American College of Psychiatrists, which is an honorary psychiatric society, I think for, approximately, 12 to 15 recipients throughout the U.S. and Canada.

Q. Now, I think you told us you started your job at Lilly after you completed your residency in psychiatry?

A. That's correct.

Q. And what year was that?

A. That would have been 1987. It was 7/7/87.

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Q. So you've been at Lilly now, how long?

A. A little over 19 years.

Q. Now during those 19 years I'd like to ask you to tell us about the nature of your work. And first, with respect to the study and research on new drugs to treat psychiatric illnesses, what has been your job with respect to that?

A. Well, that has been the core if, or certainly the large component of my job. Through my first 17 years or so here I think I, probably, supervised, wrote, directed, the analysis of probably something around 20 clinical trials in that time period with several drugs we talked about yesterday.

Q. And there's also been questions during your deposition with respect to analysis of observed adverse events with drugs. Do you remember questions like that?

A. Yes.

Q. Would you tell us what has been your job, if any part of it, at Lilly for the last 19 years concerning the

evaluation and analysis of observed adverse events in patients taking a drug?

A. Well, that's, that's an integral part of running and analyzing any clinical trial. That has been very much sort of my focus and, frankly, the thing that the company at this point views me relatively expert in, which is why I'm in the consulting position I'm in.

MR. ALLEN: Objection, nonresponsive.

QUESTIONS BY MR. ALLEN:

Q. You were earlier asked some questions with respect to your expertise on treating patients with diabetes in an office practice. Do you remember being asked questions in that area?

A. Yes.

Q. Let me ask you from a slightly different perspective, Dr. Beasley, if we were looking for someone who was well qualified to perform study and research on both the usefulness and safety of proposed new drugs to treat mental disorders, like

schizophrenia, how would your qualifications and your experience stack up regarding that question?

A. I certainly have a great deal of experience in that area, as I understand it, relative to my peers both within and outside Lilly.

Q. And if we were looking for someone well qualified to evaluate, question whether an observed adverse event in patients taking a particular drug are, in fact, caused by the drug or, perhaps, caused by or the result of other factors, how would your experience and qualifications stack up to that question?

A. Well, that's certainly something that I have been involved in with my colleagues, particularly my statistical colleagues, since my employment, at the beginning of my employment at Lilly.

Q. You've been asked some questions about whether you are personally a, an expert in endocrinology or the disease diabetes. Do you recall those questions?

A. Yes, I do.

Q. And are you?

A. No, I have not had that type of formal training.

Q. All right. Tell us were there specialists at Lilly in endocrinology, and in particular in diabetes, who participated in the review and evaluation of this issue about hyperglycemia and diabetes as it concerns Zyprexa?

A. Yes. There were at several levels.

Q. All right. First, have there been specialists in endocrinology and diabetes at Lilly who were principally focused in their careers on these questions?

A. Yes. There have been a series of endocrinologists and diabetologists that were, actually, assigned to work on the Lilly team.

So although not psychiatrists or neuroscientists, their principal assignment was to the team, the product team.

Q. And other than the

specialists in endocrinology and diabetes who were assigned to work principally on the team, have there been other individuals with those specialties who have been involved in studying the hyperglycemia issue as it concerns Zyprexa?

A. Yes. There certainly have been individuals. And we discussed one yesterday on, I think it was on one of the e-mails, a number of the endocrinologists and, specifically, the diabetologists have had the opportunity to review data and give advice and suggestion about continued experimentation in the work.

Q. Now, Dr. Beasley, I want to ask you some questions about how controlled clinical trials with drugs are, actually, conducted. And let me just ask you, would it be helpful for you to actually draw a diagram in order to explain your testimony regarding that?

A. I could do that, yes.

MR. SEE: I think we need to maybe change the location of your

C D E

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seat so that you can, actually, draw the diagram. And so we'll go off the record for just a minute in order to do that. So we're off the record.

MR. ALLEN: Also I need to turn this back on for you because I turned it off. It's just a warm up.

(At this time, the parties went off the record, after which the following proceedings were had:)

THE VIDEOGRAPHER: We're back on the record.

QUESTIONS BY MR. SEE:

Q. Dr. Beasley, we're back on the record now and we've had you come over and sit at the machine that will project what you put on the paper.

Do you see the screen and how what you put on the paper will be projected there?

A. Yes, I do.

Q. All right. Now questions

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that I want to ask you right now have to do with performing clinical trials with proposed new drugs, okay?

A. Yes.

Q. First, let's start with an uncontrolled trial. Can you explain, and if it's helpful make a diagram, of what, what you actually do in performing an uncontrolled trial with a new drug?

A. I can.

Q. And tell us what you're doing?

A. First off, I'm writing the title, uncontrolled, and this is the type of trial that's done early in development that we talked about yesterday where --

Q. All right.

A. -- where there is only a group of individuals that are treated with the drug. There are no other treatments in this trial.

Q. Now tell us what you, actually, do in an uncontrolled trial with the drug?

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A. Let me illustrate some individuals in this trial. We're going to have ten people in this trial.

Q. And the circles represent what?

A. The circles represent the people. So this group of ten people in this uncontrolled.

Q. You've got nine of them there. You better put one more.

A. Got to put the one more. Are treated for some period of time with the proposed drug. There is nobody else being treated with anything but the drug in this particular trial.

Q. All right, then, what do you do?

A. Well, you observe these individuals. You observe them, you do physical examinations, you do blood studies, you collect your history of medical problems, you collect the minor symptoms that they might be having, such as headaches, prior to being treated with drug. And then you repeat

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these examinations periodically during the course of treatment.

Q. All right. Now --

A. You observe things.

Q. All right. Now give us an example of what kind of observations are made in an uncontrolled trial?

A. Well, if we're talking about something like an adverse event, we could say flu-like symptoms, and a number of these individuals might have flu-like symptoms, let's say there's seven of them. So we have seven, ten, flu-like.

Q. Now, Dr. Beasley, if in your example the seven out of the ten in the uncontrolled drug trial were observed to have flu-like symptoms, what conclusions could you draw, if any, whether the drug caused the flu-like symptoms?

A. Well, in this particular trial you wouldn't draw any conclusions about causation or causality. You would simply draw the conclusion that there were a lot of flu-like symptoms experienced in these

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individuals during this trial.
Q. Could you, in fact, make any conclusion with respect to the question does the drug cause flu-like symptoms?
A. No. That would not be considered scientifically appropriate.
Q. Why not?
A. Because there are many things that could cause flu-like symptoms since this is a very common occurrence. It could be the flu virus, it could be common cold viruses, it could be environmental exposures, it could be contaminated sushi that someone ate the evening before or if it were served on an inpatient unit to all these individuals, lots of different potential causes.
Q. Now, if you would, could you tell us about a controlled trial and illustrate that on your diagram?
A. Well, that would be the next step in terms of types of studies. And here we would have --
Q. What does the second box you're drawing represent?

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A. This is going to be a comparison treatment. A comparison group with placebo.
Q. As you're writing the word "placebo" there. You'll have to tell us what that means?
A. This would be a, an inactive substance. It could be corn starch, it could be lactose. It is a capsule or a pill that looks identical to that given to patients who are receiving the drug but it is an inactive or inert substance. It has no chemical action in the body.
Q. All right. And who is in the placebo group?
A. Well, generally, these would be done with similar-sized groups. So, obviously, in clinical trials the numbers are, actually, larger. But in this illustrating example we're having ten drug-treated patients, ten placebo-treated patients. I'll just draw that to make that clear that that's all that one, and that was just the uncontrolled.

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Q. If you have a controlled clinical trial you described two groups and you initially described the observation of adverse events. Would that also be observed in the placebo group?
A. You would do everything identically to the individuals in the drug group and the placebo group.
Q. All right. And provide an example for us regarding the observation of adverse events in the placebo group?
A. Well, if you had a similar number, suppose we had seven of ten, okay?
Q. Now what does that represent?
A. This represents seven of the ten placebo patients also experiencing flu-like symptoms.
Q. Now if you, in fact, had a controlled clinical trial with the observations of adverse events that you have portrayed in your diagram, what, if anything, would you be able to conclude about whether the drug caused the flu-like symptoms?
A. Well, here's where we used

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the mathematics of statistics to compare the percentage, in this case it would be the percentages of patients. And given the very similar number, we would conclude that there is not a significant difference here. And the way that we would interpret that is that it would be unlikely, because there is similarity, it would be unlikely that the drug caused the flu-like symptoms.
We would conclude that other things, unknown to us, but again, with a lot of possibilities, would have caused the flu-like symptoms.
Q. Now, are you familiar with the term called "blinded" as it refers to controlled clinical trials?
A. Yes, I am.
Q. Could you tell us what that means?
A. That means that neither the, the doctors who are giving the drug or, and/or evaluating the patients, performing the examinations, nor the patients know which patient is receiving drug and which patient

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is receiving placebo.
Q. And why is that important, if it is?
A. The reason that that is important is to prevent the, the, either the reporters, the doctors, or the reporters, the patients, from believing that they might have something, some effect because they know what they're receiving and reporting consistent with their belief. It's done to do what we call prevent bias in reporting.
Q. All right. Now Dr. Beasley, if you would, could you draw a vertical line down your diagram there so we can let me ask you questions about a related but different topic.
And now I want to ask you, are you familiar, and we've already heard some questions today about something called a spontaneous report of an adverse event. Are you familiar with that?
A. Yes, I am.
Q. Can you tell us what that is and illustrate that for us, please?

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A. That would be a report that would be received by the company from a wide variety of sources about a patient treated with the drug. When I say wide variety of sources it could be from a physician treating the patient, a pharmacist who had heard about the patient, the patient, him or herself, a relative of the patient. Many different individuals that would call us and report that a patient had experienced a particular event, a spontaneous adverse event --
Q. All right. Now --
A. -- such as flu-like symptoms.
Q. All right. Now, so in your diagram when you put an X on the circle under the spontaneous column, what is that intended to represent?
A. That's intended to represent that the patient has had something that, that whoever the reporter was, considered adverse. So in this case flu-like.
Q. Now, with a spontaneous report of an individual taking a drug who reports experiencing flu-like symptoms, what

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can, what conclusions can you draw, if any, about whether the drug is somehow related to the flu-like symptoms?
A. Well, this does two things: One, what it does is alerts us to the fact that similar to this uncontrolled trial we have an individual who was taking the drug, who at the same time what we call a temporal association, was having flu-like symptoms. Past that, we would draw no conclusions based on this report.
Q. And why could you not draw any conclusions about whether the drug caused the flu-like symptoms in the spontaneous report?
A. That's because we really don't have a control group with which to make comparisons. And this is particularly the case when you've got something that would be relatively common in the population that could be occurring due to a great many possible causes, or what we call etiologies.
Q. All right. Now tell us, Dr. Beasley, suppose the company received

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several or many spontaneous reports of, following your example, patient who's took a drug and experienced flu-like symptoms? And tell us what you're representing there.
A. This would be additional reports, spontaneous adverse event reports.
Q. All right, now tell us what conclusions, if any, can be drawn from the receipt of numerous spontaneous reports from these patients who took a drug and then experienced flu-like symptoms?
A. Particularly with a common event, like flu-like symptoms, we would not be able to draw, again, any sort of causal conclusion or association. It would certainly alert us to the fact that these things, again, had been reported in temporal association and would alert us to the need to further investigate this what had been observed as a temporal link, in clinical trials, in prospective studies, in a number of potential ways.
MR. SEE: Thank you, Dr. Beasley, I think we're finished

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with the camera. So we'll go off the record for just a second and adjust where you're sitting and then we'll go on with the questions.

(At this time, the parties went off the record, after which the following proceedings were had:)

THE VIDEOGRAPHER: We're back on the record.

(Whereupon, Deposition Exhibit(s) 5 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SEE:

Q. Dr. Beasley, the diagram regarding the controlled clinical trial and spontaneous events, we've now put an exhibit sticker on that. Has it been marked Beasley Exhibit 5?

A. It's been marked 5. I don't see a Beasley on it.

Q. Let's add that. Has it now been marked as Beasley Exhibit 5?

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A. Yes, it has been.

Q. Now, Dr. Beasley, in your earlier testimony in the deposition I believe you told us that Zyprexa was approved by the Food and Drug Administration in 1996. Do you remember that?

A. That's correct.

Q. And was there labeling for Zyprexa that was a part of that initial approval in 1996?

A. Yes, there was.

(Whereupon, Deposition Exhibit(s) 6 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SEE:

Q. Let me hand you what we've marked as Beasley Exhibit 6. And ask if you can identify that?

A. This is a Zyprexa label.

Q. Can you look at the date on the last page and orient yourself?

A. Let me look on the back. This is marked, this is dated

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10/02/96. So I believe this would be the original label.

MR. ALLEN: I'm sorry, is this Beasley 6?

MR. SEE: Yes.

MR. ALLEN: Okay, thank you. I apologize.

QUESTIONS BY MR. SEE:

Q. Dr. Beasley, to whom is the product labeling or package insert directed?

A. This would be to the individuals who would be prescribing the medication.

Q. And who is it, Dr. Beasley, that decides what information is included in the Zyprexa labeling or package insert?

A. The FDA.

Q. Now there have been questions during your deposition about weight gain as an adverse event observed in patients taking Zyprexa; do you recall that?

A. Yes.

Q. Let me ask you to turn over to Page 2 of Beasley Exhibit 6, and I want to

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ask you generally were prescribing physicians provided information on weight gain observed with Zyprexa in the original product labeling or package insert?

A. Yes, they were.

Q. First, I want to direct you to table one on the second page. And can you tell us what information was provided about weight gain as an observed adverse event with Zyprexa?

A. Well, again, this was both observed and the information provided here was in reference to what was both observed and then reported as an adverse event by the clinicians conducting the studies.

And it was reported that weight gain occurred and was reported in 6 percent of the olanzapine-treated patients and 1 percent of the placebo-treated patients. These data were the aggregation or the combination of all the placebo controlled data on the medication.

Q. Now let me ask you to turn over to the, essentially, the next table over

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on the next page. Do you see that one?
Called common treatment
emergent adverse events?
A. Yes.
Q. And would you tell us,
please, what's reported about weight gain in
that table?
A. This is the table that
represents what were called common, or most
common treatment adverse events that were
reported at 5 percent or greater. And this
reports the same numbers, weight gain
6 percent and placebo 1 percent.
Q. Now if I could direct your
attention to the bottom of that page. And if
you could tell us is there additional
information about weight gain provided to the
prescribing physician in the original package
insert for Zyprexa?
A. Yes, there is.
Q. Tell us what that is, please?
A. In addition to restating the
information regarding weight gain reported as
an adverse event, this is a summary of

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information regarding what was observed when
patients were weighed on scales to, actually,
determine their weight.
And the first set of
information that is contained describes the
olanzapine patients compared to placebo
patients during the acute or short term or
six week trials. And then it goes on to
describe the experience of all patients
treated in the longer term extensions of all
studies.
And it reports that the
olanzapine-treated patients gained an average
of 2.8 kilograms compared to an average of
0.4-kilogram loss in the placebo patients.
And that when we look at the 7 percent or
greater gain in body weight that that was
29 percent of olanzapine-treated patients
compared to 3 percent of placebo-treated
patients. And again, this is in the acute
phase of the study.
Q. All right.
A. It goes on to describe the
data to, regarding long-term. And again,

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here's where all patients were used with a,
what we call a median or sort of central
point between the fewest number of days and
the longest number of days of treatment being
238 days.
And this reports that
56 percent of patients gained 7 percent or
greater of body weight. And that the average
weight gain during this period was
5.4 kilograms.
The additional information is
provided that the greatest amount of weight
gain was seen in patients who, based on what
we call body mass index or BMI, with patients
with the lowest value for that at baseline.
Q. Now there's also been some
question during your deposition about the
adverse event of hyperglycemia and diabetes
and diabetic acidosis, do you recall that?
A. Yes, I do.
Q. Is there information about
those adverse events observed in patients
taking Zyprexa included in the original
package insert?

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A. They are listed in the other
adverse events observed during the
premarketing evaluation of olanzapine.
Q. And could you particularly
let me reference you to under that column,
the column of endocrine system?
A. Yes.
Q. And can you tell us what is
provided to the prescribing physician
regarding the information regarding diabetes
there?
A. That diabetes mellitus was
observed infrequently and that diabetic
acidosis was observed but rarely.
Q. Now could I refer you to the
metabolic and nutritional disorder section
and ask the same question.
What information was provided
in that section regarding hyperglycemia
observed in patients taking Zyprexa?
A. In this section,
hyperglycemia was indicated to be an event
that was observed with an infrequent
frequency.

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Q. Dr. Beasley, because these events of hyperglycemia and diabetes and diabetic acidosis are included in the package insert for Zyprexa, does that mean Zyprexa causes them?

A. No. What that means is that they were observed during the conduct of trials in patients who were included in the clinical trials.

Q. Dr. Beasley, why was information about weight gain and hyperglycemia and diabetes included in the original package insert for Zyprexa?

A. That, along with the other information that is provided here, is so that physicians take the entirety of the information, judge, make a risk/benefit analysis for use in their patients and be aware of what had been observed.

Q. Now we've had some testimony from you with respect to spontaneous reports of adverse events, do you recall that?

A. Yes, I do.

Q. And did Lilly receive

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spontaneous reports of adverse events from patients taking Zyprexa after Zyprexa was approved and went on the market?

A. Yes.

Q. And tell us what did and does Lilly do, if anything, to monitor its receipt of reports of adverse events?

A. Well, this would be the, the primary function of the Pharmacovigilance and Pharmacoepidemiology department or now, Global Product Safety. And the first component is, actually, taking and receiving the reports.

So these are generally called in to us, and entered into computer systems by individuals.

The next thing that is done with this group of individuals would follow-up on these reports to attempt, I really should emphasize attempt to obtain additional clinical information that might have been missing from the initial report when it was presented to the company.

Q. What do the people at Lilly

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actually do to try to follow-up spontaneous reports of adverse events?

A. They can make telephone calls, they can send letters. This is the -- this is the collection process for the individual cases.

The next step in the process is for these to be reviewed as groups of reports. And here there are physicians and what we call surveillance scientists that would be involved, along with pharmacoepidemiologists.

And there would be a number of types of reports that would be, that would be prepared. There are periodic reports to the Food and Drug Administration, periodic reports to other regulatory agencies that summarize these data.

There is the potential for what we would call ad hoc requests, meaning that an agency would send a specific request outside the, the routine periodic reports for information. And then the group could also provide periodic internal review.

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Q. Let me ask you about that, specifically. And after Zyprexa went on the market and Lilly received reports of hyperglycemia in particular, was there any particular internal review that Lilly performed with respect to those events?

A. Well, there was a, there was a sequence of them. We had weekly or biweekly meetings, actually, the pharmacovigilance function, the product team, the U.S. Affiliate, to discuss all adverse events that were being observed.

My first recollection of a, of a specific review of the topic of hyperglycemia was, I think, sometime early in 1997.

Q. All right. And what was done at Lilly?

A. I think there was something on the order of ten to 15 cases, some with rather high glucoses. We felt that we should obtain the consultation from an endocrinologist/diabetologist. So these cases were summarized and presented to one of

our internal diabetologists who then provided us with a, a verbal report.

Q. And what was the report with respect to the review, the spontaneous reports of hyperglycemia at that time?

A. His belief was that the cases were sufficiently confounded to make it impossible to conclude that there was a causal association in these cases he reviewed.

Q. You've used the word "confounded." Would you explain for us what that means?

A. That would mean there were alternative, multiple alternative risk factors or frank causes, in his opinion, or that the cases really did not show sufficient change to constitute an event that would not be expected as just fluctuation in the normal course of a patient with diabetes.

Q. After that internal review of the spontaneous reports of hyperglycemia, do you recall, Dr. Beasley, whether Lilly received any inquiry from a Dr. Wirshing with

respect to that topic?

A. I believe that we received a request for information from, at the time, Dr. Donna Aims and her, subsequently, her husband, Dr. Wirshing, our understanding was that they were intending to potentially publish a case series and they were requesting information from us on what had been observed in our clinical trials.

Q. What, specifically, did Dr. Aims and Wirshing ask of Lilly and how did Lilly respond?

A. Well, they asked what data we had pertinent to the topic.

Q. And did Lilly provide them with anything?

A. My recollection is that we provided them with a, both a summary of the data from our integrated summary of safety analysis, and I believe that may have also included some summary of the post-marketing data, but I'm less certain about that.

MR. SEE: Let me hand you what I've marked as Beasley

Exhibit 7.

(Whereupon, Deposition Exhibit(s) 7 duly received, marked and made a part of the record.)

QUESTIONS BY MR. ALLEN:

Q. And ask you if you could recognize that and tell us what that is?

THE WITNESS: I need to.

MR. SEE: Surely, take a look at it.

A. Review of glucose changes in patients treated with olanzapine. And it says for Donna Aims Wirshing. So this was, probably, the record that was provided. There's an internal date of September 1997. It's a fairly lengthy document. It appears to be, again, based on our integrated summary of safety. Some of the analysis that we talked about. And let me see if there are -- we also appear to provide them with a reference, a reference list. So this would be information from got the, the haloperidol controlled clinical trials and the placebo

controlled clinical trials and a copies of a literature search on the topic.

It appears to be, again, based on our integrated summary of safety. Some of the analysis that we talked about. And let me see if there are -- we also appear to provide them with a reference, a reference list.

So this would be information from both the, the haloperidol-controlled clinical trials and the placebo-controlled clinical trials and copies of a literature search on the topic.

Q. All right. And to your knowledge, Dr. Beasley, did Dr. Ames and Wirshing eventually publish?

A. This was an article that I think we discussed yesterday in which they reported on a series of cases that they had observed.

Q. Now, Dr. Beasley, at the time Lilly pulled together the information contained in what we've marked as Beasley Exhibit 7, what were the conclusions that

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were permitted by the data that Lilly had with respect to whether Zyprexa was causally related to hyperglycemia?

A. Well, given the data that we had at the time of our submissions which are reflected here, we did not see an association.

Q. Now after that, Dr. Beasley, did Lilly receive -- well, you were asked some questions early in your deposition about an inquiry from the drug regulatory agency in South Africa, do you recall that?

A. Yes, I did.

Q. And did Lilly receive an inquiry from the drug regulatory agency in South Africa asking for some information?

A. I believe that we did.

Q. And what did Lilly do in response to that inquiry?

A. Well, the pharmacovigilance department would have prepared a report on the, the spontaneous adverse events to date that had been observed.

MR. SEE: Let me hand you

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what we've marked as Beasley Exhibit 8.

(Whereupon, Deposition Exhibit(s) 8 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SEE:

Q. And ask if you can tell us what that is?

A. It's marked Appendix Seven Review Of Blood Sugar Alterations. The date is October 1997. I believe that because it's marked Appendix Seven it was part of a larger document. Let me look at the --

So this appears to be a, the analysis that would have been put together for South Africa. Given that it's marked as an appendix I believe that it would have been, this specific document would have been an inclusion, probably, in a larger regulatory report to the U.S. and/or Europe or other regulatory agencies.

Q. Okay. Now at the time Lilly provided or pulled together the information

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in response to the inquiry from the South African regulatory agency was it possible to draw any conclusion from spontaneous reports whether Zyprexa was causally related to hyperglycemia?

A. No, based exclusively on this data we would not draw any sort of firm conclusion about causality. But let me just review the summary.

MR. SUGGS: May I ask which page he's looking at?

THE WITNESS: Page 19.

A. And what we indicate given the exposure we, it was considered that the number of events reported was, actually, quite small, and that post-marketing spontaneous adverse events reports of alterations in blood glucose are consistent with the safety profile observed in the clinical trials.

Q. All right. And did Lilly subsequently receive a request from the drug regulatory agency in Europe with respect to spontaneous reports of hyperglycemia

Page 568

regarding Zyprexa?

A. Yes, we did.

Q. All right. And what did Lilly do in response to that request?

A. That would, again, have been a review of the spontaneous adverse events performed by the pharmacovigilance and epidemiology group.

MR. SEE: Let me hand you what we've marked as Beasley Exhibit No. 9 and ask if you can tell us what that is.

(Whereupon, Deposition Exhibit(s) 9 duly received, marked and made a part of the record.)

A. It's titled A Review Of All Spontaneous Cases Of Hyperglycemia Reported In The Lilly Safety Database, Clintrace, that was the name of the computer system, In The First 21 Months Of Marketing Of Commercially Available Olanzapine. And it would be through data through 30 June of '98.

And, okay. I wasn't sure,

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specifically, what, it says in the introduction: This task was undertaken to fulfill the commitment made to CPMP in the PSUR covering the period December 1997 to March 1998. So --

Q. And what is the CPMP?

A. That is the scientific branch of the European medicines regulatory agency. So this was a report prepared to specifically address the question of analysis and review of the spontaneous adverse events for Europe.

Q. Now, Dr. Beasley, you, I think previously gave testimony that you were involved directly and primarily regarding Zyprexa through the early part or some early part of 2001, is that -- am I correct in that?

A. 2000, I had very direct involvement through early 2001. I had more focused involvement in that period from 1997 through 2001.

Q. All right. And toward the end of your direct involvement with Zyprexa, were you involved in any review, overall

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review of the Zyprexa data?

A. Yes. I think this is something that we have discussed that there was a large review undertaken, primarily, negotiated out of both pharmacovigilance and myself representing the team that I have referred to as the Beasley/Kwong analysis, I believe.

The work, actually, extended over a significant period of time with a lot of individuals involved in actual completion of that work that was ultimately submitted to the Food and Drug Administration.

MR. SEE: All right, let me hand you what's been marked as Beasley Exhibit No. 10.

(Whereupon, Deposition Exhibit(s) 10 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SEE:

Q. Which is a rather large document that I'll put in front of you. Can you look at that and tell us what that is, please?

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A. The cover letter says response to FDA request. Enclosed is our response to your May 2000 letter requesting information about olanzapine.

This review had been, again, internally initiated and not in response to a request from FDA. But toward the end of its preparation such a request arrived. So this document was provided to them.

Q. All right. Now, can you tell us, Dr. Beasley, what was involved and what kinds of data were included in the overall review that resulted in the document submitted to the FDA we've marked as Beasley Exhibit 10?

A. There were a number of different aspects of data included. The ones that I'm most familiar with are the analysis of the clinical trial data. But also, the spontaneous adverse event data.

I believe this also includes a, a review of the literature, both clinical and preclinical. And given that it was

Page 572

submitted to the FDA, I believe it would have included regulatory correspondence regarding hyperglycemia and diabetes as well.

Q. All right. And Dr. Beasley, based upon the review that you participated in, and submitted to the FDA that we've marked as Beasley Exhibit 10, can you tell me the date of that submission?

A. This would have been, let's see the cover letter but also let me see if I can -- would have been July 2000.

Q. Now based upon the review that was submitted to FDA in July of 2000, Dr. Beasley, were any conclusions possible with respect to the question whether Zyprexa is causally related to hyperglycemia and diabetes?

A. Taking the data in total, all the extensive material, we believe that the data did not support an association between the drug and hyperglycemia slash diabetes.

Q. All right, thank you, Dr. Beasley. Now, in addition to Lilly's review of the spontaneous reported data, and

Page 573

Lilly's review and analysis of the controlled clinical trials with Zyprexa, were there other different types of studies that looked at the specific question whether Zyprexa was exerting some direct effect to cause hyperglycemia?

A. There were a large number of studies and activities going on both clinically and preclinically under this group that Dr. Breier had organized. I'm most familiar with two studies that were conducted in humans referred to as clamp studies.

Q. First, tell us, you said there were two studies referred to as clamp studies?

A. That's correct.

Q. Tell us first what was it that the two clamp studies were directed at looking at?

A. Okay. Type two diabetes is thought to be caused by two types of what we call pathophysiology together, or abnormalities in the body, is what pathophysiology means.

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One is the, the failure of what we call the insulin receptor. And this is a molecule on cells in the body that insulin, which insulin, which is a hormone, interacts with to allow glucose to move into the cells.

So you've got to have this receptor working right in order for glucose to move into the cells so that you lower blood glucose levels and the cells are able to use glucose's energy.

Q. Are you familiar with the term, Dr. Beasley, insulin sensitivity?

A. Yes.

Q. Tell me what that means?

A. That would be a measure of how well these insulin receptors work.

Q. All right.

A. The other thing that seems to be necessary for the development of type two diabetes, clinical type two diabetes would be the failure of the pancreas, which is an organ that sits in the abdominal cavity close to the stomach, to put out sufficient amounts

Page 575

of insulin.

The pancreas is signaled to release insulin when glucose is high in the blood. It releases this insulin, goes to insulin receptors, and this allows glucose to be transported into cells. So the thinking is to be frankly or actual clinical type two diabetes you have to have failure of the insulin receptor, decreased insulin sensitivity, and a decrease in the pancreas' ability to make enough insulin to compensate for poor insulin sensitivity.

Q. All right. Let me ask you first about, actually the second thing you mentioned, that is the failure of the pancreas to actually produce insulin or to produce enough insulin. Was there one of the clamp studies directed at that question?

A. Yes, there was. And again, why did we, we take on these studies? The thinking behind this was that it was important to us to do a study that would look at whether or not olanzapine was causing the effects in the body that would lead to type

Page 576

two diabetes. So that was the purpose in doing the studies.

Q. All right. Now first I want to ask you to describe the clamp study that was directed at the question whether Zyprexa exerted some adverse effect that would cause the pancreas not to produce insulin or not to produce enough insulin.

First, tell us what was that study called and how did you perform it?

A. That's a hyperglycemic clamp study.

Q. And please tell us in layperson's language how that's done?

A. First of all, you have your parallel treatment groups, as we talked about this morning. You have in this case it was placebo, another antipsychotic, and olanzapine. And before patients, or, actually these were what we call normal volunteers, these were healthy subjects. They were tested.

And the way they were tested was by this thing that's called a

Page 577

hyperglycemic clamp. They have an intravenous line inserted into their arm. They are then given glucose, actually --

Q. Glucose is what?

A. Is sugar. Large amounts of glucose, blood sugar, into this line into their body. And then the pancreas has the opportunity to react to this. And what is measured is the amount of insulin that the body produces in response to this extra glucose. Then the patients, or the subjects are treated.

Q. When you say "treated", what do you mean?

A. They receive double blind either placebo or olanzapine or this other medication. In this case they received it for two weeks and then they were retested. I think it was probably worth stating that, that this, this type of sophisticated study was -- I did not design this study.

Q. Who did design it?

A. This would have been designed

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by our --

MR. ALLEN: I have to object to the last answer as not being responsive.

A. -- by our endocrinology colleagues.

THE VIDEOGRAPHER: End of tape seven. We're off the record.

(At this time, the parties went off the record, after which the following proceedings were had:)

THE VIDEOGRAPHER: This is -- we're back on the record. This is the beginning of tape No. 8 of the deposition of Dr. Beasley.

QUESTIONS BY MR. SEE:

Q. All right, Dr. Beasley, before we changed the tape I was asking you about the hyperglycemic clamp study. And now let me just ask, were the results of the study performed by Lilly looking at whether Zyprexa exerted an adverse effect on the pancreas to produce insulin, were the results

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of that study published?

A. They were published in a peer reviewed journal.

MR. SEE: Let me hand you what's been marked as Beasley Deposition Exhibit 11.

THE WITNESS: Actually, it's not. You need to add the Beasley.

MR. SEE: Let me add the Beasley on it, sorry.

Let me now hand you what's been marked as Beasley Deposition 11. And can you tell us what that is, please?

(Whereupon, Deposition Exhibit(s) 11 duly received, marked and made a part of the record.)

A. This would be the academic publication regarding the results of the study we just discussed.

Q. All right. Now, Dr. Beasley, tell us what did the results show of the study done by Lilly to see whether Zyprexa

Page 580

exerted an adverse influence on the pancreas such that the pancreas produced a little or insufficient insulin?

A. The results are summarized in the last paragraph of the abstract. "We found no evidence that treatment of healthy volunteers with olanzapine or the other drug," left that one out, "decreased the insulin secretory response to a prolonged hyperglycemic challenge. The results of this study do not support the hypothesis that olanzapine or the other drug directly impair pancreatic beta cell function."

Q. All right. Dr. Beasley, let me ask you, this hyperglycemic clamp study methodology, is that a recognized methodology to look at the question whether the pancreas is affected to produce insufficient or no insulin?

A. That's my understanding from my endocrine colleagues.

Q. Now, Dr. Beasley, turning to the second prong of these clamp studies, did Lilly perform a study looking at the question

of whether Zyprexa produced insulin insensitivity?
A. Yes. That was what was referred to as the euglycemic clamp study.
Q. All right, the euglycemic clamp study. Can you tell us again in layperson's language, what was the euglycemic clamp study looking at?
A. Well, this looks at insulin receptor sensitivity. And here in contrast to the last study you first give a lot of insulin and you also give some glucose. And you determine, essentially, how much glucose you can give, a fixed amount of insulin, and how well the body uses that amount of glucose.

(Whereupon, Deposition Exhibit(s) 12 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SEE:
Q. Let me hand you what we've marked as Beasley Exhibit 12 and ask first were the results of the euglycemic clamp

study performed by Lilly published?
A. Yes, they were.
Q. All right. Now let me ask you to look at Beasley Exhibit 12 and ask you to tell us what that is?
A. This would be the academic publication of the study that we just discussed.
Q. Can you tell us, Dr. Beasley, what were the results of the euglycemic clamp study performed by Lilly to look at the question whether Zyprexa affected insulin sensitivity?
A. That's probably, again, best summarized in the abstract, in the last part of the abstract. "In summary, this study did not demonstrate significant changes in insulin sensitivity in healthy subjects after three weeks of treatment with olanzapine or a different drug."
MR. SUGGS: Counsel, could we get a copy of that?
MR. SEE: I thought I handed you one.

MR. ALLEN: No, you didn't.
MR. SEE: I thought I did.

QUESTIONS BY MR. SEE:
Q. Now, Dr. Beasley, given the results of the two clamp studies performed by Lilly, based upon the results of those studies, what conclusions, if any, did Lilly draw regarding whether Zyprexa demonstrated a causal and a mechanistic effect on producing type two diabetes?
A. Well, these studies certainly did not support the hypothesis that olanzapine was causing either type of pathophysiology that would cause diabetes. It was not causing the things that would cause diabetes in these two studies.
Q. Earlier in your deposition, Dr. Beasley, you were asked some questions about the diagnosis of your own type two diabetes, do you recall that?
A. Yes.
Q. At what age were you diagnosed with type two diabetes?
A. I think it was age 51.

Q. Dr. Beasley, do you know the general recommendations from the American Diabetes Association with respect to screening blood glucose for type two diabetes?
A. I believe that I do.
Q. All right. Can you tell us what those are?
A. I think it's a recommendation of a fasting blood glucose every three years at age 45 and older. And I believe there is some discussion about if an individual is obese and has other risk factors conducting these investigates or blood tests at an earlier age.
Q. And those recommendation by the American Diabetes Association for screening blood glucose for type two diabetes, to whom did they apply?
A. Well, all Americans. I mean, they, that's a universal health care recommendation by this organization.
Q. So I mean, do they apply whether the person is suffering from

schizophrenia?
A. Yes.
Q. Or do they apply if the people are not suffering from schizophrenia?
A. To my understanding yes. I mean, they don't draw any distinction. The only distinctions are the age cutoff and then earlier if risk factors are present.
Q. And would those general recommendations regarding screening for type two diabetes by looking at blood glucose, would that apply to people who were taking antipsychotic medication like Zyprexa?
A. They would apply to, as we've said, anyone.
I mean, again, irrespective of their, of their health status with the exception of this age cutoff.
Q. And let me just ask, would the general recommendations of the American Diabetes Association to have a screening for type two diabetes by looking at blood glucose also apply to people who were not taking antipsychotic medication like Zyprexa?

A. Yes.
Q. Dr. Beasley, earlier in your deposition I think you testified that if it were up to you the warning about hyperglycemia would not be in the current Zyprexa product label; do you recall that?
A. Yes, I would not have advocated that warning.
Q. Can you explain your rationale for that feeling?
A. We discussed yesterday my understanding of the criteria for placing a warning. That you have to, one, establish a reasonable association and that the event has to be clinically serious. And my understanding, my interpretation of the data, having been personally involved through 2000, is that a reasonable association had not been established.
And my secondary understanding of the data since that time still remains consistent with failure to establish a reasonable association.
Q. All right. Let me hand you

what's marked as Exhibit 13, Dr. Beasley, can you tell us what that is?
A. Do you want to --
MR. SEE: I beg your pardon. I keep forgetting to write Beasley on there.
Let me hand you what's marked as Beasley Deposition Exhibit 13.
(Whereupon, Deposition Exhibit(s) 13 duly received, marked and made a part of the record.)
QUESTIONS BY MR. SEE:
Q. Can you make reference to the date on the last page and then tell us what that is?
A. Well, it's a Zyprexa package insert and I'll need to check the date.
I see a copyright 2006 date here, literature revised as of March 20, 2006, so this was the package insert that was approved as of that date.
Q. Could you turn to Page 8 of that document, please?

A. Yes.
Q. And in particular, I want to ask you about certain language contained in the warning section related to hyperglycemia and diabetes mellitus. Do you see that?
A. Yes, I do.
Q. All right. Now could you read the first three sentences of that for us, please?
A. Yes. "Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not

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completely understood."
Q. Let me first ask you, Dr. Beasley, that the reference there to an increased background risk of diabetes mellitus in patients with schizophrenia. Can you explain for us in layperson's language what that means?
A. I believe that means what we were discussing yesterday, that there is the belief, understanding, and data, to support that a higher percentage of individuals with schizophrenia than without schizophrenia, everything else being equal, would have diabetes.
Q. And then making reference to the increasing incidence of diabetes mellitus in the general population. Can you explain in layperson's language what that means?
A. I understand that to mean that there is a continuing increase in the number of new cases of diabetes being observed every year. So that it's becoming more frequent in the population.
Q. All right. And in the second

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sentence is it those two things that are referred to as confounders?
A. Those two things would be confounders, "given these confounders."
Q. Now can you tell us just in layperson's language what does "confounder" mean?
A. That means things that are present that make understanding or interpretation difficult or impossible.
MR. SEE: Dr. Beasley, thank you very much.
MR. ALLEN: Okay, I have some questions. At some point we're going to have to take a break but I'm going to proceed now and get this screen back to me. But let's go ahead and let me ask a couple questions and then we'll take a break.

EXAMINATION,
QUESTIONS BY MR. ALLEN:
Q. Dr. Beasley, Scott Allen, how

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are you?
A. Good.
Q. When you testified to me earlier today and yesterday was your testimony truthful and accurate?
A. Yes, it was.
Q. And when you wrote your e-mails concerning the clinical trials to the people throughout Eli Lilly, were your e-mails truthful and accurate?
A. To the best of my knowledge those data were correct at the time I wrote them.
Q. Right. So if a jury looks at your e-mails when you say things like "olanzapine is the worst offender," the jury can know that Dr. Beasley truly believes that Zyprexa is the worst offender concerning weight gain in the second generation antipsychotic class?
A. No, you have, I believe, slightly mischaracterized what I said. I believe I said second, because I would include clozapine as an atypical

Page 592

antipsychotic.
Q. But if your e-mail says, if it says, "olanzapine is the worst offender," the jury can know that you're telling the truth in your e-mails?
A. I believe that e-mail made reference to clozapine.
Q. Okay. So we can count on your e-mails, right?
A. And again, my understanding of the data at the time.
Q. If your e-mails say things like "it would be ludicrous to conclude that weight gain associated with Zyprexa does not put one at increased risk of cardiovascular disease" the jury can count on that to be true, correct?
A. Again, with the understanding that if you did empirical analysis that showed otherwise part of the e-mail, yes.
Q. If your e-mails following a meeting in Atlanta, Georgia, in October of 2000, indicate that when the endocrinologists wanted to see the continuous data -- you

reviewed English language clinical studies. Those are the things you discussed with Mr. See on direct-examination, right, clinical studies?

A. This would have included only those that were published.

Q. Yes, sir, I agree. You and I are agreeing. Clinical studies. And it says most of the known peer review, that means experts, had reviewed the studies, right?

A. That's correct.

Q. And then all these panel members, in order to get this consensus, they looked at all the data and all the published information concerning these clinical studies in order to reach this consensus statement, right?

MR. SEE: Object to the form.

Q. Sir?

A. I would understand that to be correct from what is written here.

Q. Yes, sir. Now it's important as what's written here -- you read articles like this all the time. That's what you do,

you're an academician, are you not?

A. I guess I have not thought of myself as an academician but I read articles.

Q. Yes, sir, that's what you do. So you know how to read articles like this, don't you?

A. Yes.

Q. And by the way, you told Mr. See something on direct-examination that one of the things we like to do in studies is to blind them so in order to prevent -- what's the word?

A. Bias.

Q. Bias.

A. On reporting by the investigator or the patient.

Q. And how does blinding prevent bias?

A. That prevents both the, both the investigator and the patient from knowing the medication they're on and because of knowing the medication they're on making assumptions or coming to beliefs about what they're experiencing and then reporting it.

Q. Right. If you blind the study, if the individual does not know, the doctor doesn't know, such as a researcher, right?

A. Correct.

Q. And the patient doesn't know which medication they're taking, you're more likely to get an objective as opposed to a subjective biased analysis, correct?

A. That's correct. That is the intent of blinding.

Q. And if you unblind information, unblind it, and a person has a bias, it might interfere with their objective interpretation of data, correct?

MR. SEE: Object to the form.

A. We've been talking about blinding in the, the actual conduct of the studies. So while the data are being collected. Are you, are we now, I thought that you switched to a different topic.

Q. I did. You are following me precisely. We're now talking about -- but the reason, see, it's logical. And you tell

me if I'm not logical because I'll correct it, but I think I'm being logical. You told me the reason you want to have this blinded study is to prevent bias, to have objective analysis done, right?

MR. SEE: Object to the form.

A. That you want to collect the data in a blinded fashion to prevent bias.

Q. Right. The same logic would also entail an analysis of data. Wouldn't you rather have an objective analysis of the literature, an objective analysis of the data, an objective analysis of the studies, as opposed to let Eli Lilly determine what the final conclusion is regarding their drug?

MR. SEE: Object to the form.

A. What I would want would be the best analysis of the totality of data available.

Q. From objective review, correct?

A. From an objective review.

Q. Right. Let's go back to the document. And I would suggest to you, and I

C D E

IN THE SUPERIOR COURT OF THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,

Plaintiff,

vs.

ELI LILLY AND COMPANY,

Defendant.

Case No. 3AN-06-05630

VIDEOTAPED 30(b)(6) DEPOSITION OF
STATE OF ALASKA
DESIGNEE: DAVID CAMPANA

Tuesday, September 18, 2007
10:00 a.m.
Volume I

Taken by Counsel for Defendant
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ANCHORAGE, ALASKA; SEPTEMBER 18, 2007
10:00 A.M.
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VIDEOGRAPHER: We're on the record at 10:01. This is the video deposition of David Campana taken by the defendant in the matter of State of Alaska versus Eli Lilly, Case Number 3AN-06-05630 Civil in the Superior Court for the State of Alaska, Third Judicial District at Anchorage.

This deposition is being held in the offices of Lane Powell located at 301 West Northern Lights Boulevard, Suite 301, Anchorage, Alaska on September 18, 2007.

My name is Eric Cossman, here today on behalf of Pacific Rim Reporting located at 711 M Street, Suite 4, Anchorage, Alaska 99501. The court reporter is Sonja Reeves, also with the firm Pacific Rim Reporting.

Will counsel and all present please identify themselves for the record?

MR. ROTHSCHILD: Eric Rothschild from Pepper Hamilton for the defendant, Eli Lilly and Company.

MR. JAMIESON: Brewster Jamieson with Lane Powell on behalf of Eli Lilly and Company.

MR. HAHN: Blair Hahn on behalf of the State.

MR. SNIFFEN: Ed Sniffen, Assistant Attorney General here on behalf of the State of Alaska.

MR. STEELE: Joe Steele on behalf of the State of Alaska.

MR. JAMIESON: And Barry Boise from Pepper Hamilton is attending telephonically just listening.

-o0o-

DAVID CAMPANA,
deponent herein, being sworn on oath, was examined and testified as follows:

EXAMINATION

BY MR. ROTHSCHILD:

Q. Good morning, Mr. Campana.

A. Good morning.

Q. Have you had your deposition taken before?

A. Yes.

Q. How many times?

A. Three times.

Q. What were the proceedings for which those depositions were taken?

A. Two were drug cases, one was a civil suit.

Q. When you say "drug cases," what do you mean by that?

A. The first one was a pharmaceutical manufacturer, Mylan, and they had conspired to raise prices

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inappropriately for generic drugs. And it was a national AG office effort to go after them for damages for our Medicaid program.

The other deposition was for the Neurontin case. And I served as a trustee on the State Employees Health Trust, and they were suing Pfizer for promoting the unlabeled uses of Neurontin.

Q. And the third case that you gave a deposition for?

A. That was stemming from serving on the trust and one of the trustees was suing the other trustees.

Q. Did you give any trial testimony in any of those matters?

A. No.

Q. I'm sure you understand the process fairly well from your prior experience, but I'm going to be asking you some questions today.

I need you to give your answers verbally with words, not other sounds or nods of the head so that we can get a clear transcript of my questions and your answers.

Do you understand that?

A. Yes.

Q. My experience is that you will be able to anticipate many of the questions I'm going to ask you,

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and, as we would do in normal conversation, you're likely to sort of chime in before I'm finished so that you can answer the question.

I'm going to ask you not to do that today so that we can get a clear record and not drive Sonja, the court reporter, crazy. I will endeavor to do the same.

I will wait for you to finish your answers before I ask my next question. If at any time you feel like I haven't given you the opportunity to do that, I have cut you off, please let me know. I want to get your complete answer.

A. Okay.

Q. If you need a break, let me know.

A. Okay.

Q. Who are you employed by?

A. The State of Alaska, Department of Health and Social Services, Division of Health Care Services.

Q. How long have you been employed in that division?

A. 17-plus years.

Q. What position do you hold right now?

A. Medicaid pharmacy program manager.

Q. How long have you held that position?

A. For 17 years.

Q. What did you do before then?

A. I worked as the pharmacist for the Pay and Save

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chain. I was at the level of head pharmacist for the one store, the Boniface Pay and Save.

Q. How long did you do that?

A. 14 years.

Q. Have any professional experience before then?

A. I worked at the Anchorage Professional Pharmacy as a pharmacist for a year and a half.

Q. Anything besides that?

A. Prior to that, I served my internship.

Q. Where did you go to school?

A. University of Montana.

Q. What degree did you -- did you graduate?

A. I graduated with a bachelor of science in pharmacy.

Q. Any formal education after that?

A. No major education other than continuing education.

Q. Can you describe what you do as the Medicaid pharmacy director?

A. I manage the program. I'm the answer man. I promote several different programs or work with several different programs as a Medicaid pharmacy program manager.

The various programs that I work with are the drug utilization review, the pharmacy and therapeutics

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committee, the preferred drug list.

Currently, we're working on a dispensing fee survey for the network providers and we're trying to implement the tamper resistant prescription pads that Congress so nicely dropped on us to implement.

Q. You referred to the P&T committee and said quickly after it the PDL preferred drug list.

A. Right.

Q. Are those related concepts?

A. They are related concepts. The pharmacy and therapeutics committee works to determine whether drugs are safe and effective and whether there is a class effect on a particular class of drugs.

And once that is determined, then we set different drugs on the preferred drug list.

Q. Am I correct in understanding that not all classes of drugs have been reviewed for the preferred drug list?

A. That's correct.

Q. And am I correct in understanding that anti-psychotics have not been reviewed for the preferred drug list?

A. The atypical anti-psychotics or the typical anti-psychotics have not been reviewed under the preferred drug list.

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Q. Let me make sure I understand, the atypicals have not been?
A. That's correct.
Q. And that's Zyprexa and Respidol and all of those kind of medications?
A. Right.
Q. And what's the status of the typicals?
A. The typicals also have not been reviewed; however, we do say that mental health drugs have been reviewed, and that includes the sedative hypnotics, the ADHD drugs, the anti-depressants. Some people basically classify all of those as anti-psychotic drugs.
Q. So some mental health medications have been reviewed, some have not, and what we're calling the atypical anti-psychotics, which include Zyprexa, has not been?
A. That's correct.
Q. Similarly, the typical anti-psychotics, like Haldol, have not been?
A. That's correct.
Q. I wanted to make sure I understood what you were saying about the P&T committee. Does the P&T committee have any responsibility for reviewing the safety and efficacy of drugs that are not on the PDL or not being reviewed for the PDL?

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A. They have reviewed one class of drugs outside of the ones that would not be or would -- actually, let's try this again.
The P&T committee did review a class of drugs that did not have any kind of rebate connected, supplemental rebate connected to it, and that was the Levothyroxine, just because an issue came up and one of our providers had suggested that we review it and the P&T committee did review that.
Q. But, for example, for atypical anti-psychotics, the P&T committee has not done anything?
A. That's correct.
Q. You called yourself the "answer man". What did you mean by that?
A. Well, I sit by my phone and answer questions. And as I sat by my phone, and Tuesday seems to be a busy day, this morning before I came over here, I answered several questions.
Q. Questions from whom?
A. One was a drug manufacturer wondering whether his drugs were up for review at this September pharmacy and therapeutics committee meeting, and then several questions from one provider.
And then talked to another state, pharmacy program manager for another state who had some

Page 12

information I wanted to obtain about a dispensing fee for a common provider.
Q. You said you managed the program. What does that entail?
A. Oversight of the program, trying to determine what the spend for the next year is going to be as far as budgeting, looking at any avenues for cost containment or slowing cost increases, making sure that we meet the federal guidelines and the new guideline coming up.
October 1 is tamper resistant prescription pads, so that's a good example of that. Of course, the feds have a reimbursement methodology, the federal upper limit drugs, make sure that we're meeting the qualifications under that.
Q. Do you have any responsibility for any aspects of the Medicaid program other than prescription drugs?
A. Well, I have aspects of prescription drugs, but they are not necessarily the pharmacy aspect. I price and determine whether drugs that are administered in physicians' offices are going to be covered under the Medicaid program, and then I set the reimbursement levels for that.
Q. But outside of medications, do you have any responsibility vis-a-vis the Alaska Medicaid program,

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such as for hospital providers or physician providers?
A. Not other than just some medications.
Q. Explain what the drug utilization review program is.
A. Sure. The drug utilization review program is a program that was mandated by over 90 and it's also in section 1927 of the Social Security Act.
It's required by the Medicaid program in order to obtain the federal financial participation for medications. There is several different aspects to that that I oversee, and that's the prospective drug utilization review.
And we have a system that's state of the art pharmacy claims processing system that reviews medications as they come into the system for payment to the pharmacies. And we review that for appropriateness as far as doses, drug-drug interactions.
The drug-to-pregnancy interactions and then the drug-drug interactions that are highest significance, we actually deny those and request that the pharmacists review those drug interactions, and even consult with the prescriber about those.
That's one aspect. The other aspect is that we have a retrospective drug utilization review where the computer processing system melds the pharmacy data,

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A. No, I don't.
Q. When did you become aware that the state -- well, let me withdraw that for a moment.
Did you participate in the decision by the State of Alaska to sue Eli Lilly?
A. No.
Q. Do you know who did?
A. No, I don't.
Q. When did you become aware that the state had sued Eli Lilly? Just to sort of put a time frame, the lawsuit was actually filed in March 2006.
A. It was in 2006 when I became aware of it.
Q. The first half of the year, second half of the year?
A. Well, let's see. Probably first quarter.
Q. How did you find out?
A. I'm not sure if I was -- if it was in discussion with Ed or I know there was a news release about it too. And I can't remember whether it was discussion with Ed or the news release was first.
Q. And when you are referring to Ed, you are referring to Ed Sniffen?
A. Ed Sniffen, Assistant AG.
Q. When you found out that the state had sued Eli Lilly regarding Zyprexa, did you go and talk to anybody

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at the Department of Health and Human Services about it?
A. I think I -- let's see. I remember talking to my director at that time.
Q. Who was your director?
A. Our director at that time was Dwayne Peeples, P-e-e-p-l-e-s. Our current director is William Streur.
Q. When you say "director," the director of the Medicaid program?
A. Yeah, director of the Medicaid program and director of health care services.
Q. That's your direct report?
A. Actually, my direct report -- I directly report to the deputy director.
Q. Who is that?
A. Randall Shlapia.
Q. That's the deputy director of what?
A. Of health care services.
Q. So what's your reporting relationship to Dwayne Peeples?
A. William Streur is our present director who was just promoted to the deputy commissioner.
Q. Why don't we actually lay this out a little better? You are the pharmacy director. Who do you report to?
A. I currently report to Randall Shlapia.

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Q. Who is the deputy director of health care services?
A. That's correct.
Q. Who does Mr. Shlapia report to?
A. To William Streur.
Q. William Streur is the deputy commissioner of Health and Human Services?
A. Health and Social Services.
Q. And for the Medicaid program and health care services?
A. Right.
Q. And Mr. Streur reports to the commissioner?
A. Commissioner Karleen Jackson.
Q. Has this -- I know the people have changed, but has the reporting structure remained the same during the 17 years you have been with the program?
A. No. The reporting structure has been all over the board. I originally reported to the medical director, and that was Tom Porter.
And then it switched about eight years ago, and then I reported to Terry Keklak, and she was the manager of the -- let's see. What was it?
Manager of the, I guess, provider unit. And then that switched about five or six years ago and my supervisor became Pam Muth who was the deputy director

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for at that time division of medical assistance.
And then it changed to division of health care services, and she stayed on until about four years ago. And then that position, the deputy director was vacant for at least two years, and then Randall Shlapia filled that position.
And within two months after that, Dwayne Peeples left and then it wasn't until April that we had a new director, and that was William Streur.
Q. Has there been a person at the deputy commissioner level in this reporting structure the whole time?
A. Yeah. The deputy -- there was a deputy commissioner pretty much all the way through, and if we have to go back 17 years, I'm not going to remember the names.
Q. But Streur holds that role now?
A. Right.
Q. Peeples held it before him?
A. Peeples held the director position, not the deputy commissioner. While Mr. Peeples was director, our deputy commissioner was William Hogan.
Q. And before Hogan?
A. Before Hogan, Karleen Jackson was our deputy commissioner and Joel Gilbertson was our commissioner.

IN THE SUPERIOR COURT OF THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,
Plaintiff,
vs.
ELI LILLY AND COMPANY,
Defendant.

Case No. 3AN-06-05630

VIDEOTAPED 30(b)(6) DEPOSITION OF
STATE OF ALASKA
DESIGNEE: DAVID CAMPANA

Wednesday, September 19, 2007
9:30 a.m.
Volume II

Taken by Counsel for Defendant
at
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301 West Northern Lights Boulevard, Suite 301
Anchorage, Alaska

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I-N-D-E-X

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ANCHORAGE, ALASKA; SEPTEMBER 19, 2007
9:36 A.M.
-o0o-

VIDEOGRAPHER: We're on the record at 9:36. This is Volume II of the video deposition of David Campana taken by the defendant in the matter of State of Alaska versus Eli Lilly, Case Number 3AN-06-05630 Civil in the Superior Court for the State of Alaska, Third Judicial District at Anchorage.

This deposition is being held in the offices of Lane Powell located at 301 West Northern Lights Boulevard, Suite 301, Anchorage, Alaska on September 19, 2007.

My name is Eric Cossman, here today on behalf of Pacific Rim Reporting, located at 711 M Street, Suite 4, Anchorage, Alaska 99501. The court reporter is Sonja Reeves, also with the firm Pacific Rim Reporting.

Will counsel please identify themselves for the record?

MR. ROTHSCHILD: Eric Rothschild from Pepper Hamilton for the defendant, Eli Lilly and Company.

MR. HAHN: Blair Hahn for the state.

MR. SNIFFEN: Ed Sniffen, Assistant Attorney General, for the state. And also with us today is Joe

Steele from Garretson & Steele, also representing the state.

EXAMINATION

BY MR. ROTHSCHILD:

Q. Good morning, Mr. Campana.

A. Good morning.

Q. You understand you are still under oath having been sworn yesterday?

A. Yes.

Q. Thank you. Your counsel has provided me with a couple of documents this morning. I haven't had a chance to examine them closely yet, but I want to go ahead and mark them as exhibits and have you tell me what they are.

A. Okay.

(Exhibit No. 13 marked.)

Q. I'm going to mark a document as Exhibit No. 13. Can you tell me what Exhibit No. 13 is?

A. Sure. This is a document that contains the fields that were on the data that were provided back in April and gives the field name that is on the data tables, the system field name, if it's known by any other name and the data element from the data element dictionary.

And the subsequent pages include the page from

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asking for the individuals most knowledgeable about the selection of drugs for Alaska's formulary. We got the response it was David Campana and Tom Porter.
You looked at those interrogatory answers, correct?
A. Correct.
Q. It may just be a miscommunication there, but there is no formulary?
A. Well, there is a drug list. As far as a formulary, and my definition of a formulary is that you would have a list of drugs.
On there would be drugs that are covered and drugs that are not covered. It would be nice and easy to find and it would be go search on it by NDC and find what is covered what is not.
We don't have that, so we have a regulation that tells generally classes that are covered and not covered.
Q. It tells by list what are not covered and everything else --
A. Is covered.
Q. -- is covered?
A. Correct.
Q. If, for example, anti-psychotics are a class of drugs that are covered, correct?

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A. Correct.
Q. And if since it's not listed, therefore, the class of anti-psychotics does not appear in that regulation, correct?
A. Correct.
Q. And that means that every drug in that class is covered, correct?
A. Correct, as long as there is a federal rebate.
Q. You sound like you are a fan of formularies. Why doesn't Alaska have one?
A. Well, formularies really don't fit in the Medicaid program. They fit in a PBM program, PBM insurance program where you can say, "Well, we don't cover this. We don't cover that."
Unfortunately, with Medicaid, it's out there in federal law what you can cover and what you can't cover. And if there is a federal rebate, you virtually can't not cover it.
Q. Does the state have the discretion to disallow reimbursement of a medication because of safety issues?
A. We can put it on restriction for safety issues, and our regulation allows us to do that.
Q. What regulation is that?
A. That would be 7AAC43.598 or 594.
Q. What does that do? What does that regulation

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allow Alaska to do?
A. Allows us to place, under some type of restriction, medications for safety or abuse issues.
Q. What kind of restrictions can Alaska impose on drugs that fit that description?
A. We can put quantity limits on those. We can change the definition for early refill on those.
We could do step edits, and we could also do prior authorizations.
Q. What is a step edit?
A. Step edit is a process where you are doing edits on a medication. They would have to fill one type of medication before they can get another type of medication.
The good example of that is when Vioxx was available, you had to take Ibuprofen or you had to take Naprosyn before you could get a prescription of Vioxx filled.
Q. This was before, obviously, Vioxx was taken off the market?
A. Correct.
Q. Do you remember the date of that, estimate when Vioxx went off the market? I'm just trying to orient ourselves.
A. It was September of '04 or '03.

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Q. Was the step edit in place for Vioxx in Alaska -- was the step edit in place the entire time Vioxx was on the market?
A. Actually, we did not implement it. We had the programming ready to go and then did not implement it.
Q. When did Alaska start the process of, you know, developing the step edit?
A. In 2003.
Q. Do you remember when in 2003?
A. It was when we were implementing HIPAA. It was February to May of 2003.
Q. What caused the state to start the process of developing this step edit?
A. Due to safety issues with Vioxx and then also cost issues. Vioxx was much more expensive than Ibuprofen was.
Q. Were you sort of the person in HSS who was leading this effort to put in this step edit?
A. Yes.
Q. What safety issues did you -- caused you to -- were you the one who suggested the step edit?
A. I'm not -- I don't remember as to whether I was or it was suggested by our fiscal agent, First Health.
Q. You agreed with it?
A. I agreed with it.

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A. At one meeting, correct.
Q. That was which one again?
A. The American Drug Utilization Review Society meeting.
Q. What year did you speak?
A. I don't remember.
Q. What topic did you speak about?
A. NSAIDs and gastric upset.
Q. Was it before Vioxx went off the market?
A. Yes.
Q. What was the subject of your presentation?
A. I can't remember the exact subject or the exact title, but the subject was whether there is a difference in the gastric upset between COX-2s, the drugs like Vioxx and Celebrex, versus the typical NSAIDs.
Q. Other than attending these conferences, do you communicate with peers, your peers in other states about safety issues?
A. Yes.
Q. What's the process for doing that?
A. Just e-mail or phone.
Q. Is that something you have done a fair amount of?
A. Yeah. I mean, a small percent of the time is probably spent in discussing the issues with other colleagues.

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Q. Are there a particular group of colleagues you speak with?
A. Just the Medicaid pharmacy program managers.
Q. Any in particular states?
A. I have talked to Utah. I talked to Montana yesterday. I have talked to Florida. I have talked to New York, Nebraska. Just all different states.
Q. And you have been doing that over the years?
A. Over the years.
Q. For various different medications?
A. Correct.
Q. The state -- we talked a little bit yesterday about the state having a preferred drug list?
A. Yes.
Q. Explain what the preferred drug list is.
A. The preferred drug list is a list of medications that actually lists preferred medications and non-preferred medications.
The list is developed by the state through or with the pharmacy and therapeutics committee.
Q. So when did Alaska start developing preferred drug lists?
A. It was in the fall of 2003. We put together a pharmacy and therapeutics committee. We had amended our contract with First Health to use their services for the

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project and we went out with their national pooling initiative and then gained CMS approval for that.
Q. What do you mean by "national pooling initiative"?
A. They have what's called a National Medicaid Pooling Initiative where it pulls the members or the eligibles from various states into one pool and then contracts with manufacturers for supplemental rebates for the drugs that are added to the preferred drug list.
Q. I want to get back to this, but it just occurred to me I left one issue hanging in terms of state procedure or a couple of issues.
You talked about the step edits and I want to talk a little bit more about that. But you also said that the regulations allow prior authorizations?
A. Correct.
Q. Let me just clarify, you had said that the regulation that allowed restrictions on reimbursements is 43598?
A. Yeah, or 594.
Q. Okay. Let me just show you. I think that's what I wanted to confirm. I'm going to show you 594, and I have the book as well. Did you mean to say 594?
A. Yeah. It's changed. It had been 598 and back to 594.

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Q. 594 seems to describe a prior authorization process, correct?
A. Correct.
Q. Maybe I'm not reading it correctly, but I don't see the step edit process included in 594. Am I missing something?
A. Under B it says, "As necessary to prevent waste and to address fraud and abuse, the division may place limitations on the maximum or minimum quantities allowed of a specific prescribed drug or therapeutic class, or on the number of refills of a specific prescribed drug or therapeutic class," so as far as placing limitations.
Q. In the section on prior authorization, it talks about considerations of cost and clinical effectiveness, correct?
A. Correct.
Q. And clinical effectiveness would include safety issues?
A. Correct.
Q. In the section B, which you are referring to, it talks about waste or fraud and abuse, and it doesn't talk about cost effectiveness or -- I'm sorry -- clinical effectiveness or safety.
Is there a distinction, as you understand the regulation, in terms of when step therapy, step edits

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can be used relative to prior authorizations?
A. Well --
Q. I'm sorry. Let me withdraw that and ask it this way: Is it your understanding that the state may institute step edits to address safety issues?
A. Yes.
Q. And similarly, can use prior authorizations to address safety issues?
A. Yes.
Q. What is a prior authorization?
A. Is that an exhibit?
Q. We don't need to mark that as an exhibit. What is a prior authorization?
A. A prior authorization is an edit that is placed on medications to prevent the filling or the paying of that medication unless certain criteria or certain administrative references are fulfilled before that is authorized.
Q. What do you mean by that? What has to be done?
A. The physician, the prescriber or the pharmacist who is filling the prescription has to call an 800 number, let us know what the -- or what the diagnosis is, and then we determine whether or not the prescription drug can be paid for by the Medicaid program.

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Q. And the prior authorization, that's a mechanism to address safety issues with the medications?
A. That's one of the tenants on that.
Q. What are the other tenants?
A. To address safety, to address the utilization, keep it within the labeled indications, and to address fraud or abuse.
Q. Has Alaska instituted prior authorizations for medications because of safety issues?
A. Yes.
Q. What medications?
A. The opioid medications.
Q. Can you give me some examples of those?
A. Morphine, Methadone, Oxycodone, Fentanyl patches, Fentanyl lozenges.
Q. Any other medications which have -- where you have instituted prior authorizations because of safety reasons?
A. I'm not remembering any right now.
Q. Do you think there have been others?
A. I'm drawing a blank right now. In fact, it's a good time for a break.
VIDEOGRAPHER: Going off record. The time is 10:54.
(There was a short break.)

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VIDEOGRAPHER: Back on the record. The time is 11:06.
Q. Mr. Campana, in terms of the prior authorizations, sort of mechanically, if you had a medication that had a safety issue, what would the prior authorization process do?
I mean, what would the doctor have to do? What discretion would the persons receiving the communication have regarding the prescription?
A. The doctor would have to supply information as far as a diagnosis, the person, what other medications they have been on in the past, why other medications or why they have discontinued other medications before going on the new medication.
Q. And once the doctor has communicated all of that, the person who is receiving the information, what are their options?
A. Their options are to either approve the prior authorization or deny the prior authorization. If they approve it, then they approve it for a certain amount of time, usually six months, and then put an indicator in the system so the pharmacy may fill the prescription and the prescription will go through the system.
Q. And how does the -- well, who are the individuals who are making the determinations about whether to issue

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the authorization?
A. It's a couple of different sections at First Health. One section is the pharmacy tech desk or help desk, and they have a certain amount of prior authorized drugs that they can review and enter authorization for.
And then there is another desk called the Manage Access Program that is staffed by pharmacy technicians and pharmacists and they review the drug, review the information coming in from the physician and apply that against the criteria set.
Q. In addition to having that process work for medications where there are safety issues, I think you indicated that you could have a prior authorization process to make sure that medications are only being used for indicated uses, correct?
A. Correct.
Q. Would that process sort of operate in the same way?
A. Yes.
Q. Would -- can you identify any medications reimbursed by Alaska where a prior authorization has been put in place based on the indication issue?
A. Yes.
Q. Give me an example.
A. Lupron Depot is one of the first ones that we

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did. Our concern was that it could be used for fertility issues off label. The labeled indications are for endometriosis and prostate cancer, plus a couple other diagnoses.

Another one is Ravadia, which is the new name for Viagra, and CMS had issued a notice two years ago that Medicaid programs could no longer pay for ED drugs, erectile dysfunction drugs, so we could not pay for Ravadia for that use, which would be an unlabeled use for the drug name Ravadia. Ravadia could be used for pulmonary hypertension.

Q. Going back to the preferred drug list, you explained that that is implemented by HSS in conjunction with the P&T committee, correct?

A. Correct.

Q. Am I correct in understanding that the P&T committee was formed for the express purpose of assisting HSS in developing PDLs?

A. In developing our preferred drug list, yes.

Q. And there was no P&T committee before the PDL process started?

A. Correct.

Q. And Alaska -- and the P&T committee doesn't do anything except work on the PDL, correct?

A. Correct.

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Q. Does First Health have a P&T committee?

A. They have indicated that they do.

Q. You don't use that function?

A. Well, we use at least the -- First Health produces information for us to provide to our P&T members to read about each drug class that we will be reviewing.

Q. Prior to the PDL process, the Alaska Medicaid system didn't avail itself of any P&T committee, correct?

A. Correct.

Q. Any sort of knowledge and expertise built up around the medications was built up amongst the employees of HSS?

A. Correct.

Q. How is the P&T committee selected for Alaska?

A. We are provided -- we initially went out with the idea of the preferred drug list. The commissioner and myself went to meet with various groups throughout the state and talk about the preferred drug list.

After or following that, and within that time span, numerous organizations had submitted names to be on the pharmacy and therapeutics committee.

We had names from the Alaska Psychiatric Association, the Anchorage Surgeons Association, the

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Alaska Medical Association and the Nurse Practitioners Association, Alaska Pharmacists Association, members that wanted to serve on that committee.

Q. So you selected names from that list?

A. Correct.

Q. How did the idea of having a PDL start in Alaska?

A. Well, it was actually an idea that came out of Florida and Michigan. They were the first two states that had developed the preferred drug list. Another state that had even done it longer than those was California has done it indefinitely.

But Florida started, and then Michigan also started, and it came out from that.

Q. Who suggested the idea in Alaska?

A. Well, in reading court cases, because Florida had been sued by pharma and it was an idea that we had talked about in our department.

And in 2003, my supervisor said, "Let's do it."

Q. Who is your supervisor?

A. At that time, my supervisor was Terry Keklak.

Q. Is the PDL something you had been promoting prior to that?

A. I thought it was a good idea. Actually, I thought when I looked at the California model back in the early nineties it was a good idea to do it at that

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time.

However, without having enough staff to do it, it was virtually impossible to try to do it.

Q. By this point, you had enough staff?

A. Well, you never have enough staff. I have, working with the contractor, I have enough staff at least to do the job that I think is adequate.

Q. What contractor are you referring to?

A. First Health.

Q. Is there any legislative authority or regulations that permit you to do the PDL?

A. No.

Q. Has the department ever sought that legislative authority?

A. We actually have a regulation that has been written for that. It was out for public comment and it's at the Department of Law currently.

Q. But it's been the department's interpretation or conclusion that it can go ahead and develop and administer this PDL without that regulation in place?

A. Correct.

Q. Is there any sort of authority or is this sort of the department's general authority to run its Medicaid program that causes you to believe you can do this?

A. General authority to run the Medicaid program and

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do it cost effectively.
Q. What is the purpose of the PDL?
A. The purpose of the PDL is to obtain supplemental drug rebates from the manufacturers for keeping their drugs on that list.
Q. Am I -- is it fair to say that the only purpose of the PDL is economic?
A. Well, it's not fair to say that because it isn't -- I mean the end result is that it keeps costs down in the Medicaid program so that services can continue to be provided.
Q. But in developing the PDL -- I mean, for example, is safety or effectiveness a reason that a medication would be preferred versus non-preferred?
A. Yes. The P&T committee determines whether a medication should be preferred or not preferred. Their normal decisions, and can be found in minutes of the P&T, is that they determine a class -- within a class, there is a class effect for the major indications in that class.
They may come up and say, "You know, this drug should be non-preferred." And in our state plan amendment, we have given the feds that information and the feds were looking or CMS was looking for that information, that we would allow the P&T to make a

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designation that one drug would be covered or would be on the preferred list as preferred or one would be not preferred.
Q. I'm a little confused about sort of what determines -- it seems like there is sort of two sets of consideration about whether a drug can be preferred.
One is the committee's conclusions about safety and effectiveness. And the other is whether the company would then agree to the supplemental rebate.
Is that fair?
A. That's fair, but there is still another determination in there as to whose rebate is best in that class.
Q. Okay. So explain the sort of steps you go through. I mean --
A. Well, the steps are starting from the ground up as far as, say, our meeting is coming up in the end of September. Prior to that, we get a room. That's basic.
We get the court reporter. We get the audio people lined up. Then we get a schedule put out as to what classes we're going to review, put that out ahead of time on our website so that the manufacturers can supply us with information that they want about their drugs.
Then we put out a date. This is the date that

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any clinical submission from a manufacturer has to be received in order that we can get that information out to the P&T members prior to the meeting.
So on this last or this next meeting, we said, "Okay, well here is the cutoff date," and the manufacturers who have drugs coming up would submit either a dossier or information that is relevant for that -- their particular drug.
Then we mail out all of that information, plus the information we get from First Health, the drug class reviews, to the P&T committee. We also publish an agenda.
We publish a public notice in the newspaper, public notice online that the meeting will take place and where it will take place at.
Then we take information from the manufacturers as far as if they are going to have a speaker at the P&T meeting. We allow them five minutes per class per manufacturer to speak at the meeting.
Prior to any testimony from the manufacturers, we allow public physicians or public citizens to present to the P&T committee. And they can speak for five minutes.
Then we get into the class review. We would take any input or public testimony from manufacturers prior to any other discussion.

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If the P&T members have discussion or questions, they will ask that manufacturer representative. Then First Health will give a synopsis of the drug class, prior claims count, as far as a break-out of the claims within that class, if it's a rereview.
Then following that, there would be P&T member discussion and then a vote as to whether it's any motion made, whether it's a motion to declare it a class effect or a motion to non-prefer one drug out of the class or prefer all the drugs out of the class.
Q. When you say a motion on a class effect, what does that mean?
A. A motion would be made among the members that drug class X appears to show that there is a class effect that the majority of drugs in that class exert the same or very similar effectiveness.
Q. So that could be one conclusion that basically these drugs, they pretty much work all the same?
A. Pretty much work all the same. They have some differences, but the differences aren't large enough to exclude or make a special note to include those as preferred.
Q. And in that situation, then would the next step be that the state can negotiate supplemental rebates and make those that agreed to it the preferred class,

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preferred drugs in the class?
A. Yeah, although the negotiation on the supplemental rebates is actually done once a year by First Health.
They do that by submitting an RFP to the manufacturers and say, "You know, here is your drugs. Which ones do you want to bid on for this national Medicaid pooling initiative."
And manufacturers can come back and say, "Okay, for this level of population, we'll give you this kind of price."
Q. So you actually know going into the review which ones would give the supplemental rebate to your state?
A. Correct.
Q. It might change the next year, but you know going in what the status is for that drug as you are doing the review?
A. Yes.
Q. So if it's been voted out as a class effect, then you basically know whichever one, three or six of the drugs in the class have agreed to that, those will be the ones who are preferred?
A. Correct.
Q. So that's one conclusion that the P&T committee can reach. The P&T committee, what considerations are

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they -- what are their considerations?
A. Well, they look at, as far as the indications for the drug, look at any kind of side effects. They look at abstracts of studies on the drugs within the class as far as what the outcome of those studies are.
And from that, and from their own experience, they can determine different avenues to go as far as how they want to do a motion.
Q. But is it fair to say the P&T committee is -- their job is to to look at safety and effectiveness issues, but not cost issues?
A. Correct. The P&T looks at the clinical issues, not the cost issues.
Q. So they can vote on a class effect. What else can they vote on?
A. They could vote that none of the drugs should be preferred or they could vote that one of the drugs should be preferred in addition to any supplemental rebates that are available.
Q. So if that occurs, what they voted out, is that one drug, even if everything else is the same, and it's going to be -- its status on the PDL is going to be contingent on the supplemental rebate, this particular drug or two drugs have qualities, clinical qualities that warrant it being on the PDL, even if they don't

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give a supplemental rebate?
A. Correct.
Q. And all of these conclusions by the P&T committee, does the state treat them as binding in terms of the PDL?
A. Yes, we do treat those as binding.
Q. Okay. Could this work in the opposite way that all -- there is ten drugs in a class and nine of them you say class effect they are all pretty much the same, but there is one you actually want to drop, treat as non-preferred, could that happen?
A. That could happen.
Q. And that would again happen for clinical reasons?
A. Correct.
Q. So if there is a safety problem with one particular drug in the class, that might get non-preferred for that reason?
A. Correct.
Q. So now we have got a PDL. What does that mean in terms of reimbursement for the medications?
A. What that means is if a drug is non-preferred, in order for Medicaid to reimburse that drug, the physician would have to indicate that it's medically necessary on the prescription or if the prescription is phoned in the physician or the person that's calling in the

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prescription would have to indicate that the physician has determined that this is medically necessary. It's a non-preferred drug.
Q. Are there criteria that physicians are supposed to use to determine that a drug is medically necessary?
A. No.
Q. Once a physician certifies that the medication is medically necessary, is that the end of the process, the drug is then reimbursed?
A. Unless there is a prior authorization on the drug also.
Q. The fly in the ointment of the PDL would seem to be that doctors can just sort of ignore it and just say, "I am going to keep prescribing what I want because I will just certify it as medically necessary."
Is there any monitoring supervision, any process that stops that from happening?
A. We have a couple of different things. There is a retrospective review of who is prescribing the non-preferred drugs. And there is a pharmacist working for First Health back in Virginia that sends a letter to the physician.
"We see that you're prescribing these non-preferred drugs at a higher than average level. Why are you doing that or, you know, could you consider

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going to the preferred drugs?"
So we have that retrospective part. Also, physician claims and physician charts are open to audit.
Q. What do you mean by that?
A. They could be audited and anything that is placed on prescription or orders could be a subject of an audit.
Q. So you can actually go to a prescriber and say, "Give me all your medical records for a patient, the following ten patients"?
A. We could do that.
Q. Is that done?
A. Sometimes.
Q. And the physicians are required to produce in that situation?
A. That's correct.
Q. Is there any sanction with teeth in it, so to speak, anything that can happen to the physician in terms of reimbursement beyond this communication process?
A. Nothing with teeth. I would like to say that the compliance with this program is very high and in the 80 percent range.
Q. So if you -- if this process results in a medication being non-preferred for whatever reason, your

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experience is that it will be prescribed quite a bit less?
A. Correct.
Q. And safety reasons is one of those reasons?
A. Correct.
Q. Not all classes of drugs have been reviewed for the PDL?
A. That's correct.
Q. What is the process for deciding which drugs are going to be reviewed for the PDL?
A. Basically, the drugs that First Health gets bids on, drug classes.
Q. Is that the only trigger for a drug to be reviewed?
A. That is one trigger. As I mentioned yesterday, we had reviewed Levothyroxine also.
Q. And the reason for that again?
A. Prescribers in the community had wanted that reviewed.
Q. And the reason -- what was the issue there?
A. Well, the issue was that it was -- there is a number of generics that are manufactured for Levothyroxine and there is one brand name, and the use of the generics was basically higher than what some of the physicians wanted, so they wanted to see if we could

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just prefer all the different brands and then there wouldn't be substitution of medications, generic substitution in that class.
Q. They thought that was a medical issue?
A. That was a medical issue.
Q. HSS could determine to review a class of drugs for reasons other than the prospect of supplemental rebates, correct?
A. Correct.
Q. You could take a class of drugs and decide we're going to review it for clinical effectiveness and safety, correct?
A. Correct.
Q. And the result of that could be that the class of drugs is segmented into preferred drugs that you think are safer and more effective than non-preferred drugs that are less safe and less effective, right?
A. Correct.
Q. And that could be done even though it's not going to change the financial arrangement at all?
A. Correct.
Q. Is it possible for First Health to have a class of drugs where some manufacturers have agreed to supplemental rebates, but the state determines not to put that class up for review anyway?

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A. That could happen.
Q. Has that happened?
A. Not to my knowledge.
Q. Anti-psychotic drugs have not been reviewed for the PDL, correct?
A. For our PDL, it has not been reviewed. It is a class of drugs that have been reviewed by other states.
Q. Do you know what states?
A. I know Oregon has reviewed it. Washington has reviewed it. I know those two for sure.
Q. Why haven't anti-psychotics been reviewed for the Alaska PDL?
A. Because we just have not wanted to do that yet.
Q. When you refer to the "we," I'm guessing you are part of that, right?
A. I'm part of that, correct.
Q. Let me just, before I get that specific, is there a sort of working group that says, "Okay, here is the six drugs we want to put up for review in September"?
A. There is a working group of myself and the pharmacists from First Health.
Q. Is that one particular pharmacist?
A. Yes.
Q. Who is that?
A. Melinda Sater.

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MR. ROTHSCHILD: Counsel, I'm prepared to go off the record if you want to give him a few minutes.

MR. HAHN: Let's let him look at it and see what he wants to do first.

Q. You know, actually, let me just pause for a minute before I ask you to do that. When you had this conversation with Mr. Peeples, this was shortly after the lawsuit was filed, correct?

A. Correct.

Q. Do you know whether you had seen the complaint at that point?

A. I don't believe I saw the complaint at that time.

Q. So maybe this is a better question for me to ask you: What was your understanding about what the lawsuit was about when you found out about it?

A. I would have to speculate. I don't exactly remember.

Q. Do you have any sort of recollection of your understanding about what the lawsuit was about?

A. I really don't remember.

Q. Do you have an understanding about what the lawsuit is about now?

A. I have a lot better understanding of what it is about now.

Q. What's your understanding about what the lawsuit

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is about?

A. The lawsuit is about the problem of discovery that Zyprexa causes diabetes, that the knowledge of that was not disclosed early enough to the prescribing community, and that there was improper marketing going on by Eli Lilly that was not disclosing that to the prescribing community.

Q. Not disclosing what to the prescribing community?

A. Was not disclosing the causation of diabetes.

Q. So that -- you know, the understanding of the lawsuit you just described, I mean was that consistent with what you had understood before the lawsuit was filed?

A. Yes. We did have an understanding of Zyprexa causing diabetes.

Q. Before the lawsuit was filed?

A. Before the lawsuit was filed.

Q. You say "we". You are referring to yourself?

A. I guess I have to get rid of the "we". It's myself and I.

Q. How did you develop your understanding that Zyprexa caused diabetes?

A. I don't remember where I got the knowledge originally. I know we did do a drug utilization review study on the atypicals and diabetes, diabetes drugs, and

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that was back in 2004. And then we did an intervention on that also.

Q. At the time you did the drug utilization review, did you have the understanding that Zyprexa caused diabetes?

A. Yes.

Q. Was your understanding that Zyprexa caused diabetes a precipitating event to the drug utilization review? Is that why you did it?

A. Well, and I don't remember and I don't have any documentation of why we did that study, but I know that I had read information that there was a cause and effect with Zyprexa in causing diabetes.

Q. Where did you read that?

A. I don't remember.

Q. When did you read that?

A. I don't remember the exact date on that either or a time period. It was probably in August of 2004.

Q. Did you say what materials you read that caused you to reach that conclusion?

A. I don't remember.

Q. You said you did an intervention on that. What was the intervention?

A. Well, we had pulled the drug utilization review profiles, and I mentioned that yesterday, I believe, how

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the profiles come out and give you the pharmacy claims and the medical claims.

And the drug utilization review committee had reviewed those and then we produced a letter that we were going to send to providers, to the prescribing providers about monitoring for the side effects of Zyprexa that could be associated with diabetes, the metabolic side effects.

Q. Did you actually create that letter?

A. Yes.

Q. Was it sent?

A. It was sent.

Q. When was that sent?

A. In the fall of 2004.

Q. Did that letter address only Zyprexa, or other medications?

A. That I don't remember.

Q. Do you still have a copy of that letter?

A. I think it was provided with the interrogatory.

Q. Prior to August 2004, had you read any literature relating to any relationship between Zyprexa and diabetes?

A. I don't remember.

Q. And let me extend the question to atypical anti-psychotics and diabetes.

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A. That I don't remember either.
Q. Prior to August 2004, did you have any awareness about whether Zyprexa had any relationship to weight gain?
A. I did have some information prior to that, and that came in on a prior authorization request for one of the anorexic drugs, the drugs to help cause weight loss. That was basically an anecdotal piece of information, but I had seen that.
Q. Other than that anecdotal episode, any other -- did you have any other knowledge about any relationship between Zyprexa and weight gain?
A. No, I don't.
Q. So it's fair to say that by the fall of 2004, you had come to the conclusion that Zyprexa caused diabetes?
A. I had information indicating that.
Q. Other than diabetes, is it the state's position that Zyprexa causes any other medical condition?
A. Well, there is a whole list of side effects that Zyprexa causes that are listed in the package insert.
Q. Other than the package insert --
A. Well, and, you know, it is listed in there that diabetes and heart disease and high lipids and all of that is mentioned in the package insert.
Q. When you received this information that Zyprexa

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causes diabetes, what did you do about it?
A. Developed a drug utilization review study about that.
Q. What conclusions, if any, did you draw from the drug utilization review?
A. That it appeared that a number of the people who were taking Zyprexa had diabetes and were taking diabetic drugs.
Q. Did you, through that drug utilization review study, conclude -- reach any conclusions about whether the number of Zyprexa users taking diabetes medication was higher than would be expected?
A. I don't remember.
Q. Did you take any other actions besides the DUR study, and I think you mentioned the letter, anything else?
A. That's all we have done up to that point.
Q. Up to what point?
A. Up to this point now based on the information that or that letter from the FDA, we're looking at another intervention.
Q. Did you take any action as a result of what you found out from the DUR study?
A. Well, as far as the action we had taken was just doing the intervention, sending out a notice to the

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prescribers that watch out for these metabolic effects that could happen while patients are taking Zyprexa.
Q. That's the letter you referred to?
A. That's the letter.
Q. Again, you don't remember sitting here today whether it was Zyprexa specific or a class specific?
A. Correct.
Q. The FDA letter you were referring to, what letter is that?
A. The letter on CBX that the FDA sent to Eli Lilly requesting that they improve the labelling on the causation of diabetes.
Q. When did you receive -- do you remember the date of that letter?
A. It was March 28th.
Q. Of --
A. Of -- well, actually, there wasn't an actual date from the FDA, but there was a date on the letter of March 28th.
Q. 2007?
A. 2007.
Q. When did you receive that letter?
A. It was in my notebook again, and so I had received it as from counsel.
Q. And you said -- do you know when you received it?

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A. I don't remember exactly when I had received it.
Q. But you said that's now motivating another intervention?
A. That's correct.
Q. What intervention?
A. That will be an intervention to look at Zyprexa and to also remind prescribers that it can cause diabetes and to be on the watch out for metabolic changes.
Q. So let me just make sure I understand that. One intervention is to look at Zyprexa?
A. Well, one study or one review is to look at Zyprexa and look at whether or not diabetes drugs are being used in those who are taking Zyprexa.
Q. So one intervention that you were talking about as a result of this letter is to do another drug utilization review?
A. Correct.
Q. And another intervention that you are considering is to send another communication to prescribers?
A. Well, the intervention would grow out of the drug utilization review.
Q. So you would do a drug utilization review and then after that is completed, you might or might not send a letter to prescribers?

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A. Correct.
Q. Anything else, any action you are taking as a result of --
A. We may put a study or something else with that letter.
Q. I don't understand what that means.
A. Well, as far as a study that shows, if there is another one available, that shows where diabetes may be the result of taking the Zyprexa.
Q. Are you talking about a study that Alaska would perform?
A. That's a published study.
Q. Not based on Alaska data, but what else, what's out there in the national literature?
A. Right.
Q. But that action hasn't been taken?
A. That action has not been taken.
Q. Do you have a particular study in mind that you would provide to physicians?
A. Not at this time.
Q. How would you go about finding that?
A. Look on Pub Med or one of the resources, medical resources.
Q. Other than the actions you have described or the actions you are considering, any other actions that

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Alaska has taken as a result of your learning that Zyprexa causes diabetes?
A. Well, the other action that we do use, it's not tailored to Zyprexa individually, but it is tailored to the anti-psychotic drugs is the behavioral pharmacy management program.
And we send letters to prescribers once a month through that program, and that's done for us by the Comprehensive Neuroscience Company.
Q. And I do have some questions for you about that, but those activities, that's the BMPS program?
A. BPMS program.
Q. The activities that would come out of the BPMS program are all related to your findings about Zyprexa's relationship to diabetes?
A. No.
Q. Would any letters to prescribers coming out of that program have anything to do with safety issues?
A. It does have information about the safety issues as far as the use of atypicals and how many atypicals are used in a person, the age of the person that's using the atypicals.
Q. I want to return to that subject, but let me put that aside for now. When we talked about this issue of your knowledge, yesterday you referred to the list

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serves.
Was the list serves a source of information to you about risks associated with Zyprexa?
A. I don't know for sure.
Q. That may be the case that even prior to August 2004, information about safety-related issues with Zyprexa were communicated to you through the list serves?
A. It's possible.
Q. As a result of the information you learned, you did not institute a step edit for Zyprexa, correct?
A. That's correct.
Q. Why not?
A. It would just be a difficult edit to implement, and doing it with atypicals would not be the place you would want to start with the step edit.
Q. Why is that?
A. There would be too much negative energy directed towards the Medicaid pharmacy program manager.
Q. You do agree -- you have come to the conclusion that there is a safety issue with Zyprexa, correct?
A. Correct.
Q. And you told me that step edits is one way to address a safety issue in the medication, correct?
A. Correct.

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Q. Can you explain to me why negative energy directed toward you would impede you from addressing a safety issue?
A. As far as doing a step edit, you would want to do that with a different type of drug rather than the atypical anti-psychotics.
Q. Why?
A. There would be -- well, the mental health community is just not where you would want to start that.
That community is highly financed by pharma organizations through the advocates and they get irate if you try to put any kind of restriction on their medications.
Q. Do you have an understanding of why they get irate?
A. Because they want what they want, and their doctors want what they want.
Q. As the pharmacy director for Medicaid, do you feel like you have a responsibility towards Alaska Medicaid recipients to protect their safety interests?
A. Yes, I do.
Q. And you take -- do you take all steps necessary to protect the safety of Alaska Medicaid recipients?
A. All within reason that are available and wise to

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do.
Q. Okay. Is step edits one available mechanism you have to protect the safety of Alaska Medicaid recipients?
A. It is one avenue I would have.
Q. And it's a reasonable method?
A. It's a reasonable method for other classes.
Q. Is the only reason you're singling out the anti-psychotics as not being a reasonable method because the mental health community is active as advocates?
A. No, that's not the only reason.
Q. What other reason?
A. Well, I guess for all practical purposes, that's the main reason is just that they are quite active, and as far as going against that, is it worth it to create a lot of negative pressure in the community.
Q. Putting aside the negative pressure, do you think it would be the right thing to do to put Zyprexa on a step edit protocol?
A. No.
Q. Why?
A. Well, the right thing would entail looking at all different angles, all different possibilities for backlash, and while we are looking at the interests of the patient, the overall interest, I just -- I don't

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think that's the place to start with a step edit.
Q. I'm having trouble understanding. I want to put aside what I will call sort of advocacy pressure and political pressure and understand just sort of on the merits for this medication, which you have identified safety issues for, why wouldn't you use a step edit?
A. I wouldn't start with the atypicals for a step edit.
Q. Why?
A. Actually, the CATIE study says that the typical anti-psychotics are better and less prone to cause side effects, so there would be a possibility to say, "You got to go through this, try typicals before you go to the atypicals."
Q. So why not have that step edit process?
A. I don't want to do it.
Q. This is your job. You have testified that part of your job is to protect the safety of Alaska Medicaid recipients. You have identified a safety mechanism.
I'm going to ask you these same questions for some of the other procedures you have at your disposal for protecting the safety of Alaska Medicaid recipients.
You have told me you don't want to do it, but I'm not getting a clear answer for why.
MR. SNIFFEN: I have to object to that. I

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think he has said why. I think he said there is a lot of political pressure that has prevented him from doing that.
MR. ROTHSCHILD: He has also testified that even absent that political pressure, it would not be his recommendation to do that, and I want to understand why.
MR. HAHN: It's been asked and answered.
MR. ROTHSCHILD: It hasn't, Blair.
MR. HAHN: It has, because the political pressure -- just because you magically wave it away and ask him the question without it doesn't mean it goes away. It's there and he said that's why.
Q. Mr. Campana, am I correct in understanding that even if the political pressure wasn't there, you would not be recommending a step edit for Zyprexa?
A. If this was a perfect world and there was no political pressure, I would consider a step edit for the atypical anti-psychotics.
Q. For all atypical anti-psychotics?
A. All atypical anti-psychotic, and I would consider one for just Zyprexa.
Q. Okay. And so what is the step edit you would recommend in this world that doesn't have the political pressure?
A. Step edit that you would have to fail on at least

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one or more of the typical anti-psychotics.
Q. What would be the reason for that step edit?
A. To make sure that prescribers had tried the earlier drugs, the older drugs, and make sure that the patient had actually failed on that medication before going to the typical or to Zyprexa.
Q. The atypical or Zyprexa?
A. Or Zyprexa.
Q. When you -- that protocol that you described, would that be directed at keeping costs lower or safety issues?
A. It would be both. It would be, first of all, the safety issue with Zyprexa and then the second is that there would be a cost issue.
Q. And the impediment to that that you have described is that there is political pressure?
A. There is political and advocate pressure to not do that.
Q. How do you know that? I mean, what is the source of that pressure?
A. That pressure is -- comes from when we had or originally had Clozapine on prior authorization. We have had prior authorization on that drug since '89.
And in the years after that, and after I had started with the state, I had calls, "Why do you have

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this on prior authorization? Why don't we get every drug we want?"

Also, psychiatrists are one group of physicians that, in my opinion, think that every drug should be available on their arsenal to every patient, and they have a stronger opinion of that than other practicing physicians.

Q. Do you understand why they hold that opinion?

A. No, I don't.

Q. Clozapine was subject to a prior authorization process?

A. It is subject to a prior authorization process.

Q. And what is the reason that Clozapine is subject to a prior authorization process?

A. Safety issue for Clozapine causes blood dyscrasias.

Q. So that's an example of a mental health medication which, notwithstanding the political pressure, the state has implemented a prior authorization process?

A. Correct.

Q. Has the state instituted a prior authorization process for Zyprexa?

A. No.

Q. Why not?

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A. We haven't.

Q. Is it the same reasons that you haven't done a step edit?

A. Correct.

Q. So the state is capable of doing it for safety reasons, but has chosen not to for Zyprexa?

A. Correct.

Q. And you have been able to resist the pressure from the mental health community and psychiatrists in keeping Clozapine on prior authorization?

A. Correct.

Q. And you have experienced that pressure?

A. I have experienced that pressure.

VIDEOGRAPHER: Off record. The time is 12:18.

(There was a lunch break.)

VIDEOGRAPHER: On the record. The time is 1:31.

Q. Good afternoon, Mr. Campana.

A. Hello.

Q. Your counsel has given me two disks. One of them has just a tape label on it that says "gender control". One has a label, and the other one has a label that says "gender tally and gender zip".

I have looked at those disks, and I'm just going

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to give you some representations about the numbers, unique Medicaid recipients that I saw there just to confirm that's consistent with your understanding of what was expected.

On the disc that includes the gender tally file, that appears to just be a duplicate of the gender file that we looked at earlier today which had relatively small numbers, 700 or so Zyprexa users and about 8,000 other users.

Then there is a file "gender Zyp" and it has 6,455 unique recipients. Is that number consistent with your recollection about the number of Zyprexa users who you received gender data for?

A. That's closer to consistent to my number.

Q. I mean, is there anything about that number that sounds wrong to you or you just don't have a perfect recollection of the number?

A. I don't have a perfect recollection of that number, but it's more than 700, and 6,000 sounds better.

Q. Other than that, you can't -- you don't know whether it was 8,000 or 4,000?

A. Right.

Q. It was in the thousands?

A. Thousands.

Q. The other disk, which is "gender control," has

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256,772 unique recipients. Does that sound roughly consistent with the information you pulled for the gender of what you would label the control group?

A. That sounds like a number more consistent with the control group.

Q. Thank you. For the prior authorization of Clozapine, I understood your testimony to be that that prior authorization was already in effect when you became part of the Department of Health and Social Services; is that correct?

A. That is correct.

Q. Has that treatment, reimbursement treatment of Clozapine, been up for review during your tenure?

A. We have reviewed it. I have reviewed it and I changed the criteria set for that and developed a specific form for authorization of Clozapine.

Q. It's been up for review and you have made changes. Is that subject to any kind of public proceeding or comment period or anything like that?

A. No.

Q. You have indicated that you felt political pressure regarding that treatment of Clozapine.

What was the context where you would receive pressure?

A. I have met at different times with different

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psychiatrists in the community and we have been -- this was at a time when Dr. Porter and I worked together on the program. We met with psychiatrists, and they requested we take the prior authorization off of Clozapine.

I have met with different psychiatrists at different times and there have been requests to take the prior authorization off of that.

Q. And you have always declined that request?

A. Basically, I have declined that request.

Q. And in the course over the years where you have been dealing with issues of prior authorization for Clozapine, have you had any interactions with representatives of the mental community or their advocacy groups regarding the prior authorization of Clozapine?

A. No.

Q. Have you felt political pressure from those groups regarding the issue?

A. No.

Q. Have you had any dialogue or heard from the mental health community advocates regarding possible changes to the reimbursement treatment of Zyprexa?

A. No.

Q. Before lunch, you were talking quite a bit about

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the sense of political pressure from those groups as it related to possible changes in the treatment of Zyprexa, and I'm trying to understand where you would have received that from if you are not meeting with them or hearing from them.

A. As far as the pressure would be in discussion with psychiatrists or phone calls. They may call in and say, "You know, we would like to make sure you don't put prior authorization on that."

As far as the mental health drugs, in looking at states across the country, very few states have any of the mental health drugs on prior authorization.

Q. Does that include Clozapine?

A. That could include Clozapine. Some of the states have legislation that prevents them from having any of the mental health or any of the atypical anti-psychotics on prior authorization.

Q. So Alaska distinguishes itself to some extent from other states by having Clozapine on prior authorization?

A. Correct. There are states that do have Clozapine under prior authorization still.

Q. But it's not the norm?

A. I can't answer that.

Q. The name Thomas Porter has come up in our

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dialogue and, in fact, his name appears in some of the interrogatory answers. I think I need a better understanding of where he fits in the picture.

He was the medical director?

A. He was the medical director for Medicaid.

Q. For what time period?

A. Approximately to '90 or late '89 through to 2001, I believe.

Q. And what was -- what roles or functions or responsibilities did he have regarding medications, and particularly anti-psychotic medications?

A. Well, he basically reviewed the prior authorization for Clozapine. He also reviewed the prior authorization requests for growth hormone.

And then he reviewed prior authorization requests for gastric bypass, different hospitalization, different issues that would come up under the surveillance utilization review program.

Q. Who replaced Mr. Porter?

A. There was no replacement for him until this year, this spring. Dr. Malter was hired as the medical director.

Q. Did somebody fill Dr. Porter's responsibilities during this period where there was no medical director?

A. I took over the prior authorization for growth

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hormone and Clozapine.

Q. If I'm understanding you correctly, during Dr. Porter's tenure, he worked with you on some medication issues, and, after his departure, you didn't have a counterpart to work on medication issues?

A. Correct.

Q. Another way that you described that the state could address safety issues with the medication is to review the medication for the PDL, correct?

A. Correct.

Q. And the outcome of a review for that reason could be that the medication is put on -- is treated as non-preferred, correct?

A. Correct.

Q. And -- or the outcome could be that all the atypicals are preferred?

A. Sure.

Q. And, again, as you said before lunch, becoming non-preferred wouldn't stop any prescriber from prescribing the medication, it would just mean that the prescriber has to explain the medical necessity?

A. Correct.

Q. And as we have discussed, you have not reviewed Zyprexa or any of the other anti-psychotics for the PDL, correct?

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A. The typical or atypical anti-psychotics have not been reviewed for the preferred drug list.
Q. Why didn't you review Zyprexa after you learned the information you have described about Zyprexa's relationship to diabetes?
A. We did review it as far as under the drug utilization review program.
Q. Why didn't you review it for the PDL?
A. We didn't take over that class or didn't review that therapeutic class in the preferred drug list.
Q. And that was the decision of you and your First Health counterpart?
A. Correct. And as reasons I had previously stated, and also the mental health community is under terrific pressure here due to low funding and due to over-abundance of patients and small infrastructure to take care of those patients, so why do we want to add one more hoop to that whole overrun entity?
Q. So was that resource issue the reason? I want to be very precise about my question here. There came a point in time when you had gathered information about Zyprexa's relationship to diabetes, correct?
A. Correct.
Q. And you interpreted that information to be communicating that Zyprexa actually caused diabetes?

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A. Correct.
Q. And that was sometime around fall of 2004, correct?
A. Correct.
Q. And could have been even earlier?
A. Could have been even earlier.
Q. And one of the things you could have done about that is reviewed Zyprexa for the PDL?
A. Correct.
Q. And the P&T committee might have come to the conclusion that the safety issues warranted Zyprexa being non-preferred, correct?
A. Correct.
Q. As you said, putting a drug -- making a drug non-preferred has actually been fairly effective in causing prescribers to prescribe those medications less than they previously did?
A. Correct.
Q. But you elected not to do that?
A. Correct.
Q. I want to make sure I understand. Why in this juncture, after you have come to these conclusions about Zyprexa's relationship with diabetes, did you not take that step?
A. Well, we didn't take that step at the time.

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There were political issues about that. And as I mentioned just a minute ago, the over-burdened community, mental health and mental health community, and lack of psychiatrists out there, lack of practitioners for the mentally ill.
Q. So are those the two reasons that after determining that Zyprexa causes diabetes you didn't elect to review Zyprexa for the PDL?
Those are the only two reasons, the political pressure and the resource issue?
A. Those are the main two I can think of right now.
Q. Can you think of anything else?
A. At this point. I might have a brain storm in a minute, but that's the two.
Q. I'll put up the umbrella. Just let me know.
So let's break these down. One issue is lack of resources. In what way does the lack of mental health resources bear on the issue of whether a drug you have concluded has a safety issue should not be reviewed for that safety issue for the PDL?
A. Well, as far as making it any more onerous for those prescribers to prescribe the drug. Even though writing -- the only requirement we have is to write "medically necessary," do we want to impact that resource with another hoop or another restriction to

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getting that -- getting the services for the mentally ill.
Q. Are there any mental health medications that are on the PDL?
A. There are mental health as far as drugs that are used in the treatment of mental health conditions.
Anti-depressants are on there. The anti-convulsants, the sedative hypnotics, and the ADHD drugs.
Q. That's actually most of the mental health drugs, isn't it?
A. Well, that's most of the other mental health drugs that are used in the treatment of mental illness other than the atypical or typical anti-psychotics.
Q. The people who prescribe all of those drugs you just described, anti-depressants and anti-convulsants, they pretty well overlap with the group that prescribes anti-psychotics, correct?
A. Correct.
Q. And you have nevertheless put those drugs on the PDL, correct?
A. Correct.
Q. And made those prescribers jump through those hoops, correct?
A. Correct.

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Q. And did you -- was it a consideration when those drugs were put on the PDL that this scarce mental health treating community would be burdened?
A. Yes, it was.
Q. But it didn't stop you from doing it?
A. It didn't stop us from doing it.
Q. When those drugs were put on the PDL, the reason for it was -- the reason they were reviewed for the PDL was more economic than safety; isn't that right?
A. Well, it was the effectiveness, the clinical effectiveness and for economic reasons.
Q. Were any of these -- for any of these classes of drugs that you just described, anti-depressants, anti-convulsants, was there a medication amongst the group that had a particular safety issue that you were concerned about?
A. Well, as far as the stimulants that are used for attention deficit disorder, there is somewhat of a safety concern on those as far as diversion on those.
Q. What do you mean by diversion?
A. As far as people looking for stimulants. There is a big methamphetamine problem out in the world and methamphetamine is one of those drugs.
Q. So that's a safety issue based on misuse of the drug as opposed to a safety issue that comes with using

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it for its expected use?
A. Correct.
Q. In the case of Zyprexa, you have identified a safety issue that you understand to come with its regular use, indicated use, correct?
A. With its labeled indications and unlabeled indications that it's being used.
Q. Any of the classes -- were there any medications within the class of drugs that have been put on the PDL that had sort of safety issues that were inherent even when it was being used for its indicated use?
A. Well, the opioids are on the preferred drug list and they have safety and abuse issues, and they are also on prior authorizations, so there is at least one example of that.
Q. That's not a mental health drug?
A. It's not a mental health drug per se.
Q. So for all the mental health drugs that we just talked about, they don't have any safety issue that's inherent in their indicated use, correct?
A. At least there is not a major safety issue.
Q. Okay. And as we said, they are prescribed by the same physicians who prescribe anti-psychotics?
A. Correct.
Q. But you determined that they should be on the

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PDL?
A. Correct.
Q. Is it fair to say that anti-depressants are prescribed more often than anti-psychotics?
A. Without having the data, I wouldn't make a statement as that.
Q. You just don't know one way or the other?
A. I don't know.
Q. Did you ever recommend filing a lawsuit against Eli Lilly based on what you had learned about the safety issues with Zyprexa?
A. Not that I remember.
Q. I have gathered from your testimony today that the state has filed lawsuits against other prescription drug manufacturers?
A. It's my understanding that we have joined lawsuits filed against other drug manufacturers.
Q. What other drug manufacturers, and if you can identify it by medication as well?
A. Well, as far as the other manufacturers, the first case I worked on was Mylan. That was a national suit that was done through the AG's office where Mylan had conspired to raise prices of generic drugs.
Q. I'm actually glad -- let's put aside price issues and just talk about lawsuits that the state has filed

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because of, you know, safety issues or improper promotion kind of issues.
A. There are two other cases I know of. I don't know all the particulars about the cases. The OxyContin case where improper marketing was done by the manufacturer, and that case has been recently settled.
Then there was the Neurontin case where I believe it was a qui tam issue and done by the AG's office due to the improper labelling and marketing of the drug.
Q. In either of those cases, has there been any lawsuit filed against the manufacturer of Vioxx?
A. I can't answer that. I don't know.
Q. In either of the cases you identified, OxyContin and Neurontin, did you play any role in deciding whether to file a lawsuit or join a lawsuit?
A. No.
Q. So one reason you said you hadn't reviewed Zyprexa for the PDL after drawing your conclusions about the safety issues was the over-burdened mental health community, and we had discussed it.
You again refer to political issues, and I want to make sure we're on the same page. What do you mean by that exactly?
A. The political issues were carryover from a previous administration. And as far as the current

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Q. Just we're not doing it right now, that kind of thing?
A. We're not going to do it right now.
Q. Eventually, though it was allowed?
A. Eventually, we were able to prevail and say that, you know, the preferred drug list is up and running, we have good buy-in with the prescribers and we have compliance over 80 percent.
This is what it's going to do for these drugs and it will, you know, basically be okay to do this. And it just took a while to get buy-in to do that.
Q. When you made the case to your superiors, was your case based on the economics?
A. It wasn't totally based on economics. It was based on, and I don't have the recollection as far as what I put in the memo to do that, but I believe part of that was the compliance issue, compliance with the drugs, so I don't know.
Q. Meaning some people -- one of the rationales for preferring a drug was that some drugs resulted in better patient compliance than others? Is that what you mean by compliance?
A. No, it wasn't patient compliance. It was compliance with the preferred drug list.
Q. Thank you for clarifying that. So the case you

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were making was we can reduce costs and prescribers are agreeable to complying with this?
A. Correct.
Q. That was really the main argument?
A. That was at least one argument, and there was good buy-in with the preferred drug list at that time. And if anyone wanted to come to present or to talk at any one of the P&T committee meetings, there was an open time and place for them to do that.
Q. So you felt political pressure, but ultimately what you perceived to be the correct result, the recommended result was able to overcome that political pressure?
A. That's correct.
Q. Did you ever make the same case in your agency or above for putting the anti-psychotics on the PDL?
A. No, I haven't, but I will.
Q. What do you mean by that?
A. I'm going to go ask to do that and see how it goes as far as to see what kind of backing I have from the commissioner to do it now.
Q. You didn't do it yesterday?
A. I didn't do it yesterday, but I'm going to go forward at some point and do that.
Q. What has caused you to decide to do that?

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A. Well, I think that there is no reason not to do it.
Q. Okay. Now, you have been operating under the -- let me withdraw that for a moment.
What are the reasons that you have now decided to recommend a PDL for the anti-psychotics?
A. I think we have a good product with our preferred drug list and there is no reason at this point not to ask for it.
We have -- you know, there is going to be political pressure. There is always going to be some political pressure.
Q. Any other reasons that you have decided to do this?
A. That's the main reason.
Q. When do you expect to make that recommendation?
A. I'll have to dig out from being gone for the last couple of days. Next week is going to be a busy week, so it's going to be sometime in the future.
Q. When did you come to the decision that you were going to recommend anti-psychotics to the PDL?
A. At lunch.
Q. Is there anything that has taken place during this deposition that's caused you to come to that conclusion?

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A. Well, reviewing the facts and reviewing what we have done. Maybe it's worth reviewing again. Reviewing the decision to do that.
Now, as far as reviewing a decision to do that, and implementing that, may be two different things.
Q. At lunch, did you discuss your testimony -- did you discuss your testimony with counsel over the last day and a half?
A. Not the individual testimony. I mean, there were some comments.
Q. Did you discuss the issue you just -- the topic you just communicated to me that you have now concluded that you are going to recommend the anti-psychotics be reviewed for the PDL?
A. No.
Q. Did you come -- when you walked in here yesterday morning, did you have any intention of reviewing anti-psychotics for the PDL?
A. As far as intention, I have intended to do that at some point. It's just that the time had not been right and maybe now is the time, but it's still a time to review a decision towards that, not necessarily to implement that.
(Exhibit No. 15 marked.)
Q. I'm going to mark as Exhibit No. 15 Plaintiff's

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Response to Defendant's First Set of Interrogatories. I don't have an extra copy. If you could turn to page 16 of the document.

We asked the question, "Did you ever take any steps to reduce the payment you were paying or reimbursing for any anti-psychotic drug?"

The state answered, "The state is and has been working on a formulary aimed at reducing the amount paid for all pharmaceuticals, including atypical anti-psychotics."

Is that accurate?

A. Well, unfortunately, formulary is in there and it should be preferred drug list. And then I'm tripped up on including atypical anti-psychotics.

Q. Even if you substitute the word "PDL" for "formulary," that statement is not accurate, is it?

A. No, it isn't.

Q. These were the responses to interrogatories we talked about earlier today and they were sent to us by your counsel on April 23, 2007.

You said you do have a copy of these in your file, correct?

A. Yes, I do.

Q. Did you review this document before April 23, 2007, or in that general time period?

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A. I'm not sure when I had reviewed it.

Q. Do you know whether you reviewed it before it was finalized and sent out?

A. I reviewed it before -- actually, I reviewed the interrogatories, but I don't remember reviewing the answers.

Q. Okay. And looking at the answer that I just showed you, is that familiar to you at all?

A. Part of that is familiar. At least the bottom part is familiar. And as far as working on a formulary, working on a PDL, it sounds like an answer that I would have made.

I'm not clear where that atypical anti-psychotics came in though.

Q. It wouldn't be accurate for atypical anti-psychotics or typical anti-psychotics, correct?

A. Actually, it could be because even though we have gone out with information that we are not including the atypicals in our preferred drug list, it's not saying that we won't ever consider it.

Q. Mr. Campana, this is important. Let's look at the answer very -- it says, "The state is and has been working on a formulary aimed at reducing the amount paid for all pharmaceuticals, including atypical anti-psychotics."

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It is not true that the state, and this would have been as of April 23rd, 2007, it was not true at that time that the state has been and was working on a formulary that involved atypical anti-psychotics or a PDL involving atypical anti-psychotics, correct?

A. As of the time that this answer was provided, we were working on a PDL, but we have not been working on including the atypical anti-psychotics.

Q. So even if you substitute the word "PDL," it was inaccurate at the time and it is inaccurate now, correct?

A. As far as being in the present tense, it is inaccurate.

Q. Only in the future tense could it be accurate?

A. In the future tense it could be accurate.

Q. But you don't read this statement to be in the future tense, do you?

A. I don't see that it's in the future tense.

Q. And even if we substituted "typical anti-psychotics" for "atypical," it would also be inaccurate, correct?

A. That's correct.

MR. ROTHSCHILD: Counsel, we have asked repeatedly for verifications of these interrogatories, and it's really being reenforced to me now why that's

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necessary, so I would ask that that be supplemented immediately.

And if there needs to be corrections to the interrogatory answers, please do that.

Q. You said that after that first sentence we have been focusing on that the rest of the text looked familiar to you?

A. I'm sure that the information about the BPMS program was provided by myself.

Q. I just want to make clear, when you say "familiar," are you talking about the actual sort of words on the page you saw or the content is familiar to you?

A. The content is familiar.

Q. You didn't necessarily see a response that included the sentence, "The state participated in the BPMS program sponsored by Lilly"?

A. Correct.

Q. The next sentence says, "Additionally, the state has investigated the possibility of joining with other states to negotiate further rebates."

Is that accurate as applied to anti-psychotic drugs?

A. Well, that statement is sort of incorrect because we have -- we are already -- have already joined with

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A. Based on the literature that is or based on the package insert that is shown that diabetes is a side effect of Zyprexa, it can -- I have drawn a conclusion that there would be at least one recipient in Medicaid that has developed diabetes after taking Zyprexa.

And also back in that 2004 study, DUR study, we had found people that had taken Zyprexa associated with diabetes.

Q. So you found some Zyprexa users who had diabetes?

A. Correct.

Q. You didn't do any further analysis to determine whether their diabetes was as a result of Zyprexa, correct?

A. Correct.

Q. You agree that some Zyprexa users will get diabetes -- would get diabetes no matter what, correct?

MR.HAHN: Objection. That's outside the scope of this witness's expertise and the notice, but answer if you know.

A. Please repeat the question. Or let's take a break and then you can repeat the question.

VIDEOGRAPHER: Off record. The time is 2:44.

(There was a short break.)

VIDEOGRAPHER: On the record. The time is

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2:58.

Q. Mr. Campana, I'll withdraw my last question. Let me ask you this question: Do you know whether Zyprexa users in Alaska have developed diabetes at a greater rate than other Alaska Medicaid recipients?

A. I don't know.

Q. Do you know whether Alaska Medicaid recipients who use Zyprexa have developed diabetes at a greater rate than Alaska Medicaid recipients that use other psychotic medications?

A. I don't know that.

Q. In addition to meeting with representatives from Eli Lilly, you meet with representatives from other medication manufacturers, correct?

A. That's correct.

Q. Do you meet with representatives of any anti-psychotic medication?

A. I have met with representatives from other manufacturers of anti-psychotic medications.

Q. In those interactions, have they ever provided to you information about safety issues relating to Zyprexa?

A. Not to my knowledge.

Q. You have referred to CNS and BPMS quite frequently in the deposition. I have not followed up, but I would like to now. Tell me what the BPMS program

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is and what CNS is.

A. The CNS is Comprehensive Neuroscience. They are a company that does or provides a similar product to our drug utilization review program where they have developed a number of different criteria statements.

One of the criteria statements is a person who has taken five or more anti-psychotics over a certain period of time, over six months.

So there is criteria statements for that. They are based on five, four, three, two, different anti-psychotics.

There is statements about use of opioids. There is statements about use of the atypical anti-psychotics in children. They get a download of pharmacy data once a month and then run it against those criteria, and then they produce reports and do intervention letters to the prescribers mentioned on those profiles.

Q. So this is a -- BPMS is a program run by CNS?

A. Right.

Q. And they are -- it's basically a drug utilization review program?

A. Correct.

Q. Is it a utilization review limited to anti-psychotic medications?

A. It's limited to anti-psychotics and opioids. And

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in, say, in the anti-psychotics, that includes the anti-depressants, the stimulants, the anti-epileptic or anti-convulsants and anti-depressants.

Q. So it's not just --

A. It's not your atypical or typical. It's the atypical and typical and other classes of mental health drugs.

Q. How long has Alaska been participating in this BPMS program?

A. Let's see. We started in, I believe it was 2005, and continued it 2005 through 2006. Then the contract for it had expired earlier this year and we did another contract for another two years.

Q. I'm sorry. So it started what year again?

A. 2005.

Q. It started in 2005?

A. Started in 2005 in Alaska.

Q. So really you have been participating continuously since 2005 under two separate contracts?

A. Correct.

Q. How did it come to be that Alaska enrolled in the BPMS program?

A. The product was presented to us back in 2004, and it was also presented to the Alaska Psychiatric Association by Eli Lilly.

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And when we started looking at the program, we said, "We can't do it right now because we're in the middle of implementing the preferred drug list." Once we had that up and running, then we looked at the program further in 2004.

Looked at it. Eli Lilly was going to provide a grant for the service provided by Comprehensive Neuroscience.

And so they did provide the grant for it and we took it on for the two-year period. And over the course of that, they started off initially with just doing the mental health drugs, and then they added the opioid drugs in there.

They are a progressive company so that they continually reevaluated and changed the criteria. They went from a small amount of criteria for children to many more different criteria statements.

Went from a medium-sized amount, as far as like there were about 15 different indicators for adults, and then expanded that to some over 25 indicators.

Q. Who from Eli Lilly presented the program to Alaska and the API?

A. That was Kevin Walters.

Q. Is he basically the Eli Lilly person that you identify with this program?

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A. Yes.

Q. He is the only person you have interacted with regarding the program?

A. He is the local person that I have interacted with. Actually, he is out of Seattle. I have interacted with his supervisor, who is Joe Busby, out of Salt Lake.

Q. In person or over the phone?

A. In person and over the phone.

Q. Have all of your interactions with Mr. Busby been about this program?

A. Yes.

Q. And, again, there is nothing that Mr. Busby has said about Zyprexa that you have concluded was a misrepresentation?

A. Correct.

Q. Eli Lilly provided the grant for the BPMS program when it started?

A. Yes.

Q. Did that cover it completely?

A. It covered the complete cost of the program.

Q. When the contract was renewed, did Eli Lilly issue another grant to cover the contract?

A. They initially were hesitant to provide a grant for that program. It looked like they weren't going to

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fund it at all, and then they came back with half the funding.

Q. Where does the rest of the funding come from?

A. Well, actually, we reduced the scope of the project to accommodate the full grant. Now, the "we" in that is different than the "we" for other things.

Q. Who is the "we"?

A. The "we" for that is Dr. Hobson and myself, as he is the medical director of Alaska Psychiatric Institute, the medical director for behavioral health, the division of behavioral health, so he and I coordinated on that project.

And there is another individual that assists us on that who hardly ever makes a meeting, and that's Robert Hamacher.

Q. Who is he?

A. He is a person that works in behavioral health.

Q. Are most severely mentally ill patients in Alaska treated at API?

A. I don't know.

Q. You said Lilly was hesitant to fund the grant at all. How do you know that?

A. I had discussions with Mr. Walters on that. And there was information coming from other states that Eli Lilly was balking at providing that grant, and the

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information also came from CNS.

Q. Do you know why they were balking?

A. I don't know why.

Q. And then they decided to do the half grant?

A. Right.

Q. Are they still funding everything that CNS does with the BPMS program in Alaska?

A. Yes, other than the individuals who work, oversee the program for the state.

Q. Does the BPMS program benefit the State of Alaska?

A. Yes, I believe it does.

Q. How does it benefit?

A. It provides this overview of the mental health drugs and, basically, edits on the criteria or runs the pharmacy claims against its criteria.

And for those who out lie (as spoken) from that criteria, they are sent a letter about the prescribing habits, notice that overshoot the criteria.

Q. And I guess some of the criteria is poly-pharmacy using, multiple mental health drugs simultaneously?

A. Correct.

Q. Another one would be frequent changes in prescriptions to a patient?

A. That's one. The other one is like five

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psychotropics in one person over a period of time, four, three, two, psychotropics, use of Benzodiazepines in children, use of more than one stimulant in a child. Items such as that are the criteria.

Q. Does the program reveal off-label prescribing?

A. It really doesn't come up against off-labeled prescribing.

Q. And I guess the data that is being used for this is the same as the claims data?

A. As the claims data, pharmacy claims date only at this time.

Q. Does the program in any way look for side effects?

A. No, it doesn't. There is no diagnosis information used at this point.

Q. Has the BPMS program -- I mean you have described how the program works, but how does the state actually benefit from the output from the program?

A. By sending letters to the prescribers of those medications. It let's the provider know who else may be working on the case, so it let's the provider know about poly-pharmacy and who other prescribers are; therefore, increase in the safety of medication use.

Also, it indicates to a prescriber you have X number of patients or these patients listed on this

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letter have exceeded this criteria, five or more psychotropic drugs within this period of time.

We compare utilization for different periods of time, and we have shown that there has been decrease in that offending issue after a provider has been noticed on that.

Q. Does that help the state cut costs?

A. It helps the state by cutting costs, cutting side effects that could be an issue with many different prescription drugs.

It basically helps to provide a safety net for those recipients that are taking those medications.

Q. So economically helpful to the state and medically helpful to patients?

A. Correct.

Q. How is your relationship with Kevin Walters?

A. Pretty good.

Q. Do you ever talk to him about the lawsuit?

A. No.

Q. Did you -- you have never ever talked to him about the conclusions you reached that the product that his company is selling causes diabetes?

A. No.

Q. Why not?

A. I don't know.

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Q. You told me a little while ago that you had concluded that Eli Lilly had misrepresented Zyprexa in its package insert?

A. Correct.

Q. Did you ever tell him that?

A. No.

Q. Why not?

A. I just don't go out and pick fights.

Q. The response to interrogatory 28 -- I think you have the complaint. Actually, it's this one.

A. Interrogatories. All of these legal terms. 28?

Q. We asked the question, "Identify any algorithms or protocols adopted by Alaska for treatment of schizophrenia, bipolar disorder and/or any other algorithms or protocols that include Zyprexa."

The response is: "The State of Alaska has used a protocol for the use of atypical anti-psychotic medications, although it does not specifically address Zyprexa.

This protocol was developed by grant from Eli Lilly. It is generally known as the BPMS program and is run by a contractor, CNS."

What protocol is being referred to in this response?

MR. HAHN: Objection. It's outside the

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scope of your notice.

MR. ROTHSCHILD: No, it's not.

MR. HAHN: Sure, it is.

MR. ROTHSCHILD: The notice talks about CNS and BPMS, and this response directly refers to that.

MR. HAHN: Same objection. If you know the answer --

MR. ROTHSCHILD: That's an improper objection, Blair.

A. I don't know.

Q. There is no protocol, is there?

A. At least my understanding of a protocol is a guideline for use, and this is not a strict guideline for use, but it's a guideline for review.

Q. You would not characterize it as a protocol for treatment of schizophrenia or bipolar disorder?

A. No.

Q. You are familiar with algorithms, guidelines and protocols for treatment of schizophrenia?

A. I am familiar with the Texas algorithm for treatment of mental health issues.

Q. You would -- if Alaska had adopted that, you would consider that a response to this kind of question, correct?

MR. HAHN: Objection; calls for speculation.

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Q. Do you know -- can you estimate when they started doing audits?
A. I'm not sure when it was. I think it's been the last couple of years. The contract is just up and they are reviewing an RFP right now for a new contractor.
Q. And when you say "very little errors," do you have an estimate for the percentage?
A. No, I don't.
Q. Was the audit you are describing just pharmacy audits?
A. They were all provider audits.
Q. Do you know whether the other providers had low error rates such as you are describing for pharmacy providers?
A. I know that DME providers had high error rate.
Q. What is DME?
A. Durable medical equipment. And there was some other areas that had a significant error rate. I don't know what it was. And I'm not -- I don't have the information as far as the other providers.
Q. Do you have documentation of the audit as it applies to pharmacy providers?
A. I have had documentation. I probably still have documentation of the pharmacy audits that have been conducted.

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Q. And do you know who would have the documentation of the rest of the audits?
A. All of the audits are with Margaret Summers.
Q. Who is she?
A. She is the manager for the -- what is it? Quality assurance unit, program integrity unit.
Q. When we're talking about these audits, in order to conduct these audits, did Myers and Stauffer seek backup to the claims such as medical records and prescriptions?
A. Yes.
Q. This audit also doesn't sound like it's an audit of the MMIS system itself; is that fair?
A. Right. It's an audit for what's provided for backup to claims.
Q. Has there been any audits of the MMIS system?
A. You previously asked that.
Q. I'm sorry. What was the answer?
A. The answer was I believe so, and you should contact Linda Walsh for that.
Q. I apologize for repeating. Other than the PERM audit that we talked about, has the federal government previously done audits?
A. I can't answer that.
Q. Have you heard of a PAM audit?

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A. No, I'm not familiar with that.
Q. Who would be the best person to ask about other federal government audits?
A. Either Linda Walsh or Margaret Summers.
(Exhibits No. 16 and No. 17 marked.)
Q. Mr. Campana, do you recognize the two documents I have marked as Exhibits No. 16 and No. 17?
A. Yes, I do.
Q. What are they?
A. They are letters to the drug utilization review committee.
Q. Who is the drug utilization review committee comprised of?
A. It's a committee of pharmacists and physicians who are providers to the Medicaid program and sign up for a three-year term as a volunteer on the committee.
Q. Each of the letters to the committee has an attachment of meeting minutes, do you see that?
A. Yes.
Q. And it lists who was present at the meeting?
A. Yes.
Q. The first Exhibit No. 16, which has a November 2nd, 2004 letter, has meeting minutes for October 22, 2004 and it has a list of individuals present and excused. Do you see that?

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A. Yes.
Q. Is that list of names, if you include both present and excused, are those all the members of the DUR committee as of that time?
A. I believe that is.
Q. And of the individuals on the committee, and I think the list would be the same for the October 22nd meeting as the November 19th, are any of those committee members psychiatrists?
A. Yes. Alex von Hafften is a psychiatrist.
Q. And would you agree that these meeting minutes reflect some discussion and presentations regarding the issue of mental health medications and metabolic issues?
A. Yes.
Q. And these are the only DUR committee meeting minutes that were produced to us in the litigation.
To the best of your recollection, are these the only occasions on which the DUR committee discussed these issues?
A. These are all that I could find for where the DUR committee had discussed these issues.
MR. SNIFFEN: I'm sorry. These issues being what issues?
MR. ROTHSCHILD: The mental health medications and metabolic issues.

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Q. Is that your understanding?
A. Yes.
Q. That was what you tried to do was try to find DUR meeting minutes that addressed that topic, correct?
A. Correct.
Q. You didn't try and give me all the DUR minutes?
A. That's correct.
Q. These are obviously two meetings pretty close in time, late 2004. Have there been any DUR committee meetings where -- in the last few months or anything where the issue of anti-psychotic medications and metabolic disorders have been discussed?
A. I don't know. I don't remember.
Q. Is it accurate to say that one of the things these meeting minutes report is that reports were run on anti-psychotic drug users to see whether they were also being treated for diabetes?
A. That's correct.
MR. ROTHSCHILD: Let's go off the record for a minute.
VIDEOGRAPHER: Going off record. The time is 3:46.
(There was a short break.)
VIDEOGRAPHER: On record. The time is 3:47.
Q. Mr. Campana, is it the case that you had reports

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run that showed diabetic medication use among anti-psychotic users?
A. That's my understanding of what we did here.
Q. And what precipitated the committee reviewing this issue and running these reports at this time in late 2004?
A. I don't remember exactly, although we do get a list of items that we can run in our drug utilization review, and it may have been an item that came up in the criteria set that we could run.
Q. You always could run it, but you don't always run it, do you?
A. Well, we run based on what comes up in the criteria set. As far as what I remember, we did determine that it would be a good idea to go ahead and run the mental health drugs and look for diabetic use or the diabetic issues coming up for mental health drugs.
Q. You don't know where that good idea came from?
A. I don't remember exactly where that came from.
Q. After this time, after this late fall 2004 period, has that report been run again by the state?
A. I don't remember us running that exact type of report again.
Q. Why not?
A. I don't remember.

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Q. You didn't think it was important to run?
A. Well, I can't say I didn't think it was important to run. It's just that other issues came up and other issues took precedence over that.
Q. So you concluded sometime in the fall of 2004 that there was an issue of Zyprexa and diabetes, correct?
A. Correct.
Q. You had drug utilization reviews where that topic was focused on?
A. Correct.
Q. You ran your claims data to find out are we seeing some of this, right?
A. Right.
Q. And then just stopped?
A. Well, we did the intervention letters on that and then that continued into the next month, and sent out notice to the providers about that.
Q. But you never checked again to see if there was a problem?
A. We never ran that criteria again.
Q. At the drug review -- drug utilization review meeting on October 22nd, did Mr. von Hafften make a presentation about the issue of mental health diseases, mental health treatments and metabolic disorders?

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A. Dr. von Hafften had made a presentation as noted in the minutes.
Q. And what did you understand Dr. von Hafften to be communicating?
A. Communicating about the risk of diabetes and metabolic disorders in conjunction with the ingestion of the psychotropic drugs.
Q. Did he say that there was a greater risk of metabolic disorders for those taking atypical anti-psychotics?
A. Yes, he did.
Q. Is that reflected here anywhere?
A. He also gave us a table, and that's a bad copy of it at the back of this.
And he had listed out the anti-psychotic medications and the chance for diabetes with different medications.
Q. You are referring to the page that's Bates-stamped 3351?
A. Correct.
Q. Who prepared these meeting minutes?
A. I prepared the minutes.
Q. Did you try and record everything important that Dr. von Hafften said?
A. I tried to record as much as I could while

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running the meeting and taking notes from the meeting.
Q. I don't see anywhere in this -- would you agree that paragraph four is your description of what Dr. von Hafften presented?
A. Yes.
Q. And I don't see anywhere in this paragraph where you record that he stated that the atypicals increased the risk of metabolic disorders or caused metabolic disorders.
A. Well, actually in four, as I read it, he did make presentation on the mental health disease process and the effect on metabolic disorders, as indicated in the month's profiles.
Q. When we're talking that that's a reference to the mental health disease process, it doesn't refer to mental health treatments, correct?
A. That's the mental health disease process.
Q. Do you remember, did Dr. von Hafften talk about the fact that individuals with severe mental health illnesses are more prone to obesity and diabetes than the general population? Do you remember him talking about that?
A. I do remember that.
Q. If you look at that chart you are referring to on 3351, and I agree it's hard to read, this is basically

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how we received it, there is a heading that says "Medical Disorders". And it's hard to read, but it says "obesity" and then something else. Can you tell --
A. Looks like metabolic disorders, obesity, hypertension, HTN, and dyslipidemia.
Q. And so there you have -- and then the numbers there run 22 percent in the community, 31 percent psychiatric, right?
A. Right.
Q. Then it says "prior to atypical"?
A. Right.
Q. And then there is -- next it says, "General class," and it says 31 percent typical, and then it looks like, "50 percent," question mark and it's hard to read.
It says "60," but I don't know what else it says there for atypicals.
A. Yeah. I can't read that either.
Q. That's not actually for diabetes, right? That's for other sort of obesity, dyslipidemia, right?
A. Right. Diabetes is just under that.
Q. Right. That says for the community 1 to 6 percent, psychiatric 10 to 15 percent?
A. 10 to 13 percent.
Q. And then for the class it doesn't have anything,

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right?
A. That's correct.
Q. And then you have some handwriting at the bottom of the document. Is that your handwriting?
A. Yes, it is.
Q. It says, "These problems should be expected"?
A. Correct.
Q. Then below that, "Clear problem not warrant D/S meds"; is that right?
A. No. "Clear problem does not warrant discontinuing medicine." An acronym for discontinuing is D/C.
Q. So those are your notes based on what you were hearing from Dr. von Hafften?
A. That was correct.
Q. What do those notes mean?
A. The notes mean that it was his opinion that while this may be a problem about the psychotropic medication, that in his opinion it didn't warrant discontinuing those medications.
Q. When you are talking about discontinuing, was he talking about discontinuing reimbursement or was he talking about discontinuing patients on these drugs?
A. Discontinuing the drugs in the patients.
Q. So did you have an understanding of why he took

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that position?
A. No, I don't.
Q. Was the information that Dr. von Hafften was communicating at that meeting anything different than what you already understood?
A. I don't remember.
Q. Huh?
A. I don't remember.
MR. ROTHSCHILD: Let's take a ten-minute break, and I will wrap up quickly after that.
VIDEOGRAPHER: Going off record. The time is 3:58.
(There was a short break.)
VIDEOGRAPHER: Back on the record. The time is 4:08.
Q. Mr. Campana, you said that you sort of reached the conclusion at lunch that maybe you ought to recommend or at least consider recommending anti-psychotics for the PDL.
Is there anything that you learned at this deposition that caused you to come to that conclusion?
A. Well, it seems like Eli Lilly and yourself are questioning us why we didn't do that, why, if our process is a good process to review drugs, that we don't review drugs.

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So maybe we need to revisit that and look at that process again, and look at all of the processes as far as if we need to do some other action on the atypical and psychotropic drugs.

Q. So this was a conclusion that you didn't come into this deposition -- a position you didn't come into this deposition holding, but during the course of this deposition, you have come to the conclusion that, based on the questions that I have asked you, that perhaps you should review the atypical anti-psychotics?

A. Correct.

Q. Are the medications that the state has reimbursed through its Medicaid program the same today as were reimbursed in 1996?

A. No.

Q. Are there more?

A. There is many more.

Q. If I was trying to figure out which medications have been added or subtracted from the list of medications that are reimbursed by Alaska, how would I go about doing that?

A. You would look at the formulary file and determine what drugs or what NDCs have come in and what the dates are that they have come into the system.

Q. So the formulary file is a reference file that

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lists the NDCs that are reimbursed by the state?

A. Well, there is a reference file for the MMIS system and that has formulary files on it. It has NDCs on it.

We used to use an indicator on that that you could determine whether or not medication is covered or not.

The present processing system doesn't use that formulary file. It uses a different formulary file that is set up for use by more than one benefit program. And on that, the indicators are not out there as to whether it's covered by Alaska Medicaid.

So finding that out would be more difficult now than what it used to be. It used to be everything was in a file, there were edits that were in effect and would show that this drug is not covered.

And if there were absent of those edits on the formulary file, the drug was covered. But present with that, we don't have a way to easily find out that a drug is covered or not.

It's built into the rules for the processing, but as far as going out there and pulling a list, we wouldn't know whether they are covered or not unless they fell out in the non-covered drugs.

Q. Okay. When did this sort of new reference

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formulary come into place?

A. In May of 2005, when we went with the HIPAA compliance system.

Q. Do you know whether it's the case whether the medical services and procedures reimbursed by Medicaid has stayed the same from 1996 to 2006?

A. It has changed.

Q. Are more services and procedures covered now than were --

A. Yes.

Q. -- in 1996.

A. Yes.

Q. How would I go about figuring out what was covered in different time periods?

A. Actually, there is a fee schedule that's available on the internet. You can go out to the internet and look at the fee schedule.

It covers all the different CPT codes and HCPC codes that are covered under the program.

Q. Would I find that at First Health's website?

A. Yes.

Q. That would tell me what's covered now?

A. That would tell you what's covered now. As far as the backup previous years, I don't know for sure where that is or who would have that.

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Q. Who do you think would be the best person to ask?

A. Well, actually, there is that list. There is the list basically providers can look at.

Now, as far as procedure codes, those are used in the MMIS claims processing for physician claims and hospital claims and what have you.

It's basically -- the reference file it is on the system has the coverage information on it for the procedures, so that's available, you know, as a reference file.

Q. Right. But would that be true -- if I wanted to find out what procedures were covered in 1998, would that be available in the system?

A. Yes.

Q. And so there would be a reference file that would let me know what procedures and services were covered at any given point in time?

A. Yes, as long as it's procedures and not drugs.

Q. And what about for revenue codes?

A. I'm not sure. You would have to talk to Linda about the revenue codes.

Q. When you came to the conclusion that Zyprexa had the safety issues we have discussed, did you communicate in any written form to anybody else in the department?

A. No, I didn't.

Q. Did you talk with anybody else in the department about the safety issues that you had determined?
A. I don't remember.
MR. ROTHSCHILD: I have no further questions. I know this has been a long two days and I appreciate your patience with it. Thank you very much.
MR. SNIFFEN: We have no questions.
VIDEOGRAPHER: This concludes the deposition of David Campana. The time is 4:16.
(Proceedings concluded at 4:16 p.m.)
(Signature reserved.)
-o0o-

WITNESS CERTIFICATE
RE: STATE OF ALASKA V. ELI LILLY
CASE NO. 3AN-06-05620
DEPOSITION OF: 30(B)(6) STATE OF ALASKA, VOL. II
DATE TAKEN: SEPTEMBER 19, 2007

I hereby certify that I have read the foregoing deposition and accept it as true and correct, with the following exceptions:

Page	Line	Description/Reason for Change

SIGNATURE DATE

Please sign your name and date it on the above line. As needed, use additional paper to note corrections, dating and signing each page.

(SLR)

CERTIFICATE

I, SONJA L. REEVES, Registered Professional Reporter and Notary Public in and for the State of Alaska, do hereby certify that the witness in the foregoing proceedings was duly sworn; that the proceedings were then taken before me at the time and place herein set forth; that the testimony and proceedings were reported stenographically by me and later transcribed by computer transcription; that the foregoing is a true record of the testimony and proceedings taken at that time; and that I am not a party to nor have I any interest in the outcome of the action herein contained.

IN WITNESS WHEREOF, I have hereunto set my hand and affixed my seal this 21st day of September 2007.

SONJA L. REEVES, RPR
My Commission Expires 8/7/11

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,

Plaintiff,

vs.

ELI LILLY AND COMPANY,

Defendant.

Case No. 3AN-06-05630 CI

VIDEOTAPED DEPOSITION OF LUCY LJUBICICH CURTISS, M.D.

December 13, 2007
1:35 p.m.

Taken at:
Anchorage Community Mental Health
4020 Folker Street, Conference Room C
Anchorage, Alaska

Reported by: Sandra M. Mierop, CRR, CPP, CBC

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I-N-D-E-X

LUCY LJUBICICH CURTISS, M.D. DECEMBER 13, 2007

EXAMINATION

PAGE

BY MR. ROGOFF 5

PROCEEDINGS

THE VIDEOGRAPHER: One moment, please.

We're on the record, today is December 13th, 2007. The time is approximately 8:56 a.m.

This is tape 1 of the videotaped deposition of Lucy Curtiss, M.D. being taken on behalf of the Defendant in the matter of the State of Alaska versus Eli Lilly & Company filed in the Superior Court for the State of Alaska, Third Judicial District at Anchorage; Case No. 3AN-06-05630 Civil.

We're in the office of Dr. Curtiss, located at 4020 Folker Street in Anchorage, Alaska.

My name is Steve Miedzwiadok, and I'm the videographer. My business is 545 East 12th Avenue in Anchorage, Alaska.

The court reporter is Sandra M. Mierop with Northern Lights Realtime & Reporting.

Would counsel identify themselves for the record, please?

MR. STEELE: My name is Joe Steele. I represent the State of Alaska.

MR. JAMIESON: Brewster Jamieson with Lane Powell. I represent Eli Lilly & Company.

MR. ROGOFF: Andrew Rogoff with Pepper Hamilton; and I also represent Eli Lilly.

MS. MANDALA: Cheryl Mandala with Jermain, Dunnagan & Owens. And I represent Anchorage Community Mental Health Services and Dr. Curtiss.

LUCY LJUBICICH CURTISS, M.D.
having been duly sworn, testified as follows:

EXAMINATION

Q. (BY MR. ROGOFF) Good morning, Dr. Curtiss. You heard my name is Andrew Rogoff. I represent Eli Lilly & Company in a lawsuit brought by the State of Alaska against the company.

Are you aware -- were you aware of this lawsuit before you found out you were going to have your deposition taken?

A. Yes.

Q. How did you hear about it?

A. I'm not sure whether it was the newspaper or from colleagues.

Q. Do you know how long ago?

A. **I also don't know the answer to that.**
Q. Do you recall any discussions with any colleagues about the case?
A. **I don't.**
Q. Do you remember what your reaction was when you heard about the case?
A. **I don't.**
Q. What is it that you do know about the case?
A. **That it has to do with Zyprexa, and disclosure of risks related to Zyprexa.**
Q. Anything else?
A. **That's about it.**
Q. Dr. Curtiss, have you ever had your deposition taken before?
A. **Yes, I have.**
Q. In what kinds of cases?
THE WITNESS: How would I describe that?
MS. MANDALA: In, I guess just a --
THE WITNESS: Civil matter?
MS. MANDALA: -- yeah, civil matter.
Q. (BY MR. ROGOFF) Did it involve Zyprexa?
A. **No.**

Q. Just one time?
A. **Just one time.**
Q. Have you ever been an expert?
A. **Yes, I have.**
Q. In what kinds of cases?
A. **In civil matters. It usually has to do with guardianships.**
Q. Dr. Curtiss, you're a psychiatrist?
A. **Yes, I am.**
Q. How long have you been practicing psychiatry?
A. **I completed my residency in 1995.**
Q. Where did you go to medical school?
A. **I went to the University of Washington School of Medicine. I graduated from there in 1991. I stayed at the University of Washington for my residency, which I completed in 1995.**
Q. Was your residency in psychiatry?
A. **Yes.**
Q. Are you board-certified?
A. **Yes, I am.**
Q. Did you engage -- did your residency involve any subspecialization?
A. **Not formally. I informally focused on community psychiatry and geriatric psychiatry.**

Q. Were those particular interests of yours?
A. **Yes.**
Q. Have you continued to focus on them in your practice?
A. **Yes.**
Q. When did you become board certified?
A. **In January, 1997, I believe. It was the first opportunity.**
Q. You're licensed in Alaska?
A. **Yes, I am.**
Q. Anywhere else?
A. **I had a license in Washington during my training.**
Q. Do you have to be recertified in Alaska?
A. **Yes. The certification is a national, and it's every ten years. I was recertified last summer. And so my board certification expires the end of 2016.**
Q. Did you bring any documents with you?
A. **I did not.**
Q. Have you ever published anything -- anything in the psychiatric journals or medical journals?
A. **No.**

Q. Where did you go to work after you completed your residency in 1995?
A. **I've been here the whole time.**
Q. What's here?
A. **Anchorage Community Mental Health Services.**
Q. Could you describe what Anchorage Community Mental Health Services does?
A. **Anchorage Community Mental Health Services is a private nonprofit organization which is the largest community mental health provider in the state of Alaska. We provide services for people throughout the lifespan from toddlers to seniors. We work with people that have a range of diagnoses, but we tend to work with the people that have the most severe illness. At this time, in our adult programs, our referrals preferentially come from hospitals, psychiatric hospitals, emergency rooms, Department of Corrections. I also do psychiatric consultation for the two nursing homes in town.**
Q. The description of the patient population that you gave outside of what you do in nursing homes was for the center itself or for you?

A. For the center itself. That we work with children -- the children that we see are severely emotionally disturbed; so these are children that have been either removed from parental custody or at risk for removal due to the severity of their behavior problems.

The adults that we work with are people that have severe, persistent mental illness which has a federal definition that involves essentially anyone who has functional impairment persistently related to problems with their brain or their behavior. So it could be classic mental illness, schizophrenia, bipolar disorder. It can also be chemical dependence. We see a lot of people that have comorbid addictions, people with brain injuries, people that are developmentally disabled who have behavioral problems as a result of -- as a result of that.

We work with a lot of medically frail people, people with personality disorders.

Q. How would you characterize the population that you treat personally?

A. All of the adults that I just listed.

Q. No children?

A. I do not work with children.

Q. You work with geriatric patients?

A. I do.

Q. What percentage of your patient population do you think is geriatric?

A. It has varied over time. At this point, 20 percent. That's an estimate.

Q. And the remainder of your patients are adults?

A. Yes.

Q. Before geriatric?

A. Before geriatric.

Q. Within the geriatric population, is there a low percentage of schizophrenia and bipolar disorder or a lower percentage than you find in the adults?

A. It depends on the setting that -- a lot of the referrals that we get for geriatrics have to do with behavioral signs and symptoms associated with dementia, and so the relative number of people that have primary mental illnesses is lower because of that. But we certainly have people that have aged through our system and are now seniors.

Q. Would you characterize the presenior

adults as seriously mentally ill?

A. Severely persistently mentally ill which is its own -- it has its own definition.

Q. Legal definition?

A. Yes.

Q. And would you -- how would -- what percentage of the presenior adult population that you see would you characterize as suffering from either schizophrenia or bipolar disorder?

A. You're counting schizoaffective disorder in there as well?

Q. Yes.

A. Probably a majority.

Q. Or one or the other or both?

A. As -- as -- most of the people that come to our services have multiple diagnoses. That people don't come here unless they have failed less restrictive or less comprehensive treatment programs. You have to be very impaired to qualify for services at -- at this agency.

And so probably a majority of the people in my caseload do have a diagnosis of schizophrenia, bipolar disorder or shizoaffective disorder.

Q. Are all of your patients treated on an

outpatient basis?

A. Yes.

Q. Do you ever see patients at API?

A. I do not.

Q. You said you go to two nursing homes?

A. I do.

Q. Do you practice anywhere besides the two nursing homes and the community mental health center?

A. I have a small private practice.

Q. What is the patient population of that practice?

A. The diagnoses of the people that I see are more mood and anxiety disorders.

Q. What percentage of the patients do you see in your -- break it down three ways, the private practice, the geriatric -- the nursing homes, and the mental health center?

A. Right. What percentage --

Q. Can you break it down by -- if they all added up to 100 percent, what percent of your patients do you treat here at the mental health center? What percentage do you treat at the geriatric facilities? And what percentage are in your small private practice?

A. The vast majority are here. I see a handful of patients, very small number in my private practice. And at the nursing home it's consultation. So I don't have a caseload that I consistently see. I see whoever the primary care providers ask me to see on any given visit.

Q. You're working full time?

A. Yes.

Q. Have you worked full time here since you came to the community mental health center?

A. Yes.

Q. Does this mental health center have a formulary of medications?

A. No, we do not.

Q. What percentage of your patients here and in your private practice are Medicaid eligible?

A. No one in my private practice has Medicaid. Here, the statistics have changed over time. We are seeing fewer and fewer Medicaid-eligible patients. At this point -- I'd have to think about the breakdown. We've got -- maybe 40 percent of our patients are dual eligibles so they've got primary Medicare, secondary Medicaid; they don't use the Medicaid

formulary.

25 percent are primary Medicaid here?

Q. Why are you seeing fewer Medicaid patients than previously?

A. Because the people that we are getting are sicker. They are more likely to have comorbid addictions; and less likely, as a result of their addictions, to qualify for entitlements. That if -- Social Security has gotten much harder to get over the years. It used to be that you could come in, you could apply for your benefits and within a year you would have Social Security and Medicaid. Now people can come in, it can take years, if they ever qualify at all. And my experience has been that anyone who has any sort of history of substance use, they don't get benefits, period.

Q. Do you know why?

A. Well, you would have to look into federal regulations that it's their fault that they're ill.

Q. And how do those individuals pay for their care?

A. We pay for it. We have grant -- grant

dollars that we get from various sources. We have a grant from the State of Alaska. We also have a number of federal grants and Mental Health Trust Authority grants that help to offset some of the costs of providing care for unresourced patients.

Q. Does the center here have any restrictions or place any restrictions on what you may prescribe for your patients?

A. No.

Q. Do you, in your practice, use anti-psychotic medications?

A. Yes.

Q. Which ones do you use?

A. I use all of the atypicals, and some of the traditional anti-psychotics.

Q. Which of the traditional anti-psychotics do you use?

A. I use Haldol, Haldol Decanoate, Prolixin, Prolixin Decanoate and perphenazine. And occasionally some chlorpromazine.

Q. What kinds of -- we'll come back to that.

Do the psychiatrists in this community mental health center ever meet as a

group?

A. Yes, we do.

Q. Do you discuss your cases?

A. Yes, we do.

Q. Why else do you meet?

A. We meet for administrative purposes.

Q. What does that mean?

A. That we have a medical team. We have at this point three psychiatrists and three advanced nurse practitioners. I am the medical director; so I'm also half-time administrative.

We meet on a weekly basis to talk about issues relating to the care of our patients, agency, news. We are -- the way that our center is organized, we are not -- we are a team; the nurses are a team; and each of us works with different clinical teams that specialize in people that may be homeless, people that may be coming out of Corrections, people that live in a certain part of town. So we each spend time with different teams.

Q. How long have you been medical director?

A. For --

THE WITNESS: How long has it been?

A. Since May, '04, I believe.

Q. (BY MR. ROGOFF) What are your responsibilities as medical director?
A. I have responsibility for the medical staff. I do the hiring, the firing. I set the standards. I write the budget. I maintain the budget. I am the lead clinician for the agency; so if there is an issue of a dispute about what ultimately can we or can we not do, I have the final say on that. I work with the directors of the different parts of the agency in determining what are our standards of care.
Q. In prescribing medications, even though the center doesn't impose any restrictions on you, does -- does the State or any other authority impose any restrictions upon your ability to prescribe anti-psychotic medications?
A. With clozapine we have to have prior authorization.
Q. Anything else?
A. In regard to anti-psychotics?
Q. Any other restriction --
A. No.
Q. With regard to any other mental health medications?
A. Naltrexone, I don't know if that still

has a prior authorization process. There are times that we prescribe female hormones for men; that requires prior authorization. Nurse practitioners have a limited licensure where they can only prescribe psychiatric medications. M.D.s can prescribe any medications, but we as a practice choose to limit our scope to psychiatry.
Q. Do you know why clozapine requires prior authorization?
A. Can you rephrase that?
Q. Do you know why you have to obtain authorization to prescribe clozapine?
A. I can answer that different ways. I mean, one is that the State has implemented a prior authorization program, and so I can't prescribe it without going through that process. Clozapine does have risks associated with it in terms of a agranulocytosis, in particular. And so for patients to take clozapine they have to be listed in the National Registry. We have to have it set up where they are following the protocol for have bloodwork drawn at specified frequency.
The lab results have to come to us and to the pharmacy; and the meds are not released from the pharmacy unless the lab work

has been received, reviewed and is -- meets certain criteria.
Q. Have you been involved in the -- any of the administrative processes of the State where a P & T Committee has attempted to establish a preferred drug list?
A. I am on the P & T Committee.
Q. How long have you been on it?
A. I have been on the committee for approximately -- again, this is an estimate -- a year and a half, maybe. I was not one of the original members.
Q. Has the P & -- now, this P & T Committee is part -- is run under the auspices of the Medicaid program in the state?
A. Yes, it is.
Q. And who is the chair of the committee?
A. Richard Brodsky.
Q. Who else sits on the committee?
A. It is a collection of physicians, nurse practitioners, pharmacists, there's a dentist on the committee. The membership changes over time. People serve terms and may or may not sign up again.
Q. How many psychiatrists are on the

committee?
A. There are two of us.
Q. Who is the other one?
A. Duane Hopson.
Q. During your tenure on the committee, has it ever sought -- has it ever considered imposing any restrictions?
(Cell phone ringing.)
Q. (BY MR. ROGOFF) In your tenure on the P & T Committee, have you ever considered whether to place any anti-psychotics on the preferred drug list?
A. We have never reviewed the anti-psychotics.
Q. Do you know whether the committee before you joined it ever reviewed anti-psychotics?
A. They have not been reviewed.
Q. Do you know why?
A. I don't know.
Q. Did you -- before you were on the committee, did you ever speak with anyone on the committee or appear before the committee when it was discussing anti-psychotics?
A. No, I did not.
Q. Did you ever write any letters to the

committee?
A. I don't recall. I am aware of conversations I had about other agents that were under consideration by the committee and conversations that I had with other psychiatrists about those.
Q. Does Dave Campana sit on the committee?
A. He does.
Q. Have you ever discussed with him whether anti-psychotics ought to be considered for a preferred drug list?
A. I have not discussed that with Dave Campana.
Q. Have you discussed it with any members of the committee?
A. Melissa (sic) Sater has mentioned to me that they may come under review within the next year.
Q. What is Melinda Sater's position?
A. Melinda Sater --
Q. I'm sorry.
A. She is -- is it Melinda or Melissa? Melinda, I believe. It's Mel.
Q. We won't tell her.
A. She is -- she -- I'm not sure what her

formal job title is. She is the one who provides the information that we review. She is the one who takes down the recommendations of the committee and then goes back and reviews bids and determines which agents meet the criteria and have bid within budget.
Q. Have you ever expressed an opinion publicly about whether anti-psychotics ought to be reviewed for purposes of a PDL?
A. Could you clarify your question?
Q. Have you ever expressed to anyone your view of whether anti-psychotics ought to appear on the PDL in Alaska?
A. When Mel Sater asked me, I said I thought it was fair. That other medications come up for review; it's fair that these come up for review as well.
Q. If they do come up for review, do you know what criteria -- under what criteria they will be reviewed?
A. I don't know. The classes that the P & T Committee reviews don't -- they're not always consistent. That we have a sedative hypnotic class, for instance, that has agents from -- that have different mechanisms of action,

but not all of the agents that have those particular mechanisms of action are reviewed. We have an anticonvulsant group. But anticonvulsants as a group have very broad usage for very different indications by different -- people of different specialties. And so I don't know how anti-psychotics would be classified.
Q. Is it your view as a psychiatrist with the experience you have that it's possible to classify second-generation anti-psychotics other than Zyprexa as equally efficacious with Zyprexa?
MS. MANDALA: Do you understand the question?
A. I'm sorry. No, I don't understand the question.
Q. (BY MR. ROGOFF) You know, let me come back to that and ask you some questions about prescribing.
A. All right. All right.
Q. What do you prescribe perphenazine for?
A. Psychosis. Occasionally, for -- now, this was in my training -- that was the primary anti-psychotic that we used in our training. And so there would be times that we would also use it for intense anxiety, for emotional flooding, we

call it. People that have histories of trauma sometimes emotionally flood and cannot think. You work on getting people out of that state of mind to where they can think.
Q. Were there any second-generation anti-psychotics available to you during your training when you were using perphenazine?
A. Risperdal came out in 1994; that was toward the end of my training. That was the last year of my training that it became available.
Q. Do you prescribe as much perphenazine now as you did when you were in your training?
A. I do not.
Q. Why?
A. The older anti-psychotics have greater risk of extrapyramidal symptoms and may have greater risk of tardive dyskinesia, and oftentimes require use of a side effect medication an anticholinergic.
Q. But, given all those risks, you nevertheless prescribe perphenazine in certain circumstances?
A. Yes, I do.
Q. And why is that?
A. It typically is a matter of patient

preference. Patients have been on medications for a long period of time. They know what works; they know what they trust.

Q. Any other factors that would militate in favor of using perphenazine besides patient preference?

A. Well, it has anti-psychotic effect. You know, I'm looking for effectiveness of a medication, and acceptability to a patient.

Q. For new patients who have not used perphenazine and therefore wouldn't have a preference for it, do you, nevertheless, from time to time prescribe perphenazine for such patients?

A. At times.

Q. And what are the factors you consider in those cases?

A. The patients that come here, it is very rare that I would see a patient who has -- is treatment naive. That, by definition, the people that we take are people that are coming out of other treatment facilities, and generally have been started on an agent. And so I'm not the first one that is prescribing for somebody. They typically have experience with treatment.

And so often people will have come here after having failed other treatments.

Q. For a treatment-naive patient, have you used perphenazine?

A. Not since my residency, no.

Q. Why is that?

A. Well, first, I don't see very many treatment-naive patients. But in terms of options that are available, I do preferentially use the newer anti-psychotics.

Q. Have you ever received -- do you recall ever receiving a letter from the State regarding the use of anti-psychotics?

A. I don't. I don't know.

Q. Are you familiar with the Behavioral Pharmacy Management Steering Committee?

A. I am aware of the process.

Q. What do you know about it?

A. That there is -- the BPMS, it is -- I believe it is sponsored, paid for, by Eli Lilly, and they have a number of indicators that they review, and they send out notification to prescribers every other month when patients that we're -- for whom we're prescribing meet certain indicators. If they're on three or more

psychotropics, if they're on a subtherapeutic dose, if they're on a higher-than-recommended dose, if they're not filling their prescriptions, if they're getting prescriptions from more than one provider, we get those lists every two months.

Q. Have you personally received them?

A. Yes, I have.

Q. Have any of those notifications affected your practice with any of these patients?

A. There have been times when I have learned that patients are seeing more than one provider; that's useful information.

Q. And receiving more medication than you're aware of?

A. Yes.

Q. Any other times it's affected your practice?

A. Overall, I'd say not.

Q. Dr. Curtiss, are you ever involved in treating patients who are involuntarily committed?

A. Yes, I am.

Q. Where do you treat them?

A. I treat them here as outpatients. We do

get patients who are on -- it's called an early release. It is an outpatient commitment that -- it starts as an inpatient commitment, and then patients can agree that they will adhere to treatment recommendations specified in the early release. We as an agency would accept responsibility for their care. And if they don't follow through with what they've agreed to, then -- well, then, it's our responsibility to seek rehospitalization. So, yes, I have treated patients like that.

Q. Are those patients coming out from API?

A. Yes.

Q. Are any --

A. There -- I'm sorry, there are also patients who are in court-ordered treatment who as conditions of their parole or probation are mandated to -- to follow treatment recommendations, in which case I would recommend to someone this is -- this is what I think you should do; if you disagree, go to your P.O. about it. That's involuntary. Coercive.

Q. The folks who are coming out of API, are any of them, when you receive them, on Zyprexa?

A. Some.

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Q. Do you know if any of them had at any point been involuntarily medicated while at API?
A. Patients that -- wait. Please restate your question.
Q. You said that you're treating patients who had been involuntarily committed to API --
A. Yes.
Q. -- and are now being seen by you on an outpatient basis involuntarily?
A. I have none of those right now.
Q. You've had them?
A. I have had them.
Q. You've had them within the past two years?
A. I've had probably two within the last two years.
Q. Do you know whether either of those patients had been treated at API with Zyprexa?
A. I don't know.
Q. Have you ever received patients from API who had been treated involuntarily with Zyprexa?
A. I don't know. I don't -- I don't know the internal processes of API and at what point people go from being involuntary to voluntary.
Q. Have you ever sought to -- to medicate a

patient against his or her will?
A. Not directly. No.
Q. Have you ever sought a court order to medicate somebody?
A. No. We don't do that in the outpatient setting. If we think that someone is at imminent risk, we seek hospitalization; we would never seek a court order to medicate someone in the community.
Q. And the hospitalization would be typically in this community at API?
A. At API.
Q. For what kinds of conditions do you use Zyprexa in your practice today?
A. In my practice today, I have patients that take Zyprexa for schizophrenia, schizoaffective disorder, bipolar disorder, PTSD, and behavioral disturbances associated with dementia.
Q. And for several of those illnesses, the treatment with Zyprexa would be off label; is that correct?
A. Yes.
Q. Why do you use Zyprexa off label?
A. Well, in psychiatry there is very much

off-label prescribing; and particularly in the field of geriatric psychiatry, there are no FDA-indicated treatments for behavioral disturbances associated with dementia. All of that prescribing is off label. And so I think as -- as a field, we are more comfortable with off-label prescribing than other fields may be.
Q. How about for post-traumatic stress disorder?
A. That is also a diagnosis for which most prescribing is off label.
Q. Have you found in your practice that using Zyprexa for schizoaffective disorder, post-traumatic stress disorder and behavioral disturbances associated with dementia has been effective for your patients?
A. For some patients, yes.
MR. STEELE: Is there a "T" in that word?
MR. ROGOFF: Yes, no, does not have a T in it.
MR. STEELE: He's got a "T" in his "schizo," "schizo."
MR. ROGOFF: No.
MR. JAMIESON: It's the German

pronunciation.
MR. STEELE: It's the Philadelphian pronunciation.
MR. ROGOFF: Anyone else?
MS. MANDALA: I'm good, thanks.
MR. ROGOFF: Okay.
Q. (BY MR. ROGOFF) What are the side effects of Zyprexa with which -- of which you are aware?
A. The common side effects -- you know, I'm not going to speak to every side effect I've ever seen in every patient; that's not possible. The most common side effects are weight gain, sedation, elevated blood sugar, elevated lipids.
Q. Do you see those side effects in other second-generation anti-psychotics?
A. Yes. The frequency with which I observe it varies from agent to agent.
Q. Does it also vary from patient to patient?
A. Absolutely.
Q. You'd said earlier, Dr. Curtiss, that you prescribe all the second-generation anti-psychotics, as well as several of the typical anti-psychotics. Are you able to

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articulate a percentage, first of all, from second-generation versus first generation?

A. I would say the majority is second-generation. Beyond that, no.

Q. Can't break it down among the second-generation anti-psychotics?

A. I use all of them.

Q. Has your use of them varied over the years? And I'm talking about the atypicals.

A. Yes.

Q. For what reasons has your usage varied?

A. Availability. And they weren't all available at the same time. My experience and comfort in prescribing them. It takes probably a couple of years to really have a good feel for an agent and how to use it, when to use it, who is most likely to benefit from it. Side effect profiles. All of the concerns about metabolic effects, definitely we think more about that now than we did in the past.

Q. When did your concern about metabolic side effects change?

A. Again, I can't tell you what year, but it has been within the last few years.

Q. Do you recall a classwide label change

in 2003 with regard to the second-generation anti-psychotics?

A. I don't. I'm sorry.

Q. Do you recall any label changes for either Zyprexa or the class of medications? And I'm not asking you for a date, but just the -- the event or the fact of it occurring.

A. Well, I know that it has definitely become more of a focus. In my practice what stands out more is the black box warnings about patients with vascular dementia and use of anti-psychotics.

Q. But -- I'm not asking you whether you've memorized the labels. But do you read the labels when you use medication for the first time?

A. Generally.

Q. What else do you do to familiarize yourself with new medications?

A. I tend to be a bit of a late-adopter. That -- I read about a medication. I talk with my colleagues. I hear about what their experiences have been. I talk with patients about options. I'm very straightforward with my patients about "I don't have experience with this agent yet." There are particular patients that

they want the newest treatment the moment it becomes available, and so they're typically the first to try them. But I am more likely to hang back and see what my colleagues experience before I jump in with a medication.

Q. You also read the literature?

A. Yes.

Q. Are there publications that you regularly read in your practice?

A. There is not any publication that I regularly read. There's the Green Journal; there is Journal of Clinical Psychiatry. I get this much mail every week (indicating). I pick and choose.

Q. Do you typically read articles about medications that you -- that are available to you to use with your patients?

A. I don't know how to answer that question. Again, I get reams and reams of material. I read some of it. I read when a particular question comes up. I read when I'm considering treatment options for a particular patient.

Q. Have you read the results of the CATIE trials?

A. Yes, I have.

Q. Do you keep any kind of folders in your office where you collect literature on topics of interest?

A. I keep as little paper as possible.

Q. Before you use a medication for the first time, do you do any research on it? Other than talking to your colleagues and --

A. Reading journal articles and reading the package insert, and I'm not sure what else you would be --

Q. Well, do you -- do you meet with pharmaceutical company sales representatives?

A. I do.

Q. Do you meet with reps from Lilly?

A. I do.

Q. And have you met with reps from other companies?

A. Yes, I do.

Q. Do you know how often you meet with them?

A. Probably each company sends a rep every couple of months.

Q. Do you meet with the reps when they come?

A. I have -- I have over time changed my practice. I used to have a 30-minute block every other week in which reps could schedule up to 15 minutes. I am less -- much less available now. It's if they catch me between patients.
Q. When did that practice change of having a block and not having a block of time?
A. Probably when I became medical director.
Q. Which was a few years ago?
A. Which was a few years ago.
I am also more cautious, being on the P & T Committee.
Q. Because?
A. Because I am being visited by reps that -- that detail agents that I would never prescribe ophthalmologic agents and all kinds of other things. And I'm -- I'm also very clear that I don't -- I am turned off by sales.
Q. What do you mean by that?
A. That if a rep comes in -- I did one time have a rep say, "I want you to promise to prescribe this for your next X number of patients." I didn't meet with him again.
Q. Do you know what company that rep was from?

A. I'm not sure what company it was.
Q. To what extent do you rely on sales representatives for information about medications that you prescribe to your patients?
A. It's a small, small percentage.
Q. Why is that?
A. Because I assume that they are in the business of sales and that they will tell me good things about their product.
Q. And so you're skeptical of sales reps?
A. Yes.
Q. Has that always been the case?
A. Yes.
Q. When you've met with sales reps from various companies, do they take -- have they taken notes while talking to you?
A. Not often.
Q. Now, since you became medical director, can you characterize how many minutes a week or month that you would spend with a sales rep?
A. Probably less than -- less than 30 minutes a month for all reps.
Q. How many companies are you visited by?
A. Several.
Q. Are you visited by AstraZeneca?

A. Uh-huh.
Q. That's "yes"?
A. Yes.
Q. Johnson & Johnson?
A. I don't think so.
Q. Janssen?
A. I'm sorry?
Q. Janssen?
A. Yes.
Q. Are you visited by reps from GlaxoSmithKline?
A. Yes.
Q. Wyeth?
A. Yes.
Q. Merck?
A. What do they market?
Q. Just about everything.
A. I don't know. I don't know offhand.
Q. How about Pfizer?
A. Yes.
Q. When you've met with sales reps from various companies, do they oftentimes talk to you about their competitors' products?
A. I discourage that.
Q. Why?

A. Again, it is negative and it's not an effective sales technique with me.
Q. Can you recall any instances where you've been -- where you've met with a sales representative from a pharmaceutical company and you believed you've been misled by that representative about his or her product?
A. Possibly.
Q. Can you think of any particular instances?
A. Oh, the one that comes to mind is when Remeron went to solutabs that the representative suggested that pills would not be available. That the only possible switch if I wanted to prescribe mirtazapine was to switch to the solutabs.
Q. Do you recall any other instances?
A. Of reps appearing to try to misinform me?
Q. Yes.
A. Not offhand.
Q. Have you ever been a speaker for any pharmaceutical company?
A. No.
Q. Do speakers from pharmaceutical

companies ever come to your practice here?
A. Yes.
Q. What companies bring in speakers?
A. A number of companies do. I ask that the trainings be coordinated by our nursing manager; and I don't personally attend them.
Q. Have you ever attended them?
A. Not for years.
Q. Why don't you go?
A. I'm too busy, and I am -- again, skeptical that I don't trust that the information truly is unbiased.
Q. How long have you felt that way?
A. I think that has always been my inclination, but I have attended presentations at times, so -- but it has probably literally been years since I did.
Q. Dr. Curtiss, you said earlier that the side effects of Zyprexa that have concerned you included weight gain and metabolic blood sugar issues and lipids. Was there anything else?
A. Sedation. Dizziness. Sure.
Q. How does your knowledge of those potential side effects affect your prescription habits?

A. I talk with patients and my -- my practice is that it is a collaboration. I am not particularly directive in my approach. That my philosophy is that it's about the relationship. That it's my job to try to understand my patient, who they are, what they value, what they want, and what's acceptable to them in terms of treatment. And does the treatment that I am providing help them meet their goals. I tell people that any negotiation, any result of that has to be acceptable to both of us, and that ultimately it is the patient's life, the patient's body, and they should not agree to anything that they're not prepared to -- to accept.
Q. So in each case you're making an -- you and the patient are collaboratively making an individualized judgment?
A. Most of the time. I would say the -- the exception to that is when someone is grossly psychotic or very, very demented, in which case I am less likely to talk in that detail about treatment options, potential side effects; or if someone is extremely paranoid that I tend to tailor my information where I focus more on the

relationship than about immediate risks of the medication until that person has reached a degree of health where they can say, "Yeah, I feel better now."
Q. You learned in medical school that excess weight was a risk factor for diabetes?
A. I don't know where I learned that.
Q. You've known it your entire practice?
A. Yes.
Q. And, nevertheless, with the risk of weight gain and blood sugar issues with Zyprexa, you prescribe the medication?
A. Yes, I do.
Q. Why is that?
A. There are patients for whom it is the only thing that works.
Q. Are there other reasons?
A. If it works and the patient understands the potential risks and wants the treatment, I prescribe it.
Q. So then to go back to a confusing question I asked a long time ago --
A. Yes.
Q. -- which relates, really, to individual prescribing decisions, is it really possible to

say that -- as a blanket matter, that any anti-psychotic medication is equally efficacious with any other anti-psychotic medications?
A. They're all different. And you don't necessarily know what will work for any given patient. You focus on desired side effects and risks. All things being equal, I preferentially will choose one of the agents with less risk for metabolic abnormalities. Ziprasidone and aripiprazole. However, their side effect profiles aren't always ideal.
Q. Is there an anti-psychotic medication that has no side effects?
A. There is no medication that has no side effects.
Q. You said before, Doctor, that you're familiar with the CATIE study?
A. Yes.
Q. Are you familiar enough with the conclusions of the studies to say whether or not your clinical experience has been consistent with the results published about CATIE?
A. I can't say that.
Q. Are they inconsistent, or are you just -- it's impossible to generalize?

A. Well, my concerns with the CATIE study would be how the results would be interpreted and that -- that could be ultimately disadvantageous for patients.

Q. What do you mean?

A. That -- my take on CATIE is patients with mental illness quit their meds anyway so we might as well just give them whatever's cheap.

Q. That's how you interpret CATIE?

A. That's -- that's, I think, the potential dangerous interpretation of it.

MS. MANDALA: Do you want to go off record so we can get that loud noise to stop?

THE WITNESS: Let's do that.

MR. ROGOFF: Great. Thank you.

THE VIDEOGRAPHER: Going off the record at approximately 9:48 a.m.

(Break.)

THE VIDEOGRAPHER: We're on the record. The time is approximately 8:58 a.m.

MS. MANDALA: No, it's not.

MR. ROGOFF: 9:58.

THE VIDEOGRAPHER: Oh, 9:58. I apologize.

Q. (BY MR. ROGOFF) Dr. Curtiss, how many

patients do you see now on a weekly basis now that you're medical director?

A. Good grief. Oh, it varies tremendously. 50? And that's just really a rough estimate.

Q. How many did you see before you became medical director, rough estimate?

MS. MANDALA: Per week?

A. Per week? Probably not a whole lot more.

Q. (BY MR. ROGOFF) So you're working harder?

A. I am working harder and faster. Very fast.

Q. How many of your severely, persistently mentally ill patients are using psychiatric medications?

A. The majority.

Q. Have you -- have any of your patients, while using any of the psychiatric medications, developed diabetes?

A. Yes.

Q. Were some of them on Zyprexa?

A. Yes.

Q. Were some of them on other medications?

A. Yes.

Q. For those who are taking anti-psychotic medications, do you regularly monitor any of their -- their blood levels -- the glucose levels?

A. I try to.

Q. How long have you been doing that for your patients?

A. Oh, it's been a few years.

Q. Do you know how long?

A. I don't know exactly when I started.

Q. For which patients do you test glucose levels?

A. I check for anyone who is on -- well, I try to get all my patients to have at least yearly physical health care. For people that are on anti-psychotics, I try, all of them, to get them to do it.

Q. All of them being typicals and atypical users?

A. All of them that I have just in general tried to become more thorough in addressing physical health considerations for my patients. There is lab work that is routinely associated with different mood stabilizers, and it is more cost-effective to do panels than individual

tests, and so I will do a comprehensive metabolic panel for a patient who may be on Depakote, but not an anti-psychotic, and then in that case I'll get their blood sugar.

Q. Dr. Curtiss, do you know whether you have in your possession any promotional or marketing materials from my pharmaceutical company?

A. In my personal possession or in the clinic?

Q. In your office.

A. I try to throw it all away. There probably is something in there that I haven't thrown away.

Q. But you can't identify it as you sit here; is that right?

A. If I went and looked, I could find things, but, no, I don't hang on to materials from drug companies.

Q. And I may have asked this before, and I apologize if I did, but do you recall receiving any written communications from any arm of the State of Alaska regarding anti-psychotic medications?

A. I don't know.

Q. Nothing comes to mind?
A. Nothing specifically, no.
Q. Doctor, thank you. I have no more questions.
A. I do have one more comment on that last question, though.
Q. Okay. I'm sorry.
A. That the Drug Utilization Review Committee is another pharmacy committee that is part of the State. And so I have received communications from them. And I receive communications from the P & T in my role on that committee.
Q. What do you remember receiving from the Drug Utilization Committee?
A. I have at times -- you know, there are different -- private insurance companies also have utilization reviews, so if -- highlights about a specific patient's medications concerns, combinations of medications that would not routinely be used together or -- but I don't remember specific examples.
Q. Any -- but did you receive any warnings from the State from the P & T Committee, Drug Utilization Committee, Department of Health and

Social Services or anyone else regarding safety concerns about anti-psychotic medications, including Zyprexa?
A. I don't specifically remember.
MR. ROGOFF: I have no more questions.
THE WITNESS: All right. I have no more answers.
MR. STEELE: I don't have any questions at this time.
THE VIDEOGRAPHER: Here ends today's deposition of Dr. Lucy Curtiss being taken on the 13th of December, 2007. The total number of tapes used today is one. The time is approximately 10:04 a.m.
We're off the record. Stand by.
(Deposition adjourned at 10:04 a.m.)

WITNESS CERTIFICATE

LUCY LJUBICICH CURTISS, M.D. taken October 13, 2007
State of Alaska v. Eli Lilly
Case No. 3AN-06-05630 CI

I hereby certify that I have read the foregoing deposition and accept it as true and correct, with the following exceptions:

PAGE	LINE	CORRECTION/REASON
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Date LUCY LJUBICICH CURTISS, M.D.

(Use additional paper to note corrections as needed, signing and dating each page.) (SMM)

REPORTER'S CERTIFICATE

I, SANDRA M. MIEROP, Certified Realtime Reporter and Notary Public in and for the State of Alaska do hereby certify:
That the witness in the foregoing proceedings was duly sworn; that the proceedings were then taken before me at the time and place herein set forth; that the testimony and proceedings were reported stenographically by me and later transcribed under my direction by computer transcription; that the foregoing is a true record of the testimony and proceedings taken at that time; that the witness requested signature; and that I am not a party to, nor do I have any interest in, the outcome of the action herein contained.
IN WITNESS WHEREOF, I have hereunto subscribed my hand and affixed my seal this 27th day of December, 2007.

_____
SANDRA M. MIEROP, CRR, CCP
Notary Public for Alaska
My commission expires: 9/18/12

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,
Plaintiff,
vs.
ELI LILLY AND COMPANY,
Defendant.

Case No. 3AN-06-05630 CI

VIDEOTAPED DEPOSITION OF JOEL GILBERTSON

December 6, 2007
9:03 a.m.

Taken at:
The Offices of Lane Powell, LLC
301 West Northern Lights Boulevard, Suite 301
Anchorage, Alaska

Reported by: Leslie J. Knisley
Shorthand Reporter

A-P-P-E-A-R-A-N-C-E-S

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BY: DAVID C. RIGGS
(801) 266-0999

STATE OF ALASKA
Department of Law, Civil Division
Commercial/Fair Business Section
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BY: CLYDE "ED" SNIFFEN, JR.
Assistant Attorney General
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BY: ERIC ROTHSCHILD
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BY: BREWSTER H. JAMIESON
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Also Present: STEVE MIEDZWIADOK, VIDEOGRAPHER

I-N-D-E-X

JOEL GILBERTSON DECEMBER 6, 2007

EXAMINATION

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BY MR. ROTHSCHILD	5, 78
BY MR. SNIFFEN	76

EXHIBITS

NUMBER	DESCRIPTION	PAGE
(No exhibits were marked.)		

PROCEEDINGS

THE VIDEOGRAPHER: One moment, please.

We're on the record. Today is December 6th, 2007, and the time is approximately 9:01 a.m. I'm sorry. I have to go back off the record.

(Off the record.)

THE VIDEOGRAPHER: One moment, please.

We're on the record. Today is December 6th, 2007, and the time is approximately 9:03 a.m. This is Tape 1 of the videotaped deposition of Joel Gilbertson, being taken on behalf of the defendant in the case of State of Alaska versus Eli Lilly and Company, filed in the Superior Court for the State of Alaska, Third Judicial District at Anchorage, Case No. 3AN-06-05630 Civil.

We're in the offices of Lane Powell, LLC, located at 301 West Northern Lights Boulevard, Suite 301 in Anchorage, Alaska. My name is Steve Miedzwiadok, and I'm the videographer. My business address is 545 East 12th Avenue in Anchorage, Alaska. The court

reporter is Leslie Knisley with Northern Lights Realtime & Reporting.

Would counsel identify themselves for the record, please?

MR. BIGGS: David Biggs for the State of Alaska.

MR. SNIFFEN: Ed Sniffen, assistant attorney general for the State of Alaska.

MR. ROTHSCHILD: Eric Rothschild from Pepper Hamilton, LLC, representing the defendant, Eli Lilly and Company.

MR. JAMIESON: Brewster Jamieson with Lane Powell representing Eli Lilly and Company.

THE VIDEOGRAPHER: We ask now that the court reporter please swear the witness.

JOEL GILBERTSON,

having been sworn, testified as follows:

EXAMINATION

Q (BY MR. ROTHSCHILD) Good morning, Mr. Gilbertson.

A Good morning.

Q I represent Eli Lilly and Company in a lawsuit that has been brought by the State of Alaska against Eli Lilly, and your deposition is

A That's a good question. What was it? Political science.
Q And when did you earn your law and master's degrees?
A '99 for my law degree. I believe 2001 for my master's degree, but it could have been 2000. I think it was 2001.
Q Did you have any full-time employment after the time you graduated from college until you received your two degrees, graduate degrees?
A Not full time during a full calendar year, no. I did the summer associate thing and worked in the general counsel's office for the National Association of Social Workers, but they were not full time.
Q Describe for me your work history after you received your master's degree in 2001.
A I worked in the -- well, I was employed before I finished my master's degree but after my law degree, in that time period, and that job continued past my master's degree. I was employed by the United States Senate and was the staff director and legislative director for United States Senator Frank Murkowski. That continued -- that was from 1999 until 2002.

December of 2002 I was appointed as Commissioner of the Alaska Department of Health and Social Services, confirmed by the legislature in February of 2003. I remained in that job until the end of September of 2005. Literally the last day of September. Took from Friday, ended in that job Monday, started at Providence Health and Services.

So that would have been the first couple days of October of 2005. And I'm in that current employment now where I serve as regional director for the Alaska region.
Q And can you just tell me again when you began as Commissioner? What month?
A December of 2002, December 9th, 2002, continuing through the end of September, 2005.
Q And that was a position that you were appointed by the governor?
A Yes.
Q And who was the governor at that time?
A Frank Murkowski.
Q I've been accused of this before, but you speak very quickly and --
A I'm from the East Coast, too. I will slow down. I'm with you on this one. I'll talk slower.

THE REPORTER: Thank you.
Q (BY MR. ROTHSCHILD) Are you represented by counsel today?
A I am.
Q And who are you represented by?
A Mr. Sniffen and Mr. Biggs.
Q Okay. And how did they become your counsel for this deposition?
A I believe from my -- I'm essentially being deposed from my role as when I was Commissioner, so it's in that function, as the State is defending my deposition.
Q When were you -- when did you first speak to them about them representing you in this deposition?
A First met them this morning. First -- had only one other contact with Mr. Sniffen, which I think was about a week ago, notifying me that there was an interest in taking my deposition.
Q Prior to -- and that conversation you had with Mr. Sniffen, that first conversation, was it anything other than sort of notification and logistics?

A It was notification, asking me when I would be available for the deposition. Gave me very high-level background of what the case was and then asked me dates I was available. And other than that, I've had no contact with Mr. Sniffen.
Q How long did you meet with Mr. Biggs and Mr. Sniffen this morning?
A Thirty minutes, 35 minutes.
Q Were you shown any documents?
A No.
Q Other than that 30-minute session, did you do anything else to prepare for this deposition?
A Not one thing.
Q Prior to speaking to Mr. Sniffen a week ago, were you aware that the State of Alaska had sued Eli Lilly regarding its prescription drug Zyprexa?
A No.
Q Do you have an understanding now about what the lawsuit is about?
A Not well, but I have a general explanation.
Q Okay. What's your general explanation?

A That it involves Eli Lilly, an allegation of promoting off-label use of Zyprexa in Alaska, and a claim that the Medicaid program suffered a financial harm as a result of that. And I'm not even sure I'm even restating it accurately. I apologize for that.

Q And is the only alleged misconduct that you're aware of off-label promotion?

A I may have been told something else. That's all I remember right now. I really have -- I have very limited knowledge of this case.

Q Have you seen the Complaint that was filed by the State of Alaska?

A No.

Q Have you read any articles, news articles about the case?

A Not one.

Q Prior to talking to Mr. Sniffen and then later Mr. Sniffen and Mr. Biggs, have you had any conversations with lawyers, whether employed directly by the State or retained by the State, about Zyprexa and Eli Lilly's conduct regarding Zyprexa?

A No.

Q Nothing during the time that you were Commissioner?

A The only -- well, I would have had conversations with the Department of Law around regulations and the process for establishing a preferred drug list, but nothing that was specific to any one pharmaceutical product.

Q This is a pretty broad question, but tell me, what were your duties and responsibilities as the Commissioner for Health and Social Services for Alaska?

A Okay. Well, as Commissioner, you are essentially the chief executive officer of operations. The Department of Health and Social Services is the largest State agency; has a work force a little over 4,000 employees. The time I left, I managed a budget of about $2 billion, which is a combination of state, federal and other funds. Manages a collection of programs. It's sort of an umbrella agency that has divisions within it.

The functional responsibilities of the Department include overseeing all public health powers, so operating public health laboratories, overseeing the medical examiner's

office, public health functions, running public health clinics, disease surveillance, bioterrorism preparedness, those types of functions. Overseeing the Juvenile Justice System for the State of Alaska, so operating juvenile detention facilities, overseeing juvenile probation services.

Overseeing the Medicaid program and its tentacles into other programs, of course. Overseeing the child protection system, so foster care, investigating reports of harm, general social work, targeted case management. Overseeing senior and disability services, so that would include running the Pioneer Home system, which is a collection of assisted living facilities in the State of Alaska.

Overseeing the Developmental Disability Waiver program, the Senior Waiver program, the Personal Care Attendant program. Would also include overseeing all behavioral health programs for the State of Alaska, so that includes running the State Psychiatric Institute, and managing behavioral health grants, which are grants that go out to local community mental health providers for delivering clinic-based

outpatient services.

And then there's a collection of regulatory functions, Certificate of Need, licensure certification. I'm probably missing some, but that's sort of a -- it's your broad health and social service functions for a State agency.

Q I've read a little bit about you on the Internet. You've been described as accomplishing a lot for someone your age, which sounds accurate.

Is there any -- are there any particular accomplishments during your tenure as Commissioner that sort of stand out? Initiatives you took?

A Bring the Kids Home, getting that launched, off the ground, which was a process to ensure that we had facility-based and residential and outpatient behavioral health services so we could keep our kids in state rather than send them to out-of-state facilities. At any one point in time during my tenure -- when I came in, we had over 450 kids out of state. It's a long journey and the State's not done with that journey yet, but our goal was to keep those kids

closer to their families.
A lot of time around -- one other division I didn't mention, Public Assistance, all the welfare-to-work programs. We had great success in welfare to work. I think the State once had 13,000 families on its public assistance roles, and we got that down to below 4,000. So a lot of work in getting people into jobs and infrastructure development in rural areas.
During my time as Commissioner, I also co-chaired the Denali Commission and spent a lot of time on rural infrastructure development, clinic construction, infrastructure development that's geared towards expanding health care access.
So, you know, I would -- I'm not going to tout one accomplishment, not to give you the typical answer, but it's a great Department that accomplishes great things on a daily basis, and I happened to be there for three years.
Q What were your responsibilities and the agency's responsibilities regarding the Alaska Psychiatric Institute?
A It operated it. It was a -- all employees, save for vendors, are State employees.

It manages it, runs it. The administrator of it reports to the director of behavioral health which was -- which reported to me. It is a State facility.
Q Was the agency responsible for submitting the budget for API?
A Uh-huh. Yes.
Q And was that -- were you involved, you personally involved in developing that budget?
A I was involved in overseeing the budget process. I was involved in making final decisions on the budget at an aggregate macro level, and I was responsible for representing it before the Office of Management and Budget, the governor's office and the legislature and then administering the funds.
Q What were the major items of expense for API?
A The major items of expense for API are similar to virtually any other health care facility, which is labor, depreciation expense and supplies.
Q And do supplies include medications?
A I'm certain they do, but the way the State budgets at that line item level, I would never see that.
Q Okay. And what were -- what are the agency's functions in regard to the Medicaid program?
A The State had broad functions similar to every other state, in that it is a state/federal partnership where states are given fairly broad discretion in operating their Medicaid program within certain laws that are set up either through regulation, through consent agreements or through statutory authority that comes from either a federal agency or Congress.
The State sets eligibility levels within certain parameters. The State sets optional services within certain parameters. The State manages enrollment, eligibility, manages claims processing, manages general administration policy decisions within it, and then works with the federal government on funding it.
Q Did any component of the agency have any responsibility for monitoring or supervising the safety of medications that were prescribed to Alaska Medicaid recipients?
A Not in the sense of doing -- no, not in the sense of doing -- vetting clinical literature

for safety, no. It does not regulate drug products, no.
Q And why -- why not?
A It's a function of the Food and Drug Administration.
Q How do you know that?
A Personal knowledge. I couldn't cite the source.
Q And was that the understanding of employees of the agency, that that's not our job to supervise the safety of the medications?
A The generally-accepted philosophy within the Department is that there are drugs approved under the -- I'm not what the technical term is -- but a list of pharmaceutical products that are approved for the Medicaid program where states are allowed to draw down matching funds. So there's sort of a Medicaid list of drugs.
And then the State has the right to prior authorize certain drugs. The State does not have the authority to say, this drug or that drug is not going to be covered by the Medicaid program, but it can put up controls over the prescribing and the authorization of those drugs.
Q And one of the controls, as you said, is

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prior authorization?
A Correct.
Q And how does that work?
A Prior authorization involves a process, and it can be handled many different ways. But, essentially, there is some function or process that determines drugs that will be prior authorized. And then in those drugs that are prior authorized, there is a hurdle put up that the prescriber has to get over to be able to prescribe the drug, to allow a pharmacy to dispense it, and then submit a claim that will be paid by the Medicaid program.
States handle that differently. In Alaska the prior auth -- the authorization that would be necessary is the prescriber would have to write for a -- in the case of a drug that was being prior authorized through a preferred drug list, the prescriber would have to note on the script that it's medically necessary to prescribe a drug that was not an approved drug within a drug class. And that would be -- that's all the authorization that was required.
Q And I just -- I want to ask you some questions about the preferred drug list, but that

was not in effect for your entire tenure as Commissioner, correct?
A The preferred drug list?
Q Right.
A The preferred drug list came into effect within months of me coming into office and to my knowledge continues to this day.
Q Was the preferred drug list the only context in which there could be a prior authorization mechanism?
A No, but I was not involved in those other authorizations.
Q Were you aware that, in fact, that prior authorizations existed outside the PDL?
A Sure. Prior authorizations existed for Oxycontin. It existed -- some states had done prior authorization on growth hormones. I mean, there are authorization processes; I just was not involved in them.
Q Could those -- who -- who was involved with them?
A Those would have been done through the -- at that time the Division of Medical Assistance, now the Division of Health Care Services. So that would have been the division

director who at the time was Bob Labbe, and the pharmacy program manager, Dave Campana, and then a collection of staff.
Q To your understanding, could a prior authorization be used in order to deal with the safety issue that has arisen with a drug?
A I'm not aware of that having been done. I don't know.
Q Are you familiar with the antipsychotic drug Clozapine?
A Not as a clinical drug -- in a clinical sense, no, but I've heard of the drug.
Q Do you know whether there was a prior authorization for the use of Clozapine by Alaska Medicaid recipients?
A I do not know.
Q Did you do anything as Commissioner to keep yourself apprised about the medications being reimbursed by the State of Alaska?
A At the individual drug level, no. Simply not enough time in the day.
Q You qualified it, so is there -- there some extent that you did keep yourself apprised?
A Well, I was -- I was apprised as we were going through the process, for example, of

implementing a preferred drug list. I was aware at a very high level of -- though I couldn't recall what they are now -- I was revised -- I was notified on a periodic basis of which drug classes were being reviewed, but not at the results level of which drugs were selected by the P&T committee. That was done by an external group, and I let that be resolved by the clinicians. I'm not a clinician.
Q Did you in your role as Commissioner interact with representatives from pharmaceutical companies?
A Yes.
Q Okay. And for what purposes?
A I didn't seek them out, but they seemed to want to visit frequently to lobby the Department on various issues.
Q Was Eli Lilly one of the companies that --
A Eli Lilly hired lobbyists and Eli Lilly did lobby the Alaska state government during my years in office.
Q Okay. Did they personally interact with you?
A Yes, yeah.

that was offered and defeated, thankfully, to stop the preferred drug list, and so obviously the majority of the legislature agreed with me.

And with the public there was dialog, but, you know, the reality was, after we got going and within a few months, it just died out.

I once had a request from a legislator prompted from an industry lobbyist -- I don't know who it was -- to scour the records of how many complaints there were and problems with folks getting the drug that they needed or providers being able to prescribe the drug that they needed. And we had to scour. We didn't get a single one after we implemented the preferred drug list. Save for at that point in time -- save for, I remember once it was a specific pharmacy in town that wouldn't dispense a drug and we had to call them and explain to them what the override process was. And once they were clarified, they got it out the door. It was largely a nonissue once it went into implementation.

Q During your tenure at the Department, the safety issues around Vioxx arose, correct?

A I remember national literature of the safety issue around Vioxx. I couldn't tell you what year it was. It wasn't my role with the Department.

Q Again, Mr. Campana testified when I took his deposition that as safety issues arose regarding Vioxx, he recommended something called a step edit.

Are you familiar with what a step edit is?

A I've heard the term, but I would not -- that would not be something where I would sit down with Dave Campana in my office and go through that type of work, no.

Q And what he testified was you actually stopped him from implementing the step edit. Is that consistent with your recollection?

A I have no recollection of that at all.

Q Did you take -- did the Department take any steps regarding Vioxx during your tenure?

A I don't recall a single meeting I had about Vioxx while I was Commissioner.

Q Did the State file any lawsuits against prescription drug manufacturers during your tenure as Commissioner?

A I don't know.

Q Did you ever have any conversations with anybody about, you know, considering filing a lawsuit against any drug manufacturer?

A Not that I recall. I know that there was a -- when I first came in, the Department was in some type of dispute. I don't know if it was a lawsuit or if it was agency action or whatever it was. But it was a multi-state issue around something that are called J-code rebates. It's such a knit policy decision.

It was how to get the rebates for pharmaceuticals that are administered -- administrated -- or administered in physician offices where the drug cost is embedded in the claim for the physician's professional fees. So you had to go through this complex process of vetting out all the claims for a physician's fees that are being billed by the physician, and figure out which ones of those had embedded in that cost them administering a drug, which had the drug costs in it, and it was a dispute. And whether that was in court or not, I don't know, but I remember something around J-code rebates that I was not actively involved in. Other than

that, there was pretty broad separation between the Department of Law and the Department of Health and Social Services.

Q And did you ever make any recommendation to the Department of Law to pursue litigation against any kind of prescription drug manufacturer?

A Not that I recall.

Q Or tobacco manufacturer?

A Not that I recall.

Q You described some of the interactions you had with either employees or representatives of Eli Lilly. In any of those interactions was there any dialog about the characteristics of Zyprexa?

A I know for a fact that in my meetings with drug reps we never got to that level of detail about drugs. So, no.

Q Okay. Were you ever made aware of any interactions between representatives of Eli Lilly and employees of the agency regarding the characteristics or uses of Zyprexa?

A Not that I recall.

Q Are you aware of Eli Lilly making any misrepresentations about Zyprexa to the State of

Alaska?
A I have no knowledge of that. I don't recall.
Q Are you aware of any -- sitting here today, do you believe that Eli Lilly omitted, failed to tell the State anything that they should have?
MR. BIGGS: Objection; calls for speculation.
A I have no knowledge.
Q (BY MR. ROTHSCHILD) Did anybody employed by the State of Alaska ever communicate to you that Eli Lilly had made misrepresentations to them about Zyprexa?
A I don't recall.
Q In your tenure as Commissioner, did anybody employed by the Department ever communicate to you that the Department had been misled about any drug?
A I have no recollection of that.
Q And did anybody ever communicate to you that they felt that prescribers in the State of Alaska had been misled about any drug?
A I don't recall that.
Q You've used the word "atypical

antipsychotics," which shows that you probably have a little bit more knowledge on this subject than the average member of the public.
What's your understanding of what that phrase means, "atypical antipsychotic"?
A I'd rather not get into -- I'm not going to get into a clinical discussion of what an atypical antipsychotic is. I'm not a clinician, but I did go through my boot camp and as we talked about different mental health drugs, familiarized myself. I don't -- I've left some of that knowledge behind when I left the Department. And it would be probably a quasi-inaccurate statement now for me to recall what I knew about atypical antipsychotics four years ago.
Q But you used the term. I mean, I actually was using the term antipsychotics, and you periodically interspersed our dialog with the phrase "atypical," so that obviously means something to you.
A Well, that's how we referred to it, so that's sort of the name in my head.
Q Okay.
A I'll use antipsychotic, if that's

easier.
Q You understand that Zyprexa is an atypical antipsychotic?
A I am aware of that, yes.
Q Did you, during the course of your -- of being Commissioner, come to any understanding about what effect the atypicals had in terms of hospitalization rates for the mentally ill?
A I don't recall that.
Q If it turned out to be the case during your tenure as Commissioner that the State -- anybody employed by the State had come to the conclusion that a pharmaceutical company was misrepresenting the characteristics of a prescription drug reimbursed by Medicaid, if the State actually became aware of that, is that something you would expect you as Commissioner would be made aware of?
A I would hope I would be made aware of it. I don't know if I could expect it. I mean, at the end of the day, buried in that question is: Would I be aware of it? And I can't tell you that everyone would have made sure that I was aware of it. I would hope I would have been aware of it.

Q Why is that?
A Because I don't know what the process would have been for the State to make that evaluation. I can tell you that I would hope I would have been made aware of it, but I don't know.
Q Right. And I'm asking: Why would you hope to be? Would it be the case that you would figure that was important to your role as Commissioner?
A Well, I think for an agency head who oversees a health agency for the State, there's very little bit of -- very little information regarding health care in Alaska I wouldn't want to be aware of.
Q And potentially, depending on what the issue is, you might want to take action about it?
A I certainly would want to have deliberations around the merits or the authorities for that.
Q The State has told us during the course of this litigation that it became generally aware of Lilly's misrepresentations about the safety and efficacy of Zyprexa in the summer of 2005.
The summer of 2005 was during your

tenure as Commissioner, correct?
A It was; however, I had recused myself of virtually all of my responsibilities beginning May or June of 2005.
Q And why was that?
A Because I was -- I had filed a disclosure with the Department of Law that I was going to seek employment outside of the State of Alaska. I met with the ethics attorneys from the State of Alaska. They developed a plan for me on how to firewall me off from anything that could create a conflict of interest. So we created memos to the file, delegation authorities.
And I basically spent my last four months in office, or more, more in the PR function of a Commissioner. You know, meeting with groups and giving the speeches, but was basically firewalled off from a good portion of the business of the Department.
Q Who would have filled your role on sort of the policy end of things during that summer?
A Deputy Commissioners would have, plus the Division Directors. It would depend on the subject matter.
Q Okay. You know, we've talked about this

issue of -- raised this issue that the State was aware of misrepresentations about Zyprexa during that timed period.
Who would you have expected that to be deliberated amongst in the group you just described?
A I can give you a broad net. That would have been the Division Director, who at that time I believe was Dwayne Peebles. Jerry Fuller, who was in the function -- that was essentially the Medicaid Director. Tony Lombardo, a Deputy Commissioner, and there may have been others.
Q You had just one Deputy Commissioner?
A No, I had three.
Q Okay. And so who -- Mr. Lombardo was one. Who else?
A Karleen Jackson, the current Commissioner, and -- let's see. In 2005 it would have been -- changed jobs -- someone changed jobs during that year. I'm trying to remember who was there at that time. I believe Tammy Sandoval was the other Deputy Commissioner at that time. She was incoming as our new Deputy Commissioner who oversees the Office of Children's Services, which is all the CPS functions.

Q The fact of -- the alleged fact of misrepresentations about Zyprexa -- given the firewalling arrangement you've just described, would you have expected that information to have percolated up to you under the arrangement you were working under?
A I don't know if I would have expected it. I mean, I don't know.
Q Would you, to use your phrase, hoped you would still find out about that?
A I would hope, yeah. I wanted to know everything in office. Who wouldn't, right?
Q I take it it's the case that you have no recollection of misrepresentations about Zyprexa being brought to your attention at any time?
A I don't recall that.
Q Are you familiar with something called the BPMS program?
A I don't recall that I am. I might be.
Q A drug utilization program that's delivered by an organization called CNS?
A CNS, yes.
Q Does that ring a bell now?
A Yes, it does.
Q What's your recollection of what that

program does?
A I was not involved in it, so my recollection is very narrow and limited. During the time period in which we were developing the preferred drug list and my exit, we remained interested in looking at ways in which we were continuing to get better value and better results for beneficiaries in the Medicaid program.
And my understanding, which could be incorrect, but my understanding is that the Division of Behavioral Health continued to work, and the Medicaid office continued to work on different solutions for mental health drugs. One of them was working with a vendor, CNS, on a product, but I was not actively involved in that project.
Q Did you -- was it -- I mean, did you approve it being -- it being used in Alaska?
A I certainly did through delegated authority.
Q Okay.
A But not in the formal sense of overseeing it, no.
Q Did you have an understanding of how that program was funded?

A At the time I may have. I don't recall it.
Q If I told you that Eli Lilly funded it, would that ring a bell or --
A Wouldn't ring a bell. It wouldn't surprise me, but it wouldn't ring a bell. We were always very open on collaborations where it made sense.
Q Do you know whether that program was beneficial for the State?
A I don't.
Q Don't know anything to the contrary either?
A No. I didn't review, you know, empirical evidence that came out of it and did my own analysis, no.
Q Were you aware that, putting aside the BPMS program, that the Department sometimes did drug utilization reviews?
A I'm available -- I'm -- I am aware that we did. I was not personally involved in it.
Q Are you aware that in 2003 the FDA required the manufacturers of atypical antipsychotics to change their warning, their label to address issues relating to diabetes?

MR. BIGGS: Objection; it assumes a fact not in evidence.
A I'm not aware. I don't recall; that's probably a more accurate answer.
Q (BY MR. ROTHSCHILD) During your tenure as Commissioner, did you ever become aware of any issues around metabolic and side effects of antipsychotics drugs?
A I don't recall being involved in those discussions.
Q Sitting here today, do you have any knowledge about metabolic issues, things like diabetes and the like, having any relationship to antipsychotic drugs?
A I'm not a clinician. I don't -- I don't review -- I leave that to the experts. That's why you have chief medical officers.
Q Okay. But notwithstanding the fact that you're not a clinical expert, do you have any awareness of that?
A Not -- not really, no.
Q Okay. That's fine. But as someone who lives and works in the medical community, you may have knowledge of it.
A I'm an administrator.

THE VIDEOGRAPHER: Pardon me, Mr. Rothschild. We have about five minutes left on this tape.
MR. ROTHSCHILD: Why don't we take a break now.
THE VIDEOGRAPHER: Here ends Tape 1 of today's deposition of Joel Gilbertson being taken on December 6th, 2007. The time is approximately 10:25 a.m. We're off the record. Stand by.
(Break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. This is the beginning of Tape No. 2 in today's deposition of Joel Gilbertson, being taken on December 6th, 2007. The time is approximately 10:34 a.m.
Q (BY MR. ROTHSCHILD) Mr. Gilbertson, you testified that if employees of the State had become aware that Lilly was misrepresenting Zyprexa, that is something you would hope you would become aware of in your role as Commissioner, correct?
A I would think so, yes.
Q But you have no recollection of that

occurring?
A I don't recall it, no.
Q You also talked about how you had an understanding that the State's lawsuit alleged that Lilly was engaged in off-label promotion of Zyprexa, correct?
A Correct.
Q Is that also a fact that if it was known during your tenure as Commissioner, you would have hoped you would have been made aware of?
A Probably, yes. I'm not sure whose responsibility that would have been in State government to enforce or to be involved in. I mean, I don't know the authorities, but it's something I would want to know, yeah.
Q And you were not made aware of that during your commissionership?
A Not that I recall, no.
Q You're interrupting a little bit.
A I'm sorry.
Q The State has also -- has alleged that Lilly misrepresented the safety and efficacy of Zyprexa, including a risk associated with diabetes. To the extent that was known in the State during the time you were Commissioner, is

that something you would have hoped you would have been aware of?
A I would want to know, but I would not have been involved in any -- what the agency would have done. I mean, that's up to the clinicians and the program managers. So it would be only for information purposes, but I would want to know.
Q Okay. You would want to know?
A I'd want to know anything. I like knowledge, so I'd want to know.
Q And, again, you were not made aware of any facts of that nature during your tenure?
A Not that I recall.
Q You're currently employed by the Providence Health System?
A Providence Health and Services, yes.
Q What is that?
A We are an integrated health care system. We're the largest health care system in the Pacific Northwest. We have health care operations in Alaska, Washington, Oregon, Montana, California; about 50,000 employees. We run hospitals, nursing homes, assisted living facilities, primary care practices, medical

practices, air ambulance programs, critical access hospitals, behavioral health programs. Everything from birth to death and every service in between. We run them, and we are the largest health care provider in Alaska, Washington and Oregon.
Q Do you know whether the health system purchases Zyprexa to be prescribed to patients?
A I would not be involved in that at all. I have no knowledge.
Q You don't know whether they were -- whether Zyprexa is prescribed to patients within the system?
A I have no personal knowledge of any prescribing habits in the system.
Q Okay. And do you have any knowledge about any restrictions put on prescriptions of particular medications?
A I have no involvement or knowledge of that.
Q Do you have any role in negotiating with pharmaceutical companies regarding rebates or purchases of medications?
A None.
MR. ROTHSCHILD: No further

questions. Thank you.
MR. SNIFFEN: Can we just take one quick break? I may have a couple follow-up questions.
THE VIDEOGRAPHER: Going off the record at approximately 10:38 a.m.
One moment, please.
(Break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 10:42 a.m.
EXAMINATION
Q (BY MR. SNIFFEN) Mr. Gilbertson, Ed Sniffen. I'm an Assistant Attorney General with the State. We've talked earlier pertaining to this deposition. Just a couple of follow-up questions to some questions posed to you by Mr. Rothschild.
He'd asked you if you had hoped to know or become aware of certain issues during your tenure as Commissioner relating to Zyprexa, for example, whether it was used for off-label purposes.
Do you recall that question?

A I do.
Q He also asked you if you had hoped to become aware of any safety issues with Zyprexa.
Do you recall that?
A I do.
Q Does the fact that you were not aware of those things mean to you that they did not happen or that you just don't recall?
MR. ROTHSCHILD: Objection.
A It means I don't recall. I think it's fair to say that, you know, there's a good portion of the Department, particularly that which is at the program level, at the clinician level, at the skill professional level where those decisions are made, and those experts manage it. There's a certain level of detail that you get involved in at the Commissioner's office, and that I was not aware of it doesn't mean much in terms of did it happen or not.
Q (BY MR. SNIFFEN) So, is it fair to say, then, that there would have been times when some of those issues may have come to the Department's attention through its program administrators or other employees and they would not have been brought to your attention?

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,

Plaintiff,

vs.

ELI LILLY AND COMPANY,

Defendant.

Case No. 3AN-06-05630 CI

VIDEOTAPED DEPOSITION OF DUANE HOPSON, M.D.

December 11, 2007
10:18 a.m.

Taken at:
The Offices of Lane Powell, LLC
301 West Northern Lights Boulevard, Suite 301
Anchorage, Alaska

Reported by: Leslie J. Knisley
Shorthand Reporter

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I-N-D-E-X

DUANE HOPSON, M.D. DECEMBER 11, 2007

EXAMINATION

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EXHIBITS

NUMBER DESCRIPTION PAGE
1 E-mail, 5/1/07 96
Bates Nos. ZYP-AK-05302 to 05305
2 E-mail, 1/24/07 101
Bates Nos. ZYP-AK-05218 to 05241

PROCEEDINGS

THE VIDEOGRAPHER: One moment, please.

We're on the record. Today is December 11th, 2007, and the time is approximately 10:18 a.m. This is Tape 1 of the videotaped deposition of Duane Hopson, being taken on behalf of the defendant, in the matter of State of Alaska versus Eli Lilly and Company, filed in the Superior Court for the State of Alaska, Third Judicial District at Anchorage, Case No. 3AN-06-05630 Civil. We're in the offices of Lane Powell, LLC, located at 301 West Northern Lights Boulevard, Suite 301 in Anchorage, Alaska.

My name is Steve Miedzwiadok,and I'm the videographer. My business address 545 East 12th Avenue, Anchorage, Alaska. The court reporter is Leslie Knisley with Northern Lights Realtime & Reporting.

Would counsel identify themselves for the record, please?

MR. SNIFFEN: Ed Sniffen, assistant attorney general for the State of Alaska.

MR. STEELE: Joe Steele, assistant

attorney general for the State of Alaska as well, sort of special assistant attorney general to be exact.

MR. JAMIESON: Brewster Jamieson with Lane Powell on behalf of Eli Lilly and Company.

MR. ROGOFF: Andrew Rogoff, Pepper Hamilton, on behalf of Eli Lilly and Company.

Did you get sworn in?

MR. STEELE: No, but I get a badge.

MR. ROGOFF: Let's you ride the Anchorage subway for free.

MR. STEELE: Well, you can use it in public restrooms actually. We can get you one if you want one.

THE VIDEOGRAPHER: We ask now that the court reporter please swear the witness.

DUANE HOPSON, M.D..

having been sworn, testified as follows:

EXAMINATION

Q (BY MR. ROGOFF) Dr. Hopson, as you heard, I represent Eli Lilly and Company. I'm going to be asking you some questions about the lawsuit that the State has brought against our client.

Are you represented by counsel today?
A I am.
Q Did you bring any documents with you?
A No, I did not.
Q Have you ever had your deposition taken before?
A Many years ago.
Q What kind of case?
A I was working with Dallas County Homeless Services and an individual brought a case against the clinic, and I had seen that individual one time while I was covering for a doctor and so -- I was later released from it, taken off.
Q Is that the only time you've testified at a deposition?
A Yes.
Q Have you ever testified at any public hearings or trials?
A No.
Q Dr. Hopson, you're a psychiatrist?
A Yes.
Q Where did you get your -- where did you obtain your medical degree?

A University of Arkansas for Medical Sciences in Little Rock.
Q What year?
A 1985.
Q Did you start your residency training right after that?
A I did. The following year at Timberlawn Psychiatric Hospital in Dallas, and I did my general psychiatry residency there and then my child and adolescent fellowship at the same location.
Q What years were you at Timberlawn?
A Timberlawn would have been '86 through '88, and then '88 through '90 was my child fellowship.
Q What did you do between 1985 and 1986?
A Year of transitional internship at Baylor University Medical Center.
Q After -- are you board certified?
A Board eligible.
Q All right. Did you go into private practice after your fellowship?
A No. I joined the staff at Timberlawn and was on staff for six years in their Department of Outpatient Services.

Q That takes you through 1996?
A Uh-huh. Well -- yes, exactly. And then I joined a group practice in Dallas, Holiner Psychiatric Group.
Q What was that? I'm sorry.
A Holiner, H-o-l-i-n-e-r, and was on staff at Medical City, Dallas. And was there two years and then I went into private practice in Garland, Texas, a suburb of Dallas, and remained there in private practice until 2000, December of 2000. And I was recruited to Fairbanks to be the medical director of mental health there, and moved there in January of '01. And I remained there until July of '03, at which time I was recruited to API to be the medical director, and I've been there ever since.
Q Did you limit your practice in Texas after your fellowship to child psychiatry?
A About half and half.
Q What was the nature of the patient population that you treated that were -- one-half of which was juvenile, or --
A The kids? What type of kids? A whole lot of ADHD, oppositional defiant, some depressed kids.

Q What was the adult population?
A Really the full gamut. Schizophrenia, a lot of major depression, bipolar.
Q You were at Holiner when Zyprexa first came on the market?
A That would be about right, yes.
Q Did you treat patients at Holiner with Zyprexa?
A I'm sure I did. I don't recall specific, but --
Q And your private practice in Garland, Texas was also half and half, child and adult?
A Yes.
Q Similar populations, similar problems?
A Very similar.
Q When you say you were recruited to become medical director of mental health at Fairbanks?
A Uh-huh, Fairbanks Memorial.
Q What kind of hospital is Fairbanks Memorial?
A It's a community-owned general hospital, and they were just opening a 20-bed psychiatric unit. And they did a nationwide recruitment for a medical director and so --

Q And they found you?
A They did.
Q And you became the director of that 20-bed unit?
A Yes, that's right.
Q Did you have -- was your practice confined to that unit?
A Yes.
Q Did you see -- did the unit see patients on both an outpatient and an inpatient basis?
A No, just inpatient.
Q How many psychiatrists worked in that unit?
A Two --
Q You and a --
A -- including myself. That's right.
Q Who was the other person?
A Well, it was -- it varied. We had a locum tenens much of the time, and that was Bill Carroll. And then I was finally able to recruit Jan Kiele, J-a-n K-i-e-l-e, and Dr. Kiele was with me until I left.
Q Is she still there?
A He. No, he's gone.
Q Is -- where is Bill Carroll?

A He's doing locum tenens in California.
Q Do you know where Jan Kiele is?
A He's working here in Anchorage, I believe. I'm not sure what organization.
Q And what kind of patient population were you treating in this 20-bed unit in Fairbanks?
A Pretty much the full gamut. Depression. Of course, you know, people to be in the hospital, suicidal, so severe depression, psychosis, danger to self or others. Pretty much the commitment criteria.
Q Were most of the patients involuntarily committed?
A Yes. Initially at least and then would later sign voluntary usually.
Q How were their -- how was the treatment paid?
A My understanding was that, of course, if they had a commercial payor, you know, the hospital would bill that. If they had Medicaid, they would bill that. If not, there is a State-funded program for indigent. The DET program is what it's called, diagnostic and evaluation and treatment, and that would pick up the other.

Q Were you responsible for formulating a budget there?
A No.
Q Did you face any restrictions in Fairbanks in terms of what kind of medications you could prescribe?
A No.
Q Was the unit typically full?
A No. It averaged about, as I recall, 10 to 12 patients. There were a few occasions during my time there that it was full, but --
Q Were those patients also treated from time to time with Zyprexa?
A I would assume so, as I recall. I would imagine, yes.
Q Do you have any doubt in your mind?
A No. It's commonly prescribed.
Q You left Fairbanks to come to API?
A Yes.
Q When did you start at API?
A July 1 of '03.
Q You started at API as its medical director?
A Yes.
Q Did you succeed Dr. Kletti in that

position?
A Yes, I did.
Q What professional organizations do you belong to?
A The American Psychiatric Association and the Alaska Psychiatric Association.
Q Have you ever held an officer position in either of those?
A Yes, I'm the president of the Alaska Psychiatric Association.
Q How long have you been president?
A Completing my second year in April, so almost two years, and I was president elect for two years prior to that. So I've had an office for almost four years.
Q How long will -- when does your term end?
A The -- the last day of the annual meeting in May, so about May 25th.
Q 2008?
A Yes.
Q Do you expect to be president for another term?
A No.
Q Have you ever appeared on television or

radio here in Alaska?
A Here in Alaska, yes.
Q How many times?
A I was on the radio, I think, twice in Fairbanks on a talk show, evening talk show. Can't recall the name of it, but there would be a topic and people would call in and ask questions about it in the evening hour, and there was a moderator and it lasted about an hour. And I think I did it twice. Topics like depression or seasonal affective or something like that.
And then I've been interviewed once or twice since I've been here on the TV as the medical director of API for various reasons.
Q What were the reasons?
A You know, I can't recall. I'm fairly certain one dealt with depression. I can't recall the first one. It was right after I started.
Q What network were you on?
A Channel 13, I believe, was one. Maybe Channel 11 was one of them.
Q Have you been quoted in the Anchorage Daily News, as far as you know?
A Have I been quoted? I can't recall.

They've made reference to API before and the medical director, but I don't know that I've been quoted.
Q Have you ever served as an expert witness or an expert consultant in any litigation?
A No.
Q Have you published any articles in your -- in the field of psychiatry?
A Many years ago I co-authored a chapter in a textbook. For 14 years I worked with homeless services in Dallas, on the streets of Dallas, and a social worker and I co-wrote a chapter of a book that was pretty much used for training social workers and their training about homelessness and how to treat it. And so I did one chapter on -- mostly it dealt with the development and how we set up our clinics and the shelters of Dallas.
Q What was the name of the organization?
A That I worked for?
Q Yes.
A Community Outreach Coalition.
Q When did those 14 years with Community Outreach Coalition begin?

A They began in 1986, and I left them when I left to go to Fairbanks in 2000.
Q Is that a charitable organization?
A No.
Q What kind of organization is it?
A It was set up initially -- in the initial days of it was set up with some grant funding from the City of Dallas. And as it grew and there was increase in need, it was finally, before I left, taken over by Dallas County Mental Health, Community Mental Health. So it became kind of under their umbrella, but we functioned pretty much autonomously and different because we weren't located in one clinic. We had five different clinics in the different shelters.
Q What was the mission of the organization?
A To treat the homeless mentally ill that would not go into the -- into the regular clinic, so we went to them. We, you know, worked under bridges and things like that.
Q Did this -- did the -- was this in addition to the work that you did at Timberlawn?
A Yes.
Q Was it a paid position?

A Yes.
Q What was your title?
A Just psychiatrist. It was just one clinic. I was -- there was another psychiatrist on and off through the years that also worked alternating clinics, but I kind of took the lead, I guess, in it since I had been with it almost from its inception.
Q Does it still exist?
A I would assume so, but, again, under the umbrella of Dallas County.
Q Were the homeless people that this organization reached out to -- were many of them mentally ill?
A They were all mentally ill.
Q Were you able to treat them with medication?
A Yes.
Q Did you treat them also with psychotherapy?
A We didn't do individual psychotherapy. We had a social worker that worked with us as part of the team and would do some group type social skills, you know, therapy.
Q What were the mental illnesses that

these people were suffering from?
A Schizophrenia and bipolar and depression, for the most part.
Q Would you characterize them for the most part as severely mentally ill?
A Yes.
Q What medications did you use to treat them?
A At that time it was the typical antipsychotics, Stelazine, Navane, Thorazine, Haldol.
Q Did you use Perphenazine?
A We did some. It was on -- our formulary was through Dallas County MHMR always, so that was the pharmacy we used. And that was -- that was on their formulary.
Q Did you use it?
A Probably, yes.
Q But just not as often as the others?
A No.
Q Am I correct?
A That's correct.
Q You were with the Community Outreach Coalition until 2000; is that right?
A Right.

Q Did you never use atypical antipsychotics even through the year 2000 with this homeless population?
A I don't believe so. Not that I recall.
Q You know, I asked my question in a confusing way. I said, did you never use it? Let me try it again.
Did you ever use atypicals?
A Not that I recall.
Q Why is that?
A Partly because the formulary that Dallas County MHMR had at that time, and this was -- this was a very budget-conscious group because it was all indigent services, everything. No one paid for any of their care there. So we, you know, really tried to watch what we prescribed and how much. Conscious of that.
Q Were the atypicals not on the formulary?
A I -- I really can't remember.
Q Do you remember any discussions with anybody in the organization about whether to use atypicals in this population?
A No.
Q Nevertheless, during that same period, you were treating patients in your other -- the other part of your practice with atypical antipsychotics?
A Yes.
Q Dr. Hopson, you became medical director at API on the 1st of July, 2003, correct?
A That's correct.
Q And have you been medical director ever since?
A Yes.
Q What are your responsibilities as medical director of the Alaska Psychiatric Institute?
A It's primarily an administrative position. So I have supervision of the other psychiatrists, of which there are seven, and the director of nurses reports to me, and the clinical director reports to me as well. And he's a clinical psychologist and oversees social work, rehab and psychology. So, essentially, if you look at it, all clinical services within the hospital report up to me and I report to the CEO.
Q Who is the CEO?
A Ron Adler.
Q To whom does -- is it Dr. Adler?
A No.

Q To whom does Mr. Adler report?
A His boss is Melissa Stone, division director, the Division of Behavioral Health.
Q Of HSS?
A Yes, that would be the Department, right.
Q Today you supervise seven psychiatrists?
A Yes.
Q Has it always been seven?
A We're funded for seven positions. At times there have been six. We've had turn-over and we tried to fill in with locums tenens. Currently I just have six.
Q How many social workers?
A There are eight.
Q And how many psychologists are there at API?
A Two Ph.D.s and two master's level.
Q You also said that there were rehab?
A Yeah, rehab therapists.
Q How many rehab therapists are there at API?
A Four, five, something like that.
Q Then there's also psychiatric nurses?
A Yes.

Q How many of those are at API?
A Within the Department of Nursing, there's like 156 nurses, but they're not all licensed nurses. We use psychiatric nursing assistants, but they're all within the department.
Q So there are 156 people who perform nursing activities?
A Yes.
Q Are patients treated at API both inpatient and outpatient?
A No, just inpatient.
Q How many beds are there?
A Eighty.
Q Are those 80 beds full today?
A No.
Q Are they typically full?
A No.
Q What's your average patient load?
A Sixty-eight.
Q You sure?
A (Witness nods head.) It averages really close to 68 every -- for the last several years. We do have some peak days certain times of the year where we're at 80, but it's usually

short-lived.
Q When are the peak times?
A Break-up and usually -- actually, at the very early part of winter. This year we've not experienced that census increase, though.
Q What was the first thing you said? Break-up?
A Break-up. When all the snow melts. I'm sorry. So we're talking --
Q Thank you.
A -- April -- April, May, early April.
Q So before the winter and after the winter are your peak seasons?
A Yeah.
Q Why is that?
A Well, you know, people speculate a lot of it. The first peak people are really upset, feel hopeless because they know the long, dark winter is setting in. And then break-up is a real teasing time for people. They've been locked in, it's frozen, it's dark, and the sun starts to come out and they get hopeful that spring is around the corner, and then it -- we have this freezing again. And so their hopes are dashed and people just can't tolerate that, and

they get overwhelmed and suicidal. So we think that that's the phenomenon.
Q When you -- you said that the medical director is an administrative position?
A Yes.
Q Do you see any patients?
A I do. I make rounds every day. I mean, I get report every morning on every patient in the hospital, and then I make rounds to every unit and so I know what's going on. I'm asked by the staff to see certain patients in a consultation perhaps or to run something by me, the staff does that, and so I do have contact. And I have on occasion filled in for a doctor when I don't have a locums. I will go down to the unit and work for two or three weeks during a vacation.
Q You function as an attending psychiatrist?
A Yes.
Q Does API have any outreach responsibilities?
A Not -- not in the typical sense of outpatient outreach. The only thing, we have a new program, it's a telebehavioral program. And

it's actually -- it functions like an outpatient program, but it's not typical. So that's why I said we don't have a typical outpatient clinic when you asked that. But we are getting high band width connectivity to rural Alaska clinics, and we're providing psychiatric consultations, medication, evaluations, things like that to help out the rural sites where they have no mental health provider.
Q Is that done through a television or a computer hookup?
A Yes, television, and it's using digital technology, high band width T-1 lines.
Q In that process, do you interview patients, or do you consult with their physicians or something --
A You can do both. You can do both.
Q And does API do both?
A Yes.
Q How many facilities around the state do you have this connection with?
A Four or five. It's still growing. That's really the brainchild of Ron Adler, so he kind of spearheads the development end of it.
Q Is the plan ultimately to cover as much

of the state as is possible?
A Well, I think the plan is to cover the rural clinical sites. There's still a lot more areas out there that would benefit from having connectivity, but you have, you know, a lot of distance between us and them. You have to lay -- these are land lines, so they're very expensive for some of these villages to run land lines to, so --
Q Are there any other psychiatric institutions in the state besides the unit that you used to supervise in Fairbanks?
A Yes.
Q Where are they?
A Juneau, Bartlett Hospital in Juneau has a psychiatric unit, and then Fairbanks Memorial. Those are the two that have dedicated psychiatric. Aside from here in town, Providence Hospital has an adult unit, twelve beds.
Q Where is that?
A It's next door to API. It's across from the university on Providence Drive. So they have a 12-bed adult, 6-bed adolescent.
Q Is the population of that facility different from the population you treat at API?

A Yes.
Q How so?
A They're an unlocked facility, so they do not take aggressive, violent or committed patients. It's all voluntary. So it's an open unit just like any other unit in a general hospital, so --
Q Could you describe the patient population that averages at about 68 at API?
A Yes. The majority of the census is made up of schizophrenia, bipolar disorder, major depression. Admitting criteria for API is -- we follow State statutes, so it's gravely disabled, homicidal, suicidal, risk to self or others.
Q How many of the 68 on average are committed there involuntarily?
A Well, essentially 99.9 percent of our patients come to us on an involuntary hold. That's the way you get into API, but within the first day after meeting with their psychiatrist, the majority sign voluntary to remain in the hospital to avoid going to court. As far as how many committed patients that have gone to court and are on a 30-day commitment at any one point in time, maybe 7 to 10.

Q How many of those patients, if you can state, are being medicated involuntarily at any given time?
A It's a very small number. We don't do that many unvoluntary medication commitments at API. So at any one time there might be 4, 5.
Q And over a year, that might be how many people?
A Let me see. I've seen those stats. Over the course of a year, it may be 20 or so people.
Q And that's pretty consistent year over year?
A Those numbers have actually been dropping, of the number of involuntary medication, in part, an effort for us to better educate patients about medications and things like that.
Q So that through the education they become voluntary takers of those medications?
A Yes.
Q Are patients at API involuntarily treated ever with Zyprexa?
A Yes.
Q Right through today?

A It's possible, yes.
Q It is -- Zyprexa is in the treatment arsenal for patients who are being medicated involuntarily; is that correct?
A Yes.
Q Have you -- since you became director of API -- let me start all over.
Since you became medical director of API, has API had to go to court to obtain orders to involuntarily medicate patients?
A Yes.
Q Have any of those -- and have you obtained court orders?
A Yes.
Q Do those court orders specify the medications that the patients will be involuntarily medicated with?
A They generally do.
Q Have any of those court orders specified Zyprexa?
A Yes.
Q Do you know what percentage of the people who are involuntarily medicated at API today are receiving Zyprexa?
A No.

Q Do you keep such records?
A The pharmacy does have access to and I think can do a search for that sort of thing.
Q Who is the pharmacy director?
A Patty Deren.
Q Can you spell both names?
A Yeah. Patrice is her first name; she goes by Patty. Deren, D-e-r-e-n.
Q Has anyone from -- in the chain of command ever -- you know, going up your reporting relationships, ever suggested to you that you not use Zyprexa when patients are involuntarily medicated?
A No.
Q That would mean -- that's from the head of the Department of HSS on down; am I correct that not one of those people has ever suggested that you not involuntarily medicate anyone with Zyprexa?
A No.
Q I'm correct?
A You're correct.
Q Has anyone from the head of HSS on down every discussed medication of your patients with Zyprexa one way or the other?

A Not that I recall.
Q As the medical director at API, are you required to create budgets for the institution?
A We're pretty much given our budget from Juneau and, you know, we can ask for increases from year to year if we can substantiate it, but we have to account for it, but we don't get to really set it. You know, I have a set amount, and we try to make it work within that.
Q Do you have any input into the creation of the budget?
A Minimal, yes.
Q Are you asked annually for any thoughts about the budget?
A Yes.
Q What kind of -- who asks you for input?
A The CFO.
Q Who is the CFO?
A Currently, it's Tina Williams.
Q What information does Tina Williams seek from you?
A Well, she might ask, do I foresee any capital budget expenditures for the next year for medical staff. And do I foresee any changes in the cost of medical care that we provide, CT,

things like that. We end up paying for that for a lot of patients. Those sorts of things.
Q Does the medicine -- I'm sorry, let me start all over.
Does the cost of medicine come out of your budget?
A It -- there's a budget item for it. The pharmacy is on its own budget, but, yes.
Q Have you ever been unable to prescribe a medication that you wanted to prescribe or that your psychiatrists wanted to prescribe for budgetary reasons?
A The only one that I -- we have an open formulary, to begin with, so the answer overall is no. There -- there is a restriction on Risperdal Consta that I have placed on it because of the cost of it. Our docs still prescribe it, but they review those cases with me before just to make sure it's appropriate.
Q Are there restrictions on any other psychiatric medication?
A No.
Q Are -- does Medicaid reimburse for the cost of much of the medication that's used at API?

A We don't -- we don't -- we can't bill for our medications, so Medicaid does not reimburse the hospital, no.
Q Then, the cost of the psychiatric medications used at API comes right out of the API budget?
A That's correct.
Q And that's for all psychiatric medications, correct?
A That's right.
Q So that every time a psychiatrist at API prescribes Zyprexa, the State of Alaska pays for it?
A In essence, yes.
Q And that's right through today in December of 2007, correct?
A Yes.
Q And as long as you've been director of API, that's been the case?
A Yes.
Q Has any State official ever suggested that you at API cut back on the amount of Zyprexa that you prescribe?
A No. Not to me, I would add.
Q And not to you through any of your

superiors; is that correct?
A No one has spoken with me about that.
Q Putting aside the cost of medications, is the cost of inpatient care for patients at API reimbursed at all through Medicaid?
A Is the cost of care? Yes.
Q What costs are reimbursed?
A We can -- we bill for physician fees. We bill Medicaid for that. We are an IMD, which is an institution for mental disease, so we cannot bill Medicaid for the age 21 through 64, I think. So we have this big window when we cannot bill, but we can bill on either end Medicaid.
Q Can you bill for taking up space for the bed?
A They -- they do bill for that, yes.
Q Do patients from time to time at API receive medical care in addition to the psychiatric care they're receiving?
A Yes.
Q Do they -- do doctors other than psychiatrists come in to treat them?
A Yes. We have an on-staff family practice doctor.
Q And that doctor is charged with the

medical care of all of these patients?
A Yes.
Q Do specialists, other specialists come in from time to time?
A They wouldn't come in. We would refer out, if Dr. Love felt that there was a need for a special consult for someone.
Q If any of your patients at API have diabetes, is Dr. Love going to be treating them?
A Initially, yes.
Q As long as they're patients there?
A Yes.
Q Does someone else assume their care while they're still in API?
A Well, they'll be assigned to a psychiatrist as well and then she does -- her and her staff take care of all the medical aspects while they're hospitalized.
Q Is the Alaska Native population treated at all at API?
A Yes.
Q Is the situation the same for them with regard to who pays for the medication? Talking about the psychiatric medication.
A Yes, while they're hospitalized, yes.

Q So the State is paying for it?
A Yes.
Q When they're released from the hospital, do you know who pays for their medication?
A They get their medication through the hospital, through ANMC, Native Medical. They have an outpatient pharmacy.
Q Is there any restriction on the admission of Native patients to API?
A No.
Q Are all of the patients at API adults?
A No, we have a 10-bed adolescent unit, ages 13 to 17.
Q Is anybody treated who's younger than 13?
A No.
Q If a child is younger than 13 and needs inpatient psychiatric care, where would he or she receive that treatment?
A North Star Hospital here in Anchorage.
Q Is that a juvenile facility?
A Yes.
Q Or children's --
A Adolescent, yes.
Q Of the 68 people who are in API on

average, how many of those are adolescents?
A They typically run a census of about 8 on that 10-bed unit.
Q Are the adolescents suffering from the same disorders as the adult population suffers from, on average?
A Less schizophrenia, less bipolar, of course, but certainly a lot of depression, family issues, that sort of thing.
Q Does API have any policies regarding the use of psychiatric medications?
A We have in our policies and procedures P&Ps that address the prescribing, but it doesn't address, you know, which drug, that sort of thing. It's more how orders are to be written, that sort of thing.
Q Is it, therefore, up to the individual psychiatrist in each case to decide the treatment plan for his or her patients?
A Yes.
Q Do you ever meet as a group to discuss your patients?
A Yes.
Q How often?
A We have weekly medical staff meetings,

and as part of that, cases come up for discussion.
Q Is it the policy that all psychiatrists should attend the weekly staff meetings?
A Yes.
Q Do other professionals also join those meetings?
A Once a month.
Q Which professionals come to those meetings?
A The quality improvement director, the CEO, the director of nurses and the pharmacist.
Q Have there ever been any directives -- let me start over.
Have there ever been any policies or procedures as long as you've been at API regarding what medications a psychiatrist may prescribe for his or her patient?
A No.
Q Does any psychiatrist have to get approval from anyone else before he or she prescribes a psychiatric medication for an API patient?
A Just the Risperdal Consta, right.
Q You said you put a restriction on

Risperdal Consta because of the cost?
A Yes.
Q Are there medications that you would use in place of Risperdal Consta before using it?
A Not necessarily. That medication is considered usually for someone who is noncompliant with their oral medications. So, you know, a patient who fits that category, their doc is generally going to think about that, if that's something they agree to.
Q What are the medications you might use in place of Risperdal Consta?
A Seroquel, Abilify, Geodon, Zyprexa. It would depend.
Q Is the cost of those alternative medications lower than Risperdal Consta?
A Yes.
Q What other considerations do you take into account in deciding whether -- let me start all over.
In order to prescribe Risperdal Consta, a psychiatrist has to come to you?
A Yes.
Q What criteria do you use to decide whether or not to approve the use of Risperdal

Consta?
A Well, typically, what we try to base it on is, No. 1, the patient -- does the patient agree to it, because they're going to have to get an injection every two weeks. Where are they going to get follow-up? Are they going to be in a rural site where they have access to it? Even though it's on formulary at Native Health, not all rural clinics have it. And, then, is this a new start or is this a continuation? And if it's a continuation, we certainly want to continue and not break up what they've been on.
Q In what kind of situations would you urge a psychiatrist to use, for example, Zyprexa instead of Risperdal Consta?
A Well, whether or not I would -- I would not necessarily encourage one or the other of the other atypicals. But if it was a patient that, you know, after looking at them or talking with them or the doctor presented it, that they may or may not take the medication, you know, it's kind of iffy whether or not they would be adherent. you know, are we going to go down that road? Would it be better to choose something else? Those are the types of clinical situations.

Q In each case you make an individual prescribing decision based upon the medicine, the patient and your knowledge of the medications; is that right?
A Yes.
Q In fact, that's true every time you prescribe a psychiatric medication?
A Yes.
Q When the patients are involuntarily medicated in your institution, you said that sometimes you have to go to court to get the court approval; is that right?
A Yes.
Q Who represents the institution in those situations?
A Attorneywise?
Q Yes.
A We have an assistant AG that's assigned to our hospital for those purposes.
Q And that's an assistant attorney general from the State of Alaska?
A Yes.
Q What is the purpose of your weekly staff meetings?
A Well, it's an opportunity to -- for me

to convey information to them, things that are happening, things -- upcoming things. We convey quality improvement data to the doctors. I review different data, you know, that the hospital tracks as a whole, that the hospital has a great deal of data that we're required to track for JACHO. We're a JACHO-accredited organization. And so, you know, the medical staff should play a large role in decision making and they should be knowledgeable about those sort of things. So I go over that with them. Then we can talk about any particular difficult cases, that sort of thing.

Q Did you ever have to convey to the staff that the State of Alaska had brought the lawsuit in which you're testifying now?

A No.

Q Have you ever discussed it at a staff meeting?

A No.

Q Outside of a staff meeting, have any of the -- have you had a discussion with any of your psychiatrists at API about the lawsuit that the State has brought against Eli Lilly and Company?

A Just within the last two weeks probably.

Q Why was that?

A After I was told about this. I told some of my staff I'd be away today and they said, why? I'm doing a deposition. What's that about? So I told them.

Q Did any of the psychiatrists you spoke with indicate to you that they were aware of the lawsuit?

A No.

Q Did any of them ask for any information about it?

A No. It's been kind of on the side. It wasn't in the course of medical staff meeting, so --

Q But when you told them you were going to be away because of this deposition, did anyone ask you what the case was about?

A No.

Q When did you first learn about the lawsuit?

A I heard something about it last year. I would say, actually, around April of last year.

Q April of '06?

A Yes, I heard something about it. It was -- I want -- maybe it was in the paper.

There was just a little bitty thread of discussion about it, and then I haven't heard anymore about it.

Q Do you recall what the source of your information was in April of '06?

A It was at the Alaska Psychiatric Association annual meeting, and I don't -- it seems like that's where I heard it, and it was in the paper apparently that morning and someone said they saw that, but --

Q Did you have any discussions with anyone at the Alaska Psychiatric Association meeting about the lawsuit?

A No.

Q And you say April, '06 because that's when the meeting was?

A Yes.

Q Then you heard nothing about the lawsuit again until you found out you were going to have your deposition taken; is that correct?

A That's right.

Q Did you ever ask anybody in the Department of HSS or -- about the lawsuit?

A No.

Q Did you ever talk to the attorneys from

the attorney general's office who represent API about the lawsuit?

A No.

Q Did you ever try to get any information from any other source?

A No. It -- it just kind of slipped my mind. There was never anymore talk about it.

Q At the staff meetings do you discuss psychiatric literature?

A Sometimes.

Q Do you discuss CMEs that people have attended?

A We don't discuss particularly. If someone went to an interesting one, they might tell the group what they went to.

Q You said you discuss individual patients.

A We do on occasion.

Q What causes you to discuss individual patients' problems at staff meetings at API?

A Ones that are considered maybe difficult to treat. Maybe there's a quandary of what to do with them. Maybe the length of stay is longer than the doctor is hoping for. And it's just -- it's just kind of a peer -- peer activity to

discuss those types of cases.
Q When you discuss the cases, necessarily you're discussing the medications that people are using?
A That could be part of it.
Q Is anyone ever asked to make a formal or informal presentation to a staff meeting?
A Yes.
Q What kinds of presentations are made?
A We occasionally have outside speakers that are brought in for educational purposes. Not necessarily a CME; that's pretty rare. But just an educational lecture or presentation.
Q Do pharmaceutical company sales reps ever attend these meetings?
A Yes.
Q How often?
A Well, typically, those are the individuals responsible for setting them up, so -- and the drug rep usually accompanies them. So, typical scenario, they're -- most of the drug reps are not located in Alaska. They're in the Lower 48. So a typical rep will bring a particular speaker up and they'll make the rounds to the different hospitals and give a lecture.

Q How often does that occur?
A I would say it averages once a month.
Q Since you're having -- and you're having staff meetings every week?
A Yes.
Q So once a month at a staff meeting, on average, you see an outside speaker who's brought in by a sales rep?
A This is -- it's done on a separate day. It doesn't take the place of medical staff.
Q Do outside speakers ever come to medical staff meetings?
A There was a time when they did. When I first came there, a medical staff meeting was used for that purpose, but we decided that it was kind of crowding that, so we moved outside speakers to a different day of the week.
Q Does the staff -- during the regular staff meetings, do sales reps ever come to those meetings?
A Not any longer, no.
Q Now, when you have separate meetings with speakers -- let me start all over.
Do you have separate meetings where there are just sales reps present and not outside speakers?
A Very rarely. Very rarely.
Q When would -- why would they occur?
A It seems like there was an instance of a particular company was releasing a new product and they didn't have a speaker, but they wanted to get the word out, pass out some information, so they would just do it on their -- they did it on their own.
Q But most of the time when you have an extra meeting with someone from outside, it's a speaker brought in by a sales rep; is that right?
A Yes.
Q Which companies provide speakers to your extra staff meetings?
A Essentially all of the ones.
Q Have any of the speakers since you've been at API been brought in by Eli Lilly and Company?
A Yes.
Q Do you recall what topics they discussed?
A Typical presentations, perhaps, on Zyprexa, benefits of it, comparing it to -- its effectiveness to other's effectiveness. That sort of thing.

Q How many times has -- has Lilly brought a speaker in about Zyprexa since you've been at API?
A Maybe 50 times. They probably more so than other companies.
Q That's 50 times in about four-and-a-half years?
A Yeah. That's a guess, but --
Q And each of those times has been about Zyprexa?
A No, not necessarily. Not necessarily. Other products that Eli Lilly might have had.
Q Generally, though, in the psychiatric field?
A Yes.
Q Do you recall who the speakers were who have appeared here?
A I can only think of one. Dave Samson, David Samson.
Q Do you recall what topic Dr. Samson discussed, or topics?
A His most recent -- he's appeared several times because he's a local psychiatrist that's retired now, and he this last time teamed up with

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an endocrinologist, I believe. They did their -- they call it a tag team kind of lecture, presenting facts and figures and things to docs.
Q Who was the endocrinologist?
A I cannot recall the name.
Q Do you recall the message or the theme they were tying to get across?
A Well, I think, you know, typical is, you know, touching on the effectiveness. Certainly the things now that we watch for with Zyprexa. The endocrinologist was there. How to handle it, what to look for, you know, talking about -- I think he did present data or graphs or something on the weight gain and increased lipids and all of those sorts of things.
Q When Lilly has brought in speakers, has there been an opportunity for the doctors at the meeting to question the speakers?
A Yes.
Q And have the doctors actually questioned the speakers brought in by Lilly?
A They do sometimes.
Q Is attendance mandatory at these meetings where the speakers come?
A No.

Q Since you're so good with averages, is there any way to determine what the average attendance is at these meetings?
A With the medical staff?
Q Yes.
A It's probably 75 percent. Out of 7 people, that's easy.
Q Are you aware of any instances where either -- at one of these meetings where a Lilly-sponsored speaker made any misrepresentations about Zyprexa?
A You know, specific misrepresentation, it's difficult to say. You know, I think each speaker has their own sense of the effectiveness or safety or whatever their story, whatever they're talking about. They have their own commitment to what they're talking about. And so, you know, I think out of that, you know, you could say, well, they didn't really talk about this particular concern very much. So whether that's purposeful misrepresentation or not, it's difficult to say, because everybody has their own commitment to their beliefs, I guess.
Q If you felt that somebody was leaving something out that was important with regard to

safety or effectiveness, have you attempted to correct that or bring it to the speaker's attention?
A There have been opportunities when questions would be asked of the speaker, particularly if it was something that was just kind of glaring and maybe one of my doctors -- I've had turn-over of doctors, as I've said. Some are more outspoken than others; some more committed to their beliefs. And they, you know, they will ask a challenging question. That's not my experience, perhaps, or something like that. Get some feedback going.
Q Do you remember whether Lilly sent any speakers in to speak to your staff around the time of the label change in 2003?
A What month was that?
Q September.
A There's a likelihood that they did, yes. That's a long time ago.
Q Well, do you have a recollection of any companies -- let me step back.
Do you remember that there was a classwide label change for the atypical antipsychotics in 2003?

A Yes.
Q Do you recall whether companies other than Lilly came in to talk about that label change?
A Yes.
Q What companies?
A It seems like probably Seroquel did. I can't recall others, but it seems like I do recall them.
Q Seroquel being AstraZeneca?
A Yes.
Q Do you recall the Seroquel representatives talking about or trying to distinguish Seroquel from Zyprexa?
A Yes.
Q In what ways?
A Well, there again, their -- their belief of a safer profile of side effects, less weight gain, less effect on lipids, all of those issues, you know, when they compare themselves to each other.
Q And even though you might not remember the specific medication or the specific company, do you think that you had representatives from other manufacturers of atypical antipsychotics

speaking to your staff after the 2003 label change?
A I would think so, yes.
Q And do you think that each of them in his or her own way tried to distinguish his or her own medications from the competitor's?
A I would think, yes.
Q And oftentimes the distinction was about issues relating to weight gain and lipids, right?
A Yes.
Q And rates of diabetes?
A Yes.
Q And the representatives from the companies other than Lilly tried to inform your staff that they had a better safety profile with regard to weight gains, lipids and diabetes than Zyprexa?
MR. SNIFFEN: Objection, a little bit. Do you know what safety profile means? I guess the objection is to vagueness as to the use of that term.
Q (BY MR. ROGOFF) Do you know what safety profile is?
A In general, yes.
Q Let me rephrase the question.

Did any of Lilly's competitors after 2003 come in to speak to your staff about the difference in the safety profiles between Zyprexa and the competitors' medications with regard to weight gain, lipids and diabetes?
A Yes.
Q When they gave you those presentations, how did -- where did -- how did Zyprexa stack up against the competitors when the competitors were giving the presentations?
A Well, typically, I think people have always felt that, you know, there's a higher weight gain, higher risk of increased blood sugars and lipids with Zyprexa. I think a lot of times you have to challenge yourself to wonder how much the other drugs cause that as well, you know, when the data is presented. And so -- that's the typical presentation that they would make and that you would have to consider those factors.
Q Well, you said that people have always felt that there was higher risk of weight gain, problems with lipids and diabetes with Zyprexa than with the other atypicals?
A Yes.

Q Which people are you referring to?
A Well, I think physicians in general, if you talk with them.
Q And when you say "have always," what do you mean by that?
A Well, as this has come to light, that people need to be mindful of this and adjust their practice accordingly, if that's appropriate.
Q Well, were you aware of Zyprexa's -- let me rephrase this. I'm sorry.
When competitors came and touted their product over Lilly with regard to these issues relating to weight gain, lipids and diabetes, did it come as any surprise to you?
A A surprise in that they were coming and saying that?
Q Yes.
A No.
Q You were aware of such issues from reading the literature and talking to your colleagues; is that correct?
A Yes.
Q And you were aware of such issues through your own use of Zyprexa with your own

patients; is that correct?
A Yes.
Q And that was true long before the label change in 2003; is that correct?
A It was a risk. I think that, you know, it was a risk that we did not know, I guess, the seriousness of the risk at that stage of the game.
Q When did you become aware of the seriousness of the risk?
A Well, probably around the time of the label change. Maybe perhaps before.
Q From reading the literature and from going to CMEs?
A Yes. And clinical practice, too, seeing your patients.
Q Were those issues before the label change that you had discussed with doctors in your staff meetings either here or in Fairbanks?
A We talked about it here. In Fairbanks, no, not that I recall.
Q But you talked about it here in Anchorage before the label change, right?
A Yes, that it was something that we needed to be cognizant of.

Q Nevertheless, you and your fellow psychiatrists at API continued to prescribe Zyprexa for individual patients?
A Yes. We tend to -- doctors continued to do that despite the --
Q Despite?
A Despite risks with all classes -- all types of medications.
Q Why is it that you would continue to prescribe Zyprexa given that higher risk of weight gain, lipids and diabetes?
A Well, I think one -- one treatment approach is you try other medications perhaps first. You go with those with a less risk profile, and if perhaps those are not effective, patients had perhaps side effects to them, didn't tolerate them, and then you would make a change in your approach and try Zyprexa. Some docs might do that, you know, rather than put it on as first line.
Q But there were also some doctors in your group who treated with Zyprexa first line; is that correct?
A That's possible, yes.
Q That's because they were making

individual prescribing decisions in each case?
A Yes.
Q Did they discuss those individual prescribing decisions in your staff meetings?
A Not on a regular or detailed basis, no.
Q Do you remember it ever coming up?
A You know, just general discussion, again, that there is this risk. It's open formulary, be mindful of it. And it was around that time that Dr. Love, you know, really began monitoring BMI, weight, lipids.
Q Dr. Love is your family care physician?
A Yes, family practice, yes.
Q Do you have any idea today -- well, you did say earlier, I'm sorry, about how many patients in API were taking Zyprexa now?
A No, I wouldn't have a clue. The pharmacist could look on the profile.
Q Do you know if anyone at API is on Perphenazine today?
A I would say no.
Q Why is that?
A It's one of the older antipsychotics, just rarely prescribed.
Q Do you know why it's rarely prescribed?

A Well, you know, in general, psychiatrists don't use the older drugs anymore, higher risk of tardive dyskinesia, side effect profile, that sort of thing.
MR. ROGOFF: Can we take a break?
MR. STEELE: Sure. You're scintillating, but a break is always welcome.
THE VIDEOGRAPHER: Going off the record at approximately 11:27 a.m.
One moment, please.
(Break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 11:59 a.m.
Q (BY MR. ROGOFF) Doctor, earlier you were discussing the regular staff meetings where it's only staff in attendance and -- only psychiatrists in attendance.
Does anybody keep minutes of those meetings?
A Yes.
Q Where are those minutes maintained?
A At my secretary's desk.
Q Who takes the minutes?

A She does.
Q And she attends every meeting?
A Yes.
Q Does someone take minutes of the meetings at which the speakers -- outside speakers come in?
A No.
Q Do you take notes of those meetings?
A Not regularly.
Q If you do take notes, do you keep them?
A No, I don't personally.
Q Do you personally keep a set of personal files in your office about work? And what I mean is -- let me -- let me try to be a little more clear.
Do you keep files or folders regarding individual medications and information about those medications?
A No.
Q Do you keep folders regarding research or reading that you've done?
A Some.
Q You'll keep articles that are important to your practice?
A Some.

Q What kind of articles do you keep?
A Oh, perhaps one that I think is going to be something that I might want to reference back to. Maybe the CATIE trial. I think I've got a copy of that. You know, things like that.
Q Do you keep any promotional literature that company representatives bring to you?
A Not for the long haul.
Q Have you kept -- beside CATIE or the CATIE study, have you kept any of the literature that you've read over the years about Zyprexa?
A I don't believe I have anything right now.
Q Do you think you've kept anything about atypical antipsychotics in general or about any particular atypical antipsychotic?
A I think I've got some -- something on some algorithms that we had considered as a medical staff at one point. It's the sort of thing that if you kept everything, you'd have to move out of your office, so I'm pretty discriminating what I keep.
Q What algorithms are you referring to?
A Like the Texas algorithm project, that sort of thing.

Q You kept that?
A I think I do have a copy of that still.
Q When did -- you said that you were considering implementation of an algorithm here?
A We considered them.
Q Who's "we"?
A Medical staff.
Q What did you do in your consideration of the algorithms?
A Well, we -- we looked at the Texas Medication Algorithm Project to see if we should institute some sort of program like that or a much simpler version of it, something like that. And the medical staff at that time did not feel that they wanted to do that and so we just did not, but we did consider it.
Q It was a consensus of the staff?
A Yes.
Q What was the reasoning behind the staff's consensus?
A As I recall, that they still wanted to have open access and to be able to, you know, prescribe the way they had been. And that was a different set of docs than I have now. We have not reconsidered them since.

Q Were you in agreement with that principle of open access?
A Yes, because I did do some checking of some other facilities asking for other copies of algorithms so we could consider more of them, and a lot of facilities did not have them, so they did not use them, so --
Q Why do you think open access is important?
A Well, I think, you know, the practice of psychiatry is a very unique specialty, and I think you have to have open access for very difficult patients just like you would if you were treating different cancers, things like that. Try different options taking into consideration the benefit versus the risk.
Q You have restricted, however, Risperdal Consta; is that right?
A Well, if you want to -- it's not really a restriction. It's a pass by me kind of thing.
Q You consider it within your authority to have a pass by you kind of restriction --
A Sure.
Q -- on any medication; is that correct?
A Sure.

Q That would include Zyprexa?
A Sure.
Q You have not instituted any restrictions on Zyprexa, have you?
A No.
Q When you fill in for doctors or are the attending psychiatrist at API, are there patients for whom you still prescribe Zyprexa?
A Yes.
Q For what types of conditions?
A Typical schizophrenia, perhaps bipolar. Those would be the top type of patient that would -- you would prescribe for.
Q That you would prescribe for?
A Yes, uh-huh. That I would prescribe for. That one would prescribe for.
Q Can you describe circumstances in which you would choose Zyprexa over another antipsychotic medication?
A Well, a typical scenario might be someone who has been treatment resistant perhaps to one with less side effects. And so, you know, you move up to a bigger gun, so to speak. And doctors are pretty accomplished at doing that, taking into account prior performance of a

medication, and so then you would consider something like Zyprexa for them.
Q Do you have a personal viewpoint regarding the efficacy of Zyprexa?
A Efficacy. I think it is efficacious. It is efficacious, I think, in lower doses than some of the others. Some of the others are equally as efficacious if you adjust their dosage accordingly.
Q And is there a problem that you see with adjusting doses?
A Well, sometimes you also run into side effects from that and getting your patients to take higher doses, even though you try to explain to them, you know, it's apples and oranges, it's not the same thing.
Q There's no formula that you can come up with for when you'd prescribe Zyprexa and when you wouldn't, is there?
A There isn't.
Q Have you ever used Zyprexa off label?
A I would say yes. Psychiatrists are keen at doing that on occasion.
Q Keen at off-label uses?
A Yes.

Q Why is that?
A Well, there again because of the, you know, the difficulty of patients, the nonresponse to different regimens, the nuances that you treat with different medications.
Q Would you say, then, that off-label prescribing is common in psychiatry?
A Yes.
Q And what medication you prescribe for a patient depends upon that patient's individual circumstances?
A Yes.
Q What sources of information do you have or have you used to learn about the risks and benefits of Zyprexa?
A Information from speakers, from CME activities, from journals, from any articles that might have been published, Psychiatric Times, Psychiatric News.
Q Also, the PDR?
A Sure.
Q Your colleagues?
A Sure.
Q Do you recall any particular CMEs that you've attended where you've learned about

Zyprexa?
A That focused just on Zyprexa, no.
Q On the atypicals?
A Yes, on the atypicals.
Q Are sales representatives a source of information for you about atypicals, in general?
A Are what now? I'm sorry.
Q Pharmaceutical company sales representatives --
A Oh, yes.
Q -- a source of information for you to learn about the risks and benefits of a particular medication?
A I think they can be.
Q Do you remember particular instances?
A Well, certainly. You know, and it's generalizable, I think, to all pharmaceutical reps that, you know, they -- they are selling their product and they're presenting it, and they're very committed to their product and, you know, they're presenting data to you. And, you know, whether or not you have the time to sit there and tease it out and get them to totally explain -- you know, a lot of times they may -- we don't challenge them on their data as much as

we should, but they do present, you know, their viewpoint of side effect profile, risks, benefits. Always that theirs is the best, always.
Q And you understand they're trying to sell a product?
A Sure.
Q And do you accept everything a sales rep says just because a sales rep says it?
A No.
Q What do you do to check it out or challenge what sales reps say?
A Well, you know, you use your own personal experience with a drug, first of all, as far as efficacy. And, you know, in my head I'm comparing my experience with what I'm being told. And then, you know, as far as side effects and risks, you know, you can talk to your colleagues or you might read an article about it.
Q And you'd find that more reliable than a sales representative's one-sided presentation?
A I would.
Q Have you ever been a speaker for Lilly?
A No.
Q Have you ever been a speaker for any

pharmaceutical company?
A No, no.
Q You mentioned before, I think, three general side effects relating to Zyprexa; that being weight gain, lipids and, I guess, metabolic disturbances?
A Yes.
Q Do you know when you became aware of each of those?
A You know, I think we were aware of the weight gain and the increased blood sugars early in the Zyprexa story. The impact on lipids, I think, came later. Then there was a lot of talk on metabolic syndrome, so it kind of snowballed as we got more information.
Q But you always knew that excess weight was a risk factor for diabetes; is that correct?
A Yes.
Q I don't mean always, but at least since medical school.
A Right.
Q When you say early in the Zyprexa story that you knew about weight gain and metabolic --
A Increased blood sugar.
Q -- an increase in blood sugar, what do

you mean by "early in the Zyprexa story"?
A Well, I think, you know, as soon as it almost came out and we put our patients on it, we began to see immense weight gain in some patients. Not every patient, but you do see it in a large proportion of patients.
Q And you saw that early on in the prescription of Zyprexa?
A Yes.
Q Do you know how early in the life of Zyprexa you started prescribing it or seeing this effect in patients?
A When was it released?
Q 1996.
A I would say sometime within that year. I typically don't jump on the band wagon first. I wait and see how some people are using it, how they like it, do some observation of it, so probably within the first year.
Q Do you -- when you use a medication for the first time, do you acquaint yourself with the information in the product label?
A Yes.
Q And you did that for Zyprexa as well; is that right?

A Sure.
Q You said that you kept, I think, a copy of the CATIE study in your office? That's correct?
A Yes.
Q What is your impression, if you can remember it, of the results of the CATIE trials or the CATIE --
A Well, you know, it -- it got a lot of interest, particularly the first round, saying that some of the earlier typicals were as efficacious as the atypicals with a dropout rate being dependent upon people having side effects and just stopping the medication. And so, you know, I think it created opportunity for us to pause and look at, should we go back and use some of those older medications? Some people, I suppose, did. I personally have not done that, and I don't know of anyone at API that has done that.
Q Why haven't you?
A Because I think there's still an increased risk of tardive dyskinesia with the older medications, and albeit there's risk with this medication as well --

Q "This" being Zyprexa?
A -- with Zyprexa, or with the atypicals, also, that's the old physician thinking of balancing efficacy with side effects.
Q You said that some people did go back to prescribing the earlier medications as a result of CATIE?
A I -- I heard stories of people trying some of those.
Q Did you hear what the results were in the field?
A Not really. I did not hear like from patients or from anyone else. I know I had one locums that came through the hospital and was doing that, was using the older drugs, but he wasn't having that great of luck with it because of side effect profile, so --
Q Is your career long enough for you to have a memory of the pre-atypical antipsychotic medications?
A Uh-huh.
Q That's yes?
A Yes.
Q Can you describe how the advent of the atypicals has changed the prescription of

psychiatric drugs?
A Well, I think the way they were introduced and marketed and presented to the physicians was that it revolutionized treatment, particularly for schizophrenia, and that it treated the positive and the negative symptoms of schizophrenia. So I think that was with lower risk of tardive dyskinesia. That was usually in the -- in the scheme of presentation, too.
Q Have you seen patients with tardive dyskinesia?
A Yes.
Q Can you describe what that is?
A It's generally a permanent and can be a very disabling disorder caused by dopamine block A from the older atypical -- from the older typical antipsychotics. And there are tremors involved, some muscular rigidity, a lot of oral dyskinesias, oral abnormal movements of the tongue. And it's not only socially embarrassing, but it can be very impairing to some individuals.
Q And in weighing the risks and benefits of using the typicals against the atypicals, why is it that you come down on the side of the atypicals?

A I think I believe and I think a lot of docs believe that if -- I've heard discussion about this -- is that we, if we're properly informed about the risks associated with a medication, we can monitor those risks. And it's all in the process of being adequately informed and then us monitoring for it. The problem with tardive dyskinesia is it can come on even with just one dose. There have been reported cases. So it's not kind of a progressive thing that we might see with the atypicals, so we have more time to intervene with it.
Q So it's your practice, then, to monitor your patients on atypicals for those side effects that you're concerned about?
A As we've become more aware and educated about the risks, yes.
Q And as you said, though, you were aware of the weight gain and blood sugar issues really from the start; is that right?
A Yes.
Q You described earlier the use of Zyprexa in an involuntary situation -- or the involuntary use of Zyprexa. How is the medication administered when it's administered

involuntarily?
A Well, ideally, orally. And, interestingly, you can convince a patient after they've gone before a judge and a judge has told them, you know, this doctor is going to give you this medication, you can usually tell the patient, you need to take this, the judge has said you have to take it, and they usually will. If not, then it can be administered to them with a shot, intramuscular.
Q That includes Zyprexa?
A Yes.
Q Have you seen the intramuscular injection of Zyprexa work for these patients?
A Yes. I would say as much as, you know, any other intramuscular.
Q Have you ever read the Complaint that the State has filed against Eli Lilly?
A No.
Q Did anyone in the attorney general's office consult with you before filing the Complaint?
A No.
Q Did you ever receive a letter from a drug utilization review committee regarding the

use of Zyprexa here in Alaska?
A Not that I recall, no.
Q Are you able to say that there are -- there is -- as a blanket statement, a drug that's equally as effective as Zyprexa in all situations, but with a better safety profile?
A In all situations? No.
Q Why is that?
A Because I think patients are unique and illnesses are unique, and you can't -- I think you would be in error to say that one particular medication in all instances is going to be superior.
Q When you prescribe Zyprexa, do you talk to your patients about the risks and benefits?
A Yes.
Q Have you always done that?
A Yes.
Q What are the risks that you've told your patients about Zyprexa?
A Well, there again, I think it's been a -- it's been a process of changing how we do informed consent over time with Zyprexa, as we've learned more about it. But now it includes the weight gain, increase in lipids, blood sugar,

information about metabolic profile, that sort of thing.
Q And with those risks patients have voluntarily agreed to take the medication in your experience?
A They have. Some patients will refuse.
Q Now, you said -- did I understand you that the way you obtain consent has changed over the years because your knowledge has changed?
A Right.
Q But with the knowledge that you had early on about weight gain and blood sugar changes that were associated with Zyprexa, you were passing that information along to patients right from the start; is that right?
A The weight gain was from the start, because almost immediately we recognized that it caused weight gain. You know, and we were told weight gain in varying degrees depending upon patient, type, that sort of thing.
Q Told by whom?
A Pharmaceutical reps.
Q Did your prescribing habits change as a result of the 2003 label change in Zyprexa?
A I would say yes.

Q Even though you were aware before the label change of the information in the label?
A Yes, I think that it did.
Q And how did it change?
A Well, I think after the label change, it -- not only me, but I think other people that made us even more cognizant. It made the things that we had perhaps suspected, you know, as side effects or potential side effects with Zyprexa, were actually, you know, real. They were being admitted to, being told to us, whatever, and so we -- I, in particular, you know, took that into consideration when you're considering a medication.
Q Does API have a P&T committee?
A We have -- yes, it's a little -- it functions differently than others. Ours is in place to really meet all the JACHO requirements of the Joint Commission. But we do and we oversee the formula -- the formulary and do some other projects in the hospital.
Q Who's on the P&T committee at API?
A Myself, the director of nurses, the pharmacist, Dr. Love, our family practice doc, our infection control coordinator. That may be

it.
Q How often do you meet?
A Quarterly.
Q What is it that you have to do to meet the JACHO requirements.
A Requirement. Well, first of all, there has to be -- they -- it used to be called pharmacy and therapeutics committee. The new nomenclature for the Joint Commission now is MMIC, medication management infection control, so they've combined some committees.
And you oversee prescribing practices. You have some drug utilization required studies that you have to collect data on and report that to the Joint Commission, like drug errors, things like that.
Infection control, we have certain required things we have to monitor, like refrigeration, refrigerator temperature where medications are stored, things like that.
Q You said, I think, that part of the responsibility of the P&T committee is to maintain or establish a formulary for the hospital?
A Well, we provide input. The medical

staff establishes the formulary, and then from medical staff, I go back to the MMIC committee and make recommendations, and the committee then will implement it and the pharmacist will order it. That's kind of how it progresses.
Q Well, is there really a formulary within the institution for antipsychotic drugs?
A It's not a restricted formulary. API has a formula -- a formulary, sorry, but it pertains less to the psychiatric medications and more to the medications that Dr. Love prescribes. There are some that we have chosen, if the doctors don't order them much, some of the older typicals, some of the older antidepressants; some of the serotonin agents are now generic and we order those. We order them all, but, you know, it really depends on the prescribing practices.
Q So there are no restrictions within API on atypical antipsychotics other than what you said about Risperdal Consta?
A Right.
Q Are you also on a P&T committee for the State?
A Yes.
Q How were you chosen for that committee?

A I got a letter from Joel Gilbertson that they were putting together the preferred drug list committee, to oversee this for Medicaid recipients in the state, and this was, I think, in '03 and I've been on it ever since.
Q Joel Gilbertson was the Commissioner of HSS?
A Yes.
Q Do you know why you were chosen?
A I assume probably because I was medical director at the State facility.
Q Who else is on the committee?
A Psychiatristwise. Initially was Lex Von Hafften, but now it's Lucy Curtis. There's been a changeover. Then the rest of the committee is made up of -- from other disciples, doctors from other disciplines.
Q What is the purpose of the P&T committee?
A The purpose yearly, on a yearly basis we essentially review every class of medication and we take testimony from -- not only from pharmaceutical companies, but also testimony from local physicians and clinicians. And we vote on -- we look at all the medications that are

available in a particular class. Like, for instance, the statins for blood pressure -- not statins -- for lipids --
Q For lipids.
A -- I'm sorry. And we will look at all the different ones and compare the data on them, considering efficacy, side effects, and then we will vote either to consider them a class effect, or perhaps there have been some very outspoken speakers who say, we must have this particular one, it works for a particular type of patient. Then we will say class effect, but this one must be on the formulary.
And we vote and the decision is made. If it's class effect, the decision is made by First Health based upon cost, if they're a class effect. It's really been a nonissue because if you feel that your patient needs a particular medication, you just have to write "medically necessary" on the prescription. It's an automatic override.
Q That's just for Medicaid patients?
A Yes.
Q Who else is on the P&T committee? Let me back up.

You're in there and Dr. Curtis is on there because of your practice in psychiatry?
A Uh-huh.
Q Yes?
A Yes.
Q And then there are doctors in other specialties as well on the committee?
A Yes, yes.
Q Do you know how big the committee is?
A I'd say 20.
Q Besides the doctors who are on there because of their specialties, who else is on the committee?
A David Campana, who works for the State and another pharmacist that works with him, also.
Q Are there any other nonmedical specialists on the committee?
A We have a Pharm.D. who works for First Health Corporation and presents information to us, and then there are a couple of pharmacists on the committee. There's a nurse practitioner on the committee who's in private practice in Fairbanks. There was a dentist. I don't believe he is on the committee any longer.
Q Anyone else you can think of?

A That is a nonphysician. No.
Q Any other representatives of the Department of HSS or the State?
A Not that I can think of.
Q Is it the responsibility of the members of the P&T committee to review medical literature regarding the safety and efficacy of the drugs that they're reviewing?
A Yes. The information that we're given is considered to be a unbiased, research-oriented compilation of data and there's a lot of it. And a lot of it is laid out in charts so you can very quickly compare.
Q Who supplies the literature to the members of the P&T committee?
A I believe it comes through University of Oregon. I believe.
Q Is it distributed by someone from First Health?
A Yes.
Q Do you ever provide any input in terms of suggesting literature that ought to go out to the committee?
A Personally, no.
Q Do others?

A Literature, no, not that I'm aware of. People -- different physicians have written letters, and you can ask for that to be distributed to the committee.

Q Does the P&T committee -- let me start over.

Is it the responsibility of the P&T committee to be concerned with the safety of the medications that it approves?

A I think that is a consideration. That is probably less of a consideration, and really more we look at efficacy. Side effects are discussed. Efficacy is discussed probably more.

Q If the members of the committee believe that a drug was unsafe, would that be a basis to not approve its use in the Medicaid program?

A It could if enough people, I suppose, were concerned about it.

Q Has the P&T committee reviewed psychiatric medications?

A On the original pass-by of those medications, we decided not to put any of them on the formulary and leave it open access. And then the following year, I believe, the State began working with Comprehensive NeuroScience and they

kind of now oversee the psychiatric medications, the atypicals anyway. The atypicals, the seizure medications, mood stabilizers, sedative hypnotics.

Q When you say "they," that being CNS?

A Yes. It's a different program that has been set up that is based on evidence-based practice and consensus-based practice. And uses a set of clinical indicators that the State has chosen to use. Again, this is just for Medicaid recipients. And if a particular prescriber sets a clinical indicator by, say, prescribing two or more antipsychotics, that's one of the clinical indicators. There are some safety issues associated with that, so as a result, that clinician will be messaged on that once a month with some clinical information.

Q But it's not CNS that decides whether or not a medication should be made available to physicians through the Medicaid program?

A No.

Q It's just reviewing the use of the medications?

A Yes.

Q And the frequency of the medications?

A Yes.

Q Actually, there's lots of ways they can slice and dice the data.

A Right, right.

Q But the P&T committee has the authority to decide whether medications are available to Medicaid patients or not; is that right?

A Yes. There again, if a patient -- if something wasn't on the formulary, you can just write "medically necessary" and it's an override.

Q All right. So the P&T committee establishes what's on the formulary, but any doctor can, in essence, override it in the State of Alaska?

A Yes.

Q Has the P&T committee considered -- well, can you explain what open access is?

A It's where there are no restrictions to medications that you can prescribe.

Q And is there -- does open access exist for antipsychotic medications in the State of Alaska?

A Yes.

Q Has the P&T committee of the State of

Alaska made that decision?

A Yes. They have upheld that because of the presence of the Comprehensive NeuroScience Program.

Q Explain that, please.

A Well, the Comprehensive NeuroScience Program exists to direct practice towards best practices. There is also some cost savings, I'm sure, associated with it. And as a result of that, my understanding is the P&T committee sees that as the mechanism to address the prescribing practices of the atypicals. So for that reason, the atypicals are not discussed within the P&T committee because they're discussed elsewhere.

Q But there are no restrictions on any of the atypicals in Alaska; is that right?

A That's right.

Q And the P&T committee would have the authority to restrict access to it if it so chose; is that correct?

A I suppose it could. It's not enacted that on any other drugs.

Q Well, has -- has the P&T committee put any restrictions on antidepressants?

A The antidepressants are on formulary,

yes.
Q Is there open access to all antidepressants?
A There is with "medically necessary" written on the scrip.
Q But the doctor has to do something extra --
A Yes.
Q -- to prescribe certain of the antidepressants?
A Yes.
Q Which of those antidepressants requires extra effort by the doctor, if you know?
A I think maybe Lexapro is one of them. Celexa, I think, is generic now and is on the formulary, as an example.
Q But some of those that have not gone generic may be -- may require extra effort by the doctor?
A Right.
Q But there's no extra effort required by any doctor in Alaska prescribing for a Medicaid patient with regard to any of the atypical antipsychotics including Zyprexa?
A At this point, no.

Q At this point there's no extra effort required?
A That's right.
Q Do you anticipate that there will be restrictions placed by the State?
A I think that that, you know, is a possibility.
Q Has it been discussed at any P&T meetings?
A Not that I'm aware of. I was not present for the most recent P&T committee. I was out of town, and so I don't know for that one.
Q Has Mr. Campana ever discussed with you whether there should be any restrictions on the -- for prescribing Zyprexa?
A No.
Q Are there any political pressures of which you're aware that have caused open access to remain in place for atypical antipsychotics?
A There were some political pressures initially when the P&T committee was developed and the class of those medications came up for review the first time. There was a lot of discussion and a lot of interest on the part of psychiatric providers within the State. And I

think that was probably out of fear or concern that it might become one extreme where we had a very restricted formulary. But since then, you know, I think people have gotten more comfortable with the P&T committee.
Q When you're referring to the doctors across the state, is that what you mean by political pressure?
A Yes.
Q Are you -- how was that political pressure exercised?
A Well, it -- you know, through a number of clinicians showing up at that meeting to testify, by sending letters. There were -- NAMI was there, so there were a lot of human interest groups there as well. So a lot of people were very concerned.
Q And the people who were concerned were expressing their opinions publicly?
A Yes.
Q These were psychiatrists and advocacy groups for the mentally ill?
A Yes.
Q Anyone else?
A Well, pharmaceutical companies, of

course. They're -- they're present always. They fill the room for every meeting.
Q Did they speak at these meetings?
A Yes.
Q And they spoke in favor of open access for all medications?
A Yes.
Q Did any pharmaceutical company ever suggest that its medication ought to be on the formulary but someone else's shouldn't?
A I don't recall.
Q Was there any pressure from within HSS that you're aware of with regard to the atypical antipsychotics?
A No, not that I was made aware of.
Q Were you on the P&T committee when it had to deal with whether Vioxx should remain on the formulary?
A I'm sure I was. I've been on it since its beginning.
Q Do you have any recollection of the discussions of Vioxx?
A Not specific.
Q Do you remember whether it was taken off the formulary?

A I don't recall.
Q But the P&T committee has the power to -- to make it more difficult for doctors to prescribe any medication --
A Yes.
Q -- for Medicaid patients?
That's yes?
A Yes.
Q What is the behavioral pharmaceutical management steering committee?
A The steering committee consists of myself, Dave Campana, the -- I guess you would call him the account manager with CNS. Paul Stuvey is his name. Lex Von Hafften. We had a pharmacist on the committee from Barrow, and I think she's had to drop off of that committee. So it's the small part of -- it's the committee that kind of oversees the implementation of the BPMS here in the State.
Q What is the BPMS?
A Stands for behavioral pharmacy management system. That's the name of the program we gave CNS's program within the State.
Q And we've been discussing a few minutes ago CNS and that's the same thing?

A That's BPMS, yes.
Q What is the mission of BPMS?
A I would say as an alternative to having the atypicals and psychotropic medications on the PDL, this was established which uses evidence-based practice and consensus-based practice to advise physicians or clinicians of best practices on certain clinical indicators that we've chosen, and provide them with some literature that they could use to change practice if they choose to do so.
Q You said the PDL or preferred drug list. Is that synonymous in your mind with the word "formulary" and the way we've been using it today?
A Yes, yes.
THE VIDEOGRAPHER: Pardon me, Mr. Rogoff, we have about three minutes left on this tape, sir.
MR. ROGOFF: Let's go on break now, if that's okay with you.
MR. STEELE: Yes.
THE VIDEOGRAPHER: Here ends Tape No. 1 in today's deposition of Duane Hopson, being taken on 11 December 2007. We're off the

record. The time is approximately 12:46 p.m.
We're off the record.
Stand by.
(Lunch break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 2:11 p.m. The date is December 11, 2007. This is the beginning of Tape No. 2 in the deposition of Duane Hopson, M.D.
(Exhibit 1 marked.)
Q (BY MR. ROGOFF) Dr. Hopson, before our break we talked a little bit about BPMS, and I have a few more questions about that.
I'm going to show you what's been marked as Hopson Exhibit No. 1 and ask you, first, if you can identify that document?
A Yes. This is -- well, the first page is an e-mail from our previous account manager with CNS, Ann Swink was her name, and Paul Stuvey is our current one. And the first is an e-mail from her sending me a copy and Dave Campana a copy of the presentation that was going to be done at our BPMS stakeholders committee.
We talked earlier about the

steering committee. The stakeholders committee happens now -- initially, it was quarterly. Now I think twice a year and we invite concerned stakeholders from around the area, some prescribers, other individuals that have an interest in it. NAMI has come before. And this was a presentation that Carol was doing updating everybody on what the new program was going to look like.
Q Who are the stakeholders?
A Anyone that has an interest in the program, basically, the way it's set up. So it could be a prescriber that prescribes to Medicaid recipients. It could be someone from NAMI. Anyone that has an interest in that program; they're notified by e-mail of this meeting.
Q Are the pharmaceutical companies considered stakeholders?
A They are, and there have been very few of them come, but on occasion there are a couple in attendance.
Q How is the -- how much does the CNS program cost each year?
A I don't know. I'm not on the financial end of it.

Q Do you know who pays for it?
A The initial year was funded by Eli Lilly. The most recent year, I think they've reduced their funding of it, and I'm not sure how much, but I do remember that they reduced their funding and as a result, we've scaled back the program somewhat.
Q What is the purpose of the program?
A The program is to provide evidence-based and -- evidence-based practice of principles to the prescribing of antipsychotic or atypical -- atypicals and certain opiates and mood stabilizers to clinicians that prescribe those medications.
Q Do you know what benefits, if any, Eli Lilly gets out of funding this program?
A None specific, other than playing a role in the whole process in Alaska and keeping their, you know, their name there and being a player in the system.
Q Is there anything that the State of Alaska has given Eli Lilly in return for its funding of this program?
A Nothing that I know.
Q Has the CNS program resulted in cost

savings for the State of Alaska?
A That's my understanding, yes.
Q Could you turn to page 3 of the slides? At the bottom it's ZYP AK 05221.
A Yes.
Q Can you describe what that page demonstrates?
A Yeah. It demonstrates -- the top line with the little boxes is a predicted cost based upon if the cost of Medicaid prescriptions had continued unaltered or unaffected by the implementation of this program. It is a prospective cost analysis, kind of a projection.
And then the two lines below it are -- they show the -- it's kind of blurred -- is it 13 percent savings, totaling -- I can't read it. It's kind of blurred. But of how much we have saved based upon this program.
Q And these are savings to the State for its pharmacy costs just in the behavioral management area; is that right?
A That is my understanding of it, yes.
Q Does the CNS program provide to the BPMS committee information concerning how many people

in the state are being treated with atypical antipsychotics and typical antipsychotics?
A Yes, I believe that's one of the indicators, are the typicals in addition to the atypicals.
Q Does it break down among the atypicals which medications are being used in what quantities?
A No, not the reports that I see.
Q Do you recall what the ratio is of the use of typical antipsychotics to atypical antipsychotics within the State Medicaid program?
A The use of atypicals is significantly higher than the typicals. I don't know a dollar amount.
Q In terms of the number of patients, do you know what the significant difference is?
A Again, weighted towards the typical -- more patients receive the atypicals than the typicals.
Q Has it been pretty much a constant ratio of typicals to atypicals over the time that you've seen the CNS reports?
A I'd have to go back and look at that.
Q Has anyone on the BPMS committee

suggested that the ratio ought to be different?
A No.
Q Has anyone expressed any concerns with the level of prescriptions of atypical antipsychotics in Alaska?
A Not to me.
Q Who sits on this committee?
A The stake -- or the steering committee? David Campana, myself, Lex Von Hafften. Paul Stuvey is the account manager.
Q So there's one representative for the State and that's Mr. Campana?
A Yes.
Q At any meetings has he asked the folks who are running this program whether there's any way to curb the number of atypical antipsychotic prescriptions in the state?
A It's not been directly discussed, no.
Q Has he sought in any way to effect the number of prescriptions being written for atypical antipsychotics?
A No.
(Exhibit 2 marked.)
Q (BY MR. ROGOFF) Dr. Hopson, can you identify what's been marked as Exhibit 2 and

place in front of you?
A Okay. Again, the first page is an e-mail from Ann Swink regarding setting up our steering committee meeting. We meet by phone, and she's presenting the agenda for it.
Q Are the last two pages of that exhibit minutes from a --
A They are.
Q -- steering committee meeting?
A Yes.
Q Have you seen those before?
A We usually review these at the next meeting, so I'm sure at some point I saw this.
Q The minutes you're looking at in Exhibit 2 are from the meeting of January the 12th, 2007; is that right?
A Yes.
Q At the bottom it says, Current BPM program in the middle; is that correct?
A Yes.
Q And the third bullet point is: How to maximize Eli Lilly dollars and go forward; is that correct?
A Yes.
Q Do you recall what the discussion was

that resulted in that being in the minutes?
A Yes. It was -- we had been notified that they were going to reduce the -- Eli Lilly was going to reduce the amount of funding for that program, and we were being made aware of the changes as a result of that. And we had some choices in frequency of mail-outs, of the number of physicians or clinicians we would mail out to. And so there was a discussion, how do we make the best use of the program, as we could do the most with it, I guess, with what we had financially.
Q Did you seek additional funds to make up for the difference from any other pharmaceutical company?
A Not to my knowledge. Again, that's not my end of the situation.
Q Was it your role, however, to send letters to physicians as a result of findings by the CNS group?
A Yes. Based upon -- we would have our meeting and then based upon a review of the spreadsheets, looking at the data from the previous quarter, I would just kind of decide upon a topic to discuss in my letter and that's how I came up with it. Then that would go out

with the mail-out that month.
Q You'd send mailings to psychiatrists across the state?
A Not just psychiatrists. Any prescriber of -- to Medicaid recipients that set one of the clinical indicators that we monitor.
Q What are the clinical indicators that you monitor?
A There's, like, 50 of them. But some examples are two or more antipsychotics for over 90 days, high-dose psychotropic use, low-dose psychotropic use, unfilled prescriptions after 30 days, multiple prescribers of the same agent. Just things that could pose safety issues. That sort of thing.
Q If this -- if your steering committee concluded that doctors were engaged in harmful prescribing practices with regard to their patients, would that be something that you would send a letter about?
A It certainly could be.
Q It's within your power?
A Yes.
Q Has this committee ever sent out a letter to this date to discourage doctors from

using Zyprexa?
A No.
Q Has it ever discussed that?
A Not that I recall.
MR. ROGOFF: Excuse me for one second. Can we take a break?
MR. STEELE: Sure.
MR. ROGOFF: Thank you.
THE VIDEOGRAPHER: Going off the record at approximately 2:25 p.m.
One moment, please.
(Break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 2:28 p.m.
Q (BY MR. ROGOFF) Dr. Hopson, I've tried to give you a clearer copy of Exhibit 1, and ask you to look again at the graph on page ZYP AK 05221, which shows the monthly behavioral pharmacy cost savings that you testified about before.
A Uh-huh.
Q And this document shows a savings, you said before, of 13 percent over -- I think the

period is from August 2004 through August -- September, 2006; is that right?
A Yes.
Q The savings that the CNS folks calculated was 13 percent; is that right?
A That is correct.
Q That's for behavioral or psychiatric medications?
A Yes.
Q And that's as a result of putting in the CNS program that Lilly paid for, correct?
A That's correct.
Q What does that savings amount to in a two-year period in terms of dollars?
A Roughly --
MR. STEELE: Can I ask a question?
MR. ROGOFF: Please.
MR. STEELE: I mean, I assume you're not asking him to vouch for their numbers. What you're just asking him to do is to read the exhibit, right --
MR. ROGOFF: Yes.
MR. STEELE: -- because he has no way of knowing whether it's right or wrong.
MR. ROGOFF: Correct.

A Roughly 6.6 million.
Q (BY MR. ROGOFF) Dollars?
A From the projected. And I do recall during the steering -- during the stakeholders committee meeting, because there were some providers there that did have question about this as to how, you know, how confident the CNS people were that the -- the projection was true. You know, would it actually have ended up costing as much?
Q Did -- I'm sorry.
A Their response was that they felt that they had enough data points to -- but there was a lot of time there -- you know, I do recall there was some discussion about that, that there was a significant amount of time had lapsed there and there might have been some other influences there, but --
Q Okay. Thank you.
MR. ROGOFF: I have no more questions.
MR. STEELE: Allow me to confer with my esteemed associate for a moment and then perhaps there will be no questions. We'll see.
MR. ROGOFF: Take your time.

THE VIDEOGRAPHER: Shall we go off the record?
MR. SNIFFEN: Yes.
THE VIDEOGRAPHER: Going off the record at approximately 2:30 p.m.
One moment, please.
(Break taken.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 2:33 p.m. Here marks the end of today's deposition of Duane Hopson, M.D., being taken on the 11th of December 2007. The total number of tapes used today is two. The time is approximately 2:34 p.m. We're off the record.
Stand by.
(Signature waived.)
(Proceedings concluded at 2:34 p.m.)

CERTIFICATE

I, LESLIE J. KNISLEY, Notary Public for the State of Alaska, and Shorthand Reporter, do hereby certify that the foregoing proceedings were taken before me at the time and place herein set forth; that the witness was sworn to tell the truth; that the proceedings were reported stenographically by me and later transcribed by computer transcription; that the witness waived signature; that the foregoing is a true record of the proceedings taken at that time; and that I am not a party to, nor do I have any interest in, the outcome of the action herein contained.
IN WITNESS WHEREOF, I have hereunto set my hand and affixed my seal this 14th day of December, 2007.

LESLIE J. KNISLEY
Notary Public, State of Alaska
My commission expires: 02/22/11

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,

Plaintiff,

vs.

ELI LILLY AND COMPANY,

Defendant.

Case No. 3AN-06-05630 CI

VIDEOTAPED DEPOSITION OF KARLEEN KAY JACKSON

December 12, 2007
1:35 p.m.

Taken at:
The Offices of Lane Powell, LLC
301 West Northern Lights Boulevard, Suite 301
Anchorage, Alaska

Reported by: Sandra M. Mierop, CRR, CPP, CBC

A-P-P-E-A-R-A-N-C-E-S

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Also Present: STEVE MIEDZWIADOK, VIDEOGRAPHER

I-N-D-E-X

KARLEEN JACKSON DECEMBER 12, 2007

EXAMINATION

PAGE
BY MR. ROGOFF 5

EXHIBITS

NUMBER DESCRIPTION PAGE
1 Complaint 5

PROCEEDINGS

THE VIDEOGRAPHER: One moment, please.

We're on the record. Today is December 12th, 2007, and the time is approximately 1:35 p.m.

This is tape 1 of the videotaped deposition of Karleen Jackson being taken on behalf of the Defendant in the matter of the State of Alaska versus Eli Lilly & Company filed in the Superior Court for the State of Alaska, Third Judicial District at Anchorage; Case No. 3AN-06-05630 Cl.

We're in the offices of Lane Powell, LLC, located at 301 West Northern Lights Boulevard, Suite 301 in Anchorage, Alaska. My name is Steve Miedzwiadok, and I'm the videographer. My business address is 545 East 12th Avenue in Anchorage, Alaska.

The court reporter is Sandra M. Mierop, CRR, with Northern Lights Realtime & Reporting.

Would counsel identify themselves for the record, please?

MR. SNIFFEN: Ed Sniffen, assistant attorney general for the State of Alaska.

MR. STEELE: Joe Steele; I represent the State of Alaska.

MR. JAMIESON: Brewster Jamieson with Lane Powell. I represent Eli Lilly & Company.

MR. ROGOFF: Andrew Rogoff, Pepper Hamilton, and I also represent Eli Lilly & Company.

(Jackson Exhibit 1 marked.)

KARLEEN KAY JACKSON

having been duly sworn, testified as follows:

EXAMINATION

Q. (BY MR. ROGOFF) Good afternoon, Ms. Jackson.

A. Good afternoon.

Q. Could you state your present employment?

A. Certainly. I'm the commissioner with the Department of Health and Social Services for the State of Alaska.

Q. How long have you been the commissioner?

A. Since October of 2005.

Q. What's been put in front of you is Exhibit 1 for your deposition. Can you identify that document?

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A. It would appear to be a lawsuit, the State of Alaska versus Eli Lilly.
Q. Have you ever seen that document before?
A. No, sir, I have not.
Q. And you're sure of that?
A. It's possible that it may have come through my office, but that -- I would not necessarily remember it, and I have not read it in detail.
Q. Have you read it -- do you remember reading it at all?
A. No, I do not.
Q. When did you first find out that the State of Alaska had filed a lawsuit against Eli Lilly & Company?
A. Actually, when I had a conversation with Mr. Sniffen.
Q. How long ago?
A. I spoke with him today.
Q. Is that the first time that you've learned of this lawsuit?
A. No. We had an earlier conversation, oh, a month or so ago.
Q. Was that the first time you've learned of this lawsuit?

A. I -- yes, that is the first time I've learned of the lawsuit.
Q. What are your duties as the commissioner of the Department of Health and Social Services for the State of Alaska?
A. Basically, to serve as a member of the governor's cabinet. To -- to, to the best of my ability, fulfill the mission of the department; promote and protect the health and well-being of Alaskans; to uphold the Constitution of the United States and of the State of Alaska.
Q. How large is the budget for your department?
A. Approximately $2 billion a year.
Q. What are the major components or divisions of your department?
A. We're what's referred to by other state agencies as a super agency. So we include everything from children's services, which is Child Protection, Division of Juvenile Justice, Behavioral Health, which is mental health and substance abuse. Boy, this is going to be a test. Division of Senior and Disability Services; our Alaska Pioneer Home System; Public Health. I'm missing a couple here. Let me think

for a minute. What am I missing.
Q. It's not a memory test?
A. I was not anticipating this one.
Q. That's all right.
How is public health related to behavioral health?
A. Public health deals with the physical health of the general population of the state of Alaska. Behavioral health specifically looks at issues of mental health, substance abuse, and those kind of more behavioral issues.
Q. Is there overlap between those two?
A. There's overlap in terms of when we're looking at the health of an individual. You can't compartmentalize mental, physical, behavioral as neatly as happens in the industries around those three pieces. There's overlap in terms of the divisions trying to work together to promote and protect the health and well-being of Alaskans. In terms of industry, they can sometimes be separate.
Q. What is the biggest component of your Department's budget?
A. The largest amount of money is involved in the Medicaid component, which includes federal

funds as well as general funds.
Q. How big is the Medicaid component?
A. Approximately $1 billion a year.
Q. So that's 50 percent of your budget?
A. Correct.
Q. That includes the funds that the State spends for Medicaid as well as federal funds that are contributed to the State?
A. That's correct.
Q. Do you know what percentage of the one billion for 2007 was federal money?
A. It would be a little more than 50 percent. The federal matching rate, I believe, in '07 was at about 52 percent; and then some of the Medicaid money includes our SCHIP program for children's health, which is a higher rate. It's at a 70-percent match rate.
Q. The State pays 30 percent and the federal government pays 70 percent?
A. For the Denali KidCare component.
Q. How big is the Denali KidCare component?
A. I don't -- I couldn't give you a guess, I'm sorry.
Q. Included in the $1 billion for Medicaid -- well, does that $1 billion for

Medicaid include prescription drugs?
A. The $1 billion would include Medicaid prescription drugs, correct.
Q. Does it include the payment for pharmaceuticals that -- for people who are dually eligible for Medicare and Medicaid?
A. Yes, I believe it does.
Q. Do you know what the State's expenses were in the last fiscal year for pharmaceuticals in the Medicaid program?
A. I'm sorry, I don't. I have wonderful budget people that do, but I don't.
Q. Let's go back a little bit, Ms. Jackson. I just want to talk about -- start with your education and then your work experience. You're a college graduate?
A. Yes, I am.
Q. Where did you go to college?
A. I got my undergraduate degree here in Anchorage at the Alaska Pacific University; and then went through The Fielding Institute and got a master's and a Ph.D. through The Fielding Institute.
Q. Master's and Ph.D. in what?
A. Master's in human development; Ph.D. in human services.

Q. When did you get your college degree?
A. My undergraduate degree from APU was in 1992. My master's in 1996. And the Ph.D. in 1998.
Q. Where's The Fielding Institute?
A. Based out of Santa Barbara, California.
Q. What kind of institution is it?
A. It's basically a distance-education program, and so has several different programs that are distance-learning model.
Q. So you actually completed the program with this institution while you were resident in Alaska?
A. Correct.
Q. Were you working while you were getting your degrees from Fielding?
A. Yes.
Q. Where were you working?
A. At Catholic Social Services.
Q. What were you doing for Catholic Social Services?
A. I did a variety of different jobs starting working in a homeless shelter and eventually working as their executive director.

Q. What years were you with Catholic Social Services?
A. From 1992 to 19- -- no, let me think. Yes, 1992 to 2003.
Q. The first job was working in a shelter?
A. Correct.
Q. Doing what?
A. Working as, basically, a case manager.
Q. And then the last job was executive director?
A. Correct.
Q. What -- what did you write your doctoral thesis on?
A. Homelessness.
Q. What about homelessness?
A. The basic premise of my doctorate degree was around social supports being the key to helping people exit homelessness and stay housed.
Q. That would include not just medical care, but family and -- and other support; is that right?
A. Correct.
Q. What jobs did you have between case manager and executive director, to the extent you can remember?

A. Case management supervisor working in a women and children's shelter here in Anchorage. Then I worked in developing a program that was basically a support model for case management of families with children called Beyond Shelter Program. And a program manager for St. Francis House that did practical supports -- does practical supports, including food, financial assistance, clothing, those kinds of things.
Q. So you actually put your Ph.D. to use?
A. I did.
Q. And did you find that in your work for Catholic Social Services that you were correct in your thesis?
A. Well, the statistical analysis showed that, indeed, without proper supports it's very difficult for people to exit homelessness and to stay housed, and that those do contribute to successful reintegration to the community.
Q. When you were working with Catholic Social Services, did you have a treatment team?
A. We did not have a treatment team in terms of what you would anticipate with a mental health agency. We were not providing mental health services, but case management services.

So it was more a coordination-of-care effort where we would refer people to mental health services, refer people to physical health services, and make sure that they were keeping their appointments and able to do what they needed to move forward.

Q. When you were a case manager or a supervisor, did you deal with any of your clients' mental health providers?

A. Absolutely, yes.

Q. Did you learn about mental health medications?

A. To some degree, yes. But, again, my -- my work was not about being an expert about mental health medication, but who to refer people to.

Q. And were you helping to coordinate care for your clients?

A. Not in the mental health model of coordination of care, but more around the -- the helping folks develop a plan for how they could exit homelessness and stay housed.

Q. Did you learn at all during your eight years -- I'm sorry, 11 years with Catholic Social Services about antipsychotic medications?

A. To some degree. I learned more about the behaviors around psychosis, and when it was appropriate to intervene on behalf of someone or encourage someone to seek help for themselves.

Q. Did you ever talk to any psychiatrists about anti-psychotic medications during that period?

A. No.

Q. Is it correct to call the people that you helped "clients"?

A. Absolutely.

Q. Do you know what kinds of mental health problems your clients had?

A. The full range that you would see in any segment of the population. The homeless population is fairly representative of the rest of the community.

Q. Did you -- did those clients suffer, in part, from schizophrenia and bipolar disorder?

A. Some did, yes.

Q. Did you learn about compliance with medication in that position?

A. My job, again, was not to be the mental health professional, but to refer. So, certainly, I know that -- that compliance with

medication is an issue for folks that need medication to stay stable.

Q. What did you do when your tenure with Catholic Social Services ended in 2003?

A. Then I went to work for the State of Alaska as deputy commissioner for the Department of Health and Social Services.

Q. Why did you do that?

A. Well, I did that because Joel Gilbertson talked me into it, to be perfectly honest. I was looking for a change, and he offered an opportunity that sounded intriguing.

Q. What was the first position that you had with the Department?

A. Deputy commissioner.

Q. For -- that's -- is that the top position after the commissioner?

A. There -- different departments are structured differently, but there are generally more than one deputy commissioner in any particular department; and that's true of the Department of Health and Social Services. So I was one of two deputy commissioners.

Q. What was the role of the other deputy commissioner?

A. The other deputy commissioner primarily had responsibility for Medicaid, for the health-care planning functions, for rate-setting, those kinds of issues.

And my responsibility was more the programmatic side around child protection, public assistance, those kinds of functions.

Q. You were deputy commissioner for -- did it have a title other -- a longer title?

A. No, it did not.

Q. But it was programmatic including child protection and --

A. Public assistance. The behavioral health unit was created under Joel Gilbertson's commissionership, so I had responsibility to work with the directors that were putting that together.

Q. How was behavioral health organized before this reorganization?

A. The substance abuse division was separate from the mental health division, which was combined with the -- the developmental disabilities.

Q. And how did it change?

A. It changed so that the mental health and

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of the Native population?
A. It could.
Q. Through what kinds of facilities?
A. Through residential psychiatric treatment facilities; through, again, community health centers; a cadre of different services.
Q. Do the community health centers operate under grants from the State?
A. Some of them do, yes.
Q. And does the State provide 100 percent of the funding for certain community mental health centers?
A. I don't -- I can't think of any that we provide 100 percent funding for, no.
Q. It varies from center to center?
A. Correct.
Q. On what basis is -- does the funding vary?
A. You know, now you're getting into an area where, again, I'm not the expert. We have an entire section of grants and contracts that deals with those issues.
Q. Do Medicaid dollars flow through the community mental health centers?
A. Medicaid dollars can go to a whole

variety. And, again, this is beyond my knowledge base, so --
Q. Okay. How long were you deputy commissioner under Commissioner Gilbertson?
A. Until he left in October of 2005.
Q. And when did you come in 2003?
A. Correct.
Q. When in 2 --
A. Oh, February of 2003.
Q. And you became commissioner in October of 2005?
A. Correct.
Q. And you've been commissioner continually since then?
A. Correct.
Q. What did you do, if anything, to prepare for today's deposition?
A. I had a conversation this morning with Mr. Sniffen and Mr. Steele.
Q. Any other things that you did?
A. No.
Q. Did you read any documents?
A. No.
Q. Is the sum total of what you know about this lawsuit whatever you've learned from

Mr. Sniffen and Mr. Steele?
A. That would be correct.
Q. Have you spoken to anyone else in the Department of Health and Social Services about the lawsuit?
A. No.
Q. Have you spoken to any physicians in the state of Alaska about the lawsuit?
A. No.
Q. Have you spoken to anyone with any advocacy groups about the lawsuit?
A. No.
Q. And by "advocacy groups," I mean a group like NAMI?
A. No.
Q. Have you spoken with any legislators about the lawsuit?
A. No.
Q. Have you spoken with the governor about the lawsuit?
A. No.
Q. Other than Mr. Sniffen, have you spoken with anyone in the Attorney General's office?
A. No.
Q. Have you gotten any information about

this lawsuit from any other sources besides Mr. Sniffen and Mr. Steele?
A. No.
Q. Do you recall the development of preferred drug lists under Commissioner Gilbertson?
A. Yes, I do.
Q. Were you involved in the creation of those lists?
A. No, I was not.
Q. What is it that you remember about the process?
A. What I remember is that this was a cost-savings effort that was done, along with several other cost-saving efforts, to make sure that we were able to keep a high level of service for clients, but minimize the cost to the Medicaid program.
Q. How was that goal -- how did the Department attempt to accomplish that goal?
A. Through -- the Preferred Drug List Committee was created to take a look at various medications to insure that they were going to be appropriately used for the client and that they could be used effectively.

Committee?
A. No.
Q. Have you ever talked with any psychiatrists about Zyprexa?
A. No.
Q. Have you talked with any other physicians about Zyprexa?
A. No.
Q. Have you talked with any State officials about Zyprexa?
A. No.
Q. Are you aware of any statements by doctors or State officials complaining about misrepresentations by Eli Lilly & Company about Zyprexa?
A. No.
Q. When you were deputy commissioner or now as commissioner of the Department of Health and Social Services for the State of Alaska, did anyone ever suggest to you that the State bring a lawsuit against Eli Lilly & Company?
A. Not -- no, not that I'm aware of.
Q. Did anyone ever discuss with you the bringing -- the possibility of bringing a lawsuit against Eli Lilly & Company?

A. Not that I can remember, no.
Q. Did you ever recommend a lawsuit be brought against Eli Lilly & Company?
A. No.
Q. Do you know of any doctors who've ever complained in the state of Alaska about being misled by any representative of Eli Lilly & Company?
A. Not that I'm aware of.
Q. And do you know of any State officials who have complained about being misrepresented by any member of Eli Lilly & Company?
A. Not that I recall, no.
Q. Either through your work at Catholic Social Services or in the Department of Health and Social Services for the State of Alaska, have you learned about the uses that doctors -- I'm sorry, I'll start all over.
Either in the Department of Health and Social Services or your prior work for Catholic Social Services --
A. Uh-huh.
Q. -- have you learned about why doctors prescribe Zyprexa for their patients?
A. I'm not even familiar with Zyprexa other

than in this context of today's conversation, so, no.
Q. Before you learned of the lawsuit, had you ever heard of Zyprexa?
A. I'm sure I probably heard of it in the media somewhere along the way. Someone probably mentioned the product. But I'm -- I'm not familiar enough to tell you when and how and who and where.
Q. Have you ever met with any representatives of Eli Lilly & Company?
A. Often in my former role as deputy commissioner and my role as commissioner we get lobbyists that come to Juneau or want to meet with the commissioner or the commissioner's representative, so I have met with representatives of the major pharmaceutical companies.
Q. Let's talk about your time as deputy commissioner. Do you recall meeting with Eli Lilly & Company representatives?
A. I am sure that I did, but I can't tell you who, when, or where. I mean, I can tell you where; Juneau. But not specifically who or when. And we get a parade of people through during the

legislative session that are lobbying.
Q. Do you have any idea what you discussed as deputy commissioner with any representatives of Eli Lilly & Company?
A. I wouldn't even frame those as discussions, but more as listening sessions when lobbyists would come through what they would want to do is talk about why their company was a great company, and my role was to listen.
Q. Do you have any recollection of any statements made by anybody from Eli Lilly & Company to you or when you were in the room and when you were deputy commissioner?
A. Would you -- I'm sorry, would you repeat that?
Q. Sure. When you were -- I'll rephrase it, because I'll never be able to repeat it.
When you were deputy commissioner -- let me start all over.
Do you remember, when you were deputy commissioner, of any specific discussions with anybody representing Eli Lilly & Company?
A. No, not specific discussions.
Q. And do you have any memory of generally what you spoke about or listened to from any

representative of Eli Lilly & Company?
A. No.
Q. Same question now for your -- during your tenure as commissioner. Since you've become commissioner for the Department of Health and Social Services for the State of Alaska, can you recall any discussions with any representatives of Eli Lilly & Company?
A. Not specifically, no. I know that they've come through on a regular basis. I'm sure I've met, shaken hands, and that's been the extent of it.
Q. Are you able to say even what they think their issues are with the State?
A. Generally, the issues have to do with funding and wanting to make sure that the State's aware of their products, those kinds of things. We get similar issues from lobbyists with every other constituency group across the state. People want commitments for funding that we're not able to give. So that's why it becomes an exercise in listening.
Q. Do you think you have in your office any documents that Eli Lilly & Company representatives provided to you?

A. It's possible that we have some things on file that they may have left behind, yes.
Q. Nothing that you consult regularly?
A. No.
Q. Do you know the names of any of the people who came through representing Eli Lilly & Company when you were commissioner or deputy commissioner?
A. No, I'm sorry.
Q. Do you recall any discussions about open access?
A. Not specific discussions. The phrase "open access" I'm sure I've heard. But can I tell you exactly what it means? No, I'm afraid I can't.
Q. Have you ever had your deposition taken before?
A. No, other than over the phone with a hearing officer.
Q. In what kind of proceeding?
A. Regarding a procurement issue.
Q. Have you ever testified at a trial?
A. No.
Q. Have you ever been an expert witness?
A. No.

Q. I think we're almost finished. If I take a break to make sure of that, I'll let you know, okay.
A. Thank you.
MR. ROGOFF: Off the record.
THE VIDEOGRAPHER: Going off the record at approximately 2:12 p.m. One moment, please.
(Break.)
THE VIDEOGRAPHER: One moment, please.
We're on the record. The time is approximately 2:14 p.m.
Q. (BY MR. ROGOFF) Commissioner Jackson, I have no more questions. Thank you very much.
THE WITNESS: Thank you.
MR. SNIFFEN: Before we go off the record, though, you have the right to read and sign this deposition, which means you can get a copy of the transcript from the court reporter, review it for accuracy, if you want to check your responses, and then sign it and send it back to her. Or you can waive that if you don't want to be bothered with having to look at the transcript. It's entirely up to you. If you'd

like to, she'll send it directly to you, and you'll send it directly back. It won't go through us or anything. So it's whatever you'd like to do.
THE WITNESS: I don't have the need to do that. Thank you, though.
THE VIDEOGRAPHER: Here ends today's deposition of Karleen Jackson, being taken on December 12th, 2007. The total number of tapes used today is one. The time is approximately 2:15 p.m.
We're off the record. Stand by.
(Deposition adjourned at 2:15 p.m.)
(Signature waived.)

IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF NEW YORK

IN RE: MDL-1596

ZYPREXA PRODUCTS

LIABILITY LITIGATION

THIS DOCUMENT RELATES TO:

ALL CASES

C O N F I D E N T I A L

- - -

November 6, 2006

- - -

Videotape deposition of

GARY TOLLEFSON, M.D.

- - -

GOLKOW LITIGATION TECHNOLOGIES
1600 John F. Kennedy Boulevard
Suite 1210
Philadelphia, Pennsylvania 19103
(877) DEPS-USA

appearance and the reporter will issue the oath.

MR. SUGGS: My name is David Suggs with the firm of Richardson, Patrick, Westbrook & Brickman representing plaintiffs.

MR. ALLEN: Scott Allen for the plaintiffs.

MR. ERTHAL: Greg Erthal, Simmons Cooper, for the third party payers.

MR. DINSMORE: Mark Dinsmore, Barnes & Thornburg, representing Eli Lilly and Company.

MR. LEHNER: George Lehner, Pepper Hamilton, representing Eli Lilly and Company.

MR. ESSIG: Bill Essig from Drinker Biddle & Reath, representing Janssen LP and related defendants.

MR. LEHNER: Is there anybody else on the phone?

- - -

GARY TOLLEFSON, M.D., after having been duly sworn, was examined and testified as follows:

- - -

EXAMINATION

- - -

QUESTIONS BY MR. SUGGS:

Q. Now, would you state your full name for the record, please?

A. Gary Dennis Tollefson.

Q. Okay. And how old are you, sir?

A. I am 54 -- 55 now.

Q. Okay. And are you married?

A. I am.

Q. And do you have children?

A. I do.

Q. Okay. You're presently employed as the Chief Executive Officer of Orexigen Therapeutics, a privately held technology company; is that correct?

A. That is correct.

Q. Am I correct it's in the business of developing drugs for weight loss?

A. That is part of the portfolio.

Q. What is the other, the rest of the portfolio?

A. We're looking at a variety of potential central nervous system indications.

Q. Okay. And am I correct that so far none of the drugs that Orexigen is looking at is, actually, in the market?

A. No, in the sense that the business strategy of Orexigen is actually one that repurposes existing or already marketed CNS molecules; however, it does them in some novel combinations, that is, putting two drugs together.

Q. Okay.

A. And that has formed the basis for composition of matter patents around the novelty of the combination of A plus B, but individually, these are drugs that have been commercialized.

Q. Okay. So your company is looking at taking drugs that are already on the market, are already being used for pharmaceutical purposes, and combining one or more or two or more of those drugs for some novel purpose?

A. That is correct.

Q. Okay. And you were formerly employed as an executive at Eli Lilly, correct?

A. Correct.

Q. Okay. Pardon me. I'm fighting off a bit of a cold today.

Your employment with Lilly and your involvement with the drug Zyprexa is going to be the focus of my questioning but before I get to that I'd like to ask you some questions about your background.

A. Sure.

Q. You are a medical doctor, correct?

A. Yes.

Q. You also hold a Ph.D. in Psychopharmacology; is that correct?

A. Yes.

Q. And I believe you went to

undergraduate graduate, graduate school, and medical school at the University of Minnesota; is that correct?

A. That's correct.

Q. In what years did you receive your respective degrees?

A. Got a bachelor's degree in psychology, summa cum laude, University of Minnesota, 1973. Degree in medicine, University of Minnesota 1976, and a Ph.D. in Psychopharmacology, 1980.

Q. And after finishing medical school I believe you did your internship at St. Paul Ramsey Medical Hospital and your residency in psychiatry at the University of Minnesota Hospitals in Minneapolis; is that correct?

A. Yes, sir.

Q. And when did you complete your residency?

A. Also around 1980, beginning of '80.

Q. And I believe you're board certified in psychiatry; is that

correct?

A. Yes. I passed the American Board of Psychiatry and Neurology exams.

Q. And in what year was that?

A. It's a good question. I'm not sure that I remember. I don't recall.

Q. Would it have been a year or two after you completed your residency, or a couple years?

A. Probably in the very early '80s, I suspect.

Q. Okay. And are you board certified in any specialties other than psychiatry?

A. No, sir.

Q. Okay. Back in 1983, well before you joined Lilly, I believe you published a report in the Journal of Clinical Psychiatry entitled "Nonketotic Hyperglycemia Associated with Loxapine and Amoxapine: Case Report." Do you recall that?

A. I recall the paper.

Q. Okay. We'll have this marked as Tollefson 1.

(Whereupon, Deposition Exhibit(s) 1 duly received, marked and made a part of the record.)

QUESTIONS BY MR. SUGGS:

Q. And I believe this was published in September of 1983; is that correct?

A. It looks like it was published in September of 1983, you are correct.

Q. And you wrote this with another gentleman, a Pharm.D. named Timothy Lesar, correct?

A. Correct.

Q. And at the time you were both at the St. Paul Ramsey Medical Center; is that correct?

A. Yes, sir.

Q. The abstract of the article notes that this was a case of nonketotic hyperglycemic coma associated with the recent introduction of loxapine. We've got some terms in there we need to talk about.

Could you tell me what nonketotic hyperglycemia coma is?

A. Well, coma refers to the level of arousal of an individual so coma is the level below stupor. Probably not easily arousable. Hyperglycemic refers to an abnormally high elevation of blood glucose. Nonketotic refers to the absence, in this case, of ketones, a degradory byproduct of biological reactions, so it's a subtype of hyperglycemic coma.

Q. Okay. And am I correct that anytime anybody goes into a coma that's a pretty severe situation, a pretty serious situation?

A. It's a concerning one.

Q. Okay. And this particular patient had recently been administered a drug called loxapine; is that correct?

A. Correct.

Q. And loxapine is a neuroleptic, correct?

A. It's a first generation antipsychotic, sometimes referred to as a

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individuals doing further research on the product.
Q. Well, weren't you, though, advocating a particular type of clinical management of patients rather than research? Because when you said "blood glucose determinations during initial trials of neuroleptic therapy appear warranted," based on what you told me before that those initial trials were not the initial testing of a drug but, rather, the initial use of a drug by a patient, you were trying to impact patient treatment, correct?
A. I was trying to underscore the importance of evaluating a patient medically, holistically, before starting treatment.
Q. Well, in fact, you would want to, if what you're saying here is correct that you were referring to initial trials with a particular patient, you would want to continue that blood glucose testing for some period of time after the patient got on the drug, correct?

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A. I think that's an individual physician assessment. But, you know, as part of a routine annual physical examination, for example, one often would get a standard laboratory panel, which would include a blood glucose.
Q. Well, this particular patient had a normal blood glucose before she started on the drug, right?
A. Correct.
Q. And it wasn't until after she took the drug that she then had the hyperglycemia and went into a coma, correct?
A. Correct.
Q. So when you're talking here about doing blood glucose determinations, plural, you're referring to sequential testing, more than one blood test, correct?
A. As I said, I think during longitudinal course and care of a patient, you would complete a physical examination on more than one occasion, you would complete assessment of their blood pressure and pulse on more than one occasion. You would get

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laboratories on more than one occasion.
Q. And the purpose of doing these multiple glucose tests on patients that you were advocating back here in 1983 was to be able to see if a patient was getting into trouble and heading toward a situation where they might go into a coma because of hyperglycemia, correct?
A. No, I don't think so.
Q. Well, if you were going to try to prevent this situation of a person going into a coma, you would need to take more than one blood test, correct? You would need to take a blood test before they began on the drug and then one or more blood test afterwards, correct?
A. I would disagree with you.
Q. How would you be able -- what would be the purpose of recommending blood glucose determinations if that wasn't with you were trying to do?
A. This patient did have a blood glucose. That did not prevent the consequence of the hyperosmolar coma. So

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having the blood glucose did not prevent any adverse outcome in this patient.
Q. Then what were you recommending blood glucose determinations during the initial trials of neuroleptic therapy --
A. Because as part of the medical care I think it's important to have a baseline assessment of a patient's health status; for example, this patient may have been diabetic. That would have been picked up on a routine evaluation as part of good baseline medical care. Whether that patient was diabetic or not is relevant to the hypothesis that was in this manuscript.
Q. Okay. Am I correct that you began working for Lilly in 1991?
A. That is correct.
Q. Okay. Can you describe your employment after you completed your medical training in 1980 up until the time you joined Eli Lilly 11 years later in 1991?
A. Well, I joined the faculty of both the University of Minnesota and the St.

Paul Ramsey Medical Center as an assistant professor of psychiatry and initially had responsibility for a discipline that was called Consultation Liaison Psychiatry, as well as doing some outpatient work and research. And I did that for, approximately, five years.

And shortly thereafter, then became the Chairman of that Department of Psychiatry. Continued actively involved with teaching research and outpatient practice. And that was the case up until '91 and joining Lilly.

Q. Okay. And you left Eli Lilly in 2004; is that correct?

A. Yes, sir.

Q. What was the date that you left in 2004?

A. I believe it was April 1st.

Q. And what was your title when you left?

A. Lilly Distinguished Research Fellow and Vice President Lilly Research Laboratories.

Q. Now, at the time you left -- well, during what period of time that you were at Lilly did you have any responsibilities for Zyprexa?

A. I assumed some responsibility for Zyprexa probably towards the end of '94 into the early part of '95, somewhere in that window.

Q. Okay. And then how long did you continue to have any responsibilities for Zyprexa?

A. Up through the late fall of 2000.

Q. And what happened in late fall of 2000?

A. I no longer was in the position of Product Group President of the Neuroscience Division. Went into a different role.

Q. And what was that different role?

A. I was for about a year a Lilly Distinguished Research Fellow I mentioned, which was a consulting role, and

then became Vice President of the medical division overseeing the early phase development for new products for Neuroscience.

Q. Okay. Do you still have any professional dealings with Lilly at this time?

A. I have done occasional consulting for them.

Q. Okay. Are you consulting for them in this litigation?

A. I hadn't considered it a consultation. I'm not sure how that would be defined. I can't answer that.

Q. Well, have you had any meetings with any of Lilly's counsel?

A. I have not.

Q. Okay. What did you do to prepare for this deposition?

A. Maybe for point of clarification, I assumed you meant in-house counsel. I have not met with in-house counsel, I have met with outside legal representation that Lilly has retained.

Q. Okay. And when did you first begin meeting with outside counsel?

A. Probably four to six weeks ago.

Q. Okay. And how many times have you met with them?

A. Probably five times.

Q. And for what total period of time have you met with them if you add all those times together?

A. Maybe 15-20 hours max.

Q. And were you paid for your time?

A. I was not.

Q. You're presently on the Board of Directors of a company called Cortex, aren't you?

A. Yes.

Q. Okay. I saw in an April 7, 2006 SEC filing of Cortex which stated that you elected to take early retirement from Lilly; is that correct?

A. Correct.

Q. Is that -- and that is an

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accurate statement?
A. Yes.
Q. But you're not really retired?
A. Yes, I am.
Q. How many hours a week do you work?
A. I thought you asked me am I retired from Lilly? And I answered, yes, I'm retired from Lilly. Yes.
Q. Okay. But you're not really retired, are you?
A. Perhaps you'd provide me your definition of retirement.
Q. My definition of retirement is that you're not working anymore.
A. I'm retired from Eli Lilly and Company, I am working for, as you established earlier, Orexigen Incorporated as CEO and President.
Q. And is that a full-time job?
A. It is.
Q. Did anyone at Lilly encourage you to leave the company?

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A. No.
Q. Okay. Before you left Lilly, were you aware that the U.S. Department of Justice was investigating allegations that Lilly illegally promoted Zyprexa for off-label uses?
A. I was not.
MR. LEHNER: Object to the form.
Q. Can you list and describe briefly the various positions that you held at Lilly after coming to the company in 1991?
A. From '91 to late '94, I was an executive director, clinical investigation, oversight for Prozac.
In late '94, early '95, became the Product Team Leader for Zyprexa. Continued in that role until probably beginning of '99, at which time I became Product Group President for the Neuroscience Division, and held that through, as we established earlier, the fall of 2000.
Q. And then what were your titles after fall of 2000?

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A. As we previously said, Distinguished Lilly Research Fellow and Vice President Lilly Research Laboratories.
Q. And did you remain in that position until you left in 2004?
A. Yes, I did.
Q. Okay. Between 1994 and 1999, when you were the Product Team Leader for Zyprexa -- well, what did that role as Product Team Leader involve?
A. I was overseeing the global clinical development and global commercial planning for the molecule up to launch and then in the post-approval environment as well.
Q. And so you would have had medical people reporting to you?
A. Yes.
Q. And marketing people?
A. Yes.
Q. Manufacturing?
A. No.
Q. Okay. Did you draw a distinction between marketing and sales?
A. Yes.

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Q. Did sales people report to you?
A. No.
Q. Okay. I'm still trying to get a handle then on what -- who was it that handled the manufacturing and distribution and sales part of Zyprexa, if you were not during that '94 to '99 time frame?
A. Those -- well, they're two different answers, so let me split them apart. Sales is a function that resides within a geography. So you'd have to go to a particular country and establish the country's management structure, and sales would report up through that local geography.
Manufacturing was a global function that existed independently. And manufacturing was coordinated under the head of manufacturing, which was a senior corporate position.
Q. Okay. Who reported to you directly regarding Zyprexa in the '94 to '99 time period?
A. I'm not sure I can recite

everyone who reported to me.
Q. Okay.
A. But it was the senior medical contributors of the team. So it would be, in essence, the chief medical officer or other senior medical people. So Dr. Charles Beasley, Dr. Alan Breier would have been involved in that way.
On the commercialization side the head of global marketing was a gentleman, Mr. James Lancaster.
Chief Operating Officer who oversaw implementation of different projects was for a while a gentleman, Dr. Jeffrey Casher, followed by Dr. Alvin Rampey.
Those would be the key functional homes within the product team.
Q. Okay. When you became Product Group President in 1999, what changed then in terms of what your function was?
A. So I no longer had direct responsibility for the Zyprexa Product Team. That role was taken over by Dr. Breier. The Product Group President role was overseeing

the entire Neuroscience portfolio. That would include marketed products, but also products that were still in the development that had not yet been approved for marketing authorization. It had to do with the oversight of the clinical portfolio, as well as overall global commercial strategy.
Q. Okay. Between '94 and '99, how much of your time did you personally spend dealing with Zyprexa?
A. Probably 110 percent.
Q. Okay. And for the 1999 to 2000 time period, how much of your time did you spend on Zyprexa?
A. That's more difficult. Perhaps, 20 percent, guesstimate.
Q. Okay. From your perspective was there any particular person or group within your organization that was responsible for identifying any safety issues with respect to Zyprexa?
THE WITNESS: At what time frame?
MR. SUGGS: Let's talk about,

let's break it up between '94 and '99 and '99-2000.
A. Well, I think the issues, it never resided in a single individual, it's a collective responsibility and obligation of the entire team.
When I was leading the team, I would say it resided, as far as maybe point people, Dr. Beasley and the chief medical officer that was Dr. Breier.
Q. Okay. And so it would be fair to say that you relied on both Dr. Beasley and Dr. Breier to keep you apprised of any potential safety issues with Zyprexa?
A. Yes.
Q. And Lilly finished conducting the clinical trials that it used to support its NDA application in 1995; is that correct?
A. The NDA was filed in '95. Typically, you know, there were clinical trials that were still ongoing at that time, and they had to be incorporated into the NDA during its review process. So there isn't a

formal end point, per se. This was an ongoing process which continues today to continue to investigate and understand the molecule better.
Q. Were you involved in or did you approve the design of the Phase 3 clinical trials for Zyprexa?
A. Yes.
Q. Were you also involved in any of the Phase 1 trials of Zyprexa?
A. Most of the Phase 1 work was done prior to my taking over the product team. There was some additional work done, it's called clinical pharmacology, that some people would designate Phase 1 that occurred during my period as product team leader. But the early exploration, quote, Phase 1 work was done principally in the latter half of the '80s, perhaps into the early '90s.
Q. Okay. Am I correct that the clinical trials that were done for Zyprexa only measured blood glucose through random blood glucose testing?
A. That was the norm for

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those studies that were part of the NDA, the outpatient studies. And I think there probably were clinpharm studies that might have done additional glucose analyses, but the standard protocol for the ambulatory schizophrenia trials, and I think for that matter, the inpatient studies, was to do serial random glucose.

Q. Okay. You used a term there. I just want to make sure we have the record clear on this. You referred to clinpharm studies. I assume you meant clinical pharmacology studies?

A. That's correct. That's an abbreviation, I apologize.

Q. That's okay. Did all the patients involved in the clinical trials of Zyprexa have the diagnoSIS of schizophrenia or did some of the studies use subjects who were healthy volunteers?

A. Phase 1 early clinical pharmacology studies may involve normal, healthy volunteers. The Phase 2 and beyond investigation of the drug would have involved

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individuals with clinical psychopathology, may have been schizophrenia, bipolar, or other forms of illness.

Q. And did healthy volunteers receive only placebo, only Zyprexa, or were they randomly assigned to either condition when they were used in any studies?

A. I think it depends on the particular study and the methodology in that study protocol.

Q. And what types of people were these healthy volunteers?

MR. LEHNER: Object to the form.

A. I'm not sure that I understand what type of people. These would be normal individuals that would opt to volunteer to participate and contribute to medical education and research.

Q. And how long would they be involved in studies?

A. Again, that's entirely dependent on the protocol of the particular study that had been approved by the local

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institutional review committee.

Q. Just sort of ballpark. Do you have a range? Is it like an hour, days, weeks, months?

A. It could be as short as a day or could extend for several weeks. Again, if we're referring to the Phase 1 studies.

Q. Okay. And, sir, isn't it true that back in the 1990s Lilly used homeless people as test subjects in those studies?

A. I'm not sure of the socioeconomics of subjects. I don't think that Lilly in any way discriminated against anyone that wanted to participate, whether they had a home or whether they didn't.

MR. SUGGS: Let me hand you what I'm going to mark as Tollefson Exhibit 2.

(Whereupon, Deposition Exhibit(s) 2 duly received, marked and made a part of the record.)

MR. SUGGS: For the record

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this is a copy of the Wall Street Journal Online dated November 14, 1996. The article has a title "Lilly's 'Quick Cash' to Habitues of Shelters Vanishes Quickly."

QUESTIONS BY MR. SUGGS:

Q. Do you remember this article coming out in the Wall Street Journal back in 1996?

A. I vaguely recall.

Q. Okay. If you look over to the side it says, "Food and Drug Administration chastised Lilly in 1994 for using alcoholics in a drug study." Do you see that?

A. I'm sorry, I don't.

Q. It's over in the little box to the right. In the small print over there. There's a one beside it?

A. Looks like a footnote.

Q. Yes. Do you recall Food and Drug chastising Lilly in 1994 for using alcoholics in a drug study?

A. I don't recall that.

Most of those interviewed used more mundane techniques to mask their additions. James Hart recalled that he would quit drinking anywhere from three to ten days before a screening and fudge those dates to Lilly staffers. "I might tell them I've been sober for two months when it was only three or four days," says Mr. Heart, who hasn't been able to get into a Lilly study since 1994, when he was diagnosed with hepatitis. Jerry Bienz, a 39-year-old who is sitting outside the Lilly Clinic waiting to be screened, confides this: "The night before you come in, drink a gallon or two of water 'cause that will get your liver count down."

Were you familiar with those techniques of the homeless people to detox before they began involvement in Lilly studies?

MR. LEHNER: Object to the form.

A. First of all, what it tells me is that anybody can lie to anyone else and misrepresent themselves. And I don't have a

crystal ball to always know when someone's lying, but these are, you know, reported folk efforts to obviate someone's alcoholism. I'm not sure that any of these resonate with me as very credible ways of blocking someone's awareness if someone is alcoholic or not.

I can allege to do a number of things that might block the diagnosis of alcoholism but these do not have much face validity when I read them.

Q. Back in 1995, before Lilly submitted its NDA to the FDA, you personally reviewed the data from those studies, did you not?

THE WITNESS: What studies, may I clarify?

MR. SUGGS: The studies that were done in support of Zyprexa's new drug application.

A. I would have reviewed at least summary reports of all the studies.

Q. Okay. And when was it that you first became aware that Zyprexa might be associated with hyperglycemia and diabetes?

MR. LEHNER: Object to the form.

A. I think that probably at the time of the submission there were cases of individuals that may have had hyperglycemia. And, in fact, in some of the longer term data there may have been individuals that had confirmation or new diagnosis of diabetes.

So in the sense of did anyone who was participating in a study have hyperglycemia or diabetes, it would have been during the assembly of the new drug application.

Q. Okay. Would it be fair to say that the focus of the clinical studies that were done in support of the Zyprexa new drug application were dealing with patients who had been diagnosed as schizophrenic?

MR. LEHNER: Objection to form. Asked and answered.

A. The first new drug application was for schizophrenia and it included, principally, individuals with

well-diagnosed schizophrenia. But it also included a smaller subset of individuals with related conditions, sometimes called schizoaffective disorder, schizophreniform disorder. The vast majority were schizophrenic.

Q. Okay. As patients get -- strike that.

As patients with schizophrenia get older, does their schizophrenia by and large tend to get better or worse?

A. Probably be more useful if you could apply an age range. We all are getting older so I'm not sure what "older" implies.

Q. Well, let's say schizophrenics in their mid-30s as compared to schizophrenics in their mid-50s. As a person with schizophrenia ages from their mid-30s to their mid-50s, do they tend to get better or worse in terms of their schizophrenia or is there any such correlation?

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A. I think it's a bit more complicated. First of all, schizophrenia can, actually, begin in later life. So I think it's more a function of the age of onset of the schizophrenia within an individual that's predictive than rather picking any particular decade or portion of life.

Typically, once the disorder begins there's a fairly rapid deterioration, and then a constant state of disability that's called the residual state of the disease.

Q. Okay. If you were to test the efficacy of a treatment for schizophrenia, would you expect to get better results in a younger population, in, say, their 30s, or better results in a population in their 50s?

A. I don't think that I could discriminate over one versus another.

Q. Okay. With respect to side effects of drugs generally, leaving aside Zyprexa, just talking about drugs in general,

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would you expect to see more side effects from pharmaceutical agents in an older population or a younger population?

MR. LEHNER: Object to the form.

A. Again, I think it's just depending on the particular side effect and the drug in question. I don't think I can overgeneralize that.

Q. Okay. With respect to hyperglycemia in particular, would you expect to see a higher incidence of hyperglycemia in an older population or a younger population?

MR. LEHNER: Object to the form.

THE WITNESS: What do you mean by "older"?

MR. SUGGS: Say, again, mid-50s versus mid-30s.

THE WITNESS: Could you restate the question?

MR. SUGGS: Sure.

QUESTIONS BY MR. SUGGS:

Q. Would you expect to see a

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higher incidence of hyperglycemia in a population in their mid-30s or in a population in their mid-50s?

MR. LEHNER: Same objection to the form.

A. I think the risk of developing Type 2 diabetes as a representative of hyperglycemia would be higher in that older patient cohort.

Q. Okay. Because by and large the older you get the more likely you are to develop Type 2 diabetes, correct?

A. No. I think -- my understanding is that probably it peaks in the fifth, the sixth decade, and then probably is level or actually may go down a little bit in the elderly.

(Whereupon, Deposition Exhibit(s) 509, previously marked, was presented to the witness.)

MR. SUGGS: Okay. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 509.

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For the record, this is a 168-page document that has a title on the first page entitled "Section 10: Clinical Studies-Safety." And down at the bottom it has a legend that says "Olanzapine LY170053 CIB, Approved by Lilly, 22 July, 1996."

QUESTIONS BY MR. SUGGS:

Q. Do you recognize this document, sir?

A. No, I don't recognize it, no.

Q. As I noted, the legend at the bottom left-hand corner states "CIB, Approved by Lilly," and then a date. Am I correct that CIB stands for clinical investigation, pardon me, clinical investigator's brochure?

A. It certainly may.

Q. And can you tell us what a clinical investigator's brochure is?

A. It's a summary of the experience with the given drug, typically, a fairly comprehensive review of the experience on efficacy, safety, clinical investigation

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risk/benefit analysis, what they do is they balance the risks with the benefits, correct?
A. Correct.
Q. Okay. And what the FDA was saying here was that the information you were giving was not balanced, correct?
MR. LEHNER: Object to the form.
THE WITNESS: I don't know what you mean by "you." Do you mean me, personally?
MR. SUGGS: Lilly.
A. It would appear that there were some materials being used where that balance wasn't optimal.
Q. Okay. If I could direct your attention to the fourth page, on this page and the following page are some items that the FDA objected to that involved you in particular, correct?
A. Correct.
Q. Okay. And at the top of the page they note that there was an interactive teleconference held on or about October 2,

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1996, by Dr. Gary D. Tollefson, Vice President of Lilly Research Laboratories, correct?
A. Correct.
Q. And who were the other participants on that teleconference?
A. This was a teleconference with a number of different investors or prospective investors in the company. These were not healthcare providers.
Q. And these teleconferences that you had with those investors were ultimately written about in various press articles, correct?
MR. LEHNER: Object to the form.
A. I do not know whether they were or were not. It wouldn't be a matter of routine to do that.
Q. They noted, the FDA noted that there were about six items that they characterized you as being misleading, correct?
MR. LEHNER: Object to the

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form.
A. Not all of them are ascribed to being misleading. Some of them in the eyes of DDMAC were.
Q. Well, at the top of the section on Page 4 it says, "The interactive teleconference held on or about October 2, 1996, by Dr. Gary D. Tollefson, Vice President of Lilly Research Laboratories is misleading in the following particulars," correct?
A. That's what it says.
Q. And then following that there is a listing of six different items, correct?
A. That's correct.
Q. And I'm not going to go through all six of them, I'm not going to take the time to do that, but there are a couple I'd like to discuss. The first is Item 1. It states, "Dr. Tollefson states that the therapeutic effects of Zyprexa are maintained over at least one year. The approved labeling states the effectiveness of the product was only

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established in short-term six week studies. Therefore, for any use over six weeks, the physician should periodically reevaluate the long-term effectiveness of Zyprexa. However, this cautionary information for the indication is never presented in the teleconference." Did I read that correctly?
A. You did.
Q. And am I correct that the labeling that came out when the drug came on the market noted that the effectiveness of the product was only established in short-term six week studies?
A. The approved labeling at the time of launch, that's correct.
Q. And are you aware, sir, now that there are a number of studies which have concluded that Zyprexa is no more effective than first generation antipsychotics that cost about one tenth of what Zyprexa costs?
MR. LEHNER: Object to the form.
A. I would disagree with that vehemently.

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Q. Are you saying there are no such studies?
A. I'm not saying there are no such studies, I'm saying that the burden of clinical research and, I think, the vast majority of clinicians believe that the second generation agents do offer advantages over the first generation counterparts.
Q. And have you been following the literature on Zyprexa in the last year?
A. Yes, sir.
Q. Okay. You agree that there have been several studies that have come out in the last year, particularly within the last six months, government-funded studies, which have concluded that the Zyprexa and other second generation antipsychotics are no more effective than first generation antipsychotics that cost a fraction of what the second generation costs? Is that correct?
MR. LEHNER: Object to the form.
A. No. I think you probably have mischaracterized a couple of things.

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One is Zyprexa is approved for long-term use. Two is that I think most of the studies have demonstrated advantages for the second generation agents, and in particular, Zyprexa, and especially when it comes to issues around a variety of extrapyramidal or behavioral side effects, even the ability to have adherence to stay on treatment longer.
MR. SUGGS: We'll leave that subject for the expert witnesses.
THE WITNESS: Very good.
QUESTIONS BY MR. SUGGS:
Q. If I could direct your attention to Item 6 -- pardon me, Item 5, in that portion of the letter the FDA stated, "When asked a question about weight gain, Dr. Tollefson's response misleadingly turned an adverse event into a therapeutic benefit. He states "So we went back and analyzed our data and saw that the vast majority of weight gain reported initially as an adverse event, in fact, was weight gain occurring in patients who had baseline before starting treatment, had been

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below their ideal body weight. So we really look at this with the majority of patients as being part of a therapeutic recovery rather than an adverse event. And that data, I think, is fairly compelling because it was included in our labeling," emphasis added. And noting that the FDA has put in bold font some of that -- what I just read, correct?
A. Correct.
Q. Okay. Then they went on to say, "The information on weight gain was indeed included in the approved labeling but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading." Did I read that correctly?
A. You read it correct.
Q. And after the FDA came out with this letter stating that you made false and misleading statements, were you punished

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in any way by Lilly after that?
MR. LEHNER: Object to the form.
A. First of all, this was a teleconference, as you pointed out, with investors, not with health care prescribers. So I was not aware that some of the same restrictions that you might use with health care providers in a continuing medical education forum would be applied here. So I was educated that those same standards might well apply in investor conferences, as well. Subsequently, I did hundreds of continuing medical education conferences and never received any kind of critique from the FDA. So was I punished? No. Was I educated regarding investor conferencing? Yes. Did I repeat it? No.
MR. SUGGS: Move to strike the nonresponsive portion of the answer.
QUESTIONS BY MR. SUGGS:
Q. Your salary was not decreased in any way after this point in time, was it?

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A. My salary was not decreased. I would just submit that I, actually, don't fully agree with the critique, though.

MR. SUGGS: Move to strike the nonresponsive portion.

Q. In fact, you were promoted within the company after this event, correct?

A. Years later.

Q. Okay. Now you noted that when Zyprexa first came out in 1996, it was indicated for the treatment of schizophrenia; is that correct?

A. That's correct.

Q. And if schizophrenia was going to be the only treatment -- strike that.

If Zyprexa was only going to be used for the treatment of schizophrenia, it was not going to be a blockbuster drug, was it, sir?

MR. LEHNER: Object to the form.

A. I would not say that. I would not agree with that.

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Q. Okay. There are a limited, relatively limited number of schizophrenics; isn't that correct?

MR. LEHNER: Object to the form.

A. Well, if you had one in your family, I don't think you would feel that way. It's a disease that is highly disabling, it is characterized by more than 1 percent of the population.

So if 1 percent is infrequent, I guess then it's infrequent, but it is one in 100 individuals are afflicted with this very serious disease.

Q. I wasn't in any way trying to minimize the severity of the disease whatsoever. It was my understanding that the incidence of schizophrenia is on the order of one or two per 10,000 people, is that incorrect?

A. I believe that's incorrect.

Q. Okay. Would it be fair to say that Lilly wanted Zyprexa to be a blockbuster drug?

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MR. LEHNER: Object to the form.

A. I don't think that anyone wants a blockbuster drug. I think one wants a drug that's going to benefit patients and addressed unmet medical needs. To what degree it does that it may or may not be economically successful.

Q. Well, you wanted -- it was the strategic intent of Lilly to have Zyprexa be the largest selling psychiatric drug in history; isn't that correct?

A. If the drug lived up to its potential in delivering benefits for patients, it had that possibility. So that was certainly an ambitious goal but one that was achievable.

Q. In fact, it was your intent that Zyprexa would be the largest selling psychiatric drug in history as early as 1997; is that correct?

A. We definitely tried to do clinical studies to demonstrate where Zyprexa was beneficial in the treatment of psychosis,

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and it was then up to prescribers as to whether or not they wanted to use the drug and as to whether it became ultimately an economic success or not.

(Whereupon, Deposition Exhibit(s) 6100, previously marked, was presented to the witness.)

MR. SUGGS: Let me hand you what has been previously marked as Zyprexa MDL Plaintiff's Exhibit 6100.

For the record, this is a sixty-four page document, appears to be a PowerPoint presentation. It has a title on the first page entitled, "Zyprexa Product Team 4 Column Summary." Then below that it has the name Gary D. Tollefson, Vice President Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana.

QUESTIONS BY MR. ALLEN:

Q. Do you recognize this

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document, sir?
A. I do.
Q. And what is it?
A. It's an Annual Strategic Planning Exercise that each and every product at Lilly went through.
Q. Okay. And to whom would this be presented?
A. It was presented to the head of the product group area. At that time it was an individual named John Lechleiter.
Q. Okay. And did you report to John Lechleiter?
A. Let me double check the dates just so I make sure I'm characterizing this right.
Q. I didn't say a date.
A. I didn't see a date on it. Yeah.
Q. I think I can maybe help with that. Page 37.
A. But these were done on an annual basis so.
Q. On Page 37 there's a

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reference year-to-date October '97. And I was wondering if that would help you place this in time.
A. Yeah, it looks like it was probably around, as you said, '97/'98. And it's about the time, I think, that Dr. Lechleiter took over responsibility for the Pharmaceutical Product Group. So I'm thinking that that's probably -- his staff is where this document was presented.
Q. And would he have been present at that meeting, also?
A. Yes, I would imagine.
Q. You know, your comments remind me I should have been more thorough in asking some earlier questions about your position at various points in time. In the 1994 to 1999 time period when you said that you were the --
A. Product Team Leader.
Q. Product Team Leader, who did you report to at that time?
A. In the earlier stage, I, actually, had a co-report. I reported to

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Dr. Douglas Morton, Mr. Robert Postlethwait.
Q. Okay. And for what period of time did that exist?
A. Probably about three, three and-a-half years.
Q. Up until about '97 then?
A. Yes.
Q. And then after that who did you report to?
A. I still had the same reports but I think the organization had changed where Dr. Lechleiter now came in above that layer. So still reporting to Dr. Morton, Mr. Postlethwait, but I believe that Mr. Lechleiter, Dr. Lechleiter, then came in that pharmaceutical products role.
Q. And who did Mr. Lechleiter or Dr. Lechleiter report to?
A. He was reporting to Mr. Taurel.
Q. Who was the CEO?
A. At that time he was transitioning. I'm not sure if he was the Pharmaceutical Operations President or if he

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had become CEO, taking over from Mr. Tobias. It was sometime around in there. I've lost track of the exact dates.
Q. Okay. And when you became the Product Group President in 1999 through 2000, who did you report to?
A. Dr. Lechleiter.
Q. Okay.
A. Reporting to Mr. Taurel.
Q. Okay. So in that '99/2000 time period, you would have been three steps or, actually two steps below the top level of the company, correct?
A. I was a member of the senior management team with -- yeah, that's a fair characterization.
Q. Okay. And then after 2000 -- I know we've got it on the record here but I just can't find my notes -- what was your title after 2000?
A. Lilly Distinguished Research Scholar.
Q. And who did you report to then?

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A. Dr. Watanabe, head of Lilly Research Labs.
Q. And who did he report to?
A. Mr. Taurel.
Q. Okay. So again, would you have been regarded as senior management in that period?
A. Yes.
Q. Okay. Getting back to Exhibit 6100. I believe you said you would have presented this at an annual meeting which would have been attended by Mr. Lechleiter and others, correct?
A. Correct.
Q. And what was the purpose of that annual meeting?
A. This was reviewing a proposed product strategy and summary for the upcoming business year.
Q. Okay. And were other members of the Zyprexa Product Team at that meeting or were you the only one?
A. I don't recall. It wouldn't be out of the question if one or two other

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senior members were there. I don't recall who was in attendance.
Q. Okay. And if, indeed, this was prepared sometime in '97, and we're both assuming that it was; is that correct?
A. Give or take a year, I'm not sure.
Q. Okay. It would have been about a year or so after Zyprexa was on the market, correct?
A. It appears that way.
Q. Okay. And if I could direct your attention to Page 7.
MR. LEHNER: I want to note for the record that several of these pages are not readable, Page 3, 4, at least.
MR. SUGGS: I would agree with you, counsel. Now you see what we have to deal with.
QUESTIONS BY MR. SUGGS:
Q. Directing your attention to Page 7. The title on this page is "Top 15 Neuroleptic Products Worldwide, MAT, Q2/97."

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Is that correct?
A. Correct.
Q. And I believe you said that the term "neuroleptic" is a synonym for antipsychotic, correct?
A. Yeah. It usually refers to the first generation antipsychotics.
Q. Okay. So this is a listing of the top 15 antipsychotic products worldwide, correct?
A. Yes.
Q. Okay. When it says "MATQ297" can you translate that for us?
A. No. No, I don't know for sure. I assume it has something to do with the mean average total, perhaps, for that particular quarter of that year in question. So these are, I think, average figures on utilization.
Q. Okay. And the second quarter of '97 would have been up through June of '97?
A. That would be convention. I'm not sure what this data -- if it represents

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that particular time frame or not.
Q. Okay. But at least as of -- even as of that early time period after Zyprexa came on the market in October of '96, this table would appear to indicate that it had already captured 12 percent of the market; is that correct?
MR. LEHNER: Objection to the form.
A. Of the -- it would appear to be the cash market as opposed to days of therapy, as best I can decipher it.
Q. And why do you think that's the cash market?
A. Well, it says dollar sales split. And so sometimes these graphics are based on the days of therapy prescribed, sometimes they're based on the cost of medication. This appears to be a cost breakout.
Q. Okay. So this may not, actually, reflect how many pills of Zyprexa were being taken relative to other folks but it was a reflection more of the money that

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heel?
A. I think it was a leading adverse event and probably the one of greatest concern for the largest number of people receiving Zyprexa.
Q. Okay. Dr. Breier goes on to state, "The most critical and immediate issue is to keep the focus where it belongs. Superior treatment and outcome -- an arena where we have no peer." Do you see that language, sir?
A. I do.
Q. For the period of time that you were involved with Zyprexa, would it be fair to say that Lilly consistently took the position that Zyprexa had superior efficacy as compared to other antipsychotic drugs?
MR. LEHNER: Object to the form.
A. I think the position was that there was clinical data that we had generated that demonstrated advantages of olanzapine that other drugs had not yet demonstrated and that differentiated it from other existing

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molecules save, perhaps, clozapine or Clozaril, a fairly unique agent.
Q. Okay. So it would be fair to say that Lilly portrayed itself and represented to prescribing physicians that Zyprexa had superior efficacy, correct?
MR. LEHNER: Object to the form. Asked and answered.
A. Not fully correct. I think the statement was based on the data that we had in hand, which was comparative data against, as we talked about earlier, either placebo or active comparators. And based on that data there were clearly select product advantages.
So speaking to those reprints yes. But I'm not aware of any efforts to make broad declarative statements that it was the best and the most effective agent relative to A, B, C and D. So it was driven by studies that had been conducted and data that had been published.
Q. Okay. The next section of Dr. Breier's e-mail is headed up Market

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Research. And he has a number of bullet points below that, correct?
A. Yes.
Q. And about the fifth one down he says, "Outliers are the main concern for physicians; 20-pound increase is viewed as threshold for concern." Do you see that reference?
A. I see the comment there, yes.
Q. Then he goes on to say, "Fact: Two-thirds of olanzapine-treated patients gain less than 20 pounds." Do you see that?
A. Yes.
Q. And the converse of that is about a third gained more than 20 pounds, correct, although that's not stated in his e-mail?
MR. LEHNER: Object to the form.
A. You could infer that from what he said.
Q. Okay. And you can infer that from what you know about the characteristics

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of the drug, correct?
A. I mean, I don't -- I don't recall the data being cut specifically at 20 pounds, so I can't speak to that. But there -- there are probably on the order of 20 to 25 percent of people that would gain on the order of, you know, five or more kilos.
Q. And, in fact, with study HGAJ, the average weight gain for people who used the drug for up to 12 months was 24 pounds, correct?
A. That is true, although extraordinarily few discontinued the treatment, but I believe that's true of their weight gain.
Q. And that's what I was asking.
A. Yes.
Q. Okay. In his next bulleted item says, "Olanzapine is viewed to have more associated weight gain than risperidone, Seroquel and traditional neuroleptics." Did I read that correctly?
A. You read it correctly, yes.
Q. And risperidone and Seroquel

are both second generation atypical antipsychotics, correct?
A. Yes.
Q. And then Dr. Breier goes on to say, "Fact: The order of weight gain among antipsychotics is clozapine greater than olanzapine, greater that Seroquel, greater than risperidone, greater than traditional neuroleptics.
A. That's what he says. I wouldn't agree with it 100 percent but that is what he's stating.
Q. At least according to Dr. Breier, in fact, olanzapine did have more associated weight gain than risperidone, Seroquel, and traditional neuroleptics, correct?
MR. LEHNER: Objection.
Asked and answered.
A. Yes.
Q. Okay. And then dropping down a couple of bullet points he states, "Physicians view EPS as something they can address with dose adjustment but not OWC."

Did I read that correctly?
A. Yes.
Q. And EPS refers to extrapyramidal symptoms; is that correct? Did I pronounce that correctly?
A. Extrapyramidal side effects or symptoms.
Q. And what are those?
A. There are several. These are classic side effects associated with the first generation agents. They range from a drug-induced Parkinsonism, much like if you've seen Michael Fox doing some of his advertisement for the foundation, characterized by involuntary movements, difficulty initiating movement, unstable gait. They can go to what are called acute dystonias, which are muscular contractions that cause significant disfiguration. The neck pulling back, for example, in spasm. Or the most severe and most concerning, which is a long-term irreversible one, tardive dyskinesia, which is a persistent involuntary movement, often of the jaw as if somebody's

chewing gum or sticking their tongue out in public. These are movements of the oral facial muscles that an individual cannot control; they're involuntary and disabling.
Q. Okay. And Dr. Breier was saying in his e-mail that physicians view that cluster of symptoms or syndromes as something that they can address by adjusting the dose of the drug but they didn't think that dose adjustment would work with olanzapine weight gain, correct? At least that's what he's saying?
MR. LEHNER: Object to the form.
A. I think he's inferring that with regards to the EPS. I don't know if he's saying here that physicians do not believe they can address it with dose or he doesn't believe they can be addressed with dose. At that time, my recollection is that there was not a clear relationship between those individuals who did gain large amounts of weight and the dose that they were on.
Q. Okay. Well, in fact, that's

when he goes on to say in his e-mail, "In fact, OWC is not dose dependent," correct?
A. Based on the data at that point as I understood it.
Q. Two questions: No. 1, I want to make sure I understand what Dr. Breier was saying here. Was it your understanding that Dr. Breier was saying that physicians thought that they could, perhaps, deal with EPS by adjusting the dosage but that physicians thought that they could not deal with weight gain by reducing the dosage?
MR. LEHNER: Object to the form.
A. I think that's partially correct. I think the inference here is that physicians believe that with lower doses of these first generation agents that they could lower, either the risk or the severity of EPS, but they may not have perceived that they could do the same thing when it came to associated weight gain.
Q. Okay. And as we noted before, Dr. Breier then goes on to say,

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that would be wrong, wouldn't it?
MR. LEHNER: Object to the form.
A. I think people would offer it as a consideration but it never should be a driver that leads to a decision.
Q. What does that mean in layman's terms, what you just said?
A. It shouldn't be the basis for any decision to include or exclude information.
Q. So now -- because when you said commercial consequences are never a consideration in regard to what will be put in a package insert, you're familiar with the fact that people on the commercial side of the business of Eli Lilly were involved in discussions about what should be put in the label, aren't you?
MR. LEHNER: Objection to the form.
A. I think they provided input into the potential consequences of label changes, considerations.

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Q. So just for a jury, I want a jury to understand your testimony, it's very clear, and you can tell us under oath, that people on the commercial side, the business side of Zyprexa, were involved in discussions at Eli Lilly about what the product label should say; isn't that true?
MR. LEHNER: Objection to the form.
A. I think across all therapeutic areas, a product label as a proposed label at the time of the launch has multiple different parties that contribute. Medical and marketing both contribute ideas to a proposed package label at the time of launch.
Q. My question to you was were people on the business side of Zyprexa, the marketing and sales side of Zyprexa, involved in meetings concerning what the label should say on Zyprexa?
A. And I think as I answered before, no one on the sales side, to my knowledge, ever was involved in those discussions.
Q. How about on the marketing side?
A. There was a marketing representative, the head of marketing, that contributed input in the process as part of the many functions that contributed input.
Q. So now we can tell this jury commercial considerations were taken into account in meetings internally at Lilly concerning what the labeling should say, true?
MR. LEHNER: Objection to form.
A. I said there's commercial input into the consequences of labeling.
Q. And when we say "commercial input" what's that mean for a jury?
A. Marketing.
Q. Thank you. And Jack Jordan, in fact, was engaged, along with you -- let me ask this. Do you know whether or not Jack Jordan, who was the Marketing Director for Zyprexa here in the United States, right?

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A. For a while.
Q. He was personally involved in labeling negotiations with the FDA on what the label on Zyprexa would say, wasn't he?
MR. LEHNER: Objection to form.
A. I'm not aware of that.
Q. Risk. What are risks of a product? Risk generally, not in regard to Zyprexa, what is your definition of risk for a jury?, if you can give us one. If you can't, just tell me "I can't do it."
A. Well --
Q. Is something I said funny?
A. No. I was thinking it was unfortunate you wouldn't give me a second to think about it so I can give you an answer.
Q. Oh, no, let me rephrase my question. What does risk mean in regard to a product? Take as long as you need to think about it.
A. Thank you. Appreciate that. Risk, typically, implies adverse events associated with treatment but

it could also imply the risks associated with not treating or inadequately treating the disease. So risks can come from the disease itself, risk can be related to the drug in question a person's taking, or the risk, in theory, could be coincidental as part of a predisposition the person might have. So risks can be multifaceted. They are multifaceted.

Q. Thank you, sir. Let's talk about -- the facet I'd like to focus on is are risks or adverse events associated with treatment. That's one of the facets you just identified, wasn't it?

A. Yes.

Q. Should a corporation who manufactures and markets a pharmaceutical ever try to minimize those adverse events associated with the drug treatment?

A. I think the company should always say the data as the data is.

Q. My question to you is -- let me just get right to Zyprexa. In identifying, I asked you to give this jury

your definition of risk. You gave us some facets and one of the facets was adverse events associated with treatment, correct?

A. Um-hum. Correct.

Q. Would it be appropriate for Eli Lilly to try to minimize adverse events associated with Zyprexa, yes or no?

MR. LEHNER: Object to the form.

A. I'm not sure what you mean by "minimize."

Q. Is that your best answer to that question?

A. I was just asking if you would like to elaborate what you meant by minimize because I'm not sure what you meant.

Q. Is that your best answer to my question?

A. Again, I think the data is the data. And you share the data, once it's been validated, and you don't maximize or minimize. The data is the data. The data tells the story. That's my view. But I'm not sure what you meant by "minimize."

Q. You just used the term "minimize," how do you use the term "minimize?"

A. If I were using it --

Q. I'm sure you've used it your entire life.

A. Probably something different than maximize. Something less than maximize.

Q. You know what maximize means. I've seen documents with your name on it talking about maximization of profit, right? You know what that means, don't you?

MR. LEHNER: Objection to form.

A. I do.

Q. To maximize something means to make it -- to highlight it, to get it as great as possible. Is that a fair definition of maximize?

A. That is a definition, yes.

Q. Okay. Minimize. What do you mean when you talk about minimizing something, you, Dr. Tollefson?

A. Not overstating it.

Q. So to minimize doesn't mean to downplay it to you? To downplay it, make it less significant?

A. That could be an extreme of it.

Q. Yes. Would it be appropriate for Eli Lilly to minimize, downplay, make less significant, an adverse event associated with Zyprexa?

MR. LEHNER: Objection to the form.

A. I think if someone is unsure whether there is a causal relationship, there is a detriment to either over or maximizing or minimizing in the absence of knowing whether there's causality.

Q. And my question to you --

MR. SUGGS: Objection. Nonresponsive.

Q. My only question to you was should Eli Lilly try to minimize the adverse events associated with Zyprexa?

MR. LEHNER: Objection to the form.

overweight and obese, correct?
A. That is correct.
Q. And you specifically say today on a website of a company that you're CEO of that obesity carries with it the independent risk factor for diabetes, correct?
MR. LEHNER: Asked and answered. It's getting to be harassment.
Q. Correct?
A. Yes.
Q. And you also say that being overweight carries risk for anxiety and depression; is that true?
A. They do co-occur, yes.
Q. Well, your website says being overweight also carries risk for anxiety and depression. Isn't that what it says?
A. That's what it says.
Q. So you're saying if someone becomes overweight they are more likely then to be anxious or depressed, true?
MR. LEHNER: Object as to

form.
A. Some individuals might.
Q. Well, your website of your company specifically says being overweight also carries risk for anxiety and depression, right?
A. As do many other things, as we talked earlier.
Q. Sir, I'm not asking --
MR. ALLEN: Objection, nonresponsive.
QUESTIONS BY MR. ALLEN:
Q. I'm asking about your company's website, Orexigen.
A. I answered very clearly some people yes, not all.
Q. Are you trying to convey to the people who are looking at your current company and are interested in your company's potential products, do you want them to understand that being overweight also carries risk for anxiety or depression?
MR. LEHNER: Harassment. Asked and answered three times.

Q. Sir?
A. Yes.
Q. Thank you, sir.
Now, I guess then if you want to be intellectually honest and consistent, if one becomes overweight or obese from Zyprexa, that can also be an independent risk factor for diabetes, true?
MR. LEHNER: Objection to form.
A. It appears not to be, based on my understanding of the FDA's analysis of this data.
Q. If one were trying to sell Zyprexa to Donna -- do you know who Donna is?
A. I do not.
Q. -- for symptoms of anxiety and depression and that caused them to become overweight, it may lead to more anxiety and depression, true?
MR. LEHNER: Objection as to form.
A. Or it may improve their anxiety and depression as part of their

psychosis. I would say that either outcome is plausible.
Q. Right. So according to you then, Zyprexa being taken by a person for anxiety or depression who then gains weight may become further depressed and further have additional anxiety symptoms, correct?
MR. LEHNER: Objection. Mischaracterizes his testimony.
THE WITNESS: He said it well. I think you mischaracterized what I was saying.
QUESTIONS BY MR. ALLEN:
Q. Who's "he said it well?"
A. Mr. Lehner.
Q. So his coaching of you helped you out?
A. No. I just agreed with him.
Q. Now, sir, all things being equal, would you rather take a product that carried with it more risk or less risk? If you took a drug product in a category would you rather take the product that carries with it additional risk or the product that

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carries less risk?
MR. LEHNER: Objection to form.
A. I'd have to consider the benefit.
Q. Would you want to take the worst offender or the least offender?
MR. LEHNER: Objection to form.
A. It depends on the benefit. It's a risk/benefit equation.
Q. Look at -- it's the last document I want to discuss with you, Zyprexa Product Team 4 Column Summary which is this document Mr. Suggs -- you recall it, right? You recall this document?
A. I do indeed.
Q. This is your PowerPoint presentation to Dr. Lechleiter?
MR. LEHNER: Objection. Mischaracterization.
Q. That was a question: Is this your PowerPoint presentation?
A. This was my team's

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presentation, not mine personally.
Q. Okay, sir, I very much apologize.
This exhibit, which is Zyprexa Product Team 4 Column Summary, Gary D. Tollefson, M.D., Ph.D., Vice President Lilly Research Laboratories at Eli Lilly and Company, this is your report and your team's report to Dr. Lechleiter, right?
A. That's what I said.
Q. If you go to Page 32, please, okay?
A. Yes, sir.
Q. Competitor analysis product profiles. Are you with me?
A. I am.
Q. Are these accurate statements you made to Dr. Lechleiter?
A. I don't know that I made these statements but what are you talking about now? Which ones? The entire grid?
Q. Yeah.
A. Let me take a moment to look at it.

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Q. Sure. I assume you're giving Dr. Lechleiter an accurate report, are you not?
A. I'd like to read something, so let me read it, please, and --
Q. I'm not asking you not to read it. My question --
A. No, you weren't giving me an opportunity.
Q. Yes, sir, I am. I have a question for you when you're through with looking.
A. Thank you.
Q. Have you had a chance to review that document, sir?
A. I have.
Q. Page 32 of exhibit -- my eyes are playing with me. What number's that, Doctor, 8100?
MR. SUGGS: 6100.
THE WITNESS: 06100.
MR. ALLEN: Yes, sir, thank you.
QUESTIONS BY MR. ALLEN:

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Q. My first question to you is when your team makes this report to Dr. Lechleiter, I assume you try to be truthful and accurate, true?
A. Yes.
Q. And I assume the information you give is truthful and accurate, true?
A. That is true.
MR. LEHNER: Objection to form.
Q. And I assume that the products that you have listed as your competitors are, in fact, what you considered as the competitors to Zyprexa, true?
MR. LEHNER: Object as to form.
A. Yes.
Q. And in regard to Seroquel, you see quetiapine/Seroquel, do you see that?
A. Quetiapine, yes.
Q. I'm sorry. Did I mispronounce that, sir?
A. Yes.
Q. Quetiapine and Seroquel, we

A. I think that's fair.
Q. Right. If these are the strengths of Seroquel and Risperdal, and Zyprexa is the worst offender in regard to weight gain, wouldn't it have been better for patients to have used Risperdal and Seroquel other than Zyprexa?
MR. LEHNER: Object to the form.
A. No.
Q. So you believe that it's better to have prescribed the worst offender in the area of weight gain, is that what you're saying?
A. No, that's not what I'm saying.
Q. And you would agree at least with me, if the worst offender caused obesity, Zyprexa, the worst offender caused obesity, that would, in and of itself, be an independent risk factor for diabetes, true?
MR. LEHNER: Asked and answered. Object to the form.
A. No.

MR. ALLEN: Thank you, sir. I'm going to pass you to Mr. Suggs because I know he has one question for you.
MR. SUGGS: Go off the record.
(At this time, the parties went off the record, after which the following proceedings were had:)
THE VIDEOGRAPHER: Back on the record.
MR. SUGGS: Mr. Allen was incorrect, I don't have another question, and so I, therefore, pass the witness.
MR. LEHNER: Okay, let's take a couple minutes' break.
THE VIDEOGRAPHER: Off the record.
(At this time, the parties went off the record, after which the following proceedings were had:)

THE VIDEOGRAPHER: We are back on the record.

- - -

EXAMINATION

- - -

QUESTIONS BY MR. LEHNER:
Q. Good afternoon, Dr. Tollefson.
A. Afternoon.
Q. Let me just ask you a couple questions. You recall your earlier testimony today where you described your background and first your educational experience and then you were a practicing physician for a period of time after that; is that correct?
A. Yes, sir.
Q. And for how long did you practice medicine before you joined Eli Lilly?
A. Approximately, 12 years.
Q. And you were practicing in the field of psychiatry; is that correct?
A. That's correct.

Q. And did you have an opportunity to treat schizophrenic patients during that period of time?
A. Yes, sir.
Q. And could you just generally tell the jury about the disease state of schizophrenia and what characterizes that particular disease based on your experience?
A. Sure. Schizophrenia in general is classified or referred to as the cancer of psychiatry just because of the devastating nature of the disease. It usually begins in the second or third decade of life. It's associated with several different constellations of signs and symptoms, but perhaps the most striking is a loss of touch with reality characterized by delusions or false beliefs, such as delusions of persecution, paranoia.
It's also associated with hallucinations, which are perceptual errors -- hearing voices, seeing threatening images, et cetera -- that aren't really there. But I think more disabling in the

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long term for the disease are what are referred to as so-called deficit or negative symptoms, and these are withdrawal from society, lack of attention to one's personal hygiene, nutrition, or good health.

Typically, they are people that have trouble with cognition. They can't make decisions well, particularly more complicated kinds of decisions. Things that you and I would take for granted, that require problem solving, presents a very significant issue for them. So on standard intellectual testing, they usually perform at least a standard deviation below their peers because of this cognitive impairment.

So there really are psychosis, social deprivation, the cognition, and they carry a fairly high rate of suicidality and depression as a fourth dimension.

Q. And did you have an opportunity to treat schizophrenic patients and people with severe psychosis with second generation antipsychotic drugs when you were

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practicing medicine?

A. Some of the early ones before I joined Eli Lilly and Company I did.

Q. And as well with the first generation antipsychotics?

A. Very much so.

Q. And could you describe again briefly what kind of risk/benefit analysis a doctor, or you engaged in when you were dealing with a schizophrenic patient and particularly when you had either a first generation or then the early generation of the second -- the early versions of the second generation antipsychotics?

MR. SUGGS: Objection to form.

A. In general, the first generation agents were marginally effective at treating delusions and hallucinations and relatively ineffective at treating other aspects of the disease state, the so-called negative symptoms, the cognitive impairment associated with schizophrenia, or for that matter, the concurrent depression or

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depressive mood and suicidal ideation that you see often in these patients. Some people even argue that they may make some of those features worse.

Probably the biggest issue from the risk side were the extrapyramidal side effects that we talked about, which were major deterrents to patients' compliance or adherence to therapy. And this is a chronic disease that often when people discontinue medication prematurely they relapse, and they're rehospitalized, and they have a progressive deterioration.

So in this case it had, I would say, I would summarize the first generation agents as saying they had modest benefit. They did have some fairly striking acute risks that often really led people to discontinue taking them.

Q. What about the second generation of antipsychotics, what experience did you have in again making a risk/benefit decision in prescribing second generation antipsychotics to schizophrenic patients?

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A. So the field designated the second generation agents with a term that's called atypical agents. And the reference to the atypicality was they were not associated with near the incidence or the severity of these extrapyramidal problems that we talked about.

I think what was, perhaps, the most interesting to people at the time when these products were introduced is they had a much broader based pharmacology than the older drugs. And there was at least the suggestion that they were more beneficial, although only incrementally so, but more beneficial on some of the other symptomatic constellations -- the negative symptoms, the social symptoms we were talking about, cognition, mood -- and again less likely to be associated with these acute extrapyramidal events or the prolactin issue that was discussed earlier.

Q. And with respect to some of the specific side effects that have been discussed today, and you've heard some of

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them mentioned, what kind of calculation did you make as a physician, and have you made in consultations with other physicians, in prescribing second generation antipsychotics as to whether or not particular risks may be worth it in light of the potential benefit and, indeed, the disease state that a patient has?

A. So, I think that many people, including myself, would view schizophrenia as amongst the most disabling diseases known to mankind. And that there is mortality associated with schizophrenia through suicide, can approach at least ten percent in the lifetime of the patient. Perhaps, moreover, there's very significant morbidity associated with the disease. Many of these people untreated, or poorly treated and managed, tend to deteriorate over time to a point where they really cannot live on their own, cannot be productive members of society, and really leave themselves at significant risk for a variety of both biological and psychological consequences.

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Q. And one final question. Going back even before the first generation of antipsychotics were developed, what was the standard of care, what kind of treatment was available to people as schizophrenics before first generation antipsychotics became widely available?

A. Well, there really wasn't effective therapy. Probably the most common therapy was, in essence, incarceration or institutionalization. They were taken away from families and society and put into state institutions were they were warehoused. On occasion they might receive electroconvulsive therapy.

Q. Is that shock therapy?

A. Shock therapy. Prior to that there was a form of shock therapy done with even insulin, but it was usually a convulsive-related therapy. Or they would just be medicated with what are called barbiturates, sedatives, merely to sedate and slow them down, but not to treat signs and symptoms of the disease. So I would say it

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was more of a custodial intervention, not a therapeutic one.

MR. LEHNER: Thank you very much, Doctor. That's all I have.

- - -

EXAMINATION

- - -

QUESTIONS BY MR. SUGGS:

Q. I have a few questions. As of 2000, how many drug therapies for treatment of schizophrenia were available besides Zyprexa?

THE WITNESS: In the United States?

MR. ALLEN: Yes.

A. I would only be able to guess, but 12, 16 --

Q. Okay.

A. -- something like that.

Q. Are you familiar with a study that was done by a Dr. Rosenheck that was published in the "New England Journal of Medicine" in, I'm looking for the date. This

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is a document I have on my computer, I don't have a paper copy.

I take it back, it was not published in the "New England Journal of Medicine" it was published in the "Journal of the American Medical Association" in 2003.

A. I think I might know what you're referring to.

Q. I'm referring to a study by Dr. James Rosenheck. You know Dr. Rosenheck, don't you?

A. I do know him, know of him.

Q. He was a consultant for Lilly, was he not?

A. He may have been.

Q. In fact, Lilly helped fund that study, did it not?

A. I believe so.

Q. Okay. And do you recall that the conclusion of his article was, "Olanzapine does not demonstrate advantages compared with haloperidol in combination with prophylactic benztropine in compliance symptoms, extrapyramidal symptoms, or overall

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
-v-	)	CAUSE NO.
	)	3AN-06-5630 CIV
ELI LILLY & COMPANY,	)	
	)	
Defendant.	)	

The videotaped deposition upon oral examination of ROBIN PITTS WOJCIESZEK, a witness produced and sworn before me, Nancy M. Kottenstette, Notary Public in and for the County of Marion, State of Indiana, taken on behalf of the Plaintiff at the offices of Ice Miller, One American Square, Suite 3100, Indianapolis, Indiana, on December 11, 2007, at 9:37 a.m., pursuant to all applicable rules.

CONFIDENTIAL

from Pepper Hamilton.

ROBIN WOJCIESZEK

having been first duly sworn to tell the truth, the whole truth, and nothing but the truth took the stand and testified as follows:

DIRECT EXAMINATION

BY MR. SUGGS:

Q Good morning.

A Good morning.

Q Would you state your full name for the record, please.

A Robin Pitts Wojcieszek.

Q And Pitts is with two Ts?

A P-I-T-T-S. That's correct.

Q And what's your occupation?

A I am a pharmacist, and I work at Eli Lilly & Company in regulatory affairs.

(Plaintiff's Exhibit 1 was marked for identification.)

Q Okay. And we'll mark as the first exhibit a copy of the renotice of the Rule 30(b)(6) deposition. I've handed you what we've marked as Exhibit 1, which is a copy of the renotice of this Rule 30(b)(6) deposition, and it indicates at the bottom of the first page and continuing over to the second page

that Eli Lilly & Company was requested to produce the person or persons most knowledgable regarding a list of eight different items there. That's going to be the focus of -- of my questioning.

However, before we get to that, I'd like to find out some of your background.

MR. KANTRA: I'm sorry, David. Just -- just for record purposes, I wanted to just read in the couple of objections we had to the -- the three different aspects of the notice just so we have that on -- on record, if we could.

MR. SUGGS: Sure.

MR. KANTRA: And get these, if you don't mind, marked as well at this point, if we could.

MR. SUGGS: Is this your written objections that you --

MR. KANTRA: Yeah.

MR. SUGGS: -- served on us?

MR. KANTRA: Exactly. Yeah, so if we could get -- I don't know if we want to mark these as Defendant's 1.

(Defendant's Exhibit 1 was marked for identification.)

MR. KANTRA: Just for the record, I wanted to note in regards to three items in the notice of

Rule 30(b)(6) deposition.

No. 3, which relates to "the changes in Lilly's Zyprexa label as described in Lilly's October 5 'Dear Health Care Provider' letter," there's an objection that we have noted in there, which I want to note.

In No. 4, which references "the clinical studies referred to in Lilly's October 5, 2007, Zyprexa label change," note at the end of paragraph 4 that Lilly is "willing to furnish a designee to discuss the clinical trials supporting the label change referenced in subject No. 4, specifically, what the pooled glucose, lipid, and weight findings from those studies are."

In No. 5, which relates to the statement in Lilly's October 5, 2007, Zyprexa label change that "Increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics," we note our objections as stated in the exhibit, and at the end state that nonethelss, we are furnishing our designee to "discuss Lilly's regulatory department's role in developing the label change referenced in Subject...No. 5."

No. 6 our objections are stated. No. 7, which relates to "any internal communications with Lilly about negotiations with FDA regarding the October 5, 2007 label change," our objections are stated.

And, finally, No. 8, which deals with "any communications with Lilly's sales force regarding the October 5, 2007, label change, "we note our objections, but then say that we are willing to furnish a designee to identify materials for Lilly's sales force that have been approved by Lilly's Medical, Legal, and Regulatory departments."

MR. SUGGS: And with respect to that last one, is Ms. Wojcieszek that designee or you talking about somebody else?

MR. KANTRA: On those as revised, yes, she is the designee on those.

BY MR. SUGGS:

Q Can you tell me a bit about your educational background?

A I have a bachelor's degree in pharmacy from the University of Connecticut.

Q Okay. And what year did you obtain that?

A In 1993.

Q Okay. And do you have any postgraduate work?

A No, I do not.
Q Okay. And when did you begin working for Eli Lilly?
A I began working for Lilly in August of 2002.
Q Okay. Between 1993 when you received your bachelor's degree and -- did you say 2002?
A Correct.
Q What did you do?
A I worked -- after school I worked in retail pharmacy at CVS Pharmacy and then was also -- I worked as a project manager at FDA in the division of neuropharmacological drug products and then transitioned to a job in regulatory affairs at Parke-Davis in 1996 and then went through the merger with Pfizer and then in 2002 came to Lilly. So all my experience has been in regulatory affairs.
Q Okay. How long were you at FDA?
A I was there from '94 to '96.
Q Prior to that time, it was strictly a retail --
A Correct.
Q -- pharmacist?
A Correct.
Q And did you have any job responsibilities regarding Zyprexa?

A Prior to coming to Lilly, no.
Q Well, I didn't think that you would before.
A Yeah. No, no.
MR. KANTRA: Just trying to be responsive.
THE WITNESS: Yeah.
Q Did you have any job responsibilities with Zyprexa after you came to Lilly?
A Yes.
Q Okay. And could you describe those for me?
A I began working on Zyprexa in April of 2003 as a regulatory scientist.
Q And who did you report to?
A Greg Brophy.
Q And who reported to you?
A I don't have anyone reporting to me.
Q How did you come to be designated as the person to testify on behalf of Lilly in this deposition?
A I was responsible for some of the supplemental applications that are referred to in this communication or in this deposition, and I have primary responsibility for interactions with FDA regarding Zyprexa and labeling changes.
Q Okay. And how long have you had that responsibility?
A Since 2003.

Q Okay. So would you have been the person responsible for interacting with FDA regarding the September 2003 label change?
A I was the -- we've had multiple regulatory scientists supporting Zyprexa. So at that time Michele Sharp was a colleague of mine, and both of us worked on Zyprexa. And she took primary responsibility of that labeling change.
Q Does she -- does she still work on Zyprexa?
A She -- she does work on some Zyprexa materials, but she has moved on to another position within regulatory affairs.
Q Do you have any responsibilities for Symbyax?
A Yes, I do.
Q Okay. Are you also the prime person responsible for communicating with FDA regarding Symbyax?
A Yes, I am.
Q Who told you that you were going to be coming here today?
A Oh, my, good old Andy Kantra.
Q And what, if anything, did you do to prepare to testify in this deposition?
MR. KANTRA: Just interposing an objection. You can answer the question as it relates to documents that you may have reviewed on your own,

but I'm instructing you not to answer the question as it relates to documents that I may have shown to you or discussions that we had.
A I reviewed interactions that occurred between Lilly and FDA.
Q And how did you go about doing that?
A I reviewed the deposition and, specifically, the items pointed out here.
Q Excuse me. When you said -- you referred to the deposition --
A This --
Q -- were you referring to Exhibit No. 1?
A That's correct.
Q So you were referring to -- you reviewed the notice of deposition?
A Notice of deposition. Sorry.
Q And -- and then what did you do?
A And reviewed the interactions that we had with FDA.
Q Okay. And would it be fair to say that because of your role at Lilly, you would have been aware of all interactions between Lilly and FDA between, say, March of 2007 to the present with respect to Zyprexa?
A That's correct.
Q Okay. And Symbyax, too?

A So...
Q And am I correct that prior to that time, prior to 2005, in the olanzapine monotherapy studies, Lilly typically used random blood glucose testing as opposed to fasting glucose testing?
A That's correct.
Q Okay. And the fasting glucose testing that was done, fasting glucose technology is -- didn't just come about in 2005. It had been available, clearly, back in the 1990s; correct?
A That's correct.
Q Okay. So the fact that these studies were done in 2005 to 2007 using fasting blood glucose wasn't the result of some new change in medical technology that made that available. It was just that Lilly chose at this point in time in 2005 to do clinical studies using fasting blood glucose as opposed to the random blood glucose testing that they had used for years before; correct?
MR. KANTRA: Objection to the form.
A We -- these particular studies, yes, collected fasting data. Previous studies that we had done, the majority of those studies were, even in consultation with FDA, that the standard was not to collect these particular laboratory analytes in a

fasting manner. And these studies actually many of them began in 2002 in support of new indications, and so, therefore, we felt it would be appropriate to also collect fasting data at the time.
Q When you said many of these studies began in 2002, are you referring to the --
A The five placebo-controlled studies.
Q Okay. So the studies were started in 2002. And when were they completed?
A Again, they're long -- longer term studies with recruitment, etc.
Q Over different spans of time?
A Correct.
Q Okay.
A But it doesn't take just 12 weeks to complete the study so --
Q Okay.
A -- they were done over a span of years.
Q These studies that are being referred to here, though, were studies where people were -- if they were exposed to olanzapine at all in the clinical study, it was only up to 12 weeks, which would be three months; correct?
A Not -- there were, if I recall, two studies in these five placebo-controlled studies that were up

to 12 weeks. Some of them were less than 12 weeks.
Q Ah, okay.
A But they were placebo-controlled.
Q So there were five placebo-controlled studies. Some of them went up to 12 weeks, but some of them -- some of the five studies were -- were less than 12 weeks?
A Were a shorter duration, correct.
Q And when you looked at that data, what you saw was that olanzapine was associated with a greater mean change and fasting glucose levels compared to placebo; correct?
A Correct.
Q Okay. And then you have in parentheses there the data showing for the olanzapine group the mean change was 2.76 milligrams per deciliter versus .17 milligrams per deciliter; correct?
A Correct.
Q Okay. And that increase in the mean was 16 times the change for the olanzapine group as compared to placebo; correct?
A That's correct. But it was -- I'd like to point out it was not statistically significant.
Q It goes on to say that "The difference in mean changes between olanzapine and placebo was greater

in patients with evidence of glucose dysregulation at baseline. (Patients diagnosed with diabetes or mellitus or related adverse events) patients treated with antidiabetic agents. Patients with a baseline random glucose level greater than or equal to 200 milligrams per deciliter and/or a baseline fasting glucose greater than or equal to 126 milligrams per deciliter." Did I read that correctly?
A Yes.
Q So in other words, the folks who were already compromised, in terms of glucose regulation, had more of an effect than folks who had had relatively normal glucose levels of baseline; correct?
A What it means is that that average increase in glucose was greater in those patients.
Q Okay. And it also notes that those patients had a statistically significantly greater mean increase in HBA1C compared to placebo?
A That's correct.
Q And could you tell the jury what HBA1C is?
A It's -- it's a -- it's a hemoglobin A1C, which is another measure used to look at -- it's kind of a surrogate of looking at glucose elevations over time.

adolescents.
Q And that --
A So numerically higher.
Q And that was the average? There were some patients who would have not gained weight or even lost weight, but there would have been others who would have gained much more weight; correct?
A That's the average, right.
Q Okay. And, in fact, we saw from that earlier e-mail of Dr. Beasley's that we looked at that at least some of the clinical studies that Lilly did there were patients who gained 80-plus pounds; correct?
A I don't know the specifics, but if that was the e-mail message, I know it's --
MR. KANTRA: I don't think he was talking about clinical trials.
MR. SUGGS: Yeah, he was. We'll let the -- we'll let the document --
MR. KANTRA: Let the document speak for itself?
MR. SUGGS: Why don't we go off the record for a second.
THE VIDEOGRAPHER: We're off the record at 3:01.

(A discussion was held off the record.)
THE VIDEOGRAPHER: We are back on the record. I'm going off the record to change the tape. This ends Tape No. 3. We're off the record at 3:02. Thank you.
(A brief recess was taken.)
THE VIDEOGRAPHER: We're back on the record. This is the beginning of Tape No. 4 of the deposition of Robin Wojcieszek. It is 3:23.
MR. SUGGS: And I have no further questions at this time. I understand that Lilly's counsel has some questions.
CROSS-EXAMINATION
BY MR. KANTRA:
Q You were shown earlier a document which was marked as Plaintiff's Exhibit No. 2368, which was identified as the ADA consensus statement regarding antipsychotic drugs and obesity and diabetes. Do you remember that?
A Yes.
(Defendant's Exhibit 2 was marked for identification.)
Q And I want to have marked as Defendant's 2. And can you take a look at this document and tell me if you recognize it?

A Yes, I do.
Q And what is it?
A It is a response -- it was a letter to the editor for diabetes care in response to the consensus statement.
Q Okay. And if I could have you turn over to page 2089 of the document.
A Yes.
Q And running from actually the bottom of 2088, the bottom right-hand side, all the way over to the middle of 2089 you see a letter that's signed by Gerard Boehm, Judith Racoosin, Thomas Laughren, and Russell Katz?
A That's correct.
Q And who are those individuals?
A They are the division director, deputy director, safety team leader, and another medical reviewer from the division of neuropharmacological drug products at FDA.
Q And this letter is in response to the ADA consensus statement?
A That's correct.
Q And if I direct your attention to the paragraph right before the -- the names of the people who wrote it, do you see the paragraph that begins in

the middle column with "although"?
A Yes.
Q Can you read that sentence?
A "Although the DNDP" -- which refers to the division -- "agrees with the ADA's recommendations to monitor patients treated with SGAs for evidence of diabetes. We do not believe that the available evidence allows the ranking of dia- -- diabetes risks for these drugs at this time.
"We agree with the ADA that additional studies are needed to clarify many of the issues surrounding the diabetes second generation anticonvulsive risk relationship."
Q When you said anticonvulsive, you mean?
A I mean antipsychotic. Sorry. "Risk relationship. In the meantime DNDP recommends that clinicians remain vigilant in monitoring all patients treated with SGAs to ensure their safe use."
Q And to this day, are you aware of the FDA having reached any sort of conclusions about rankings of second generation antipsychotics with respect to risk of diabetes?
A No.
MR. SUGGS: Objection to the form.
Q You can answer.

A No, I'm not aware.
Q Does Lilly have procedures that govern how data and literature are selected for submission to FDA?
A Yes, we do.
Q And are you familiar with those procedures?
A Yes, I am.
Q And are you aware of any instances in which Lilly with respect to Zyprexa, has failed to comply with its regulatory obligations to submit literature and data to FDA?
A No.
Q I want to show you what has been marked previously as Plaintiff's Exhibit No. 1605. You've got that probably in your...
A Okay.
Q Do you remember that --
A Yes.
Q -- exhibit --
A Yes.
Q -- that related to a data analysis from HGAJ?
A Yes.
Q There were other studies that Lilly submitted in support of its original application for olanzapine to FDA; isn't that right?
A Yeah. Dozens and dozens of studies.

Q And there would have been other analyses that would have looked at the glucose levels as well?
A Yes.
Q Is that right?
A That's correct.
MR. SUGGS: Objection, form, leading.
Q You were asked earlier whether or not this particular data run was submitted to FDA. Are you aware of procedures that govern the type of data that go into FDA when a new drug application is submitted by Lilly?
A Yes.
Q Okay. What do those procedures require with respect to the data that is submitted to FDA?
A When -- when data is submitted and, specifically, around pivotal -- pivotal studies to support the safety and efficacy that data sets that would contain information such as the raw data of laboratory tests would be included in that submission.
Q Okay. And are you aware of any documentation or other evidence that Lilly did not comply with those obligations with respect to its HGAJ submission?
MR. SUGGS: Objection to the form.
A Not aware.

Q You were asked earlier about a document 55 -- Plaintiff's -- previously marked as Plaintiff's Exhibit 5565. If it's easier --
A Yeah, yes.
Q Do you recall that document?
A Yes, I do.
MR. SUGGS: For the record, which e-mail is that?
MR. KANTRA: I'm sorry. So 5565 is an e-mail, which at the top, is sent from Mark Millikan to Jared Kerr on February 22, 2001, but -- but the --
MR. SUGGS: It has the e-mail below that?
Q Right. Exactly. The e-mail that we were discussing earlier was from Charles Beasley to Ralph Dittman on February 22 as well at 2:11 p.m.
And if you -- if you look about midway in that paragraph, there's a reference to the fact that clozapine is associated with a larger -- clozapine, I'm assuming, with a larger increase and a significant increase compared to Haldol.
Are you aware of submissions that -- the FDA submissions that Lilly made in 2001 in which Lilly would have provided clinical trial data to FDA reflecting statistically significant differences between olanzapine and haloperidol with respect to

changes in blood glucose elevations?
MR. SUGGS: Objection to the form.
A Yes, I am aware of a submission that went to FDA in May of 2001 that looked at clinical trial data related to glucose measures with olanzapine versus haloperidol, placebo, and other comparators that were available at the time.
Q Okay. I'm going to show you what was previously marked as Plaintiff's Exhibit 7802, which is titled "Listing of Treatment-Emergent Abnormal Lab Findings in Olanzapine-Treated Patients Placebo-Controlled F1D-MC-HGFU."
A Yes, I have that.
Q Do you have any information as to the context in which this data -- this document was created?
A I don't have any specific context of -- of why this particular document was created. I do know that study HGFU was submitted to FDA.
Q And would -- would the submission of study HGFU to FDA have included information about any elevations in blood glucose levels?
A Yes.
MR. SUGGS: Objection to form.
Q Thank you. And just to be clear, would it have included information about things like nonfasting

glucose levels that were in the high category?
A Yes.
MR. SUGGS: Objection to the form.
Q We talked earlier -- or you were asked earlier about what we were referred to as the New York Times -- the response to the New York Times allegations?
A Yes.
Q And in the context of that, we talked about the submission of discrepant data to -- or potentially discrepant data to FDA. Do you remember that testimony?
A Yes.
Q Can you describe the nature of the data that FDA and Lilly agreed upon would not be submitted as part of the New York Times response?
A As part of the clarification discussion that we had on January 29, we had expressed to FDA that we have numerous documents and trying to get clarification on what specifically above and beyond what we are required to submit under the regulations would be appropriate.
That is when we discussed the scope of specific data analyses would be the appropriate documents. So having some sort of a validity as

far as what type of information we would submit rather than e-mail messages on people commenting on data would be more appropriate to submit actual data analyses.
Q Okay. Let me show you what was previously marked as Plaintiff's Exhibit No. 8666. This is an e-mail from Willard H. Dere. I'm sorry. From Simeon Israel Taylor to Willard H. Dere and a number of CCs, subject being entitled "Potential Contractors."
You were asked earlier about whether or not you were aware that this was one of the documents that was submitted to FDA, and you said you did not believe it was. Can you explain why this e-mail would not have been submitted to FDA as part of the response to the New York Times request?
A This would not have been included because it did not include any specific data analyses, and we were very targeted in our approach of what documents we were reviewing and putting through kind of our decisiontry of what should be submitted in response to FDA.
And since this does not contain any specific data, but rather an individual's comments, this would not have been a document that we felt would

be appropriate to -- to review and make a decision on whether or not it should be submitted.
Q Okay. Let me show you what has been previously marked as Plaintiff's Exhibit No. 6128, which at the top is an e-mail from -- I'm sorry. From Anna Thornton to Ernie Anand. And it's marked as Plaintiff's Exhibit No. 6128.
And I want to focus on the e-mail on page 2, which is actually from Charles M. Beasley to Andrea K. Smith, and in earlier testimony, you were asked about the statement, if you look on the document itself, it says "Some patients, in clinical trials gained as much as 80-plus pounds."
What obligations are there on Lilly to submit data from clinical trials with respect to weight gain findings?
A We have done numerous submissions throughout the years, either in individual study reports, and also have done periodic reviews of pool data. And so if this was something that was coming out of a specific clinical trial, it would have -- have been submitted.
So but without any context of exactly what analysis or the time frame or what studies were included, it's difficult to say exactly where that

information's coming from.
Q And this -- this particular e-mail doesn't reflect -- doesn't relate to a particular study, does it?
MR. SUGGS: Objection.
A No, it does not.
Q But if there were a clinical study in which one or more patients had gained 80 pounds or more than 80 pounds, would that have been information that Lilly would have been obligated to submit to FDA?
A Yes.
Q And is it your understanding that Lilly has abided by its regulatory obligations to submit such data to FDA?
MR. SUGGS: Objection to the form.
A Yes.
Q I want to refer you to Exhibit No. 7 as marked by plaintiff in this deposition, which is the response to the FDA query regarding the New York Times article as Part 3, and, in particular, if I could direct you to the paragraph that begins at the bottom of page 5 and then goes over to the top of page 6.
You were asked earlier about the first sentence in the last paragraph on page 6, which

reflects Lilly's view that "After careful review of the materials being submitted, Lilly believes that the information provided in labeling regarding weight gain and hyperglycemia and diabetes is accurate."

In reaching these conclusions, was Lilly's opinion about the labeling at that point based on anything other than the discrepant data that was submitted with this submission to FDA?

A Right. It was -- it was very specific to the materials included in this particular response, not the totality of all the data.

Q And why did Lilly believe that the data that was being submitted as part of this New York Times response, that limited set of data, did not justify a labeling change?

A It was based on our, again, medical evaluation, looking at each of the materials being submitted, and the overall -- we have a particular standard of what we use as far as data quality, the strength of the data, in order to support a labeling change. And so based on our review and medical opinion of these materials, it was not warranted.

Q Okay. There has been reference earlier today to what's been called the 2003 diabetes label change

that would have been applied to atypical antipsychotics. Do you remember that testimony?

A Yes.

Q And you testified earlier, I believe, that you were aware in September of 2003 that there had been a class-wide labeling change; right?

A Yes.

Q In general terms, what did that labeling change state?

A It stated, again, across the class some confounding issues that certain hyperglycemic-related adverse events had been reported across the class and that, you know, it's a very confounding issue given the background incidence and risk of -- of diabetes in this particular patient population and was recommending, again, very specific monitoring of patients.

Q When something is referred to as a class-wide labeling change, what does that mean?

A In regulatory terms, class labeling means that it is a particular, in this instance, an adverse reactions that is seen across the class, and there's consistency as far what the recommendations would be and does not typically call out one particular product and the data associated with it.

It's across the class, and that was based on FDA's review of data that they requested from all manufacturers of SGAs at the time.

Q Did the 2003 warning contain any conclusions with respect to the issue of causation? Let me frame that differently.

Did the FDA class-wide warning in 2003 reach any conclusions about whether atypical antipsychotics caused diabetes?

A No.

MR. SUGGS: Objection.

A No, it did not.

Q Between the class-wide labeling change in September of 2003 and the Symbyax approvable letter that we discussed earlier today, which I think was Exhibit 2.

A Yes.

Q In any event, the Symbyax approval that we discussed earlier today. Yeah, it is 2.

MR. SUGGS: March 28, 2007.

MR. KANTRA: 2007, yes, exactly.

Q Did Lilly submit any other data to FDA to help in evaluating the adequacy of the diabetes warning?

A Between 2003 to 2007 we had submitted numerous documents ranging from -- ranging from clinical

trial studies that would have included our evaluation of changes in glucose. We submitted also updates of our postmarketing database.

Q What does that mean, postmarketing database?

A So those would be adverse events that were experienced not in clinical trials, but given postmarketing experience. So we also submitted any relevant literature. We were also conducting a study SO14, which is a clamp study. So we were --

Q What is -- what is a clamp study?

A A clamp study is actually looking at changes in glucose measures kind of to -- I'm not an endocrinologist but looking at if there's a specific mechanism associated with a drug versus changes in glucose levels.

Q You mentioned that -- that some of the data that was submitted to FDA between 2003 and 2007 included clinical trial data?

A Correct.

Q And you testified or were asked questions earlier about various categorical changes, changes in patients who might have been normal at baseline and became borderline or patients who were borderline at baseline and became high in terms of their levels.

Are those the sorts of analyses that would have been included in the documents that would have gone in to FDA between 2003 and 2007?
A Yes. They would have been included in specific clinical trial study reports but had also included those in supplemental applications that were submitted for Symbyax in September of 2006 and then to Zyprexa for the adolescent submission in October of 2006.
Q Did -- did those latter two submissions -- did the Symbyax TRD and the Zyprexa adolescent submissions provide more information than just the single clinical trial reports that had gone in?
A It did because we pooled numerous studies together and provided some additional summarization. We actually did special safety topics around glucose, weight, and lipids to put the data also into context.
Q Between September of 2003 when the class labeling change was put into place and the March Symbyax 2007 approvable letter, did Lilly make any decisions about -- let me start that over again.
Between 2003 and March of 2007, did Lilly conclude at any time that the warning on diabetes should be changed?

MR. SUGGS: Objection to the form.
A No. We did not conclude that the warning needed to be changed.
Q And why is that?
A We felt that the -- the conclusions of the data analyses did not warrant a change in what was currently reflected and the labeling was appropriate.
Q You were asked a series of questions earlier about the Symbyax approvable letter, and, in particular, you were asked about statements in the approvable letter that identified what were referred to as deficiencies. Do you remember that?
A Yes.
Q Within the context of an approvable letter, from a regulatory perspective, how do you understand that reference to deficiencies?
MR. SUGGS: Objection to the form.
A From a regulatory perspective, deficiencies, as outlined in approvable letter, are deficiencies in data submissions or analyses that FDA is requesting in order to make a final evaluation on what would be appropriate to include in labeling or are necessary for them to make a final action related to a particular indication.

Q You were asked about the responses to this Symbyax approvable letter. Can you tell me how it is that Lilly -- well, let me ask the question this way -- strike that. Did -- did -- did Lilly work with FDA to identify how best to respond to this Symbyax approvable letter?
A Yes, we did.
Q And what consensus did Lilly reach with FDA regarding how to respond to this letter?
A It started with a series of conversations beginning in early April. We had gotten more clarity around where FDA was as far as some of the submissions that we had made previously related to weight gain, glucose, and lipids, but also what their initial thoughts were around what type of analyses we could provide.
Based on that conversation, we provided a briefing document a few weeks later and then had a conversation in May, a face-to-face meeting, where we discussed and got very detailed feedback of what data analyses and data sets and databases FDA would like us to include.
Q How many databases were involved in the analyses that Lilly conducted in response to the Symbyax approvable letter?

A There were numerous databases, approximately 18 different databases that we committed to -- to include to look at various different subpopulations over varying durations of treatment.
Q And how many analyses was FDA asking be completed with respect to each database?
A Approximately 400 or so analyses per data set given the vast amount of studies that we had available, so quite -- quite a few.
Q We've talked about a number of different submissions that went in to FDA. In particular, I want to ask you about what was the first submission that Lilly sent in to FDA in response to the Symbyax approvable letter that generated new data analyses?
A The first submission was on August 30 of this year.
Q Okay. And what types of analyses did that include?
A It included analyses on our placebo-controlled databases for Zyprexa, both adolescents and adults, in addition to OFC or Symbyax data looking at all three of these parameters of weight, glucose, and lipids, and looking at average mean changes and various different categorical changes.
Q Before the change in October, at the beginning of October, with respect to the labeling on

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hyperglycemia, did Lilly conduct any analyses of active comparator databases?
A Prior to two thousand --
Q No. Before the October 2007 label change, did Lilly conduct any active comparator databases in response to the Symbyax's approvable letter?
A We had -- were in the process, because that was also a database that FDA wanted us to look at, which were head-to-head studies. So we were in the process of summarizing and submitting that data at that time of FDA's letter.
Q We -- we talked earlier -- if I could have you turn to Plaintiff's No. 10, which I believe is the September 17 meeting minutes. And if you can turn to the last two pages of that document, and just for the record, this is the meeting minutes dated September 17, 2007. There's a -- there's a chart that's entitled "Glucose Mean Change Analyses by Comparator"; right?
A Yes.
Q And then "Categorical Glucose Analyses by Comparator"?
A That's correct.
Q Was this the comparator data that was shared with FDA as part of discussions about what the labeling,

with respect to hyperglycemia, should look like?
A Yes, it was.
Q And when -- the reference to comparator means what?
A The reference to comparator are other atypical antipsychotics where we have head-to-head studies of olanzapine versus clozapine, quetiapine, risperidone, and ziprasidone.
Q And as you look across this first chart, this is the glucose mean change. And mean change means what?
A Mean change means the average increase in glucose that was seen in that particular database.
Q And were any of these -- were any of the differences with respect to the -- to a mean change considered to be statistically significant?
A Yes. There were two of those, both looking at clozapine, which was statistically significantly greater than olanzapine. And also the ziprasidone database where olanzapine was statistically significantly greater.
Q And with respect to quetiapine and risperidone, what were the differences there?
A Those were not statistically significant.
Q And with respect to the ziprasidone difference, what was the difference in terms of mean change

between the olanzapine group and the ziprasidone group roughly based on what this chart reflects?
A Roughly, a -- in one study it was a 5 milligram per deciliter change as far as a glucose mean change.
Q Okay. And if you look at the second page, which is the one that's titled "Categorical Glucose Analyses by Comparator," what does -- what does the word categorical mean?
A Categorical means going from one particular -- it's getting late in the day. From a -- for example, a shift of, say, 100 to 120 versus maybe going from 140 to 200. So it's a shift in a range of a particular analyte. This is looking at the percentage of patients who may have gone from one area of normal to a high level of glucose.
Q Okay.
A Their ranges.
Q And were there differences in this comparison among the atypical antipsychotics?
A The one difference that we saw was a statistically significant difference was for clozapine versus olanzapine. The others were not statistically significant.
Q The statement that -- that you were asked about earlier in regards to an apparent continuum, was

this data that was shared with FDA the basis for Lilly's statement regarding the continuum?
A Yes.
Q Was this data, as presented here, the basis for Lilly's statements regarding how monitoring ought to be handled as well?
A Yes, it was.
Q Were there -- within the company, did the analyses of these other second generation antipsychotics lead to any conclusions that there ought to be differences in the monitoring among the atypical antipsychotics with respect to hyperglycemia?
MR. SUGGS: Objection to the form.
A No.
Q You were asked also about an August 28 letter. believe this was Plaintiff's No. 8 earlier.
A Yeah.
Q Did Lilly's October 2007 label change with respect to the hyperglycemia warning implement all of the changes that FDA had initially suggested in August of 2007?
A No, it did not.
Q Why not?
A After we received this -- this letter, we felt it would be appropriate to put our most current data

and conclusions in response to this particular request.
Q When you say the most current data, how did that differ from what was in the FDA's proposal of August 28?
A So, for example, on page 2 the information that they pooled was data that was referenced and included in our TRD submission, which was in a different patient population than olanzapine was not monotherapy olanzapine data. So we felt that it would be more appropriate the olanzapine label to include that specific data.
Q Did FDA agree with that proposal?
A Yes, they did.
Q What other significant differences were there with respect to the hyperglycemia warning between the August 28 FDA suggestion and the ultimate change in October of 2007?
A It was the reflection of the apparent appearance of the continuum with regard to glucose measures.
Q And what was -- what was the -- what was the reason why Lilly changed that language?
A We did not agree or feel it was appropriate to have FDA's statement of olanzapine and clozapine treatments have been associated with a greater

potential to induce hyperglycemia than other atypical antipsychotics.
Q Did Lilly discuss its proposed labeling changes as implemented in October with FDA before implementing those changes?
A Yes, we did.
Q And when did that happen?
A We discussed it with FDA on -- during our meeting on September 17. We also followed up with FDA on September 25 with our -- our proposal and asked for comments, actually, on the "Dear Health Care Professional" letter, which included our proposed label that was implemented on October 5.
Q After you provided that information to FDA in regards to what Lilly believed the label ought to look like, did FDA object to the inclusion of the information that Lilly had proposed?
A No, they did not.
Q Why did Lilly decide to change its label in October of 2007?
A We decided to change our label because we received a request from FDA on August 28. We were in the process of including more information around these particular metabolic issues at the time, and given that we are in a regulated industry and FDA's

requesting us to make labeling changes, we complied with that request.
Q Does the current hyperglycemia warning in Lilly's Zyprexa and Symbyax labels reflect an admission that Zyprexa causes diabetes?
MR. SUGGS: Objection.
A No, it does not.
Q Why not?
A What it is reflecting is that there is -- again, it's very much the additions that were made are -- to the label are around the increases in -- in glucose and that there appears to be this continuum, but no statement with regard to any causation of -- of that to diabetes --
Q And why -- why -- I'm sorry.
A For olanzapine and diabetes, no causation statement.
Q Why isn't there a statement about causation in regards to diabetes as such?
A Because there isn't any data. I think the totality of the data -- it's extremely complicated, and there's -- there isn't distinct data that would draw that conclusion.
MR. KANTRA: Okay. Thank you.
MR. SUGGS: I have no questions.

THE VIDEOGRAPHER: This --
MR. KANTRA: Thanks for your time.
THE WITNESS: All right.
THE VIDEOGRAPHER: This completes Videotape No. 4 in the deposition of Robin Wojcieszek. We're going off the record at 4:04.
MR. KANTRA: We will read and sign.

SOA

v.

ELI LILLY

P's Trial

Depo. Designations

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

Filed in the Trial Courts
STATE OF ALASKA, THIRD DISTRICT
JAN 22 2008
Clerk of the Trial Courts
By _____ Deputy

STATE OF ALASKA, Plaintiff, vs. ELI LILLY AND COMPANY, Defendant.	Case No. 3AN-06-5630 CIV

NOTICE OF FILING PLEADING AND EXHIBITS UNDER SEAL

On this date the State of Alaska is filing a pleading titled "Plaintiff's Trial Deposition Designations." Because one or more exhibits filed with this pleading may be confidential documents under the Court's April 6, 2007 oral ruling, the State of Alaska is submitting this pleading and the attached exhibits under seal.

DATED this 22 day of January, 2008.

See Judge Rindner's 6/13/08 order, page 23 #22 Documents unsealed, Linda 8/11/08

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Exhibit 11	David Noesges	January 8, 2008
Exhibit 12	Susan Kay Schuler	February 1, 2007
Exhibit 13	Michele Sharp, Pharm.D.	November 3, 2006
Exhibit 14	Sidney Taurel	September 19, 2007
Exhibit 15	Gary Tollefson, M.D.	November 11, 2006
Exhibit 16	Denice M. Torres	December 15, 2006
Exhibit 17	Robin Pitts Wojcieszek	December 11, 2007

DATED this 22 day of January, 2008.

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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
	)	Case No. 3AN-06-05630 CI
v.	)	
	)	
ELI LILLY AND COMPANY,	)	
	)	
Defendant.	)	
	)	

PLAINTIFF'S TRIAL DEPOSITION DESIGNATIONS

Pursuant to Alaska Rule of Civil Procedure 26(A)3(B), Plaintiff, the State of Alaska, hereby designates the attached testimony to be presented at the trial in this action for the witnesses listed below. Plaintiff reserves the right to amend it's designations in accordance with the applicable rules as discovery is still continuing.

Exhibit	Desicription	Date of Deposition
Exhibit 1	Michael Bandick	June 9, 2006
Exhibit 2	Charles Beasley, Jr., M.D.	July 26, 2006
Exhibit 3	Charles Beasley, Jr., M.D.	July 27, 2006
Exhibit 4	Alan Breier, M.D.	January 11, 2007
Exhibit 5	Alan Breier, M.D.	January 12, 2007
Exhibit 6	Jerry Clewell, Pharm.D., MBA.,BCPS	October 5, 2006
Exhibit 7	Jack E. Jordan	October 26, 2006
Exhibit 8	Bruce Kinon, M.D.	July 10, 2006
Exhibit 9	Kenneth Kwong, M.D.	October 6, 2006
Exhibit 10	John C. Lechleiter, Ph.D.	March 28, 2007

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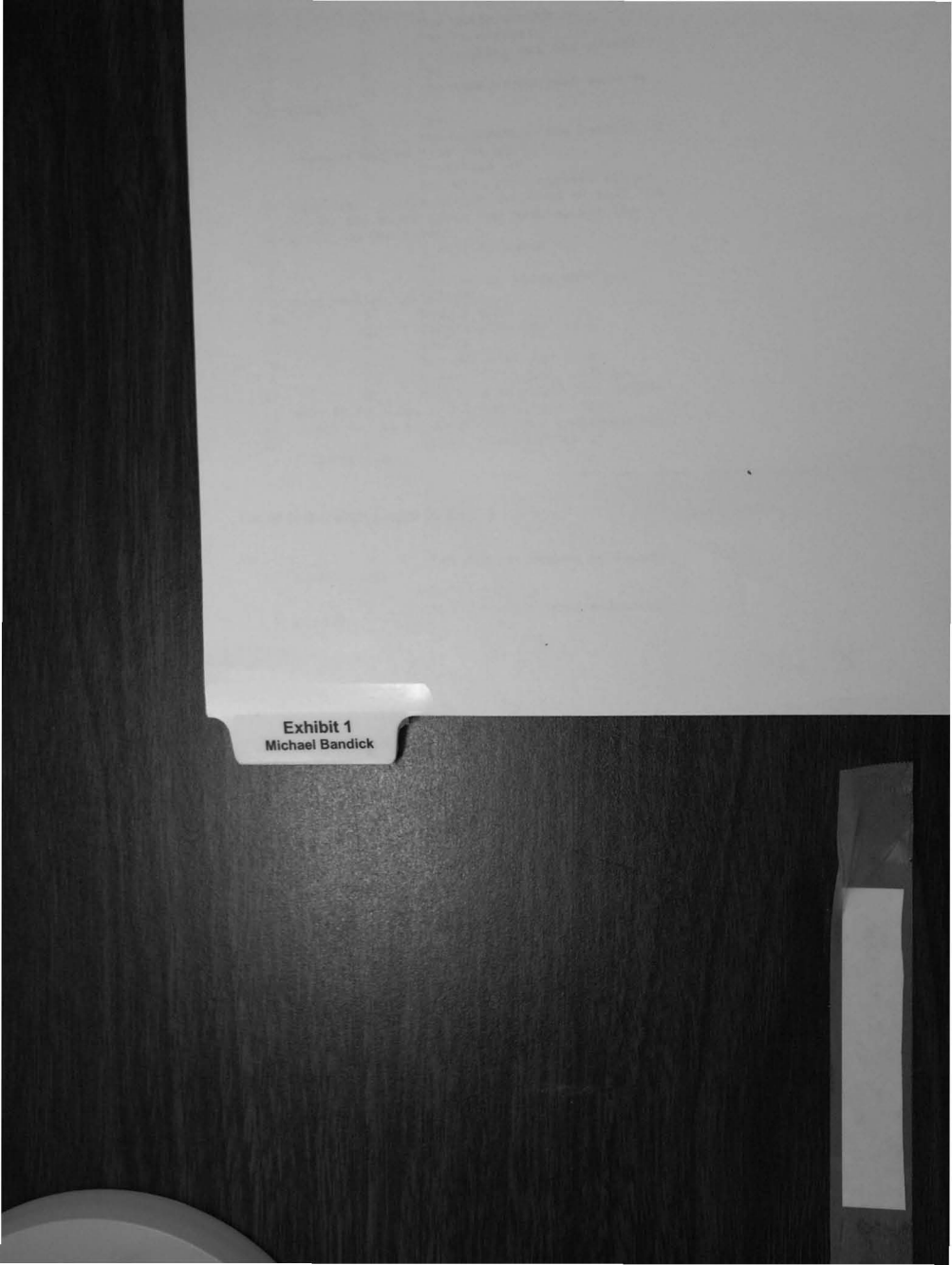
Exhibit 1
Michael Bandick

Michael Bandick (June 9, 2006)

49:12 Q. State your name for the Court
13 and Jury, please, sir.
14 A. My name is Michael Edwin
15 Bandick.
16 Q. Mr. Bandick, my name is Scott
17 Allen, I'm from Houston, Texas. I'm here to
18 take your deposition today, do you understand
19 that?
20 A. I do.
21 Q. You understand the court
22 reporter has sworn you in and you're under
23 oath?
24 A. I do.
50: 1 Q. And your testimony is being
2 taken down by the court reporter and in all
3 likelihood will be played back to a jury in a
4 court at the time of trial?
5 A. I understand.
6 Q. You understand the oath?
7 A. I do.
8 Q. You're required to tell the
9 truth, right?
10 A. That's correct.
11 Q. The whole truth?
12 A. That's correct.
13 Q. And nothing but the truth?
14 A. Yes.
15 Q. You understand your answers
16 matter?
17 A. Yes.
18 Q. You understand the meaning of
19 "answers matter," do you not?
20 A. I believe so.
21 Q. And when your answers matter
22 that means you're always supposed to tell the
23 truth, the whole truth and nothing but the
24 truth, do you agree?
51: 1 A. I will do those.
2 Q. Yes.
3 Did you do those when you
4 were working at Lilly?
5 A. Yes, I did.
6 Q. What's your age, sir?
7 A. I'm 44.
8 Q. And where do you live?
9 A. I live in Carmel, Indiana.
10 Q. And I've only been to Indiana
11 once in my life, and I don't know where
12 Carmel is; is it somewhere near Indianapolis?
13 A. It's a suburb north of
14 Indianapolis.

Michael Bandick (June 9, 2006)

54: 5 Q. When did you become employed
6 by Eli Lilly?
7 A. May of 1991.
8 Q. Directly after your education
9 and MBA at Duke?

A. That's correct.
Q. Can you tell the jury, please, the address, the actual physical address where you worked when you worked for Eli Lilly?
A. My first role was in San Francisco and I was based out of my home.

Michael Bandick (June 9, 2006)

54:17 Q. And that's very good. It's my bad question, I apologize.
(Whereupon, Deposition Exhibit(s) 1 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. I know, and Exhibit No. 1, which is right there in front of you, right?
55: 1 A. Um-hum.
Q. Is that a yes?
A. Yes.
Q. I'll explain the rules in a minute but I want to get this on the record.
Mr. Bandick, I have a document in front of me which has been identified as Bandick Exhibit No. 1 for today's deposition, and it's a marketing -- for lack of a better word, what do you call this document?
A. I would call this document an organization chart.
Q. That's exactly right. And it's an organization chart ZBT Marketing dated August of 2002. ZBT stands for what, sir?
A. Zyprexa Product Team.
Q. And your name is on this document?
A. Yes, it is.
Q. And you're at, your title's described here under Denice Torres, who was director of global marketing, there are four
56: 1 people who reported directly to her; is that correct?
A. Yes, it is.
Q. And you were one of those four individuals?
A. Yes.
Q. And your title is listed Mike Bandick, Director Marketplace Management; is that correct?
A. Yes, it is.
Q. Can you tell the jury, please, what location you worked in when you were Director Marketplace Management for Zyprexa Marketing Team in August of 2002?
A. That was based in Indianapolis.
Q. Okay. And the address was?
A. It was Lilly Corporate Center. I don't recall the zip code.

Q. Here in Indianapolis; is that correct?
A. That's correct.
Q. I've also seen documents, Mr. Bandick, that indicated you were Brand Manager for Zyprexa for Lilly?
A. I did have that role previously.
Q. Okay. And when you left -- what year did you leave Lilly?
A. 2004.
Q. What was your title when you left?
A. Director of Global Marketing for Cymbalta.
Q. For what, sir?
A. Cymbalta is the name of an antidepressant that Lilly launched in 2005.
Q. All right. Can you describe for the jury, please, what you did in your role as Director of Marketplace Management and/or Brand Manager in Zyprexa for Lilly?

Michael Bandick (June 9, 2006)

A. It's two different roles so I can describe them separately for you.
Q. Why don't we do that? What did you do as Brand Manager?
A. In that particular role I was responsible for the marketing of Zyprexa in one segment of its U.S. operations.
Q. What year were you Brand Manager, years?
A. Part of 2000, part of 2001.
Q. Okay, when were you Director of Marketplace Management for Zyprexa?
A. From the latter part of 2001 to the early part of 2004.
Q. Okay. We're going to go back into this in some detail but I just want the jury, initially, to have some idea who you were.

You said as Brand Manager for 2000/2001, your answer was something like: I handled one segment of Zyprexa's market. Right?

A. That's correct.
Q. What segment did you handle?
A. The primary care segment.
Q. That's the PCP segment?
A. It was also called PCP.
Q. I've seen documents with that name on it. Okay.

And then you took that role as Brand Manager for the PCP segment of the Zyprexa market in 2000; is that correct?

A. Yes, it is.
Q. What month of 2000 did you assume that role?
A. I believe it was July.

Q. Who had that role before you?
A. It was a new role.
Q. Right. So you were the initial brand manager for PCP, primary care physician marketing, for Zyprexa, and you took that role in July of 2000, correct?
A. Yes.

Michael Bandick (June 9, 2006)

60: 5 Now, who created that role of
6 Brand Manager?
7 A. That decision was made before
8 I came on board. I believe it was a
9 collaborative decision between members of the
10 brand team and other leadership within
11 Lilly's U.S. affiliate.

Michael Bandick (June 9, 2006)

60:15 Who informed you you were
16 going to be Brand Manager for the PCP
17 marketing of Zyprexa in 2000?
18 A. I was initially contacted by
19 my supervisor at the time who was a sales
20 director, Dave Noesges.
21 Q. Can you spell that, please?
22 A. Dave's last name is
23 N-O-E-S-G-E-S.
24 Q. He was your immediate
61: 1 supervisor?
2 A. That's correct.
3 Q. He was in sales?
4 A. That's correct.
5 Q. And his title was, sir?
6 A. Sales director for -- it was
7 a regional role. I don't know if it was the
8 midwest region or the central region, but
9 something like that.
10 Q. Okay. In regard to the
11 marketing role for the PCP marketing of
12 Zyprexa in July of 2000 as Brand Manager was
13 there anybody higher than you in marketing?
14 A. Yes.
15 Q. Who would that be?
16 A. My supervisor in that role
17 was Jack Jordan, and he reported into a
18 broader marketing organization. I believe
19 his supervisor at the time, at the time was
20 Glyn Parkin, G-L-Y-N, P-A-R-K-I-N, and Glen
21 reported into the head of what would be our
22 US affiliate commercial operations and I
23 believe that was Bill Robinson.
24 Q. As Brand Manager for PCP
62: 1 marketing of Zyprexa, the role you held from
2 July of 2000 until late 2001; is that
3 correct?
4 A. September of 2001.
5 Q. From July of 2000 till

September of 2001, you reported to Jack Jordan. And what was Mr. Jordan's title?
A. I believe his title was Brand Team Leader or Brand Leader.
Q. And in September of 2001, were you promoted?
A. Yes, I was.
Q. So for your activities, whatever they were, we're going to talk about them, but whatever you did from July of 2000 until September of 2001 impressed your superiors so much that you got a promotion; is that fair?
A. At the time I had been with Lilly for ten years and had been in four different manager level roles and I assume that the promotion was based on my performance in all those roles.
Q. Okay. That's good.
So including all of your work that you had done at Eli Lilly, including the work you had done as Brand Manager for PCP marketing in Zyprexa from July of 2000 until September of 2001, you received a promotion?
A. Yes, that's correct.
Q. Okay. Tell the jury the promotion that you received and what title that you took over in September of 2001 in relation to Zyprexa?
A. In September of 2001, I was named the Marketing Director for duloxetine, which is the molecule that later became Cymbalta. Duloxetine is spelled D-U-L-O-X-E-T-I-N-E.
MR. FAHEY: How do you spell

Michael Bandick (June 9, 2006)

Q. Did your duties and responsibilities in regard to Zyprexa cease in September of 2001?
A. They did.
Q. Tell me the brand name of that drug that you took over in September of 2001 again? Cymbalta?
A. C-Y-M-B-A-L-T-A.
Q. Did I pronounce it right, Cymbalta?
A. You did.
Q. Okay. Was Cymbalta launched in September of 2001 or was it a product in the pipeline?
A. It was a product in the pipeline.

Michael Bandick (June 9, 2006)

Q. Okay. September of 2001, you start working on Cymbalta. How long did you

do that?
A. Two months.
Q. Two months.
October/November, right?
A. That's correct.
Q. And in November of 2001 you got a new title; is that right?
A. That's correct.
Q. Tell the jury, please, what that title was?
A. Director of Marketplace Management for the Zyprexa Product Team.
Q. Exhibit No. 1?
A. That was the organization I joined, yes.
Q. Yes. And that's the title you held, which is reflected in Exhibit No. 1?
66: 1 A. That's correct.
Q. Was that a promotion?
A. That was considered a lateral move from the duloxetine role.
Q. Okay. How long did you hold the title Director Marketplace Management Zyprexa Product Team?
A. From late 2001 to early 2005.
Q. When you say "late," I think you agreed with me that was November of 2001 when you became Director Marketplace Management for the Zyprexa Product Team; isn't that right?
A. It was either November or December, I don't recall the exact date.
Q. And you held that role until January of 2004?
A. I believe that's correct, January or February of 2004.
Q. And what happened then?

Michael Bandick (June 9, 2006)

66:23 Q. What was your next role at Eli Lilly in January of 2004?

Michael Bandick (June 9, 2006)

67: 1 A. Global Marketing Director for Cymbalta.

Michael Bandick (June 9, 2006)

67:17 Q. Okay. So in January of 2004 you became Global, meaning worldwide, Marketing Director for Cymbalta; is that correct?

67:23 A. It was called the Global
24 Marketing Director of Cymbalta, if you wish
68: 1 to characterize it as worldwide, I have no
2 issue with that.
3 Q. How long did you hold that
4 position?
5 A. For about three months.
6 Q. Was that a promotion from
7 your role as Director Marketplace Management
8 Zyprexa Product Team that you had held from
9 November of 2001 until January of 2004?
10 A. No, it was not.
11 Q. Was it a demotion?
12 A. No, it was not.
13 Q. What was it?
14 A. A lateral move. Same level.
15 Q. What prompted your move from
16 Director Marketplace Management Zyprexa
17 Product Team in January of 2004 into your
18 role as Global Marketing Director for
19 Cymbalta?
20 A. It was offered to me and I
21 was interested in it.
22 Q. Who offered it to you?
23 A. Dan Hasler.
24 Q. And who's Dan Hasler?
69: 1 A. Dan Hasler is, I believe,
2 Vice-president of Global Marketing for Lilly.
3 Q. And where is the Global
4 Marketing Department for Eli Lilly located?
5 A. Indianapolis.
6 Q. So the Global Marketing
7 Department for Lilly and all of its drug
8 products is located right here in
9 Indianapolis, Indiana, of the United States
10 of America; is that right?
11 A. That's correct.
12 Q. How many countries around the
13 world does Lilly market its drug products in?
14 A. I don't know the exact
15 number.
16 Q. Well, can you give the jury,
17 please, for the jury, an estimation?
18 A. I would estimate that it's
19 more than 50 and less than a hundred.
20 Q. Okay. Somewhere between 50
21 and a hundred; is that right?
22 A. Yes.
23 Q. That's your best estimate as
24 somebody that was employed at Eli Lilly from
70: 1 1991 to 2004 in the marketing department,
2 your best estimate is somewhere between 50
3 and a hundred countries is where they market
4 drugs; is that correct?

Michael Bandick (June 9, 2006)

70: 5 A. That's correct.

Michael Bandick (June 9, 2006)

70:21 Q. So Eli Lilly is a worldwide
22 pharmaceutical manufacturer and distributor
23 of medicines and drugs; is that true?
24 A. Yes, it is.
71: 1 Q. And the marketing department
2 for Eli Lilly's worldwide operations is
3 located here, is located here in
4 Indianapolis, Indiana?
5 A. Yes, it is.

Michael Bandick (June 9, 2006)

79: 6 During the time that you were involved in any
7 way, in whatever role, in Zyprexa marketing
8 what are the names of the teams, groups, or
9 committees that you were a member of?
10 A. There are a lot of different
11 groups that would come together for different
12 reasons and even the ones that you just named
13 were for very different purposes, so I may
14 not be able to give you every last one that I
15 may have had some involvement in.
16 Primarily, I was part of the
17 Zyprexa Product Team. I was also part of the
18 Lilly U.S. Brand Team. I also had a role
19 within U.S. Market Research. Those were the
20 primary ones.
21 Q. Give me the secondary ones.
22 A. I, probably, was a member of
23 the Limitless Team. That was more for a,
24 that wasn't a specific project or
80: 1 designation, that was part of the U.S. Brand
2 Team.
3 I was also with a part of a
4 cross-functional group called the Zyprexa
5 Issues Management Team.
6 Q. Any more?
7 A. Not that I can think of.
8 Q. How about the Medical
9 Marketing Team? When I looked at a document
10 it looked like a cross-functional team of
11 medical and marketing. Do you remember that
12 one?
13 A. When I was in the market
14 research role I believe there was a group
15 called that. That wasn't something that had
16 an official designation, that was more just a
17 description of some of the different people
18 who might be invited to a discussion, but,
19 yes, that does ring a bell.
20 Q. That rings a bell?
21 A. It does.
22 Q. What about the HGFI Core
23 Team?
24 A. I was not part of that.
81: 1 Q. Tell the jury what that is?
2 A. HGFI refers to a particular
3 clinical trial. All of Zyprexa's clinical

trials would start with the letters HG. I don't recall, specifically, which trial that was. I was not part of that team.
Q. So the clinical trials on Zyprexa would all start with the designation HG; is that correct?
A. Yes, it is.

Michael Bandick (June 9, 2006)

82: 7 Q. Next question: Did you assist in writing documents that were prepared for the sales force to give to physicians about Zyprexa?
A. Sometimes.
Q. Okay. Do you remember any document in particular, or are there too many to remember, that you wrote in marketing that would be provided to the sales force that you knew would end up in doctors' hands?
MR. FAHEY: Objection to

Michael Bandick (June 9, 2006)

82:19 A. As I mentioned, I was involved in that activity. There are too many for me to recall any single one for you.
Q. Right. And that's a fair answer. You wrote a lot and lot of documents that you knew would be used by the Zyprexa
83: 1 marketing department and/or sales force that would be given to doctors concerning Zyprexa.
MR. FAHEY: Objection to

Michael Bandick (June 9, 2006)

83: 5 A. I was involved in the writing and production of several pieces and played various roles.
Q. For how many years?
A. Approximately, seven.
Q. I want to digress a minute here and we'll come back to it. While my mind's focused on this matter is there a committee at Eli Lilly with the name such as the Copy Clearance Committee?
A. If there is I'm not familiar with it.
Q. Well, in other companies that I have dealt with in other depositions, and I'll give you a description of what I'm talking about and see if it helps you, other pharmaceutical companies have had committees that they have described to me as copy clearance committees. And it was a cross-functional group of the legal
84: 1 department, the regulatory affairs

department, the marketing department, legal regulatory, medical, usually, the clinical affairs department, and they all had to approve the final copy of any document that was going to be released from the drug company providing information on a product.
Does that help you understand the kind of committee I'm talking about?
A. Yes, I think so.
Q. Okay. What's the name of that committee at Eli Lilly?
A. I knew it as MLR or Medical Legal Review.
Q. Medical Legal Review. What departments were represented on the MLR committee?
A. There was a representative from, one or more representatives from medical, typically, a representative from legal, a representative from regulatory, and then one or more representatives from marketing.
Those were the primary ones. I don't recall if there were any others that were standing members.

Michael Bandick (June 9, 2006)

Q. I think my question was, can you tell us the MLR committee's role, what they do?
A. Generally, that was a cross-functional team that would approve the materials that were ultimately used either internally for sales organization or externally for other audiences.
Q. Right. The copy clearance committee -- oh, excuse me, old habits are hard to break -- the MLR committee had to approve any copy, that means written document, does it not?
A. It can.
Q. Instead of me telling you what it means tell the jury what "copy" means?
A. Well, for purposes of MLR it included both written documents as well as documents that might have graphic design. And that would, probably, be the extent of it.
Q. Okay. And when you say "documents that may have graphic design" that would be slide show presentations, for example?
A. For example.
Q. And those could be slide show presentations for sales training internally, right?
A. I don't know if, I don't know if MLR approved internal presentations for sales training.

Q. Okay. Well, and I've got a computer over here somebody can go back and look at it for me but I don't want to do that. When I asked you what the MLR committee did part of your answer was something along these lines, it approved the copy used for both internal and external communications about the product. Isn't that what you said?
A. Yes, I did.

Michael Bandick (June 9, 2006)

Q. I was trying to understand the role of the MLR committee, and I tried to paraphrase what you said, and here's what I heard you say "the MLR committee approves copy for both internal and external communications on Zyprexa." Didn't I hear you say that?
A. Yes, I would agree with that. Thank you.
Q. All right. And it doesn't just do it for Zyprexa, it does it for all the drug products Lilly sells; is that correct?
A. Within different teams you would have different members who would play that role.
Q. Right. And it has, the MLR committee has a lawyer or two on it; is that correct?
A. There are representatives from legal, yes.
Q. And I understand that, sir, this is Jennifer Martin, she's with me. She, I guess, is in the legal department but she's not a lawyer. So my question was more specific. They have lawyers on the committee?
A. There is legal representation. That could be one person it could be more than one. Typically, it was one.
Q. That's what I heard you, in your first answer you said there could be one or more members of the legal department in this committee; is that right?
A. Yes.
Q. Do you recall the names of the lawyers that were from the legal department that were on the MLR committee dealing with Zyprexa copy?
A. I do.
Q. Tell me the names, please.
A. Gary Messplay, and later Angela Wade.

92: 1 Q. Okay. Then you said they had
2 representatives or two or more, is what I
3 thought I heard you say, from the medical
4 affairs department; is that correct?
5 A. From our medical group, yes.
6 Q. And it may be, again, my old
7 habits die hard, you call your medical
8 affairs department the medical group?
9 A. Yes.
10 Q. From the medical group can
11 you tell me the members of the MLR committee
12 involving Zyprexa that you recall that were
13 on that committee?
14 A. Different physicians would be
15 called on for different types of content.
16 The names that I can remember from that time
17 were Bruce Kinon, K-I-N-O-N, Robert Baker,
18 Don Hay, Sahid Ahmed. That's all I can
19 remember.

Michael Bandick (June 9, 2006)

93: 6 Q. You've given me the names of
7 the doctors that you can remember from the
8 medical group who were on the MLR committee;
9 is that correct?
10 A. Yes, I have.
11 Q. Who from regulatory, is it
12 called regulatory affairs?
13 A. Um-hum.
14 Q. Yes?
15 A. Yes.
16 Q. Who from regulatory affairs
17 was on the MLR committee dealing with Zyprexa
18 that you can recall?
19 A. I don't recall the name of
20 the regulatory affairs person at that time.
21 Q. Okay. Do you recall their
22 face, male or female, or anything about them?
23 A. I don't.
24 Q. Who from the marketing
94: 1 department?
2 A. Again, that would depend on
3 the content that was being reviewed, and it
4 could be Jack Jordan, it could be myself,
5 there were other marketing managers, Suzanne
6 Clifford, Mike Yost, Vince Truax, those are
7 the ones I can remember.
8 Q. Okay. And that's all I can
9 ask you is you do your very best of what you
10 can remember.
11 On the MLR committee, you
12 told me about medical, legal, regulatory, and
13 marketing. Are there any other, I want to
14 make sure there are no other departments on
15 the MLR committee?
16 A. Sometimes there would be a
17 person there as a technical editor, her name
18 was Nancy Ludwig. I recall that she would
19 sometimes sit in.
20 Occasionally, there would be

junior level marketing people that might sit in on a particular discussion but they would not have voting authority.

Q. Not have voting authority?

A. Correct.

Q. Okay. Which obviously implies to me that the MLR committee would vote on copy?

A. The group would reach agreement before something was approved and moved forward. So there wasn't a vote of hands but it was a general agreement once all the discussion had been completed.

Q. Okay. And the only reason I used vote is because you used vote before I did, right?

A. I don't recall saying vote.

Q. The record will reflect what it reflects but you said there might be some junior members from the marketing committee but they didn't have a vote?

A. I did say that.

Q. Let's put it this way, you use the word "vote" and now you said there's a general discussion, but I guess the whole point of the matter is prior to the time that any copy, and you described that as written documents or documents with graphic design, dealing with Zyprexa were released for either internal or external communications, the MLR committee would get together, meet, review the document, discuss it and approve it before it could be seen and sent out to the public or internally concerning Zyprexa, right?

Michael Bandick (June 9, 2006)

A. I can't speak to every single document that may have involved Zyprexa but I can speak to that characterization. In other words, there may have been other parts of the company that were dealing with materials that had the name Zyprexa on it. I don't know that MLR touched every single piece but it touched every piece that was developed by the brand team.

Q. Okay. The brand team. Any written document or a document containing a graphic design that was developed by the brand team for Zyprexa was approved by the MLR committee either for internal or external communication; is that correct?

MR. FAHEY: Objection to form. You can answer.

A. The MLR team approved content developed by the brand team for internal or external use, yes.

Q. Thank you. That would include things, for example, as the Viva Zyprexa slide shows, right?

A. There was content in Viva Zyprexa slide shows that was reviewed and approved by MLR, yes.
Q. That would include things like the diabetes sell sheet, correct?
A. Yes, it would.
Q. It would include the weight control, or I think, excuse me, that would include the weight gain sales sheet, correct?
A. There were materials that were, that concerned weight gain. I don't recall if that was the exact name for it but that topic was in materials that were reviewed by that group.
Q. It would include things such as issue management documents, correct?
A. I need you to be more specific.
Q. That's fine. It would include, the MLR team would approve things such as the primary care third quarter implementation guide, correct?
A. Again, I need more information on what you're referring to.
Q. Sure. We'll get to it. I can only ask you to do the best that you can.
The MLR committee would have to approve things such as the competitive and issue planners meeting documents.
A. I'm not familiar with that.
Q. How about the handling weight hyperglycemia diabetes issue handouts, did the MLR committee have to approve that?
A. Again, I don't know of a specific document by that name.
Q. Okay. Well, as we go through the documents today at times I'll ask you whether or not it had to be approved by the MLR committee. Maybe you can help me, okay?
A. Okay.
Q. But it's your best testimony, because if I forgot to ask and the jury's looking at your testimony and you've sworn under oath to tell the truth, the whole truth and nothing but the truth, it's your best testimony that any written document or a document containing graphic design concerning communications, either internally or externally, on Zyprexa, that came from the brand team on Zyprexa, had to be approved by the MLR committee?

Michael Bandick (June 9, 2006)

A. In the United States, yes.

Michael Bandick (June 9, 2006)

I'm looking down, I made myself notes, I have

my next question I wrote down is "why is there a marketing department?" So I'll ask it to you, why is there a marketing department?

THE WITNESS: Can I ask you to be a little more specific?

MR. ALLEN: Well I could, and I appreciate that. But let me tell you my train of thought and maybe this will help.

QUESTIONS BY MR. ALLEN:

Q. You talked about products in the pipeline, we talked about that earlier, right?

A. We have.

Q. Okay. We're going to talk about that some here later. You have research and development, you have products in the pipeline, you have a regulatory affairs department, clinical studies are done and the data and information is submitted to the FDA and the product receives FDA approval for its indicated purpose. You with me so far?

A. Yes, I am.

Q. Okay. You have FDA approval for its indicated purpose of a pharmaceuticals product. Are you with me now?

A. Yes.

Q. Why not just put the product on the market, ship it to the pharmacies and be done with it? You understand what I'm saying?

Michael Bandick (June 9, 2006)

A. I do.

Q. Okay. That's not what happens, is it?

A. In most cases that's correct.

Q. Okay. I mean, if you've researched the product, you developed the product, it's approved by the FDA, the package insert's included within the PDR, it's known that the product's available, and doctors can prescribe it or not prescribe it as they see fit, why not just leave it at that?

Michael Bandick (June 9, 2006)

A. The reason to not leave it at that is that it would likely not be as aware to physicians what the product's strengths and weaknesses are.

Q. Fair. I'll go back to where I started, and maybe that's the question you answered. Why is there a marketing

department for drugs that are approved and on the market?

Michael Bandick (June 9, 2006)

A. The role of the marketing department is to provide some of that awareness and detail around the product and its strength and weaknesses. There are also strategic elements of where the product might be promoted in the future, and other products, products in the pipeline, what their position might be in the market.

Q. I'm going to see if I can break that down or see if we have a clear understanding -- I tell you, we're going to have to get some quiet Coke openers -- let me see here.

In answer to my question about why there's a marketing department, you said it helps create an awareness about a product's strength and weaknesses. In addition, it also helps create such awareness involving products in the pipeline. Did I paraphrase that accurately?

Michael Bandick (June 9, 2006)

A. No.

Q. Tell me where I'm wrong, please.

A. It does create awareness for products that are approved. The strategic piece for products in the pipeline or future indications would not be for the purposes of creating awareness but rather to understand potential positioning, understand unmet medical need, things like that.

Q. Okay. So the marketing department creates awareness of strength and weaknesses of a product, but also, it helps understand, strategically, the views of the marketplace concerning potential future products and/or extended indications of existing products; is that right?

Michael Bandick (June 9, 2006)

A. That's a little different from what I think I said.

Q. All right. Where did I mess up?

A. Without the benefit of playing back exactly what I said and remembering exactly what you said, the piece that I was alluding to with the strategic piece is for both existing products and not

only future indications and disease states but understanding unmet medical need, in forming future clinical trials, understanding disease states that are unsatisfied so there can be a piece that's specific to a single product, it can be more broad to a disease state, it can even be more broader than that.

Q. Okay. Now, in your original answer you indicated that, at least one of the reasons for a marketing department was to create awareness of in doctors of the strengths and weaknesses of a product. Do you recall that?

A. Yes, I do.

Q. But doctors are not your only customer, are they?

A. There can be other audiences, yes.

Q. I use "customer" you use "audiences". Are we using those words interchangeably or is a term of art "audience" in marketing?

A. I was not using it interchangeably with customer.

Q. So when I asked you there are other customers and you answered, yes, there can be other audiences, you were not using it in the nature of my question as the word customers; is that right?

A. If what you mean by customer is a physician who has the ability to prescribe then I'm comfortable with that as customer.

Q. Okay. What do you mean by audience?

A. An audience could be a group that isn't a prescriber or a customer but could be, either an internal or an external audience; for example, an internal audience could be a sales organization.

Q. Give me some more example of some external audiences?

A. External audiences could include payors, they could include patients.

Q. Regulatory affairs at the FDA, would that be an audience?

A. Yes, it could be.

Q. I have seen a company document describing Lilly's customers as patients, doctors, payors, and regulatory agencies. Do you agree that those are Lilly's customers for its drug products?

A. That's not how I use the concept of customers and that's why I broadened it to include audiences.

Q. Okay. And that's what I thought you were going to say. So let's see if you and I can agree on this. Do you agree

that Lilly's audiences for its drug products and the marketing surrounding its drug products are patients, doctors, payors, and regulatory agencies, among others?
A. Yes, among others.
Q. Okay. But we at least agree on those four, right?
A. As audiences, yes.
Q. And where I come from -- it doesn't matter where I come from.
Let me ask you what do you mean by audience in the marketing realm?
A. A group for whom a message could be developed.
Q. So an audience is a group for whom a message can be developed; is that correct?
A. Yes.
Q. What's a message?
THE WITNESS: It's a very broad question, can you be more specific?
MR. ALLEN: No, sir.
QUESTIONS BY MR. ALLEN:
Q. What's a message?

Michael Bandick (June 9, 2006)

A. The best I can define that as is a concept that is conveyed to that audience in some form.
Q. Yeah. You use the word "message" before I did. So I -- so a message is a concept conveyed to an audience; is that right?
A. Yes.
Q. Okay. As a matter of fact, let me just look, you use the word "message" all the time in your business in marketing, don't you, every day?
A. It's a frequently used word.
Q. Okay. So when I ask you what a message was and you said that's an awful broad question, the fact of the matter is in marketing you use the terminology and the word message almost every single day, don't you?
A. Yes.
Q. Okay. And you said an audience, which includes patients, doctors, payors, and regulatory agencies, an audience is someone to whom you can give messages; is that correct?

Michael Bandick (June 9, 2006)

A. An audience could be construed as a group who would receive a message. That's not the only way I would

define an audience but for purposes of answering your question, yes.

Michael Bandick (June 9, 2006)

115:23 Q. In your role and roles in the
24 marketing of Zyprexa, why would you want to
116: 1 send audiences messages about Zyprexa?
2 A. As I indicated earlier,
3 conveying a concept can be a very valuable
4 piece of what we think those audiences would
5 need to know. And I guess the difficulty I'm
6 having in answering your question is the work
7 that we did was always in the context of a
8 particular situation. So without that
9 context it's hard for me to give you a very
10 satisfactory answer.
11 Q. I think your answer's quite
12 satisfactory. You said the reason you want
13 to send messages to audiences is in order to
14 convey valuable information that they may
15 need to know; is that correct?
16 A. Yes.
17 Q. When you send these messages
18 concerning Zyprexa to your audiences and you
19 convey this information that the audiences
20 may need to know, do you have a
21 responsibility to be truthful?
22 A. Yes. Excuse me, yes.
23 Q. Accurate?
24 A. Accurate, yes.
117: 1 Q. Do you have a responsibility
2 to tell not only the truth but the whole
3 truth?
4 A. We have the responsibility to
5 be truthful and accurate.
6 Q. And that wasn't my question.
7 When you convey this information to the
8 audiences in these messages, do you have the
9 responsibility to tell not only the truth but
10 the whole truth?

Michael Bandick (June 9, 2006)

117:13 A. I'm not sure how to answer
14 your question in the context of the way that
15 we would deliver those messages. They were
16 truthful and accurate.
17 Q. Sir, that's when we started
18 this whole deposition. Remember you raised
19 your right hand, do you remember that?
20 A. I do.
21 Q. You took an oath, do you
22 recall that?
23 A. I do.

Michael Bandick (June 9, 2006)

118: 8 Q. Your oath was to tell the
9 truth, the whole truth and nothing but the
10 truth. Did you understand that oath?
11 A. I did.
12 Q. Back to my question
13 concerning messages concerning Zyprexa to the
14 audiences. Do you have the responsibility
15 when you send messages and this valuable
16 information which the audiences may need to
17 know, do you have the responsibility to tell
18 those audiences the truth and the whole
19 truth?

Michael Bandick (June 9, 2006)

119: 1 Q. Do you have that
2 responsibility?
3 A. We have the responsibility to
4 be truthful and accurate. And I'm not sure
5 how to understand your question about the
6 whole truth. That to me, I don't make that
7 distinction. That's something that I would
8 defer to, to a legal expert, which I'm not,
9 but we do have the responsibility to be
10 truthful and accurate.

Michael Bandick (June 9, 2006)

123: 4 Q. Do you have the
5 responsibility to tell the whole truth?
6 A. I'd have to understand the
7 context of your question because --
8 Q. In the context of your job as
9 the Director of Marketplace Management when
10 you provide information concerning Zyprexa do
11 you have the responsibility to tell the whole
12 truth?

Michael Bandick (June 9, 2006)

123:15 A. The best way I can answer
16 your question is to say that in the context
17 of being accurate and truthful we had also
18 the responsibility not to provide false or
19 misleading information.
20 But I don't know how to
21 answer your question. I, honestly -- I did
22 not make that distinction. It was something
23 that, truthful was something that we abided
24 by.
124: 1 Q. I understand. You've given
2 me that answer. Let me see if I can help you
3 about the whole truth. If I told you I have
4 a car, you understand what I'm saying? I
5 have a car.
6 A. Yes, I understand.
7 Q. That's true, all right? But

if I knew -- and I said I'm going to loan you my car because you needed to borrow a car. Are you with me so far?

A. Yes, I am.

Q. Okay. And you said to me, can I drive it from Indianapolis to Louisville, Kentucky, I'd like to do that? All right? Are you with me so far?

A. Yes, I am.

Q. And I throw you the keys. Are you with me?

A. I am.

Q. So I told you I have a car. I told you you can borrow my car. And you're getting in the car and you're going to drive it from Indianapolis to Louisville in Kentucky. Are you with me so far?

125: A. Yes, I am.

Q. You look at the gas gauge before you leave and it says it's full. Are you with me?

A. Yes.

Q. You're 20 miles down the road and you run out of gas. Are you with me?

A. Yes.

Q. But the gauge never moved and it said it was full when you left, right?

A. That's what you said.

Q. Right. Well, had I lied to you at any point during the process?

A. I don't know.

Q. Well, it didn't sound like it. I told you I had a car. You could drive it from Indianapolis down to Louisville, Kentucky. I threw you the keys and you drove off and you saw the gas gauge on full, right?

A. That was your hypothesis.

Q. Right. I told you the truth, I just didn't tell you all the truth. I forgot to tell you and I didn't tell you that when my gas gauge says it's full there may be

126: only one gallon left. Are you with me so far?

A. Yes, I am.

Q. Now, back to my question. Do you have the responsibility to tell the truth about the drug product, right?

A. Yes.

Q. Do you have the responsibility to tell the whole truth?

Michael Bandick (June 9, 2006)

126: A. As I said before, without specific context that's going to be difficult. You could have told me -- you didn't tell me that the car was blue, either.

Q. That's your best answer?

A. That's my best answer.

Michael Bandick (June 9, 2006)

126:20 Q. Okay. Are there segments
21 within markets?
22 A. There can be.
23 Q. What's a market?
24 A. Broadly defined, it would be
127: 1 a group of customers or potential customers
2 for whom a product would be appropriate.
3 Q. A market is customers or
4 potential customers for whom a product would
5 be appropriate. And within markets there can
6 be segments; is that correct?
7 A. Yes.

Michael Bandick (June 9, 2006)

127: 9 let me rephrase the question. Can you
10 describe to the jury, please, sir, what
11 markets did Eli Lilly market Zyprexa to?
12 A. Primarily, physicians who
13 could be either in psychiatry or other
14 specialties. Would you like me to --
15 Is that a satisfactory answer
16 to you?
17 Q. Well, my question was what
18 markets did Lilly market Zyprexa to and your
19 answer was, primarily, psychiatrists or other
20 physicians. And so, no, it's not a
21 satisfactory answer.

Michael Bandick (June 9, 2006)

127:24 THE WITNESS: Could you
128: 1 rephrase it, please?
2 QUESTIONS BY MR. ALLEN:
3 Q. I didn't ask "primarily", I
4 asked this question, "to what markets did
5 Lilly market Zyprexa to?
6 A. Psychiatrists, primary care
7 physicians. I can't think of any others.
8 Q. What about patients?
9 A. As I mentioned, I would
10 consider them as a separate audience and I
11 understood your question to be something more
12 specific to a customer group.
13 Q. Well, let me ask this, aren't
14 patients your ultimate market for all of your
15 drug products?
16 A. No.
17 Q. They're not. Is that right?
18 A. No. That's correct.
19 Q. Okay. Aren't patients your
20 most important customers for your drug
21 products?
22 A. Patients are very important.
23 I don't know how to say they're more
24 important than another.
129: 1 Q. Okay. Can you think of

anybody that's more important -- let me rephrase that. Can you think of anybody that's more of an important customer for your drug products than patients?

A. I can't think of anything that's more important than patient safety but I would say that physicians having the responsibility to prescribe the medications also represent an extremely important market and I wouldn't distinguish between those two.

Q. Okay. The two most important markets for your products are patients and customers, excuse me, patients and doctors; is that correct?

A. Yes.

Q. Okay. So you better be truthful, accurate, fair, balanced, not withhold information, and don't make misrepresentations to them, correct?

Michael Bandick (June 9, 2006)

129:23 A. I would say that we need to
24 be truthful and accurate in all of our
130: 1 characterizations.
2 Q. What about fair and balanced?
3 A. Fair and balanced is also an
4 obligation.
5 Q. How about not lying to them?
6 A. That's part of truthful.
7 Q. How about not withholding
8 important information?
9 A. It depends on how you would
10 define "important information."
11 Q. Which word do you not
12 understand about important information?

Michael Bandick (June 9, 2006)

130:15 A. I understand all the words.
16 Q. You understand all the words?
17 A. I do.
18 Q. You agree you shouldn't
19 withhold important information from doctors
20 and patients about a drug product and in this
21 case in particular Zyprexa?
22 A. That's not what I said.
23 Q. Okay. Well, then I'll ask
24 you another question. Do you agree you
131: 1 shouldn't withhold important information from
2 doctors and patients about Zyprexa?
3 A. Without a specific reference
4 to what you might mean by important
5 information I'm not sure how to answer your
6 question.
7 Q. Thank you.
8 Now you said the doctors to
9 whom you market the products are
10 psychiatrists and primary care physicians; is

that correct?
A. Yes.
Q. Tell the jury what primary care physicians are?
A. Primary care physicians are comprised of family practice, general practice, and internal medicine. And they see patients of all ages on a wide variety of health issues.
Q. There are other primary care physicians, are there not?
A. Not that I'm aware of.
Q. Okay. So when you use the term "primary care physicians" in reference to the marketing of Zyprexa, to you, at least today under oath, it means family practitioners, general practitioners and doctors of internal medicine, correct?
A. Yes.
Q. How about pediatricians?
A. I would consider pediatrician a specialty, that's why I didn't mention it.
Q. How about obstetrician and gynecologist?
A. Also a specialty.
Q. Did Lilly, at any time, to your knowledge, market Zyprexa to pediatricians?
A. Not to my knowledge.
Q. Did Lilly, at any time, to your knowledge, market Zyprexa to obstetricians and gynecologists?
A. Not to my knowledge.
Q. Did pediatricians, excuse me, did Lilly at any time market Zyprexa to gerontologists?
A. To gerontologists?
Q. Yes, sir?
A. Within my role in Zyprexa primary care we did not, I don't know, I can't say with certainty whether we would have marketed to a gerontologist for any reason.
Q. Okay. That's fair. That's all I asked.

Now we've talked about markets and market segments. We talked about doctors and you said they're psychiatrists and primary care physicians and you've defined primary case physicians, correct, thus far?
A. Yes.

Michael Bandick (June 9, 2006)

Are there segments within the patient market?

THE WITNESS: Are we talking specific to Zyprexa or are we talking broadly?

MR. ALLEN: Let's talk

broadly first.
A. Yes, there are.
Q. We've got that established. We've got segments within the patient market. With regard to Zyprexa are there segments within the patient market?
A. Yes.

Michael Bandick (June 9, 2006)

Q. There's where we are. Tell this jury, please, the segments within the patient market to whom Lilly marketed Zyprexa?
A. Lilly marketed Zyprexa to physicians, and the patient segments for whom that was appropriate included schizophrenia and bipolar disorder setting, whether it was an office or an institution like a hospital. Severity would be another way to divide the market and was another way that we divided the market. And there could be other ways to divide patients but those represented the top ones that we looked at.

Michael Bandick (June 9, 2006)

Q. I didn't ask who you could look at and who you considered. My question is very direct and that is: I would like you to tell the jury, please, the patient segments to whom Lilly marketed Zyprexa.
A. The only example I can think of where Lilly was marketing Zyprexa to a patient segment would be for bipolar disorder patients.
Q. Okay. That's the only one?
A. That I'm aware of.
Q. Okay. What about to schizophrenics?

Michael Bandick (June 9, 2006)

A. As I indicated the only patient group to whom Lilly marketed Zyprexa directly, and I was trying to make the distinction between physicians and patients earlier, patients with schizophrenia tend not to be a direct audience for marketing messages.
Q. Okay. They tend not to be but they can be?
A. Patients with schizophrenia are very sick. And they tend not to be able to assimilate information or to understand even the basic things that we take for granted. It is possible that if there were

articles in the lay media or there were other sources of information some higher functioning patients with schizophrenia could understand that, but in general, no, patients with schizophrenia were not an audience to whom Lilly marketed Zyprexa.

Q. And you changed, I guess, and I understand, you changed it from audience to market segment. And I was not asking about audiences, I was asking about markets.

A. I would make the same comment using patients with schizophrenia as a market segment.

Q. Okay. But you agree with me, at least, I understand what you're saying, I could figure it out. But you agree with me, at least, that the patients to whom Lilly marketed Zyprexa included patients with bipolar disorder; is that correct?

A. Yes.

Q. And schizophrenia to the extent that those patients with schizophrenia could understand your marketing messages, correct?

Michael Bandick (June 9, 2006)

A. I'm not aware of any programs where we marketed Zyprexa to patients with schizophrenia.

Q. Okay. Well, who did, who did -- let me ask this: Who did you market to such that Zyprexa would hopefully make its way for a schizophrenic patient?

A. Psychiatrists and primary care physician.

Q. Okay. Now other than marketing to psychiatrists and primary care physicians for the treatment of schizophrenia, and to, I guess, psychiatrists and primary care physicians for the treatment of bipolar disease and/or marketing Zyprexa to patients with bipolar disease, did you have any other markets in the doctor and/or patient community for Zyprexa?

Michael Bandick (June 9, 2006)

A. If your question is outside of patients with bipolar disorder, psychiatrists, and primary care physicians who would treat patients with schizophrenia and bipolar disorder, did we have any other markets among patients and physicians to whom we marketed Zyprexa, I would say not that I'm aware of.

Michael Bandick (June 9, 2006)

148: 7 Q. You told us the doctors and
8 the patients to whom Zyprexa is marketed.
9 You've told us that, right?
10 A. Yes.
11 Q. And you've given us your best
12 testimony under oath, correct?
13 A. Yes.
14 Q. Okay. So I guess it's your
15 testimony here today that Lilly did not try
16 to market Zyprexa to Donnas; is that true?
17 A. What do you mean by "Donnas"?
18 Q. Do you not know that?
19 A. I'm not sure what you mean by
20 it.
21 Q. Thank you.
22 I guess it's your best
23 testimony under oath today that Lilly did not
24 try to market Zyprexa to Marks?
149: 1 A. I don't know what you mean by
2 that.
3 Q. Okay. I guess it's your best
4 testimony under oath here today that Lilly
5 did not try to market Zyprexa to Marthas?
6 A. I don't know what you mean by
7 that.
8 Q. I guess it's your best
9 testimony under oath here today that Lilly
10 did not try to market Zyprexa to Christines;
11 is that correct?
12 A. I don't know what you mean by
13 your question.
14 Q. Okay. My questions are
15 totally foreign to you about Donna, Martha,
16 Mark, Christine, you just don't understand?
17 A. I don't understand what you
18 want me to answer.

Michael Bandick (June 9, 2006)

151:17 here it is. Did Lilly market Zyprexa as a
18 mood stabilizer?
19 A. Upon receiving approval for
20 bipolar disorder, and mood stabilizers being
21 a general label for products that would treat
22 bipolar, yes, it did.

Michael Bandick (June 9, 2006)

152: 4 Q. So the answer to my question
5 is, yes, Lilly marketed Zyprexa as a mood
6 stabilizer, is that right?
7 MR. HAMMERLE: I'd object as

Michael Bandick (June 9, 2006)

152:11 A. If your question is did Lilly

at some point market Zyprexa as a mood stabilizer, I would say yes.
Q. Thank you. Did Lilly market Zyprexa for use in treating symptoms of mood?
A. No.
Q. Did Lilly market and/or promote Zyprexa for treatment of symptoms of anxiety?
A. No.
Q. Did Lilly market and/or promote Zyprexa for the treatment of symptoms of depression?
A. No.
153: Q. Did Lilly market Zyprexa or promote Zyprexa for the treatment of Alzheimer's?
A. No.
Q. Did Lilly market and/or promote Zyprexa for the treatment of behavioral disorders?
A. No.
Q. Did Lilly market or promote Zyprexa for the treatment of behavioral disorders associated with Alzheimer's?
A. No.
Q. Did Lilly market or promote Zyprexa for the treatment of symptoms of dementia?
A. No.
Q. Did Lilly market or promote Zyprexa for the treatment of decline in cognitive function related to Alzheimer's?
A. No.
Q. Did Lilly market and/or promote Zyprexa for the treatment of children with attention deficit disorder?
A. No.
154: Q. Did Lilly market or promote Zyprexa for the treatment of nausea?
A. No.
Q. Did Lilly market or promote Zyprexa for the treatment of irritability symptoms?
A. No.
Q. Did Lilly market or promote Zyprexa for thought disorders in nonpsychotic patients?
A. No.

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154:12 Q. Did Lilly market or promote Zyprexa for the treatment of symptoms?
A. No.

Michael Bandick (June 9, 2006)

158: through my notes. I'm going to try to move on here in a second but I'm trying to get

terms defined. You said the brand team. Do you recall that?
A. Yes.
Q. Tell the jury what the brand team is?
A. The brand team, the way I define it, is largely a marketing concept with support from the other members of the cross-functional team that we worked with. So I would consider a staff position, for example, to be associated with the brand team but the brand team, itself, would be, primarily, marketers.
Q. Okay. And I would, with respect -- I'm trying to get this down to where I can understand it and the jury can understand it. You said it's a cross-functional team primarily dealing with marketing. I want to see if you can help the jury understand what the brand team -- can you put that in less technical language so the jury and I can understand what the brand team is?
A. The brand team would consist of marketing personnel with different roles at different levels. And it would also include a, an associated group of members of the medical regulatory legal editing team, things like that.
THE WITNESS: Do you want me to drill down more?
MR. ALLEN: Yes, sir.
A. It would be people who are working in customer segments, which we discussed earlier, and who would play different roles depending on the needs of the team at that time.
Q. And when we're talking about -- by the way, I think it's implicit unless I say otherwise we're here talking about Zyprexa. You know that?
A. That's my assumption.
Q. Gotcha. So we're saying the brand team and your description of the brand team, you were describing the brand team with regard to Zyprexa?
A. I was.
Q. But I take it, maybe I'm wrong, that Lilly's drug products all had a brand team?
A. Many of them did.

Michael Bandick (June 9, 2006)

Q. The goals of the brand team for Zyprexa, what was the goals?
A. Effective communication to target audiences, effective strategy within the marketplace, responsiveness to customer inquiries.
Those would be the main

objectives I could think of or the main goals.

Q. And you said effective communication, effective responses to customer inquiries, and I missed the second one. Effective placement?

A. Strategy development within the market place.

Q. Explain for the jury what effective communication means in regard to the brand team of Zyprexa?

A. That really depends on the, the situation.

Q. Give the jury an example, please.

A. An example of effective communication would be providing information about Zyprexa's launch in primary care that enabled target audiences, in this case primary care physicians, to clearly understand what the drug was, what the target patient was, and what the drug was to be considered for.

Q. Okay. So you're trying to, for example, effective communication from the brand team's perspective in regard to Zyprexa would be to effectively and accurately communicate to primary care physicians those patients for whom Zyprexa was indicated?

A. That would be one example, yes.

Q. Thank you. You said another goal of the brand team was effective strategy development; is that right?

A. I did.

Q. Explain that to the jury, please.

A. Again, by use of an example, when Zyprexa received a new indication for bipolar disorder mania it was the first time an atypical antipsychotic had ever received that kind of indication, and it was important for us to understand how best to convey that, and how to maximize that opportunity clinically.

Q. When you say, as a member of the Zyprexa brand team, to maximize that indication; you said that, right?

A. I said to maximize the opportunity clinically.

Q. What do you mean when you say, as a member of the Zyprexa brand team, that once Zyprexa received a bipolar mania indication that you wanted to maximize the opportunity? Tell the jury what that means, please.

A. To maximize the opportunity clinically in the example of getting the indication of bipolar mania was to ensure that the right target patient was identified and that differences between Zyprexa and that disease state and other medications in that disease state were clearly defined. We felt

that Zyprexa offered some advantages.
Q. And what was the third goal of the Zyprexa brand team, starts with a C?
A. You read it back to me.
Q. It was effective communication, effective strategy development and effective something to customers.
A. Oh, it was responsiveness to customer inquiries.
Q. Tell the jury what that means, please.
A. For example, when customers requested information that we would have the resources to provide those answers, either through the dissemination of clinical data or other means.
Q. Okay. Sir, are there legal and regulatory limitations on how a pharmaceutical company, in this case Lilly in particular, can market a particular drug product?
A. Yes, there are.

Michael Bandick (June 9, 2006)

Do you agree that Lilly cannot actively promote and/or market Zyprexa outside of the FDA approved indications on the label?
A. Yes. I agree that Lilly cannot promote Zyprexa outside of the approved indication on its label. There are opportunities to share data that might fall outside of that.
So when you said promote and market, I'm dividing the two, and I would say it's true that Lilly would not be promoting Zyprexa outside of its approved label.

Michael Bandick (June 9, 2006)

Q. Can Lilly market Zyprexa outside the indications on the label?
A. Under specific circumstances and guidelines Lilly can share data that is outside that. And so, I wouldn't define that as marketing, per se, but it can come through the form of a sales organization or through a marketing department, but it would be governed by specific guidelines as to what is and isn't appropriate dissemination of that clinical data.
Q. Where would I find those guidelines?

Michael Bandick (June 9, 2006)

166: 8 Q. Where would I find those
9 guidelines?
10 A. I don't know exactly where to
11 point you at this point.

Michael Bandick (June 9, 2006)

167:14 Q. Now, sir, you said there's
15 some guidelines concerning marketing outside
16 the label. You said that, right?
17 A. I said there was some
18 guidelines for disseminating data outside of
19 the label.
20 Q. What do you call those
21 guidelines?
22 A. Well, in general, the
23 guidelines that the company follows are
24 called good promotional practices or GPP.
168: 1 There can be other specific guidelines for
2 that dissemination of data, and I don't, I
3 don't know where to point you to to look
4 those up.
5 Q. Well, and I appreciate that
6 answer if you just don't remember, but I
7 would assume as the Brand Manager and as the
8 Director of Marketplace Management you would
9 frequently refer to the GPPs, would you not?
10 A. Yes, I would.
11 Q. Okay. Were they kept in the
12 marketing department?
13 A. I had access to a copy of
14 them. I don't know what might have existed
15 in other areas.

Michael Bandick (June 9, 2006)

169: 1 Q. Okay. Can Lilly under FDA
2 regulations or the GPP direct the Zyprexa
3 sales force to actively proceed to a
4 physician's office on a routine sales call
5 and promote Zyprexa for the treatment of
6 symptoms?
7 A. No.
8 Q. Why not?
9 A. Company policy is clear on
10 the fact that all promotion will be within
11 the approved label and the indications that
12 follow from that.
13 Q. So the company policy is
14 clear that all promotion of drug products,
15 including Zyprexa, must be within the
16 approved indications on the product's label,
17 correct?
18 A. For promotional activities,
19 that's correct.
20 Q. Okay. What's the difference
21 between promotion and marketing?
22 A. Well, I was distinguishing
23 between promotional activities and

nonpromotional activities. I would say that the promotional activities can be part of what a marketing team assists with but I don't see them as an either/or, the difference in my mind is what's promotional and what's nonpromotional.

Q. Okay. What's the difference between promotional and nonpromotional activities?

A. Promotional activities are those that are on label and are for approved indications. Nonpromotional activities can include a wide range of interactions with clinicians. It can involve clinical data that may not be, may or may not be part of the current label. And it can involve responses to questions that are potentially outside of the label.

So that's how I would distinguish between promotional and nonpromotional.

Q. Can Lilly provide data as part of its promotional activities to a physician concerning clinical study information on Zyprexa for nonindicated uses of Zyprexa?

A. Yes, with very specific guidelines for how that discussion takes place.

Q. Tell the jury what the specific guidelines are.

A. There may be others who can describe it better than me but my recollection of how we trained sales representatives to handle situations like that was to make very clear when the discussion involved off-label information, either because it was in response to a question or at a specific time in the call there was a, an indication from the sales representative that we were now going to be in a different part of the discussion, so that would be considered a stop sign for promotional activity and then would transition into nonpromotional.

Q. Okay. So, if at any time a Lilly sales representative would discuss off-label uses of the product they were supposed to and, in fact, were required by law and by GPP at Lilly to inform the physician "that I'm now discussing off-label **uses."**

Michael Bandick (June 9, 2006)

A. There were other, there are other ways that that could occur in a call. It could be in response to a question. But Lilly sales representatives were trained to be very clear as to what the approved indications were and if there was content or

material outside of that to acknowledge it as such.

Michael Bandick (June 9, 2006)

Q. Okay. Let me ask this: Did Lilly promotional materials ever discuss off-label uses of Zyprexa?
A. A promotional material is, by definition, going to have limitations specific to its approved indications.
Q. Okay.
A. There can be other materials that I would say fall outside of promotional materials.
Q. I understand what you're saying but I think, I want to get my question answered, did Lilly promotional materials for Zyprexa ever discuss, recommend, off-label uses for Zyprexa?
A. For what I'm defining as promotional materials, no, I can't think of any examples when it did.
Q. Why not?
A. As I said, by definition promotional material would be that which is limited to the approved indications.
Q. Why?
A. That was the definition and understood guidelines around the regulations for that type of promotional activity.
Q. And by that answer you mean it would be illegal and contrary to FDA regulations to provide promotional materials on Zyprexa recommending off-label uses, correct?

Michael Bandick (June 9, 2006)

(The Court Reporter read the requested material, as set forth herein:

Michael Bandick (June 9, 2006)

A. Promotional materials that were approved by the team that we were discussing earlier, I would defer to my colleagues in legal and regulatory to be able to answer that. My understanding was that promotional materials would be limited in that regard.
Q. Limited in what regard?
A. Limited to confine themselves to discussions of approved indications.
Q. And you were involved in the preparation review and approval of

promotional pieces on Zyprexa, were you not?
A. At different points in time I was involved in some of those activities.
Q. At any point in time when Zyprexa was marketed by Eli Lilly, are you familiar with or have you ever seen a promotional document that promoted Zyprexa for off-label uses?
A. No.

Michael Bandick (June 9, 2006)

Q. Let's assume that a promotional piece on Zyprexa was prepared which promoted off-label use. Are you with me so far?
A. A promotional piece was prepared promoting off-label use. Yes, I understand the question.
Q. Should that be allowed or approved by the MLR?
A. Based on my definition of promotional material and what we've discussed, no.
Q. Right. And that's why you have an MLR, right? That's one of the reasons MLR exists?
A. That's one of the reasons.
Q. One of the reasons the MLR committee, the medical, legal and regulatory marketing committee, the MLR committee exists is to ensure that promotional material on Zyprexa did not violate the GPPs, correct?
A. That was one of their charges, yes.
Q. If a promotional piece on Zyprexa was approved by the MLR it must have then been in accordance with the GPPs, correct?
A. That would be the expectation.

Michael Bandick (June 9, 2006)

Q. The MLR committee, one of its functions was to assure that the promotional pieces on Zyprexa met legal requirements under the law, correct?
A. That's my understanding.
Q. In fact, as I've heard this when I'm taking depositions in pharmaceutical cases that the pharmaceutical industry is a highly regulated industry, correct?
A. It is a regulated industry.
Q. And Eli Lilly is one of the largest pharmaceutical companies in the entire world, is it not?
A. It's in the top 15.
Q. And I would think that

anything that Eli Lilly does in regard to the promotion and sale and distribution of its drug products they make sure that it's within the law, do they not?
A. That would be my assumption.
Q. Why is that your assumption?
A. It's my assumption because that's the expectation that I had of that group.
Q. And did the MLR committee have lawyers on that committee?

Michael Bandick (June 9, 2006)

180:18 A. As we've discussed.
Q. Yes. And was part of the lawyers' role and function on the MLR committee to ensure that the promotional material met legal requirements?

Michael Bandick (June 9, 2006)

194:20 Q. Back to my question. Would you consider the Zyprexa sales force part of the tool of the marketing department in the marketing of Zyprexa?
A. Part of the tool. I would
195: 1 consider it a channel.
Q. Okay. Tell the jury what you mean by channel.
A. There are a number of different ways in which --

Michael Bandick (June 9, 2006)

195:16 A. The sales force was a channel for marketing in the U.S. Other channels included things like direct-to-physician advertisement as you mentioned. There may be others.
Q. Okay. Fine. When you said the sales force was a channel for the marketing of Zyprexa, what did you mean by that, that statement alone?
196: 1 A. As we were discussing earlier about delivering messages and effectively conveying a concept, the sales force would be one channel, one carrier, one conveyor of those messages or concepts to an audience, in this case physicians.
Q. Okay. So the sales force delivered messages and concepts concerning the proper prescription and use of Zyprexa to physicians?
A. Yes.
Q. That was one of their main roles?

A. Yes.
Q. One of their roles to help in the marketing of Zyprexa was help to deliver samples, was it not?
A. That's correct.
Q. One of their roles in the marketing of Zyprexa was to determine physician attitudes and report those back to the company?
A. We sometimes got that feedback but we relied on other means to collect or solicit that information more formally.
Q. One of the marketing roles of the Zyprexa sales force was to overcome obstacles presented by the doctors when they would ask questions about Zyprexa?
A. That's a phrase that is used in sales training as a way to help direct a sales representative in the context of a call.
Q. One of the roles of the Zyprexa sales force in the area of marketing was to accurately respond to doctor's questions concerning the risk of Zyprexa?
A. That's correct.
Q. One of the roles of the Zyprexa sales force was to accurately convey to the doctors the approved indications by the FDA for Zyprexa?
A. That's correct.
Q. Another tool or channel for Zyprexa marketing was continuing medical education sponsored activities?
A. The key word being sponsored. The Zyprexa team didn't create that content but did provide funding for certain activities in accordance with regulations or in CME.
Q. Everything you did was in accordance with regulations?

Michael Bandick (June 9, 2006)

Q. Is that right? In regard to CME?
A. We were very careful to follow the rules and regulations of whatever the activity was.
Q. In all respects in regard to Zyprexa marketing?
A. As far as I know.
Q. Okay. Another tool or channel for the marketing of Zyprexa was the development of publication plans?
A. In conjunction with our medical group, that's true.
Q. Another tool or channel in the marketing of Zyprexa was the development of a speaker's bureau?
A. Yes, that's true.

Michael Bandick (June 9, 2006)

to my question. Part of the tool or channels of marketing for Zyprexa was Lilly giving money to medical organizations?

A. There were medical associations that received that type of funding, yes.

Q. As part of the marketing activities for Zyprexa from Eli Lilly?

A. Yes.

Q. And it was part of the Eli Lilly marketing department's budget to allocate monies to medical organizations and/or associations?

A. I don't know if that was part of the marketing group's budget or not.

Q. You just know it's part of the marketing activities?

A. Typically, funds that were assigned to medical associations would be more for clinical, that types of activities. Again getting back to who holds the budget I don't recall there being dollars from marketing that went to medical associations. It's possible, I don't know.

Q. Tell the jury, please, those medical organizations or associations to whom money was given as part of the channel or tool in the marketing of Zyprexa?

A. The only two associations that come to mind are the American Psychiatric Association and the American Diabetes Association.

Q. How many millions of dollars was given to those organizations over the period of let's say 1995 to 2004 at the time you left?

Michael Bandick (June 9, 2006)

A. I don't have any idea.

Q. It was millions, wasn't it?

A. I can't confirm that.

Q. Do you think it was in the millions?

A. I don't know.

Q. Do you have any idea?

A. I don't.

Q. Thank you.

Michael Bandick (June 9, 2006)

Q. Concerning tools and/or channels involved in the marketing of Zyprexa, you told us about the sales force, advertising, CME sponsored event, publication

plans, speaker's bureaus and grants and honoraria to medical organizations or associations, right?

Michael Bandick (June 9, 2006)

A. I talked about a couple of associations, neither of those were in conjunction with primary care, but I believe elsewhere within Zyprexa that may have been appropriate.

The only other channel or tool that I would add to your list would be in the area of direct-to-physician or peer-to-peer programming.

Michael Bandick (June 9, 2006)

Q. Oh, by the way, you agree that the CME courses are, it's what they stand for, continuing medical education, are generally directed at doctors, right?

A. They're directed at doctors.

Q. Right. And medical publications are generally directed at doctors, right?

A. Generally.

Q. Sales force is generally directed at doctors, correct?

A. Generally.

Q. Marketing materials are generally directed at doctors, correct?

A. Yes.

Q. Medical organizations are made up of doctors and they provide information to doctors, correct?

A. As we were talking about medical associations, yes, that's what I understand them to do.

Q. Okay. And, of course, the package insert or the label that's included, among other places, in the PDR is directed at doctors as well as patients, correct?

A. Primarily, directors.

Michael Bandick (June 9, 2006)

Q. Now, doctors receive information concerning Zyprexa from the package insert, correct?

A. Yes.

Q. Doctors receive information concerning the benefits and risks of Zyprexa from peers and educators?

A. Yes.

Q. Doctors receive information concerning the benefits and risks of Zyprexa

from publications?
A. Yes.
Q. Doctors receive information about the benefits and risks of the product from the sales force?
A. From the Lilly sales force, yes.
Q. Doctors receive information about the benefits and risk of the product from marketing materials?
A. Yes.
Q. Doctors receive information about the benefits and risks of Zyprexa from continuing medical education courses?
A. Yes.
Q. And doctors receive information about Zyprexa from medical organizations such as the American Diabetes Association and the American Association of Clinical Oncology -- Endocrinology?
208: 1 A. As two examples, yes.
2 Q. Okay. I'm going to show you
3 exhibit -- oh, and by the way, doctors, you
4 knew that doctors would then pass along or
5 could pass along or may pass along that
6 information they learned from those sources
7 to the patient?
8 A. That's possible.

Michael Bandick (June 9, 2006)

208: 9 Q. Right. And, of course, each
10 one of those I talked about, the package
11 insert, peers and educators, publications,
12 sales force, marketing materials, CME and
13 medical organizations were all used as
14 channels and/or tools by the marketing
15 department at Eli Lilly to market Zyprexa,
16 correct?
17
18 MR. FAHEY: Differentiating
19 from promotion of Zyprexa?
20 Mr. Allen?
21 A. I was looking at your exhibit
22 here. Could you repeat your question,
please?

Michael Bandick (June 9, 2006)

208:23 (Whereupon, Deposition
24 Exhibit(s) 2 duly received, marked
209: 1 and made a part of the record.)
2 QUESTIONS BY MR. ALLEN:
3 Q. Yes. Exhibit No. 2, we have
4 the doctor. Lilly's on the top, right?
5 A. On this document, yes.
6 Q. And then we have various
7 sources, the doctor's right there in the
8 middle and we have the sources we discussed,
9 we have the medical organization, the package

insert, the peers and educators, the publications, the sales force, the marketing materials, and the CME, are all places where the doctor gets information, right?
A. Those are all places where doctors get information.
Q. And they're also all tools and channels Eli Lilly used in the marketing of Zyprexa, correct?

Michael Bandick (June 9, 2006)

A. Each of those are channels through which certain types of information could be provided.
Q. And, in fact, was provided by Eli Lilly?
A. Different types of information would appear in different channels but each of these, in some form, were used by Zyprexa, yes.
Q. Okay. And you said that the doctor would take that information and could or might, convey to the patient, right?
A. It's possible.
Q. Therefore, when Eli Lilly used those tools and channels, such as publications or CME courses, it is important for Eli Lilly to be truthful, accurate, fair, and balanced, and to tell the whole truth, correct?

Michael Bandick (June 9, 2006)

thing, Lilly wasn't involved in the content of CME.

Michael Bandick (June 9, 2006)

For purposes of publications that was clinical trial data. And yes, it would be important to be accurate and truthful about the portrayal of those data.
Q. It's your sworn testimony under oath that Lilly never prepared slides for the use by doctors at CME courses? Is that your sworn testimony?
A. I don't know.
Q. Yeah. Well, so you're not really so positive about what your lawyer just spouted off about over there, are you?

Michael Bandick (June 9, 2006)

I assume you have a drug

product, in this case, Zyprexa, would you like it to have a bigger market or a smaller market?

A. Well, in the case of Zyprexa, the market got bigger as we expanded the label and that was seen as a positive.

Q. You mentioned that several times. So I guess I want to make sure we're communicating. In 1996, when the product was approved, being Zyprexa, it was indicated for schizophrenia, correct?

A. The actual language was a little different. It later was focused on schizophrenia, yes.

Q. So you and I are communicating and you agree with me?

A. I agree that it started with some language that later was narrowed to schizophrenia.

Q. Okay. And then I believe it was the fall of 2000, if I'm correct, that the indication was added bipolar mania; is that correct?

A. I believe that was March of 2000.

Q. March of 2000, thank you very much.

And tell this journey any other indications besides schizophrenia and bipolar mania that were ever added and approved by the FDA for Zyprexa?

A. I don't recall the date, but later, after March of 2000, there was a broadening of the bipolar indication to include maintenance, bipolar maintenance.

Q. So the three FDA approved indications for Zyprexa since it's been on the market are schizophrenia, bipolar mania and bipolar mania maintenance, correct?

A. Bipolar maintenance.

Q. Okay. Any other indications approved by the FDA other than those you just identified?

A. Not that I'm aware of.

Q. Okay. Now, in the case of Zyprexa, did you want a psychiatric only market or did you, you being Eli Lilly, want a larger market than the psychiatric physician market?

A. We were looking for markets that treated the psychiatric illnesses for which Zyprexa was indicated. The first market we went into is psychiatry but later determined that it would be appropriate to pursue a primary care market for those same psychiatric illnesses.

Q. You did so because of your company's, being Eli Lilly's, corporate

profit performance was dependent upon getting a larger market for Zyprexa, correct?
A. No.
Q. That's your best testimony?
A. Yes.
Q. Which is a larger market, the antipsychotic drug market for the treatment of schizophrenia or a market which allows Zyprexa to be prescribed as a mood stabilizing drug for mothers who have symptoms of anxiety and irritability?

Michael Bandick (June 9, 2006)

A. I don't see those as comparable concepts.
Q. They're not comparable?
A. They're not.
Q. Okay. Why not?
A. As I understood your question one had to do with the specific diagnosis and presumably an indication, the other one was not tied to a specific diagnosis or indication.
Q. Oh, the other one being the mood stabilizing drug for mothers who had symptoms of anxiety and irritability would not be an indicated and approved use of Zyprexa?
A. It would not be something we would promote within the context of our label.
Q. And it would not be an indicated or approved use of Zyprexa?
A. It would not be an indication for Zyprexa, indicated use for Zyprexa, that's correct.
Q. Or an FDA approved use?
A. That's correct.
Q. Okay. Which is a larger market, Zyprexa as an antipsychotic drug for episodes of mania in persons with bipolar disease or Zyprexa as a drug for the elderly patient with symptoms of dementia?

Michael Bandick (June 9, 2006)

A. As with your previous example I don't consider those to be comparable.
Q. And why aren't they comparable?
A. For the same reason that I stated before.
Q. And that is, Zyprexa as a drug for the elderly patient with symptoms of dementia is not an FDA-approved indication, correct?
A. That's correct.
Q. And one that it would be

219: 1 illegal and improper for Lilly to promote?

Michael Bandick (June 9, 2006)

219: 4 Q. Correct?
5 A. Consistent with company
6 policy we would not promote the product for
7 unapproved indications or things that fell
8 outside the label.
9 Q. And would promoting Zyprexa
10 for the elderly patient with symptoms of
11 dementia be illegal and outside company
12 policy?
13 A. It would be inconsistent with
14 company policy to promote for something that
15 fell outside of the approved indications.

Michael Bandick (June 9, 2006)

219:20 Q. Would it be illegal and
21 improper and outside Lilly's policies to
22 promote Zyprexa for the elderly patient with
23 symptoms of dementia?

Michael Bandick (June 9, 2006)

220: 3 A. It would be inconsistent with
4 Lilly company policy to promote Zyprexa for
5 the patient type that you just described.
6 Q. Thank you very much.
7 If you were able and chose to
8 promote to young mothers with symptoms of
9 anxiety and irritability for Zyprexa that
10 would be a much larger market than promoting
11 to the antipsychotic drug market for the
12 diagnosis of schizophrenia, wouldn't it?

Michael Bandick (June 9, 2006)

220:15 A. I can't speak to the size of
16 that market.
17 Q. Which market?
18 A. Mothers with symptoms of
19 anxiety that you just described.
20 Q. You all never looked into
21 that? You all being the marketing
22 department?

Michael Bandick (June 9, 2006)

221: 1 A. I'm not aware of any analysis
2 of the patient type that you just described.
3 Q. You're not?

4 A. No.

Michael Bandick (June 9, 2006)

221:13 Q. What about Donna?
14 A. I don't understand your
15 question.
16 Q. Okay. What about Martha?
17 A. What would you like to know?
18 Q. You all promoted to Martha,
19 didn't you?
20 A. No, we did not promote to
21 Martha.
22 Q. You promoted to Donna, didn't
23 you?

Michael Bandick (June 9, 2006)

236:10 Are you married?
11 A. Yes.
12 Q. Your wife is Mary?
13 A. Marcie.
14 Q. Marcie. That's my
15 handwriting I can't read.
16 Can you tell the jury where
17 Marcie works?
18 A. Marcie works for Eli Lilly
19 and Company.
20 Q. How long has Marcie worked
21 for Eli Lilly?
22 A. Approximately, 15 years.
23 Q. What department is she in?
24 A. Human resources.
237: 1 Q. And what's her title in human
2 resources?
3 A. She is a Human Resources
4 Director.
5 Q. And is she therefore, in
6 management?
7 A. Yes, I think you can
8 characterize that as a management role.
9 Q. Does she have, for example,
10 stock options as part of her compensation
11 plan in Eli Lilly?
12 A. She does.
13 Q. And does she -- and so, in
14 other words, the better Lilly stock does the
15 more money that Marcie can stand to make; is
16 that true?
17 A. Based on the strike price of
18 those options.
19 Q. And, of course, you all are
20 married. And how long have you been married?
21 A. We've been married 12 years.
22 Q. And I've been married almost
23 25. You treat your money as community
24 property money, do you not, you and Marcie?
238: 1 A. We do.

Michael Bandick (June 9, 2006)

238: 4 Q. Therefore, the better Lilly
5 does the more money you stand to make.

Michael Bandick (June 9, 2006)

238:10 A. As I indicated, based on the
11 strike price of options that stands to
12 reason, yes.
13 Q. How many options does your
14 family currently own in Eli Lilly stock?

Michael Bandick (June 9, 2006)

238:24 Q. My question to you was how
239: 1 many options does your family own in Eli
2 Lilly stock?
3 A. I don't know.
4 Q. Give this jury some rough
5 approximation, please?

Michael Bandick (June 9, 2006)

239: 8 A. My best guess would be
9 somewhere between five and 8,000.
10 Q. And what is the strike price
11 on those options? They vary?
12 A. It varies.

Michael Bandick (June 9, 2006)

240: 2 Q. What is the current value,
3 approximately, of your family's current Lilly
4 stock holdings?
5 A. I haven't computed that
6 recently.
7 Q. I'm certain you haven't, sir.
8 I said what is the value, approximately, of
9 your family's current Lilly stock holdings?

Michael Bandick (June 9, 2006)

240:12 A. I don't know.
13 Q. You don't know?
14 A. No.
15 Q. Can you give this jury a
16 rough approximation?
17 A. A lot of that depends on,
18 again, the strike price, the current stock.
19 I haven't looked at it. To be honest with

you it's not something I've looked at in the last six months, I don't known.
Q. When you last looked at it six months ago what was the approximate value of the Lilly stock holdings in your family?

Michael Bandick (June 9, 2006)

A. I don't know.
Q. You looked at it six months ago, you recall that, but you don't recall what you found out when you looked at it?

Michael Bandick (June 9, 2006)

Q. Okay, let me ask this. See if we can help this jury. Is your value of your Lilly stock holdings in the hundreds of thousands of dollars?

Michael Bandick (June 9, 2006)

A. I don't believe so.
Q. You left your employment -- well, you can tell the jury, you know that you have in your family Lilly stock, right?
A. That's correct.
Q. And Lilly stock options, correct?
A. That's correct.
Q. And the Lilly stock options is somewhere between 5,000 and 8,000 in number, correct?
A. Yes.
Q. Thank you.
Okay. You left your employment with Lilly. How would you characterize you leaving, did you resign or were you fired?
A. I resigned.

Michael Bandick (June 9, 2006)

Q. You said you resigned, right?
A. I did.
Q. Did somebody ask you to resign?
A. I was given the choice.
Q. Of resign or be fired?
A. Or -- yes.
Q. Okay. Who gave you the choice of either resigning or being fired?
A. Diedre Connelly and Dan Hasler.
Q. Tell me -- I didn't hear the

name?
A. Diedre Connelly and Dan Hasler.
Q. Tell the jury Diedre Connelly's title, please?
A. She was the head of the human resources function. I don't know her exact title.
Q. And who is Dan Hasler?
A. He is VP of Global Marketing.
Q. Why were you fired?

Michael Bandick (June 9, 2006)

246:
Q. Why were you given this option of resigning or being fired?
A. The company felt that my involvement in some activities with a third-party consultant had been handled inappropriately and concluded that that was grounds for the decision that I reached.
Q. Who was the third-party consultant?
A. It was a communications vendor that we had used as part of our activities.
Q. Who's the communications vendor?
A. The name of the company is Nichols Dezzinhall.
Q. And you used them as part of your activities. Are you saying you used them as part of your activities in relation to Zyprexa?
247:
A. Yes.
Q. And what activity did you engage in with this communications company, and tell me their name again, Nichols -- see, I didn't get it. Can you tell this jury and me again, please, the name of this communications company?
A. Nichols Dezzinhall.

Michael Bandick (June 9, 2006)

247:
Where's Nichols Dezzinhall located? Where are they located?
A. I believe Nichols Dezzinhall is headquartered in Washington, D.C.

Michael Bandick (June 9, 2006)

248:
Q. What did Nichols Dezzinhall from Washington, D.C., do for Lilly with regard to Zyprexa?
A. They helped to identify people who wrote articles that were then

offered for the lay media print and
electronic that were consistent with the
views that the Zyprexa team had on various
subjects.

Michael Bandick (June 9, 2006)

250: 7 **Q. I'm going to find out what**
8 **Dezzinhall did. I'm trying to find out. I**
9 **have no idea what you just said. I want you**
10 **to explain to me and this jury what it is**
11 **Dezzinhall did for Zyprexa?**
12 A. We used them to identify
13 individuals who would author articles,
14 typically, op ed types of articles, that
15 would be offered for placement in the lay
16 media, print and electronic, on subjects that
17 we, that were views that were consistent with
18 what Lilly held on certain subjects. Issues
19 in the marketplace that I can try to describe
20 for you. But I just want to make sure I'm
21 giving you enough clarity with that part and
22 if you are clear there then I can go on.
23 **Q. Yeah, I'm clear so far I**
24 **think. But let's go on. Then what else did**
251: 1 **they do?**
2 A. Well, it was in that context
3 that they, like I said, they found
4 individuals who would write articles and,
5 typically, these would be on marketplace
6 issues that were germane to Zyprexa and the
7 marketing of antipsychotics.
8 **Q. So all Dezzinhall, am I**
9 **pronouncing that correctly?**
10 A. Dezzinhall.
11 **Q. All Dezzinhall did was just**
12 **locate authors for these articles? That's**
13 **all they did?**
14 A. They were also involved in
15 the actual offering of the pieces. They
16 worked directly with the media. That's not
17 something that we did.
18 **Q. Well, did Dezzinhall,**
19 **actually, write the pieces and then try to**
20 **find a person who would put their name on it**
21 **as the author?**
22 A. No, it was the other way
23 around. They found the individuals who would
24 author the articles.
252: 1 **Q. Is there a Dezzinhall file**
2 **that you kept there at Lilly?**
3 A. There may be. It wasn't
4 something that I would have a lot of content
5 for. There was a short time that I was
6 involved in the, in that relationship, and
7 most of the interactions that we had were
8 teleconferences. So there may be a file, I
9 don't recall.
10 **Q. Who were your Dezzinhall**
11 **contacts?**
12 A. Well, the principal, the

principal's name is Eric Dezzinhall. There was an account executive, it was a woman, I'm not recalling her name.
Q. You said most of your contact with them was in teleconferences?
A. That's true.
Q. You indicated that the reason you were given this choice of resign or be fired was that these activities you described with Dezzinhall -- was it one particular event in particular, or was it a series of events that led to this choice of being fired or resigned?

Michael Bandick (June 9, 2006)

A. As it was explained to me, it had to do more broadly. There was not a single event that was cited.
Q. Were you the only person at Lilly that was in contact with Dezzinhall concerning the Zyprexa issue?
A. No.
Q. There's other people on these teleconferences and working with you on this Dezzinhall endeavor, weren't they?
A. Sometimes.
Q. Were they fired or had the choice to resign?
A. There were two other individuals who left the same week that I did. I have not been in contact with them to confirm this but I believe it had to deal with the same topic.
Q. Their names are, sir?
A. Jack Jordan and Jeff Newton.
Q. Jack Jordan was your immediate supervisor in the Zyprexa chain.
A. At one time.
Q. Who is the other guy, Newton, Jack?
A. Jeff Newton.
Q. What was Jeff's title?
A. He was director in communications.

Michael Bandick (June 9, 2006)

Q. Okay. You were fired because of this.
A. I was not fired.
Q. I'm sorry, you resigned. What was the advantage of resigning as opposed to being fired? Was there a monetary advantage or what was the advantage?
A. It better reflected the terms on which I wanted to leave the company.
Q. Did you all have a written agreement when you left?

A. Yes.
Q. So over whatever event this is in Dezrinhall you have a written agreement with Lilly at the time you resigned as opposed to being fired, right?

Michael Bandick (June 9, 2006)

256:14 A. That's correct.
Q. Did it provide you compensation as part of that written agreement?
A. Yes.
Q. How much?
A. Approximately, eight months salary.
Q. How much is that?
A. Just over a hundred thousand dollars.
257: 1 Q. Are you under any current contract with Eli Lilly or any of their affiliates?
A. No.
Q. Are you being paid to be here today?
A. No, I'm not.
Q. What is it you did wrong? You described it -- what is it that they said you did wrong?

Michael Bandick (June 9, 2006)

257:13 A. There, as I understand it, was a, essentially, an evaluation or an assessment that that relationship had not been managed to the company's satisfaction. They felt that it, potentially, put them in an embarrassing situation, and as a result I was given that choice that I -- we talked about earlier.
Q. I understand that part of the answer. And what is it that put them in an embarrassing situation and what is it that they said you did wrong?
258: 1 A. It's difficult for me to tell you that it's not entirely clear to me, because there was not a dialog that we had about it. And so I'm generally aware of what the area was, but have not -- I don't have the specifics to share with you that -- I mean, you'd have to talk to them.
Q. I'm going to. But I'm asking you what you understand they said you did wrong?

Michael Bandick (June 9, 2006)

informed you was named who?
A. There were two people, it was Diedre Connelly and Dan Hasler.
Q. You said Diedre. Diedre, probably, works for your wife?
A. No, she doesn't.
Q. She works in the same department?
A. She did.
Q. I don't want to talk about Diedre. But Diedre, that's human resources, they're always kind of their when you resign or get fired. It was this guy named Don?

Michael Bandick (June 9, 2006)

Q. Don or Dan -- what was his name?
A. The other person's name is Dan Hasler.
Q. Dan, he was the boss that was giving you your discipline, wasn't he?

Michael Bandick (June 9, 2006)

THE WITNESS: I don't understand what you mean by "discipline."
QUESTIONS BY MR. ALLEN:
Q. Let me tell you, when Dan came to your office with the lady, Diedre, from human resources, did this come out of the clear blue to you or did you have some warning it was coming?

Michael Bandick (June 9, 2006)

Q. I'm sorry. Where did this meeting take place?
A. It took place in the conference room.
Q. You were summoned to the conference room?
A. I was.
Q. On -- here at Eli Lilly?
A. It was at Lilly headquarters, yes.
Q. Okay. Did you have some warning that you were fixing to have this choice or did it come out of the clear blue to you?
A. I did not know what the meeting was going to be about.
Q. And I understand that. But had you heard anybody, had you been informed from any other source prior to the meeting that you were in trouble or they thought you

had done something wrong?

Michael Bandick (June 9, 2006)

Q. Okay. Well, wow, my only question was before that meeting -- what day was that meeting? I bet you can give us the very day in April 2004 that meeting took place, can't you?
A. It was in the second week of April, I don't remember the exact date.
Q. What date day of the week?
A. A Monday.
Q. Okay. So it was the second Monday in April of 2004?
A. Presumably.
Q. Okay. Prior to the second Monday in April 2004, had you had any indication from any source at Eli Lilly that any of your activities surrounding Zyprexa were wrong or you were about to be fired or asked to resign?

Michael Bandick (June 9, 2006)

A. No, I was not.
Q. Okay. So when you were summoned to that conference room and they told you that you had this choice to get fired or resign, it came out of the clear blue to you?
A. It was a surprise.
Q. When did you resign, that day?
A. Two days later.
Q. Did you, after you left the meeting in the conference room, did you return to your office and go back to work or did you go home?
A. I collected my things and I went home.
Q. So you were told at that meeting on the second Monday in April to get your things out of your office and to go home?

Michael Bandick (June 9, 2006)

A. I'd set up my office that day in a different building from where my office was. So to be truthful to your question I didn't clear out my personal things that day.

But I did go back to where I set up my office for that day because I moved on a couple of different Lilly campuses. And I did go back to that spot, collected my items, and then walked out to my car.

Q. Why did you move that day?
A. I'm sorry?
Q. Maybe I misunderstood you. I thought I heard you say you just moved campuses that day?
A. No. Lilly's headquarters is --
Q. Big.
A. -- across a number of different buildings. And my actual office was not where I was working out of that particular day.
Q. Okay. And I understand. So you went, how long did this meeting last?
A. About 20 minutes.
Q. You had been working at Eli Lilly in one capacity or another since 1991. You're called in on what you recall to be the second Monday in April, 2004, after 13 years of work. You had no indication you had ever been in trouble. And they gave you this choice and you had gone out of the conference in 20 minutes; is that right?

Michael Bandick (June 9, 2006)

Q. Is that right what I said?
A. It's accurate.
Q. I mean, that's got to come as a big shock to somebody. Did it?

Michael Bandick (June 9, 2006)

Q. Big shock to somebody. It was a big shock?
A. I was not expecting it.
Q. Did you ask for a written explanation?

Michael Bandick (June 9, 2006)

A. No, I didn't.
Q. Did they provide you with some, did they provide you with any documents or any writings, or show you any materials?
A. They read from a statement and I was not provided that document.
Q. They read from a prepared statement; is that correct?
A. They read from a statement.
Q. Who read it?
A. I believe, Diedre did.
Q. What did Don say to you?
MR. FAHEY: Dan.
A. Dan Hasler?
Q. Yes, sir, I'm sorry. What did Dan Hasler say to

you?
A. I don't recall his comments in that meeting.

Michael Bandick (June 9, 2006)

270: 5 Q. Have you ever talked to Dan
6 ever again?
7 A. I think I saw him once
8 outside of Lilly.
9 Q. Did you ever ask him what
10 happened --
11 A. No.

Michael Bandick (June 9, 2006)

312:18 Q. Okay. You told us that it
19 would be against federal regulations and the
20 law for Eli Lilly to promote Zyprexa for
21 indications that are not within the approved
22 label; is that correct?

Michael Bandick (June 9, 2006)

313: 1 A. It would be inconsistent with
2 company policy to do that.
3 Q. Is it also against FDA
4 regulation?
5 A. I'm not an expert in FDA
6 regulation. That's my understanding.
7 Q. It's your understanding it's
8 against FDA regulation, right?
9 A. To promote outside of
10 approved indications, yes.
11 Q. Okay. Now can you -- so
12 Lilly cannot, is not supposed to promote
13 outside the label, but can Lilly use third
14 party intermediaries to conduct such
15 activities? Sir?

Michael Bandick (June 9, 2006)

313:18 A. Not promotional activities.
19 Q. No. So in other words, if
20 Lilly can't promote outside of the label
21 Lilly cannot hire third parties and pay them
22 money to promote outside the label either,
23 can they?
24 A. No. Lilly cannot hire third
314: 1 parties to promote outside the label.
2 Q. Did Lilly ever hire third
3 parties to assist in promotion of Zyprexa
4 outside the indications on the label?
5 A. No.

Michael Bandick (June 9, 2006)

Q. Lilly's a member of PhRMA, are they not?
A. Yes, I believe so.
Q. Have you ever served in any capacity on the PhRMA board or any committees?
A. No, I haven't.
(Whereupon, Deposition Exhibit(s) 4 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. I'm going to hand you what's been marked as Bandick Exhibit No. 4. Copies for your counsel. And I will admit it's a poor copy. You can look at mine, all highlighted if you like.
That's a statement by PhRMA concerning the marketing and promotion of pharmaceuticals from PhRMA's website. Do you recognize that?
A. Let me take a look at it and I'll let you know.

Michael Bandick (June 9, 2006)

Q. Now you gave me my highlighted copy back. It's got some questions on there. I'm not trying to hide anything from you. What that thing says in sum -- you've now read it, right?
A. Yes, I have.
Q. I'm going to paraphrase what I think it says and you let me know if you agree or disagree with my characterization. PhRMA has taken the position that pharmaceutical marketing must be accurate, it must be balanced, and it must be, have full disclosure. Doesn't it say that right there? I highlighted it on there, I think, right?
Do you see where I highlighted "full disclosure"? I think I underlined it in red.
A. I'm looking for that. Yes, I see that now.
Q. Okay. That's the second paragraph. It says -- the title of this document, Bandick, is it No. 3?
A. 4.
Q. Bandick 4, comes from PhRMA. It says Marketing and Promotion of Pharmaceuticals, that's the title, correct?
A. Yes.
Q. Then you can look at my highlighted and underlined red copy, the second paragraph, it says: "The vast majority of the amount spent by pharmaceutical companies on medical marketing is on substantive information provided to

physicians." Do you see that?
A. Yes.
Q. Is that what you did in your role as marketing Zyprexa?
A. "The vast majority of the amount spent on medical marketing is on substantive information." Yes, I would say that's true.
Q. The second sentence of that paragraph: "All of it -- every word -- is regulated by the FDA to assure accuracy, balance, and full disclosure." Did I read that correctly?
A. That's what it says.
Q. Is that true?

Michael Bandick (June 9, 2006)

319: A. I can't speak to everything that the FDA does or doesn't review. I would say that, certainly, we had mechanisms internally to ensure that things were in compliance with what we understood the regulations to be.
Q. It doesn't say the FDA reviews it. It says, all of it, I'll read the second sentence: "All of it -- every word -- is regulated by the FDA to assure accuracy, balance and full disclosure." Do you understand that statement to be true?
A. I've no reason to think that it's not.
Q. All right. So you understood that your marketing and promotion, and the materials that were prepared for marketing and promotion, needed to be accurate, balanced and constitute full disclosure about Zyprexa --

Michael Bandick (June 9, 2006)

320: Q. -- is that true?

Michael Bandick (June 9, 2006)

320: THE WITNESS: Can you repeat your question, please?
Q. Yes, I'm going to just read the entire second paragraph put out by PhRMA.
Paragraph: "The vast majority of the amount spent by pharmaceutical companies on medical marketing is on substantive information provided to physicians. All of it -- every word -- is regulated by the FDA to assure accuracy, balance and full disclosure."
Did I read that correctly,

first of all?
A. Yes.
Q. Do you agree with that, second of all?

Michael Bandick (June 9, 2006)

A. The promotion of products, which is different from a broader concept of marketing, I would certainly agree with that.
I can't speak to every possible thing that could be under the umbrella of marketing. The way we worked at Lilly was to work in that regard, particularly, around promotional activities.
Q. Okay. Now I'm not going to read every word of this entire rest of the document because we have other documents we need to discuss. But let's read the first sentence of the third paragraph. "Pharmaceutical marketing serves the following positive purposes for physicians; it enables physicians to learn quickly and accurately about new therapies and diagnostic tools." Do you agree with that?
A. I do.
Q. Continuing in the third paragraph: "Pharmaceutical markets serves the following positive purposes for physicians," skipping down, "it provides FDA-regulated information that must be balanced and disclose all risks." Did I read that correctly?
A. You did.
Q. And I think, my copy I highlighted the word "all" and underlined it in red, didn't I?

Michael Bandick (June 9, 2006)

A. Yes, you did.
Q. Okay. And I want to direct your attention to the word "all." It says "the information must be balanced and disclose all risk." Do you agree with that?

Michael Bandick (June 9, 2006)

Q. My question is: Do you agree that your marketing documents must be balanced and disclose all risk?"

Michael Bandick (June 9, 2006)

A. Again, because I'm not in the

position to be a subject matter expert on those risks or their disclosure, I would say that we followed company policies that were very clear in terms of how to use subject matter experts to address those concerns.

Michael Bandick (June 9, 2006)

Q. In promotional material for Zyprexa did you disclose all of Zyprexa's risks?
A. We provided information that would have disclosed all risks, yes.
Q. All risk?
A. To the best of my knowledge.
Q. And was it fair and balanced? Was it fair and balanced?
A. Yes, that was the assessment of the members of our team.
Q. Did it constitute full disclosure as is reflected in Paragraph No. 2?
A. To the best of my knowledge it did.
Q. The last sentence of this entire document Marketing and Promotion of Pharmaceuticals it says: "More importantly it -- well, let me just read the entire last paragraph, two sentences.
"We regard pharmaceutical marketing as an essential part of the research process that brings new products into medical practice. More importantly, it serves a critical educational role in our health care delivery system."
First of all, did I read that correctly?
A. You did.
MR. FAHEY: Actually, you read --
Q. Marketing performs and serves as a critical educational role.
A. Among other things, yes.
Q. And so you knew when you prepared promotional and/or nonpromotional marketing materials concerning Zyprexa they would be utilized to educate both doctors, patients, third-party payors, and regulators, about your product; is that correct?

Michael Bandick (June 9, 2006)

A. Not all the materials that we created would be designed to go to all of those audiences.
Q. I understand. But those materials that were prepared and intended to reach those audiences, you understood would perform an educational function that is

critical to our health care system?

Michael Bandick (June 9, 2006)

A. I would say that in all of the materials that we had, both promotional and nonpromotional, there was an element of educational value in them, yes.

Q. And do you agree with PhRMA that that educational element performed a critical role in delivery of health care in the health care system?

A. That's really beyond my scope of being able to answer that.

Q. Can you hand me my copy of that back? Thank you sir.

You've heard the term "fair and balanced" before have you not, in regard to marketing documents?

A. I've heard the term "fair balance."

Q. What does that mean to you?

A. That there is an appropriate balance between what would be considered advantages or disadvantages, efficacy, safety.

Q. For example, you cannot, you, being the marketing department, in order to reach fair balance, you cannot overemphasize the benefits of Zyprexa and underemphasize the risk of Zyprexa?

Michael Bandick (June 9, 2006)

A. That's my understanding of the term fair balance.

Q. Thank you. At Lilly, in order to have fair balance can you spin the data on Zyprexa?

A. I don't know what you mean.

Q. You ever heard the term "spin the data?"

A. I'm familiar with the term "spinning." I'm not sure I understand "spinning the data."

Q. Do you think -- in your opinion, can you spin the data when marketing Zyprexa?

Michael Bandick (June 9, 2006)

A. The way we treated clinical data you would not be in a position to quote/unquote spin the data.

Q. And you should not spin the data?

MR. HAMMERLE: Same

objection.
A. Let me be clear about what I define as spinning the data.
Q. Yes, sir.
A. If by spinning you mean to mislead or to provide an untrue characterization of the data, that would be inappropriate.
I've also heard the use of the word spin more loosely in a way that would suggest to try to make things appear positive without compromising the integrity of those data.
So I want to be clear that my definition covers both of those.
Q. Okay. In marketing, be it promotional or nonpromotional materials, can you torture the data --

Michael Bandick (June 9, 2006)

Q. -- presented concerning the safety or efficacy of Zyprexa?

Michael Bandick (June 9, 2006)

A. That's not a phrase that I would use to characterize the way that we produced marketing materials at Lilly.
Q. You would agree you should not be permitted to torture the data?

Michael Bandick (June 9, 2006)

A. I'm not sure I understand what you mean by quote/unquote torturing the data, so I can't answer your question.
Q. Okay. When Lilly speaks about Zyprexa is it giving answers that matter?

Michael Bandick (June 9, 2006)

A. Answers that matter is a tag line that Lilly adopted as a corporation some years ago. That's not the context in which we created our materials. It's not a tag line that meant something to me while I was creating those materials. That was something I felt represented more of a corporate messaging campaign.
Q. Yeah. And you're a marketing professional, it was a corporate message, it's on the documents. It's Lilly, you see Lilly, and underneath it you always see

"answers that matter," do you not?
A. Some of them.
Q. Yes. What is the message that the phrase, the slogan that Lilly, answers that matter, what message does that send to the consumers of Lilly's products?

Michael Bandick (June 9, 2006)

A. The reason that you'll find it on a lot of documents is that was part of a Lilly corporate branding campaign. If you're asking me to interpret "answers that matter," to me that would imply that it's information that is relevant to the audience.
Q. Right. And, in fact, didn't Lilly represent itself in response to questions involving Zyprexa at times as being the world leaders in diabetes treatment?

Michael Bandick (June 9, 2006)

Q. Do you recall that?
A. Lilly has a long history in that disease state. I don't recall Lilly characterizing itself as such regarding matters around Zyprexa.

Michael Bandick (June 9, 2006)

Q. Is there a higher standard in the marketing and manufacturing of drug products required as opposed to, let's say, ordinary consumer products such as soap?

Michael Bandick (June 9, 2006)

A. I don't know what the standards are around consumer products. I can only speak to what I know about pharmaceutical marketing.
Q. Do you think there should be a higher standard applied to the marketing of drug products such as Zyprexa as opposed to consumer products such as soap?

Michael Bandick (June 9, 2006)

A. That's a hypothetical question that I've never considered before.
Q. Okay. Did Lilly have a problem of being overly aggressive to the point of greed in promoting Zyprexa?

Michael Bandick (June 9, 2006)

335: 7 THE WITNESS: Is there an
8 example that you'd like me to react
9 to?
10 Q. Do you know of any examples?
11 A. No, I don't.
12 Q. Okay. So the answer to my
13 question was did Lilly have a problem with
14 being overly aggressive to the point of greed
15 in promoting Zyprexa, is your answer yes or
16 no?

Michael Bandick (June 9, 2006)

335:19 A. My answer would be no.
20 Q. Was Lilly spinning the
21 medical facts and data and presenting biased
22 information in order to beat the competition
23 when it promoted Zyprexa?
24 A. No.
336: 1 Q. Did Lilly have a quote -- let
2 me rephrase. Did Lilly have a quote
3 "spinning mentality," close quote, in its
4 promotional efforts on behalf of Zyprexa?

Michael Bandick (June 9, 2006)

336: 7 A. No. In fact, great care was
8 taken to provide accurate data and in
9 appropriate context.

Michael Bandick (June 9, 2006)

347: 9 MR. ALLEN: Here's Bandick
10 Exhibit No. 6. I have copies for
11 your counsel.
12 QUESTIONS BY MR. ALLEN:
13 Q. Do you know Alan Breier?
14 A. Yes, I do.
15 Q. Tell the jury who Alan Breier
16 is?
17 A. Currently, he is Lilly's
18 Chief Medical Officer.
19 Q. Chief Medical Officer. Let
20 me go down to the third paragraph of -- so
21 it's Dr. Alan Breier; is that correct?
22 A. Yes, he is a physician.
23 Q. This is an e-mail he wrote to
24 US Medical, Medical US, Subject: 2004
348: 1 Medical Objectives. Attaching 2004 Medical
2 Objectives, Power Point Principles.
3 Do you agree with that so
4 far?

Michael Bandick (June 9, 2006)

349: 2 Q. Sir, do you agree that is to
3 US Medical Medical and it's from Dr. Alan
4 Breier?
5 A. As far as I can tell.

Michael Bandick (June 9, 2006)

349:17 Q. Sir, I want to direct your
18 attention to the third paragraph under
19 principles. Do you see the bold word
20 Principles?
21 A. I do.
22 Q. Hear what Dr. Breier says in
23 Bandick No. 6: Making medicine for people
24 facing illness is a much different and higher
350: 1 calling than making consumer products for
2 other markets. We do not sell soap. It,
3 therefore, requires a different and a higher
4 code for conducting our business."
5 Did I read that correctly?
6 A. That's what it says in this
7 document.
8 Q. Do you agree with that --

Michael Bandick (June 9, 2006)

350:11 Q. -- philosophy expressed by
12 Dr. Breier in Bandick Exhibit No. 6?

Michael Bandick (June 9, 2006)

354: 2 Q. All right, sir, you reviewed
3 this document, have you not, now?
4 A. Yes, I have.
5 Q. Okay. Do you see within this
6 document that Dr. Breier, who you said you
7 understand to be Director of Global Medical
8 Affairs in the company, correct?
9 A. I believe his current role is
10 Chief Medical Officer.
11 Q. Is there any higher doctor in
12 the whole company?
13 A. Not based on Lilly structure,
14 no.
15 Q. Based on what structure?
16 A. Not based on Lilly structure.
17 Q. So he's the highest medical
18 doctor in the whole company, right?
19 A. As far as I can tell.
20 Q. Okay. He writes this e-mail.
21 And I'm going down the third paragraph,
22 bolded sentence: "Principles. Making
23 medicine for people facing illness is a much

different and higher calling than making consumer products for other markets. We do not sell soap, exclamation point." Did I read that correctly?

A. Yes.

Q. Do you agree with Dr. Breier?

A. I agree it's much different, and my own opinion is that it is a higher calling.

Q. So, therefore, there is a higher standard required for the marketing and promotion of drugs as opposed to other ordinary consumer products such as detergent, do you agree?

Michael Bandick (June 9, 2006)

A. I'm not aware what Dr. Breier meant by that statement. And as we were talking about earlier, I don't know enough about the regulations in other areas. I know what the regulations are for pharmaceutical marketing.

Michael Bandick (June 9, 2006)

Q. Dr. Breier is not referring to regulations. He's referring, as I understand it to an issue of ethics and standards; would you agree with that?

A. I don't know what he intended by that statement.

Q. Okay. So you're not willing to concede for this jury that the marketing of drug products requires a higher standard than as opposed to Tide detergent?

Michael Bandick (June 9, 2006)

A. I'm not in a position to pass judgment on that.

Q. You're not in a position to pass judgment on that. Weren't you the Brand Manager and the Director of Marketing Management for Zyprexa?

A. Yes, I was.

Q. Did you consider your marketing activities and the statements that would be made in the promotion and nonpromotional materials to be more significant than that which would entail in the marketing of Camay soap?

Michael Bandick (June 9, 2006)

357: 5 A. As I indicated to you, I do
6 agree with the comment it is a higher calling
7 but I have no way of comparing what the, what
8 the parameters are for commercializing soap.
9 What I do know is what the
10 parameters are for commercializing
11 medications and pharmaceutical products and
12 that's what we adhere to.
13 Q. Are those standards for
14 manufacturing and marketing drugs higher than
15 those for marketing soap?
16 A. I don't know.

Michael Bandick (June 9, 2006)

357:19 Q. Dr. Breier goes on: "It
20 therefore requires a different and higher
21 code for conducting our business."
22 First, did I read that
23 correctly?
24 A. You did.
358: 1 Q. Do you agree with Dr. Breier?
2 A. I don't know the context in
3 which he intended that statement.
4 Q. So you can't answer my
5 question?
6 A. I can't answer your question.
7 Q. Dr. Breier goes on: "The
8 principles of medical research, parens, PMR,
9 close parens, provide the road map to guide
10 all human research at Lilly. PMR has been
11 fully endorsed by all key governance bodies
12 and including the Corporate Policy Committee
13 and are now the law of the land. To make the
14 principles live in our culture requires all
15 of us to understand and put into action their
16 underlying intent. We are particularly
17 challenged when it comes to presenting our
18 data in a completely objective, unbiased
19 manner because of our passion for our
20 molecules and the belief that, quote,
21 "spinning" data is sometimes necessary to
22 gain a competitive advantage. If we do not
23 abandon the quote "spinning," close quotes,
24 mentality, we will not restore confidence in
359: 1 our medical research and rebuild the public
2 trust our industry has compromised."
3 First of all, did I read that
4 correctly?
5 A. Yes.
6 Q. You agree with Dr. Breier?
7 A. I don't understand all the
8 things that he is communicating in those
9 sentences.
10 Q. But what you understand do
11 you agree with Dr. Breier?

Michael Bandick (June 9, 2006)

359:14 A. I don't know where he is
15 differentiating between Lilly and the rest of
16 industry. I don't know which, if any,
17 specific products he's referring to. I'm
18 generally able to understand the comment but
19 I don't know the full context of it. I
20 wasn't part of the audience for this e-mail.
21 Q. Do you agree with Dr. Breier?

Michael Bandick (June 9, 2006)

360: 2 A. I don't think I know enough
3 about the context to be able to answer your
4 question.
5 Q. Well, when Dr. Breier says:
6 "We are particularly challenged when it comes
7 to presenting our data in a completely
8 objective, unbiased manner because of our
9 passion for our molecules, and the belief
10 that "spinning" data is sometimes necessary
11 to gain a competitive advantage," does it
12 appear he's talking about Eli Lilly and their
13 products?

Michael Bandick (June 9, 2006)

360:18 A. It's not clear to me. And
19 the next sentence he uses the same pronoun
20 "we, and attaches that to the public trust
21 that our industry has compromised. So it's
22 not clear to me that he's speaking about
23 Lilly or if he's speaking more broadly about
24 the industry.
361: 1 Q. Okay. So when he says "the
2 belief that "spinning" data is sometimes
3 necessary to gain a competitive advantage,"
4 are you saying he's saying spinning the data
5 for the drug industry to gain a competitive
6 advantage over the cereal industry?

Michael Bandick (June 9, 2006)

361: 9 A. No, I don't think he meant
10 that.
11 Q. No. What he means is, he's
12 saying when we spin our data to gain a
13 competitive advantage over another drug
14 company, isn't that what he's saying?

Michael Bandick (June 9, 2006)

361:18 A. As I said a couple of
19 questions ago, it's not clear to me from that
20 sentence whether he's speaking about Lilly,
21 specifically, or about the industry.

Q. Did you reach all these conclusions here in the last five minutes?
A. It's the first time I've seen it.
Q. Okay. Why don't we go up to the very first paragraph of this document and let me read it to you. Dr. Breier says: "Greetings, Medical Colleagues, Early in January, the extended Medical Lead team, which comprises 25 cross functional leaders from our Component, gathered to discuss our 2004 challenges and define a set of objectives for 2004," period. Did I read that correctly?
A. Yes.
Q. Who is he talking about, the industry or is he talking about Eli Lilly?
A. I take that to mean Lilly.
Q. Okay. He says: "These objectives, which are organized around 5 Ps -- Patients, Principles, Pipeline, Productivity and People, were presented at the Medical Town Hall on January the 27th." Period. Did I read that correctly?
A. Yes.
Q. Is he talking about the industry or is he talking about Eli Lilly?
A. I presume that to be a Lilly reference.
Q. "I have attached the objectives along with our strategic intent statement, parens, also known as the medical component mantra, close parens, below and would like to share some additional thoughts about them now," period. Did I read that correctly?
A. Yes.
Q. Is he talking about the industry or is he talking about Eli Lilly?
A. I presume that's a Lilly reference.
Q. And then he goes down and he says, I'm going to provide you the Lilly principles, right?
MR. FAHEY: Objection to form.
MR. HAMMERLE: Same objection.
A. Those are the objectives for the Medical Lead team.
Q. Of what company?
A. Lilly.
Q. Okay. So this document is not dealing with the industry, this document's dealing with Lilly practices and procedures, is it not?

Michael Bandick (June 9, 2006)

A. The document, as I understand it, has to do with Lilly medical objectives.

There are other references that are broader than simply Lilly medical.
Q. What are objectives that are broader than Lilly medical?
A. No, I said there are references that are broader than Lilly medical. References like in that last sentence of the paragraph entitled Principles.
Q. Okay. Anyhow, this is what Dr. Breier says. "Below I'd like to share some additional thoughts about them now," referring to the medical component mantra. Is No. 1 Patients?
A. Yes.
Q. Now here's how I read it. I come from Houston now, you understand, so I'm going to have a hard time with this French word. He says, "The raison d'être for our industry;" is that right?

Michael Bandick (June 9, 2006)

A. I'm not in a position to address your French pronunciation.
Q. You know what that means? Doesn't that mean "the reason?"
A. The reason for being.
Q. The reason for our industry and why most of us chose to work at Lilly is to serve patients. While we have other important customers, parens, e.g., meaning for example, doctors, payors and regulators, close parens, we make medicines for only one customer." Did I read that correctly?
A. Yes.
Q. Who is that one customer that Dr. Breier says we make these medicines for?
A. The document says the patient.
Q. I asked you about that about the first 20 minutes this morning. Do you recall that?
A. I do.
Q. And do you agree with Dr. Breier here that the first and most important customer Eli Lilly has is not the doctor, it's not the payor, it's not the regulator, it's the patient?

Michael Bandick (June 9, 2006)

A. The context in which we were talking earlier this morning had to do with marketing. I would agree that from a medical standpoint the patient would be at the very top of the list. Within marketing I put patients and physicians co-No. 1.
Q. Good we got that agreement.

In your view in marketing patients and doctors are co-No. 1s, right?
A. Yes.
Q. All right. Is there anytime where the patient is not No. 1 at Eli Lilly?
A. There are times when a patient wouldn't be the primary audience for a particular message, but in terms of priority, patient safety would be at the top of the list.
Q. Now it goes on to say: "Thus the patient is our primary customer. We in medical are in the process of affirming a patient centered culture where the needs of patients are well understood and take top priority in all of what we do. Integral to a patient centered culture is putting patients in the heart of our business process. In our daily work we are faced with making decisions based on a set of priorities. Putting patients at the top of the priority list will lead to the right decisions and the most robust business results. As I have often said, quote, what is good for patients is good for business, close quotes." Did I read that correctly?
A. Yes.
Q. Is the converse true, what is bad for patients is bad for business?

Michael Bandick (June 9, 2006)

A. It certainly can be.
Q. Right. For example, if in marketing to the customer you started informing doctors and patients that Zyprexa carried with it an increased risk of diabetes different, separate and apart, from other antipsychotic medications, that you need to monitor your glucose levels because you can develop diabetes, diabetic ketoacidosis and go into a diabetic coma and die, if you relay that information about your product that would be bad information concerning the health of the patient, would you agree?

Michael Bandick (June 9, 2006)

THE WITNESS: That's a very long question. Could you break it up or rephrase it?
Q. Yeah. Let me say, Dr. Breier says "what's good for patients is good for business," right?
A. He did.
Q. I'm asking is the converse true, what's bad for patients is bad for business?
A. I think that's often the

case.
Q. Okay. So, therefore, if you're marketing a product such as Zyprexa -- we're here to talk about Zyprexa.
A. Right.
Q. And you start telling people, we believe that there is an increased risk of diabetes, diabetic coma, and diabetic ketoacidosis, that would be a bad medical condition, right?

Michael Bandick (June 9, 2006)

A. There are two parts to your question; one, is that a bad medical condition. And I think an MD would be in a better position than me but based on what I know, yes, that would be a bad medical condition.
But if the question is would telling audiences about that risk be a bad thing? I would say no.
Q. If a drug in a class has an increased risk over other drugs in a class, do you have an opinion as a marketing professional, as to how that would affect the sales of the product with the increased risk?

Michael Bandick (June 9, 2006)

A. It depends on the risk, it depends on the difference, it depends on the, on other factors, such as relative differences in efficacy. I mean, the whole risk/benefit balance is a pretty complicated thing.

Michael Bandick (June 9, 2006)

Q. Explain to the jury since you used that term "risk/benefit balance", why don't you explain what you meant to the jury, please?
A. I didn't go to medical school but my understanding is that MDs are educated as to how to perform a risk/benefit analysis with their patients, and try to optimize that balance to favor the patient.

Michael Bandick (June 9, 2006)

Q. Mr. Bandick, I handed you at the break what's been marked as Bandick Exhibit No. 7. Do you recognize this document?

372:18 Q. I handed it to you about a
19 minute ago during the break, Bandick Exhibit
20 No. 7.
21 Do you recognize Bandick
22 Exhibit No. 7?
23 A. Yes, I do.
24 Q. And how is it you recognize
373: 1 this document? How is it you recognize this
2 document?
3 A. I am familiar with the,
4 generally familiar with the content. It's
5 been a while since I've seen it. And I was
6 aware of when it was published.
7 Q. It is a document entitled the
8 "Consensus Development Conference on
9 Antipsychotic Drugs and Obesity and
10 Diabetes." And it's published by the
11 American Diabetes Association, the American
12 Psychiatric Association, the American
13 Association of Clinical Endocrinologists and
14 the North American Association for the Study
15 of Obesity, in 2004; is that correct?
16 A. It was published in Diabetes
17 Care and those four associations are
18 associated with it.
19 Q. And you read this in your
20 role at Eli Lilly before you left your
21 employment, did you not?
22 A. Yes, that's true.
23 Q. And just for the record, as
24 reflected in this exhibit, this is a
374: 1 consensus development document involving a
2 conference that was held in November of 2003;
3 is that correct?
4 A. Yes, I believe it is.
5 Q. And individuals as reflected
6 in this document, individuals from Eli Lilly
7 made a presentation at that conference,
8 correct?
9 A. That is correct.
10 Q. Along with other drug company
11 representatives and individuals from the FDA,
12 among others?
13 A. Yes, that's correct.
14 Q. And some of the drug
15 companies that made presentations included
16 were AstraZeneca, Janssen and Pfizer?
17 A. Those are the three I recall.
18 Q. By the way, did you attend
19 this conference?
20 A. Yes, I did.
21 Q. So you were, actually, there
22 at the conference itself; is that right?
23 A. Yes, I attended.
24 Q. Where was that conference
375: 1 held?
2 A. It was in -- in Virginia.
3 Q. Why did you attend this
4 conference?

A. I was part of a Lilly group most of whom are in medical, but then I also was attending for my own education.

Michael Bandick (June 9, 2006)

375:19 Q. Did they have a name for this
20 Lilly group?
21 A. No.
22 Q. Why were you selected to
23 attend?
24 A. Many of the things that we
376: 1 did involved a collaboration between
2 marketing and medical.
3 Q. So when you told me earlier
4 "I'm not a doctor," and then you gave an
5 answer, do you recall starting an answer "I'm
6 not a doctor" and then you started answering
7 the question?
8 A. I believe I did say that,
9 yes.
10 Q. But you have throughout the
11 entire experience in marketing drug products,
12 in particular Zyprexa, worked on committees
13 and teams at Eli Lilly which they call
14 cross-functional teams, and you've worked
15 with the medical affairs department, have you
16 not?
17 A. I have worked with medical on
18 a number of occasions.
19 Q. Okay. Now, this conference
20 was convened to answer several questions, was
21 it not?
22 A. Yes, it was.
23 Q. Okay. I'm just going to have
24 you skip over to Page 597 of Bandick Exhibit
377: 1 No. 7, the consensus statement, and you see
2 question three?
3 A. Yes.
4 Q. The question is: "What is
5 the relationship between the use of these
6 drugs and the incidence of obesity and
7 diabetes, question mark." Did I read that
8 correctly?
9 A. Yes.
10 Q. And when we're talking about
11 "these drugs," this conference was looking at
12 second generation antipsychotics; is that
13 correct?
14 A. Primarily.
15 Q. Okay. Including Risperdal,
16 Zyprexa, Seroquel, Geodon, is it Abilify?
17 A. Yes, is it.
18 Q. And Clozaril?
19 A. Yes.
20 Q. Those are the second
21 generation antipsychotics that were evaluated
22 in this consensus statement, right?
23 A. That's correct.
24 Q. The question is: What is the
378: 1 relationship in the use of these drugs and

the incidences of obesity or diabetes?
A. That is correct.
Q. The first heading, the bold heading, obesity, do you see that?
A. Yes, I do.
Q. It says under there: "There is considerable evidence, particularly in patient with schizophrenia, that treatment with the second general antipsychotics can cause a rapid increase in body weight in the first few months of therapy that may not reach a plateau even after one year of treatment. There is, however, considerable variability in weight gain among the various second generation antipsychotics." And it references Table 2. Did I read that correctly?
A. Yes.
Q. And you see table two underneath that statement?
A. Yes, I do.

Michael Bandick (June 9, 2006)

379:14 Q. According to table two, which is directly in front of you, at a conference you attended, what second generation antipsychotics carried the largest risk of weight gain and risk for diabetes according to Table 2?
A. According to this panel, clozapine and olanzapine, Clozaril and Zyprexa, had a higher relative risk for weight gain.
Q. And for diabetes?
380: 1 A. And to answer the other part of your question, according to this table they also identify clozapine and olanzapine as having a relatively higher risk for diabetes.
Q. And when we say olanzapine, so olanzapine being Zyprexa, for example, has a greater risk for causing weight gain and diabetes than Risperdal, Seroquel, Abilify and Geodon, correct?
A. That's what it says in this table.
Q. According to Table No. 2?
A. Yes.
Q. Of course, you'd known about that for a long, long, time before this consensus statement, right?

Michael Bandick (June 9, 2006)

380:22 A. I don't agree with that.
Q. The medical affairs or medical department -- let me ask this
381: 1 question. Roland Powell, what department did

he work in at Lilly?
A. In what time frame?
Q. In November '99.
A. I believe he would have been in marketing for the Global Zyprexa Product Team.

Michael Bandick (June 9, 2006)

Q. The marketing department and the medical affairs department at Eli Lilly had known for years prior to the consensus statement conference that you attended that Zyprexa carried a greater risk for weight gain than Seroquel, Risperdal or traditional neuroleptics; isn't that true?

Michael Bandick (June 9, 2006)

A. I'm trying to recall the launch date of Seroquel, but for Risperdal, yes, it was well characterized that Zyprexa resulted in more weight gain than the other products.
Q. And let me hand you what's been marked as --
A. I just want to note, though, my source for disagreement in your previous statement had to do with your question about also knowing about the increased risk of diabetes and that's the part I disagreed with.

(Whereupon, Deposition Exhibit(s) 8 duly received, marked and made a part of the record.)

QUESTIONS BY MR. ALLEN:
Q. Okay. I've handed you what's been marked as Bandick Exhibit No. 8. It's an e-mail from Alan Breier, you've already told us who Dr. Breier is, to various people including individuals within the marketing department; is that correct?
A. I don't know. I'll need to take a minute. I've not seen this before.
Q. Just look at the two cc's. My question right now is are people in the marketing department included in this e-mail?
A. The names in the, to whom this was addressed are senior leadership that I wouldn't characterize as marketing leadership. I would characterize them as corporate leadership.
Q. Okay. That's better. This e-mail was sent to corporate leadership in November of '99, right?
A. Apparently.
Q. Do you see where Dr. Breier says in the first sentence: "John asked me to overview the topic of

Michael Bandick (June 9, 2006)

386:18 A. I would like to take a moment
19 to review the rest of the document.
20 Q. My question, sir. You can
21 put the document down, sir.

Michael Bandick (June 9, 2006)

386:24 Q. I'm not asking about the
387: 1 document. Take the document, flip it over,
2 and I'm not going to ask you about the
3 document, okay. Do you agree to do that?
4 A. As you wish.
5 Q. All right, sir. Let me ask
6 you, was it the position of the Zyprexa
7 marketing team, the Zyprexa brand team and
8 the marketing efforts for Zyprexa, that
9 Zyprexa provided superior treatment and
10 outcome and in the antipsychotic market you
11 had no peer?

Michael Bandick (June 9, 2006)

387:14 A. That's not language that I
15 used in characterizing the brand in our
16 marketing.
17 Q. So you disagree with that
18 statement?
19 A. That's not what I said.
20 Q. Do you agree with that
21 statement?

Michael Bandick (June 9, 2006)

387:24 A. Without knowing the context
388: 1 of what Dr. Breier intended in thinking about
2 it in 1999, I don't really have a basis to
3 agree or disagree with that.
4 Q. I'm not asking about
5 Dr. Breier now. Let me ask this question.
6 Do you agree that when you were marketing
7 Zyprexa was it your position in your role in
8 marketing that Zyprexa offers the best
9 combination of efficacy, safety, and ease of
10 use, of any available treatment for
11 psychosis?

Michael Bandick (June 9, 2006)

388:14 A. That's not a verbatim for our
15 promotional marketing. It does represent, I

believe, a summary in 1999 of how we felt Zyprexa compared to other second generation antipsychotics.
Q. How about in 2000?
A. I would still say that represented, in general, our characterization of the brand.
Q. How about 2001?
A. Nothing would have changed.
Q. How about 2002?
A. Nothing would have changed.
Q. How about 2003?
A. Nothing would have changed.
Q. How about 2004?
A. I left the team at that point and was no longer involved in the marketing.
Q. How about prior to the time you left in 2004?
THE WITNESS: In January of 2004?
MR. ALLEN: Yes, sir.
A. It still represented a general summary of how we felt the brand compared.
Q. So in marketing, the general summary of how you felt the brand compared to the other anti second generation antipsychotics, would accurately state that Zyprexa offers the best combination of efficacy, safety, and ease of use; is that correct? True?

Michael Bandick (June 9, 2006)

A. It's a very broad statement. We wouldn't -- we wouldn't hold that position for every single patient. In comparing the major drugs out there it's generally a reasonable statement, again, not a verbatim that we would use in our promotion.
Q. Well, isn't it a fact that's exactly what you told doctors and patients?

Michael Bandick (June 9, 2006)

A. I'm not aware of that language.
Q. Remember -- now I'm going back to number 8, sir. I'm going to refer you back to Exhibit 8, now.
A. Then I will ask for a few moments to review the document in its entirety.
Q. Don't you want to hear a question I have first?
A. No. Actually, we've been asking a lot of questions about it and I'm feeling that I'm not going to be able to answer your question very well unless I've

read the document.
Q. So before you hear a question you want to review the entire document?
A. Yes, sir.

Michael Bandick (June 9, 2006)

391:23 Q. While you you're reviewing
24 the document, sir, I want you to keep this
392: 1 question in mind. Sir? Sir? Here's the
2 question I want you to consider while you're
3 reviewing this document.
4 In November of '99, as you
5 said, the corporate -- what do you call these
6 people, the corporate what?
7 A. I referred to them as
8 corporate leadership.
9 Q. The corporate leadership of
10 Lilly knew as a fact that among the
11 antipsychotics Zyprexa carried a greater risk
12 of weight gain than Seroquel, Risperdal, and
13 the other traditional neuroleptics. Now the
14 question's on the table as you review this
15 document?
16 A. I will keep that in mind.

Michael Bandick (June 9, 2006)

392:22 Q. And the answer to my question
23 is what, sir?
24 THE WITNESS: Could you
393: 1 repeat your question?
2 Q. Corporate leadership at Lilly
3 had known since at least November of '99 as a
4 fact that Zyprexa carried a greater risk of
5 weight gain than Seroquel, Risperdal, and the
6 traditional neuroleptics?

Michael Bandick (June 9, 2006)

393: 9 A. That's true.
10 Q. And in fact, in this
11 document, Exhibit No. 8, it states that that
12 is a fact, correct?

Michael Bandick (June 9, 2006)

393:14 A. Yes.
15 Q. Did you tell, you in
16 marketing, in your promotional activities,
17 subsequent to, at least -- let me rephrase
18 the question.
19 The date of Exhibit No. 8 is
20 November 24, 1999; is it not?
21 A. Yes, it is.

Q. Did you in the marketing department then begin to promote Zyprexa and tell the patients and doctors and your customers and your audience that it was a fact that Zyprexa carried a greater risk of weight gain than Seroquel, Risperdal and traditional neuroleptics?

Michael Bandick (June 9, 2006)

A. At that point I would say that we'd already been doing that for more than three years.

Q. Your position is you'd been telling doctors and patients for three years, since 1996, it was a fact, it was a fact that Zyprexa carried a greater risk of weight gain than Seroquel, Risperdal and traditional neuroleptics?

Michael Bandick (June 9, 2006)

A. Going back to 1996 when Zyprexa was launched Seroquel was not yet on the market so we didn't state it. And I don't know that we used that exact language saying it is a fact. But we did disclose and describe the clinical trial data that demonstrated that weight gain was higher on Zyprexa than on the other products.

Michael Bandick (June 9, 2006)

Q. Let's read the statement in Bandick Exhibit No. 8 under Market Research and go down to one, two, three, four, five, six bullet points. Do you see that?

A. I do.

Q. It says: "Olanzapine is viewed to have more associated weight gain than risperidone, Seroquel and traditional neuroleptics, Parens, Facts: The order of weight gain among antipsychotics is Clozapine is greater than olanzapine, which is Zyprexa, which is greater than Seroquel, which is greater than risperidone, which is greater than traditional neuroleptics, close parens, period." Right?

A. That's what it says.

Q. And it uses the word that's a fact, F-A-C-T, right?

A. Yes, it does.

Q. Do you recall as of November 1999, whether or not you were using and promoting Zyprexa and telling people, your audience that it was a fact that Zyprexa carried a greater risk of weight gain?

Michael Bandick (June 9, 2006)

396:20 A. I don't recall that we used
21 that exact language the way that you just
22 suggested, but continued to disclose the fact
23 that Zyprexa did have clinically significant
24 weight gain and that weight gain was, in
397: 1 fact, greater than on other second generation
2 antipsychotics.
3 Q. Do you see how in Exhibit
4 No. 8 it just says "fact," it's a fact for
5 Zyprexa?
6 A. Yes.
7 Q. Do you ever recall using that
8 terminology in the promotion of Zyprexa?

Michael Bandick (June 9, 2006)

397:12 A. I don't recall using that
13 exact terminology, no.
14 Q. You think that terminology is
15 rather clear and unambiguous? It's a fact.
16 That's a pretty unambiguous term, is it not?
17 A. I think it's fairly clear.
18 Q. And if you were trying to
19 effectively communicate whether or not
20 Zyprexa carried a greater risk of weight gain
21 than other second generation antipsychotics
22 or traditional antipsychotics, wouldn't the
23 best and easiest and straightforward fashion
24 to do is is say "it's a fact Zyprexa carries
398: 1 a greater risk of weight gain"?

Michael Bandick (June 9, 2006)

398: 4 A. That would be one way to do
5 it.
6 Q. Wouldn't it be the best way
7 to do it?

Michael Bandick (June 9, 2006)

398:10 A. I don't know.
11 Q. Why don't you turn, now, sir,
12 to Page 598 in Bandick Exhibit No. 7, which
13 is the consensus statement, and go to
14 question No. 4. Do you see that?
15 A. Yes.
16 Q. The question No. 4 reads:
17 Given the above risks, how should patients be
18 monitored for the development of significant
19 weight gain dyslipidemia, and diabetes, and
20 how should they be treated if diabetes
21 develops, question mark."
22 Did I read that correctly?

A. Yes.
Q. The answer says: "Given the
399: 1 serious health risks, patients taking SGAs
2 should receive appropriate baseline screening
3 and ongoing monitoring." Did I read that
4 correctly?
5 A. Yes.

Michael Bandick (June 9, 2006)

399:14 Q. Do you agree with that?
15 A. Based on my conversations
16 with Lilly clinicians I believe that would be
17 reasonable.
18 Q. And when did you form that
19 belief?
20 A. I don't recall.
21 Q. What year?
22 A. Probably, 2003.
23 Q. Isn't there a -- what do you
24 recall about what month you reached that
400: 1 conclusion based on your conversations with
2 Lilly medical people?
3 A. I don't.
4 Q. Do you recall the context in
5 which you reached that conclusion?
6 A. No.
7 Q. You just recall that you
8 reached that conclusion after talking to
9 Lilly medical people?
10 A. That's what I've said.
11 Q. Okay. Well, did any letters
12 go out from the medical affairs departments
13 to your customers, be it hospitals, third
14 party payors, patients or doctors, informing
15 them that Lilly believed as of 2003 that
16 given the serious health risks patients
17 taking SGAs should receive appropriate
18 baseline screening and ongoing monitoring?

Michael Bandick (June 9, 2006)

400:21 A. There were materials that
22 went out in the fall of 2003 with those
23 directions.
24 Q. What materials would those
401: 1 be?
2 A. Those materials were
3 associated with the label change that
4 occurred for all second generation
5 antipsychotics regarding association with
6 hyperglycemia and appropriate screening and
7 treatment of patients.
8 Q. Tell the jury what the PDR
9 is?
10 A. PDR stands for Physician's
11 Desk Reference. It is a compendium of all
12 major pharmaceutical products -- not even
13 major -- all pharmaceutical products that are

available with a list of their indications, warnings, dosing, other considerations. It's an encyclopedia, if you will, of clinical information.

(Whereupon, Deposition Exhibit(s) 9 duly received, marked and made a part of the record.)

QUESTIONS BY MR. ALLEN:

Q. I've handed you what I've marked as Bandick Exhibit No. 9, which I'll represent to you is a 2005 PDR reference on Zyprexa.

Do you have that in front of you?

A. It appears that I do.

Q. Okay. You know the precaution section, you know where that is, don't you? You've seen this document a lot of times, haven't you?

MR. FAHEY: The 2005 PDR?

Michael Bandick (June 9, 2006)

A. I said I'm generally familiar with the Zyprexa label.

Q. Sir?

A. I said I'm generally familiar with the Zyprexa label.

Q. Tell the jury what a precaution section is?

A. A, well, there are experts that can describe it better than me. Precaution generally is noted as something that a physician should take into account when they're considering prescribing the drug for a patient.

Q. And, of course, as we saw in the PhRMA documents or web page earlier, every single -- let me ask it this way.

This label is federally regulated by the Food and Drug Administration, correct?

A. I don't know that to be a fact.

Q. Okay. Look at the precaution section which begins on the fourth page of Bandick Exhibit No. 9.

Are you there with me?

A. I believe so.

Q. Then the precaution section goes to the next page.

Can you turn the page for me, please?

A. Yes.

Q. And there's a section in the precaution section entitled "Laboratory Tests," isn't there?

A. Yes, there is.

Q. Is there any recommendation in the precaution section of the label in 2005 suggesting that doctors or physicians

monitor fasting plasma glucose?

Michael Bandick (June 9, 2006)

A. If you could just give me a moment.

Michael Bandick (June 9, 2006)

A. No, there's language, however, that's in the warning section which is elevated, which would reflect even a greater level of awareness, that patients with an established diagnosis of diabetes mellitus who are started on an atypical antipsychotic should be monitored regularly for worsening of glucose control.

Michael Bandick (June 9, 2006)

Q. My simple question was: In the precaution section of the label is there any laboratory testing recommended for patients who take second generation antipsychotics to have their fasting plasma glucose monitored?

A. Not under laboratory tests in the precaution section.

Q. Right. Now, if you go back to the consensus statement, which is Exhibit No. 8, is that correct, sir?

A. Consensus statement is Exhibit No. 7.

Q. I'm sorry, sir. Exhibit No. 7. If you look at Page 598, and go to 599, the monitoring that is recommended includes monitoring of fasting plasma glucose; isn't that correct?

Michael Bandick (June 9, 2006)

A. Yes, that is one of the items lifted under baseline monitoring.

Q. And what is it about the fasting plasma glucose, if you know, that is relevant to the risk of Zyprexa?

A. I don't understand your question.

Q. Thank you.

Isn't it a fact, sir, that in the marketing and promotional materials related to Zyprexa, Eli Lilly touted as a benefit and a safety message to consumers the lack of a need to conduct ongoing monitoring including plasma glucose levels?

A. I'm not aware of any communication to consumers on that topic.
Q. So it was never a safety message to the audience for Zyprexa marketing?

Michael Bandick (June 9, 2006)

A. As we discussed, the primary audience for those message, clinical messages, would be physicians.
Q. And you never used the lack of ongoing monitoring as a safety and efficacy message?
A. There are different kinds of monitoring. And there, when Zyprexa was launched in 1996 one of the things that differentiated it from Clozaril was that there was not required blood monitoring for the risk of agranulocytosis.
So we did indicate in that time frame and for some time after, that no need for blood monitoring related to agranulocytosis was one of Zyprexa's safety features.
Q. Did you ever indicate -- we'll show those documents in a minute.
Sir, let's go to the summary of the consensus statement, Exhibit No. 7, on Page 600. Do you see the summary, sir?
A. Yes, I do.
Q. I'm going to read it out loud as follows: "The SGAs are of great benefit to a wide variety of people with psychiatric disorders. As with all drugs, SGAs are associated with undesirable side effects. One constellation of adverse effects is an increased risk for obesity, diabetes, and dyslipidemia." Did I read that correctly?
A. Yes.
Q. I'm going to skip down to the next paragraph, it says: "These three adverse conditions are closely linked, and their prevalence appears to differ depending on the second generation antipsychotic used. Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia." Did I read that correctly?
A. That's what it says in this document.
Q. As the Brand Manager and the Director of Marketplace Management for Zyprexa in the years you have indicated, do you agree with that statement?
A. Lilly disagreed with that statement.
Q. Do they agree with it now?
A. I don't know.
Q. Did they agree with it the last time you checked when you were at Eli

Lilly?
A. No.
Q. They did not agree with it?
A. They did not agree with it.
Q. But the fact of the matter is the consensus statement has reached a conclusion that Zyprexa is associated with the greatest weight gain and the highest occurrence of diabetes and dyslipidemia, correct?

Michael Bandick (June 9, 2006)

410:
A. That was one of the conclusions of this group.
Q. Now, of course, you in marketing, and Eli Lilly, had known about this potential for a considerable amount of time before the release of this consensus statement, had you not?

Michael Bandick (June 9, 2006)

410:
A. Lilly's conclusion, at least up through the time that I was still with the company, was that that was not borne out by the data.
(Whereupon, Deposition
411:
Exhibit(s) 10 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Sir, I'm going to hand you what has been marked as Bandick Exhibit No. 10. I have a copy for your counsel.

Michael Bandick (June 9, 2006)

411:
Q. Do you have Exhibit No. 10 in front of you?
A. I do.
Q. You have seen this document before, have you not?
A. I have.
Q. When did you see this document?
A. I first saw this document when it was published in April 2002.
Q. This document, it's dated April 2002. It's Exhibit No. 10.
Can you briefly describe for the jury what it is?
A. This is the English translation of a Dear Health Care Professional letter that was distributed to
412:
physicians in Japan following a label change for Zyprexa in Japan.
Q. And what did Japan do, in

summary for the jury, just to educate them, in regard to the label change on Zyprexa in April 2002?

Michael Bandick (June 9, 2006)

A. The Japanese regulatory agency affected a label change for Zyprexa that limited the eligible patient population for use of Zyprexa, including patients who either had diabetes or a history of diabetes. There were some other guidelines as well. I'd say a clinician or regulatory person could give you better detail on that.

Q. What the Japanese government did is they put a black box warning on Zyprexa in Japan, didn't they?

A. It was comparable to what in the U.S. we would call a black box warning.

Q. And what they said -- and let me read a portion of this exhibit -- it says: "Emergency safety information regarding diabetic ketoacidosis and diabetic coma due to increased blood glucose during administration of an antipsychotic agent, Zyprexa tablets, olanzapine. Since the marketing of this product in June 2001, nine serious cases, parens, including two cases of death, close parens, with hyperglycemia, diabetic ketoacidosis and diabetic coma have been reported for which causal relationship with this product cannot be denied, parens, estimated number of patients treated with this product 137,000 as of the end of December 2001."

Did I read that correctly, sir?

A. Yes.

Q. So at least according to the Japanese government, the Ministry of Government, Zyprexa was marketed in Japan beginning in June 2001, correct?

A. I believe that's true.

Q. And they had seen enough evidence of serious adverse consequences related to diabetes, diabetic ketoacidosis and diabetic coma to recommend and, in fact, require, the equivalent of a black box label on Zyprexa in Japan --

Michael Bandick (June 9, 2006)

Q. -- did they not?

Michael Bandick (June 9, 2006)

(The Court Reporter read the requested material, as set forth herein:

Michael Bandick (June 9, 2006)

A. What this document reflects is that the Japanese regulatory agency had decided, based on what they believed were cases of hyperglycemia, diabetic ketoacidosis and diabetic coma that such an action was warranted.

Q. "Such an action" being the placing of a black box, correct?

A. The equivalent in Japanese regulatory, yeah.

Q. The black box said, among other things, "Do not administer to patients with diabetes mellitus and those who have a history of diabetes mellitus.

No. 2. During administration of this product, observe sufficiently with such as measurement of blood glucose.

No. 3. Explain sufficiently to the patient and family members.

And it goes on to say, "Upon administration of this product, explain sufficiently to the patient and family members possible occurrence of serious adverse reactions, such as diabetic ketoacidosis and diabetic coma, et cetera. Provide guidance to them to see a physician suspending administration if such symptoms as thirst, polydipsia, polyuria, or frequent urination, et cetera, appear."

Did I read that correctly?

A. Yes.

Q. Did Lilly change its label for Zyprexa in the United States consistent with what was required by Japan in April of 2002?

A. No, it did not.

Q. Did Lilly get its sales force together and inform the sales force of the need to inform doctors, patients, third party payors and regulatory agencies -- let me rephrase the question.

Did Lilly, in its marketing and/or sales department, inform its sales representatives that they needed to tell doctors and patients of the equivalent of a black box warning being placed on Zyprexa in Japan?

Michael Bandick (June 9, 2006)

A. Lilly did provide background information to the U.S. sales organization for use in discussions with physicians if the

question arose. Lilly sales representatives were not in direct contact with patients.

So to answer your question, information was made available through the sales organization for physicians.

Michael Bandick (June 9, 2006)

421:17 Q. Did Lilly send doctors in the United States a Dear Doctor letter informing them about the equivalent of a black box warning on the Japanese label in April 2002?

Michael Bandick (June 9, 2006)

421:23 A. I don't recall a Dear Health Care Professional letter being distributed on
422: 1 that topic.

Q. Once this, the equivalent of a black box label was put on the Japanese label for Zyprexa in April of 2002, shouldn't Eli Lilly, in the interest of accuracy, fair balance, and full disclosure, let its primary care physicians and/or psychiatrists who were one of its markets, know as quickly as possible about this black box label in Japan?

Michael Bandick (June 9, 2006)

422:14 A. Lilly strongly disagreed with the regulatory outcome in Japan based on Lilly's analysis of the data. What it provided its sales organization was background information to be able to respond to questions from physicians if it did come up.

Michael Bandick (June 9, 2006)

422:24 Q. My question is assuming that
423: 1 a doctor in Cincinnati, Ohio, had no idea what the Japanese regulatory authorities had done in Japan concerning the equivalent of a black box. You follow me?

A. Yes.

Q. And you did promote Zyprexa to doctors in Ohio, did you not?

A. I believe we did.

Q. And wouldn't it be incumbent upon you as a company to, as quickly as possible, inform the doctors in Ohio and all across the United States about the Japanese regulatory action, whether they asked about it or not?

Michael Bandick (June 9, 2006)

423:17 A. I'm uncomfortable speaking
18 for people with a much deeper clinical
19 background than me. But at the time, as I
20 understand the decision, it was rooted in the
21 fact because we didn't agree with the
22 interpretation of the data, we didn't feel
23 that it represented, we didn't feel that it
24 represented actionable information for
424: 1 physicians in other countries.

Michael Bandick (June 9, 2006)

424: 9 Q. What you just said is Lilly
10 didn't agree with Japan so we thought we
11 didn't have to tell doctors in the United
12 States about Japan's actions; is that what
13 you're saying?

Michael Bandick (June 9, 2006)

424:17 A. I think that oversimplifies
18 what I said.
19 Q. How did I oversimplify it?
20 A. It's not a question of
21 because we didn't agree. It was a question
22 of because we didn't feel that the data
23 reflected that interpretation. We were
24 consistent in our communications with
425: 1 physicians about what we believe the data did
2 represent.
3 Q. Who should make the decision
4 about whether or not the, what the doctors
5 are going to do with this information or the
6 patients, should it be Lilly, or should it be
7 the doctors and the patients?

Michael Bandick (June 9, 2006)

425:10 A. I don't think I can answer
11 your question.
12 Q. Didn't you just tell me Lilly
13 didn't agree with the Japanese Ministry of
14 Health concerning the addition of the
15 equivalent of a black box?
16 A. That's correct.
17 Q. Lilly didn't agree. That's
18 clear as a bell, right?
19 A. Lilly did not agree.
20 Q. Right. But Lilly was
21 informed and was able to look at what Japan
22 did and reach its own judgment; is that
23 correct?

Michael Bandick (June 9, 2006)

426:17 THE WITNESS: And what do you
18 mean by "reach its own judgment?"
19 MR. ALLEN: About whether it
20 agreed or disagreed with the
21 Japanese Ministry of Health's
22 decision to put the equivalent of a
23 black box.

Michael Bandick (June 9, 2006)

427: 3 Q. Lilly was able to look at it
4 and make its own judgment about whether it
5 agreed or disagreed with Japan, right?

Michael Bandick (June 9, 2006)

427: 8 A. As we said, yes, Lilly
9 disagreed with that outcome, disagreed with
10 that analysis, disagreed with that
11 interpretation.
12 Q. Right. But they were able to
13 look at what Japan did and make their own
14 judgment, right?

Michael Bandick (June 9, 2006)

427:17 THE WITNESS: Make their own
18 judgment regarding?
19 MR. ALLEN: Whether or not
20 they agreed or disagreed with
21 Japan's action?

Michael Bandick (June 9, 2006)

427:24 A. I'm sorry, I feel like we're
428: 1 in circles here.
2 Q. Oh, I know we're in circles,
3 you're doing it on purpose, but I'm going to
4 keep on asking you the question.

Michael Bandick (June 9, 2006)

429: 6 Q. Mr. Bandick, I'm discussing
7 with you, I believe, is it Bandick Exhibit
8 No. 10, the emergency safety information and
9 the equivalent of a black box in Japan; is
10 that correct?
11 A. Yes, is it.
12 Q. You testified a minute ago,

and I'm paraphrasing, that Lilly looked at the data, they looked at the conclusions, they looked at the information that Japan had, they looked at the Japanese action, and made a determination that they disagreed with Japan. Is that a fact? Is that what you said?

Michael Bandick (June 9, 2006)

A. Lilly medical had analyzed and made the determination that they felt it was an incorrect decision or an incorrect analysis.

Q. And Lilly got to look at the information and reach its own conclusion, right?

THE WITNESS: Which data?

Michael Bandick (June 9, 2006)

THE WITNESS: The cases?

MR. ALLEN: The Japanese action and the reasons for it.

A. Lilly was aware of the data, Lilly was aware of the cases, and, yes, they had a chance to reach their own conclusion.

Q. Don't you think that immediately upon reaching that conclusion that you should have informed the United States doctors and United States consumers, the patients, of the Japanese action and allow the doctors and the patients to reach their own conclusion?

Michael Bandick (June 9, 2006)

A. That decision would not be mine to make, but I can tell you the policy that Lilly had to provide data that was accurate and truthful was something that we consistently applied before and after the Japanese regulatory change.

Michael Bandick (June 9, 2006)

Q. My only question is: Don't you think United States doctors and United States patients should have been told by Lilly about what happened in Japan and allow the doctors and the patients to reach their own conclusion?

Michael Bandick (June 9, 2006)

431:22 A. That was not my decision to
23 make.
24 Q. Understanding it was not your
432: 1 decision to make. As the Director of
2 Marketplace Management and as the former
3 Brand Manager for Zyprexa who communicates
4 with the audience, including doctors and
5 patients, don't you think that Lilly should
6 have told U.S. doctors and U.S. patients of
7 the Japanese action and allowed the doctors
8 and the patients to reach their own
9 conclusion?

Michael Bandick (June 9, 2006)

432:14 A. Lilly continued to provide
15 data, and I would say that it was consistent
16 before and after the label change. I'm not
17 in a position to answer a should or should
18 not question. I can tell you what we did.
19 Q. Well, sir, you, for one,
20 certainly if you wanted to, as the director
21 of, and I've all of a sudden blanked out,
22 Director of Marketplace Management for
23 Zyprexa, you certainly could have, on your
24 own initiative, informed the sales force, and
433: 1 asked them to inform the doctors about the
2 Japanese equivalent of a black box. You
3 could have done that had you wanted?

Michael Bandick (June 9, 2006)

433: 6 A. Those decisions don't take
7 place in a vacuum and that's not something
8 that I would have or could have done
9 unilaterally.
10 Q. Isn't it true, sir, as the
11 Director of Marketplace Management for
12 Zyprexa that's exactly what you can do is you
13 can inform the sales force of a black box
14 warning in a foreign country and ask the
15 sales force to inform the doctors. Isn't
16 that something you can do yourself?

Michael Bandick (June 9, 2006)

433:22 A. What I did in that role was
23 to share content that was carefully reviewed
24 and considered by members of all areas, as
434: 1 opposed to me making a decision one off as to
2 what I thought might make the most sense.
3 Q. The Japanese action, Exhibit
4 No. 10, had you wanted to, as the Director of
5 Marketplace Management for Zyprexa, you could
6 have sent that document, itself, to every
7 sales representative in the United States and

ask them to inform their doctors who they detailed, true?

Michael Bandick (June 9, 2006)

A. I stand by my earlier answer.
Q. Well, you only inform the sales force of regulatory actions in foreign countries if it helps Zyprexa but don't inform the sales force if it hurts Zyprexa?

Michael Bandick (June 9, 2006)

A. That's not the way we look at it.
Q. Have you ever informed the sales force of foreign regulatory action concerning a black box on antipsychotics?

Michael Bandick (June 9, 2006)

A. I don't recall an example.
(Whereupon, Deposition Exhibit(s) 11 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Well, let me see if I can refresh your recollection. I'm going to hand you what's been marked as Bandick Exhibit No. 11. Provide it to your counsel.
This is an e-mail you wrote, is it not? Sir, that's just a simple question, this is an e-mail that you wrote, is it not?

Michael Bandick (June 9, 2006)

A. Yes, it is.
Q. Okay. Can you tell the jury the date of this e-mail that you wrote?
A. October 18, 2002.
Q. Can you tell the jury the subject of the e-mail as reflected on Exhibit 11 that you wrote?
A. The subject is Risperidone Cerebrovascular Warning in Canada.
Q. What's risperidone?
A. It's the molecule for Risperdal.
Q. Who manufactured Risperdal?
A. Janssen manufactures Risperdal.
Q. Was Risperdal a competitor to Zyprexa?
A. Yes.

Q. Were you trying to beat the competition in sales of Zyprexa over Risperdal at the time you were marketplace manager?

Michael Bandick (June 9, 2006)

437:14 THE WITNESS: Were we trying
15 to beat the competition in sales of
16 Zyprexa over Risperdal?
17 MR. ALLEN: Sure.
18 THE WITNESS: Is that your
19 question?

Michael Bandick (June 9, 2006)

437:20 MR. ALLEN: Yes, it is.

Michael Bandick (June 9, 2006)

437:23 A. In any marketplace where
24 Zyprexa competed our goal would have been to
438: 1 realize the full commercial potential of the
2 molecule, and that would involve, at times,
3 differentiating it from other antipsychotics.
4 Q. Who is this e-mail to? You
5 don't need to read everybody's name but can
6 you be fair and accurate to the jury and
7 balanced and tell the jury who the recipients
8 of this e-mail represent?

Michael Bandick (June 9, 2006)

438:17 A. Generally, this is an
18 internal memo to members and other
19 affiliates, which we discussed earlier were
20 other countries where Zyprexa was marketed,
21 as well as to some internal Zyprexa
22 personnel.
23 Q. You sent this e-mail around
24 the world, in essence?
439: 1 A. That's true.
2 Q. And the subject is
3 risperidone, which is Risperdal, Cerebral
4 Vascular Warning in Canada, right?
5 A. Yes.
6 Q. Why would you want to be
7 informing -- and were some of these people
8 you sent the e-mail to involved in the issue
9 of marketing and sales for Zyprexa?

Michael Bandick (June 9, 2006)

439:12 A. Yes. Some of these people
13 were involved with the marketing and sales of
14 Zyprexa.
15 Q. Okay. Let me read the e-mail
16 for you out loud and for the jury.
17 From Michael Bandick,
18 10/18/2002. Subject Risperidone Cerebral
19 Vascular Warning in Canada. Yesterday some
20 of you may have received a document
21 containing a Dear Doctor letter that was
22 recently issued by Janssen in Canada. The
23 purpose of this e-mail is to provide some
24 background and recommendations regarding this
440: 1 letter.
2 Background: Earlier this
3 year Health Canada requested all
4 antipsychotic manufacturers, parens,
5 including Lilly, to provide safety data
6 regarding cerebrovascular, parens, for
7 example, stroke, close parens, adverse
8 events, CVAEs. Upon review of all of the
9 information provided, Health Canada required
10 that Janssen and only Janssen update their
11 label. Janssen and Health Canada are still
12 negotiating final details of the label change
13 and Health Canada has requested that Janssen
14 issue a Dear Doctor letter, attached, in the
15 interim. It is likely that the Risperdal
16 label will now contain a black box warning
17 pertaining to CVAEs. In addition, physicians
18 are advised to assess the risks of using
19 Risperdal in elderly patients with dementia.
20 Risperdal has an indication for this in
21 Canada."
22 Did I read that correctly?
23 A. Yes.
24 Q. Now, do you then give
441: 1 instructions to the recipients as to how
2 they're supposed to share the Dear Doctor
3 letter from Canada with the doctors to whom
4 Zyprexa is marketed in the United States?
5 THE WITNESS: I'm sorry,
6 could you repeat your question?
7 MR. ALLEN: Yes.
8 QUESTIONS BY MR. ALLEN:
9 Q. Let me just get straight and
10 to the point. When Canada took regulatory
11 action against Risperdal and required them to
12 send out a Dear Doctor letter addressing the
13 risk of cerebrovascular disease, didn't you
14 ask that the sales force for Zyprexa in the
15 United States make this fact known to the
16 doctors in the United States as a selling
17 point against Risperdal and in favor of
18 Zyprexa?

Michael Bandick (June 9, 2006)

441:21 A. The direction that was given
22 in this note is that the attached letter is
23 not approved for use in the field. This was

to provide information to affiliates around the world to keep them apprised of important regulatory events.

Q. Didn't you say under do's, "share this information selectively as appropriate?"

A. Yes.

Q. And didn't you say in this e-mail that it would be appropriate to make mention of this information when confronted with speculation and allegations regarding our label?

A. The context for that remark is that all manufacturers were required to provide data on that topic and Janssen and risperidone were the only ones who were required to make a label change. Sometimes there can be speculation that if one company has made that change it must apply to all products in the class. We felt it was important, from a safety standpoint to provide truthful and balanced information, that that did not apply to Zyprexa.

Q. Doesn't your e-mail say "it would be appropriate to make mention of this information when confronted with speculation and allegations regarding our own label. While we do not want to speculate on potential label changes, ours or competitors, we would like to point out actual label changes, such as the recent addition of a black box warning, pending finalization of language to the Risperdal label in Canada regarding CVAE."

Did I read that correctly?

A. That's what it says.

Q. And it says: "We would like to point out actual label changes such as the recent addition of a black box warning pending to the Risperdal label in Canada."

A. And the context for that remark the first part of the sentence is avoiding speculation on potential label changes, because we thought that would be inappropriate. However, if there was an actual label change that that would be something that would potentially be appropriate. And as you pointed out under do was to share information selectively as appropriate. That does not represent a proactive tell-every-customer-you've-got. If it came up that was something that could be cited as a fact.

Q. It says "we would like," sir, do you see the phrase "we would like to point out actual label changes such as the recent addition of a black box warning pending finalization of language to the Risperdal label in Canada regarding CVAE."

Did I read that correctly?

A. Yes. It's the second part of the sentence that begins by saying we shouldn't be speculating.

Q. But if a label change is made we'd like to point it out?
A. If appropriate to that situation.
Q. Yeah, okay. So it says if a label change is made, and this is your words, "we with like to point out actual label changes," right?
A. In the context of doing it selectively as appropriate as it says at the very bottom.
Q. Okay. Was an actual label change on Zyprexa made in Japan in April of 2002?
A. Yes.
Q. Would you like to point that out?
THE WITNESS: What do you mean?

Michael Bandick (June 9, 2006)

Q. Did you send out an e-mail to the same recipients or their colleagues as reflect in Bandick No. 11, and say we'd like to point out the black box label change in Japan? Did you say that?

Michael Bandick (June 9, 2006)

A. We did not send out a document that said we would like to point out the label change in Japan.
Q. Did you send out a document that says, while we do not want to speculate on potential label changes, ours or competitors, we would like to point out actual label changes such as the recent addition of the equivalent of a black box warning in Japan to the Zyprexa label regarding diabetic ketoacidosis, coma and death. Did you say that?

Michael Bandick (June 9, 2006)

A. We did not send out a document that said we would like to point out that an actual label change occurred with the equivalent of a black box for Zyprexa in Japan.

The reason for that was that we didn't believe the data warranted that outcome.
Q. Did you evaluate the data concerning the changes in the Risperdal label in Canada and reach a conclusion you agreed with?

A. We had clinical personnel who were responding to Health Canada's request for that data. And we were very familiar with the interpretation and analysis that Health Canada used.
Q. Let's look at what you did. When a label change was made in Japan concerning the Zyprexa label and diabetic ketoacidosis, coma and death, you did not send out an e-mail asking that this news be shared with doctors, correct?

Michael Bandick (June 9, 2006)

447:18 Q. Correct, sir?
19 A. That's correct.
20 Q. But when a label change was
21 made to your competition, Risperdal in
22 Canada, with a black box concerning CVAE,
23 cerebrovascular events, you sent out a world
24 wide e-mail and said to the recipients we'd
448: 1 like to share the black box warning on the
2 Risperdal label? Isn't that what happened?

Michael Bandick (June 9, 2006)

448: 9 A. I can go back to the earlier
10 answer that I gave you to a similar question.
11 Q. Just answer my last question,
12 please?

Michael Bandick (June 9, 2006)

448:15 THE WITNESS: If you can read
16 back his last question I'll do my
17 best to answer it.
18 (The Court Reporter read the
19 requested material, as set forth
20 herein:
21 "QUESTION: But when a label change was
22 made to your competition, Risperdal in
23 Canada, with a black box concerning CVAE,
24 cerebrovascular events, you sent out a
449: 1 world wide e-mail and said to the
2 recipients we'd like to share the black box
3 warning on the Risperdal label? Isn't that
4 what happened?")

Michael Bandick (June 9, 2006)

449:16 Q. I mean, can you answer that
17 question? There wasn't an answer on the
18 record to that one? What was the answer to
19 that question?
20 A. We did not intend, nor did we

communicate broadly to physicians about the Risperdal label change in Canada on CVAE. We informed members of sales and marketing in other markets of the change. We advised them to share the information selectively as appropriate, and similarly, we provided background information to the U.S. sales organization and to other affiliates on the label change in Japan, and provided them with Lilly's view on why we felt the decision was inappropriate.

Michael Bandick (June 9, 2006)

Q. Do you see any hypocrisy in the action you took regarding the changes to the label made in Japan on Zyprexa versus the actions you took concerning the black box addition of the warning in Canada on the Risperdal label? Do you see any hypocrisy in that action?

Michael Bandick (June 9, 2006)

A. No.
Q. You think the actions concerning the black box label change, the equivalent of a block box label change in Japan on Zyprexa, do you see any inconsistency in your action concerning that action in Japan versus what you did concerning the Risperdal label in Canada?

Michael Bandick (June 9, 2006)

A. I see them as very different situations.
Q. Do you see any inconsistency in what you did, sir, Mr. Bandick?

Michael Bandick (June 9, 2006)

A. I can't evaluate the consistency or inconsistency, I see them as different situations.
Q. Thank you, sir.
(Whereupon, Deposition Exhibit(s) 12 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Sir, Exhibit 12, this is your document. I have one for you and one for your counsel. This is, probably, one of the

Michael Bandick (June 9, 2006)

452: 4 Q. You know this document, don't
5 you, sir?

Michael Bandick (June 9, 2006)

452:21 Q. Sir, you recognize this
22 document, Exhibit 12, do you not?
23 A. Yes, I do.
24 Q. You wrote it?
453: 1 A. Yes, I did.
2 Q. When did you write it?
3 A. August of 2000.
4 Q. Okay. Sir, this document,
5 read the title to the jury, please.
6 A. Zyprexa Primary Care Strategy
7 and Implementation Overview.
8 Q. Why did you write this?
9 A. This was about one month into
10 my role as Brand Manager for Zyprexa in
11 primary care, and I believe this was a, an
12 overview for an internal audience, probably
13 other members of the Zyprexa Marketing Team
14 and, perhaps, other internal audiences.
15 Q. Zyprexa, had been on the
16 market since 1996; is that correct?
17 A. Yes.
18 Q. Why were you considering
19 expanding the market to primary care
20 physicians?
21 A. In studying where
22 antipsychotics were used, and understanding
23 where patients with schizophrenia and bipolar
24 disorder, or in this case bipolar mania
454: 1 presented, we determined that there was
2 significant unmet need in the primary care
3 setting and that we would be able to meet
4 some of those unmet medical needs by
5 promoting the drug in the primary care
6 segment.
7 Q. Is that a long way of saying
8 you wanted to make more money?

Michael Bandick (June 9, 2006)

454:14 Q. Sir?
15 A. It's not a way of saying
16 anything other than what I said. There was
17 unmet medical need. It's where those
18 patients presented and it's where a lot of
19 antipsychotic prescribing was already taking
20 place.
21 Q. Isn't it true that Zyprexa's
22 success was critical to Lilly's corporate
23 performance during Year X?

Michael Bandick (June 9, 2006)

455: 5 Q. You know what year X is,
6 don't you, sir?
7 A. I do.
8 Q. Isn't it true that Zyprexa
9 success was critical to Lilly's corporate
10 performance with the advent of Year X?

Michael Bandick (June 9, 2006)

455:15 A. As Zyprexa became a bigger
16 part of Lilly's overall sales, there was a
17 lot of, there was a lot of attention paid to
18 its growth potential.
19 Q. Well, wasn't it, Year X, the
20 motivating factor to expand the market for
21 Zyprexa?

Michael Bandick (June 9, 2006)

455:24 A. No, it wasn't.

Michael Bandick (June 9, 2006)

456: 1 Q. Okay. Wasn't it true that
2 with the advent of Year X, the loss of the
3 Prozac patent, and the lack of a short term
4 pipeline for new Lilly drugs, you needed to
5 expand your target markets?

Michael Bandick (June 9, 2006)

456: 8 A. The timetable for the
9 decision to go into primary care was sometime
10 in the spring of 2000. I went into the role
11 in July of 2000 and, I believe, that Prozac
12 last its patent in August of 2000.

Michael Bandick (June 9, 2006)

456:16 Q. My only question was isn't it
17 true that with the advent of Year X, the loss
18 of the Prozac patent, and the lack of short
19 term pipeline for new Lilly drugs, you needed
20 to expand your target markets?

Michael Bandick (June 9, 2006)

456:24 A. That's not the way I saw the
457: 1 launch in primary care.

Michael Bandick (June 9, 2006)

457: 3 nonresponsive. I'm not talking
4 about the launch of Zyprexa at this
5 point. You're jumping ahead of me.
6 Q. I'm asking this question and
7 this question only, isn't it true that with
8 the advent of Year X, the loss of the Prozac
9 patent, and the lack of short term pipeline
10 for new Lilly drugs, you needed to expand
11 your target markets?

Michael Bandick (June 9, 2006)

457:14 THE WITNESS: In the context
15 of Zyprexa or broadly?
16 MR. ALLEN: Yes. In the
17 context of Zyprexa.
18 A. No, I don't see it that way.
19 Q. Okay, sir, now let's look at
20 Exhibit No. 12 which this is your document,
21 you did draft it in August of 2000; is that
22 right?
23 A. Yes.
24 Q. I'll read the background.
458: 1 "Background: Following several months of
2 study by the Lilly USA Zyprexa Brand Team the
3 affiliate approved the recommendation that
4 Lilly actively promote Zyprexa to selected
5 current primary care prescriber targets."
6 Did I read that correctly?
7 A. Yes.
8 Q. But, of course, sir, in order
9 to do that you would have to face several
10 challenges, would you not?

Michael Bandick (June 9, 2006)

458:13 THE WITNESS: What challenges
14 are you referring to?
15 MR. ALLEN: The challenges
16 you have written in your memo,
17 Exhibit No. 12?

Michael Bandick (June 9, 2006)

459: 1 Q. Sir, my question on the table
2 is in order to actively promote Zyprexa to
3 selected current primary care prescriber
4 targets you would face many challenges, isn't
5 that true?
6 A. There are challenges in every
7 product launch and, yes, I've indicated a few
8 that were specific to this launch.
9 Q. One of the challenges was

very difficult to overcome, wasn't it, sir?
MR. HAMMERLE: I object as to the form of that question, counsel.
THE WITNESS: Is there a specific one you had in mind?
MR. ALLEN: Yes, sir. Let's go to challenge.
QUESTIONS BY MR. ALLEN:
Q. Tell the jury what a challenge is?
A. A challenge, in this context, would be to understand where extra care or effort might be taken so as to increase your probability of having a successful launch.
Q. Okay. Was it one of the challenges that Zyprexa's primary indications, schizophrenia and bipolar, are not viewed as primary care physician treated conditions?

Michael Bandick (June 9, 2006)

A. Yes, we had learned in market research that primary care physicians didn't acknowledge that there were patients who suffered from schizophrenia and bipolar disorder in their practice. Yet when we described how those patients presented, we learned there were, in fact, those patients in their practice who were either being undiagnosed or underdiagnosed or misdiagnosed.
Q. Okay, sir, why don't you look at your challenges section of your memo Exhibit 12, okay? Do you have it there in front of you?
A. I do.
Q. Why don't you read it out loud to the jury, please.
THE WITNESS: The whole section?
MR. ALLEN: Yes, sir?
A. Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers.
Q. Can you read it very slowly and distinctly so the jury can hear you when they hear the tape back.
A. Certainly.
Q. Go ahead.
A. "Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers. Many PCPs will refer patients in need of psychotropic treatment to a specialist rather than treat that patient. Key barriers to uptake include PCPs lack of training in this category, limited time with patients, and an aversion to perceived risk. Zyprexa's primary indications, schizophrenia and bipolar, are not viewed as PCP treated conditions so there's not a specific

indication for Lilly reps to promote in the PCP segment."

Q. Let's stop right there. These are your words: "Zyprexa's primary indications, schizophrenia and bipolar, are not viewed as PCP treated conditions, so there's not a specific indication for Lilly reps to promote in the PCP segment." Did I read that correctly?

A. Yes.

Q. I want to break this sentence down. This is your sentence, you wrote it, right?

A. Yes, I did.

Q. Let's look at the first part, "Zyprexa's primary indications, schizophrenia and bipolar." Aren't those the only indications for Zyprexa at that time?

A. Yes, that's correct.

Q. So when you said "Zyprexa's primary indications, schizophrenia and bipolar, are not viewed as PCP treated conditions," it would be more accurate to say that Zyprexa's only indications, schizophrenia and bipolar, are not viewed as PCP treated conditions?

Michael Bandick (June 9, 2006)

A. That, probably, would have been a better way to say that phrase.

Q. Okay. Then I'm going to read it like that and we're going to continue. Continuing: Zyprexa's only indications, schizophrenia and bipolar, are not viewed as PCP treated conditions. so there's not a specific indication for Lilly reps to promote in the PCP, primary care physician segment; is that correct?

A. That's what's written there.

Q. You wrote it, didn't you?

A. Yes, I did.

Q. Did you agree with it?

Michael Bandick (June 9, 2006)

A. Putting this document in context, as I mentioned, I had been in the role for about a month. As I look at it now, and even as I look at materials that were then sent to the sales organization in part of our implementation, I would agree that this is not the clearest language. However, as we got more educated about the segment and understood what the opportunities were this doesn't reflect the kind of language that we supplied to our sales organization.

Michael Bandick (June 9, 2006)

Q. Sir, you've already told us in this document you had reached the conclusion already you were going to market to PCPs. That's the whole point of Exhibit No. 12, isn't it? You'd already reached that conclusion?
A. That's not the point of that document.
Q. Doesn't it say here? "Following several months of study by Lilly USA Zyprexa Brand Team, the affiliate approved the recommendation that Lilly actively promote Zyprexa to selected current primary care prescribers targets," Isn't that what this says?
A. Yes.
Q. You had already reached that conclusion. And then you go down and say in the challenges, after reaching the conclusion you're going to market to PCPs, that Zyprexa's primary indications, which you now admit is the only indications, schizophrenia and bipolar are not viewed as PCP treated conditions so there's not a specific indication for Lilly reps to promote in the PCP segment. Isn't that what you said?

Michael Bandick (June 9, 2006)

A. What I wrote in this document, specifically the phrase "there's not a specific indication for Lilly reps to promote in the PCP segment," is, as I said, a less clear -- is a less clear way to convey what we ended up training our sales reps on.
Q. An indication, as you told me at the very beginning of this deposition, is a term of art. And that's an FDA approved indication and that's the only indication you can promote Zyprexa for, correct?
A. I don't recall using the phrase term "of art" but it is true that the promotion was limited to approved indications.
Q. And your memo here, Exhibit 12, says there is not an indication for Lilly reps to promote in the PCP segment, correct?

Michael Bandick (June 9, 2006)

A. Admittedly, that's not the clearest sentence, and certainly was better informed as I spent more time in the role.
When we launched the product there was a great deal of clarity on the indications and how we were going to be communicating with physicians.

Q. Well, at least at the time you wrote this memo, you said "there's not an indication to market to primary care physicians." When you wrote it that's what you said?

Michael Bandick (June 9, 2006)

Q. Right?
A. I would link this sentence back to the earlier comment about primary care physicians didn't acknowledge schizophrenia and bipolar as a -- those patients weren't frequently part of their practice.

So in trying to make the connection between what PCPs acknowledged, a challenge for anyone marketing Zyprexa in that segment would be to overcome the fact that they didn't acknowledge that there were a lot of patients with those diseases in their practice.

Q. That's your best answer to my question?

Michael Bandick (June 9, 2006)

A. Yes, is it.
Q. Okay. The first sentence in challenges says -- and we're going to move on -- says: "Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers." Was Zyprexa a mood stabilizers?
A. Mood stabilizer commonly refers to drugs used to treat bipolar and Zyprexa, had an indication for bipolar mania.
Q. Now, you figured out a way, and this is your document, to get around this problem of not having a specific indication for Lilly reps to promote in the PCP segment. Didn't you figure out a way to do that?

Michael Bandick (June 9, 2006)

A. We promoted Zyprexa in the primary care segment based on approved indications.
Q. What's positioning?
A. Positioning refers in a marketing context to the relative position that one product has to another. You could use a number of different axes to measure that.
Q. Why don't you go down, after challenges, which we just read, there's a segment on position, right?

A. Um-hum.
Q. Sir?
A. Yes, that's true.
Q. You underlined this sentence, do you not, the first sentence under position?
A. I did underline the first sentence in that section.
Q. And you say this: "Position: Zyprexa. The safe, proven solution in mood, thought, and behavioral disorders."
Did I read that correctly?
A. You did.
Q. Didn't you tell me hours ago in this deposition that there was no indication for Zyprexa for the treatment of mood?
A. That's correct.
Q. Didn't you tell me hours ago there was no indication, approved indication, for Zyprexa for the treatment of thought disorders?
A. That's correct.
Q. Didn't you tell me hours ago that there was no approved indication for Zyprexa for the treatment of behavioral disorders?
A. Yes, that's true.
Q. Yet, when you wrote this e-mail or this document, Exhibit No. 12, you intended to position Zyprexa as a safe, proven solution in mood, thought and behavioral disorders; is that correct, sir?

Michael Bandick (June 9, 2006)

A. A position is not the same as a verbatim. It's not the same as a message to physicians. So it is, in fact, inappropriate to compare a desired position in a prelaunch planning document to what we ultimately promoted to physicians.

Michael Bandick (June 9, 2006)

Q. My only question was: When you prepared Exhibit No. 12, you wrote that you intended to position Zyprexa as a safe, proven solution in mood, thought, and behavioral disorders?

Michael Bandick (June 9, 2006)

Q. Sir?
A. As I indicated, a position and a desired position in a prelaunch planning document, does not represent the

same as a verbatim to a sales organization or a promotion to a customer.
Q. Is that your best answer to my question?
A. Yes, it is.
(Whereupon, Deposition Exhibit(s) 13 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Sir, you've seen Exhibit No. 13, haven't you, Bandick?
A. Give me a moment with it please.
Q. The Viva Zyprexa, document? My question is: Have you seen this before?

Michael Bandick (June 9, 2006)

Q. Sir, have you seen this document before?
A. I'm refamiliarizing myself with it.
Q. So the answer's yes?

Michael Bandick (June 9, 2006)

Q. My question on the table is you have reviewed and seen this document before, haven't you, sir?
A. I have seen it and I'm almost done reviewing it.
Q. Tell the jury what the Viva Zyprexa launch meeting was without reference to that document.

Michael Bandick (June 9, 2006)

A. Viva Zyprexa launch meeting referred to the initial launch in primary care in October of 2000.
Q. And that was a launch in Orlando, Florida, right?
A. Yes, I believe so.
Q. Did you speak at that launch?
A. Yes, I did.
Q. Now, I'm confused. You're launching Zyprexa in October of 2000 but Zyprexa had been on the market since 1996, right?
A. In psychiatry, yes.
Q. So from '96 to October of 2000, Zyprexa had been launched in psychiatry, and psychiatry alone; is that correct?
A. Yes. With the neuroscience sales organization and their call targets, primarily, psychiatrists.

Q. And the approved indications on the label in '96 and in the fall of 2000 were psychiatric conditions, schizophrenia and bipolar mania, correct?
A. The bipolar approval came in, I believe, March of 2000.
Q. So what I said was correct?
A. No. You said that in '96 as in 2000 those two indications were approved. The second one came in March of 2000.
Q. Doesn't this document, Exhibit number, what number is -- 12, sir, or 13?

Michael Bandick (June 9, 2006)

477:18 Q. Thirteen. The Zyprexa launch meeting Viva Zyprexa, doesn't this document expressly tell us Lilly's motive for entering the primary care physician market?

Michael Bandick (June 9, 2006)

477:24 Q. Doesn't it answer that very
478: 1 question?
A. Well, as you pointed out there are a hundred pages. I wouldn't characterize this document as simply explaining the motive.
Q. I didn't say it simply explained the motive.
Isn't one of the things this document did is answer the question why you were entering the primary care physician market, you, being Lilly?
A. Yes, that is one of the questions that it answers.
Q. You're right there on the page I see. You're on Page 68, aren't you?
A. Yes, I am.
Q. You helped prepare this slide, didn't you?
A. Yes, I believe I did.
Q. And by the way, wasn't this launch meeting videotaped?
A. Parts of it, I believe.
Q. Including your presentation?
A. I don't know that I've ever
479: 1 viewed that. I don't know.
Q. Did you all get up -- did you all have a song that was created for this presentation?
A. Yes.
Q. Jail House Rock?
A. No, it wasn't called Jail House Rock.
Q. Oh, Viva Las Vegas but you all changed the words to Viva Zyprexa, right?
A. Yes.

Q. We're going to get to the -- by the words, when you created the song Viva Zyprexa, those words were intended to convey a message, weren't they, sir?
A. To an internal audience, yes.
Q. To an internal audience they were intended to convey a message, right, that song Viva Zyprexa?
A. Yes.
Q. Did you sing the song Viva Zyprexa at the launch meeting?
A. I did not.
Q. Okay. Now I want to go back to this question of why Lilly entered the primary care physician market, that's on Page 68, and it says right here, "Zyprexa, primary care, why are we entering this market, question mark?" Right?
A. Yes.
Q. I don't have time to read every bullet point but go one, two, three, four, five bullet points down. Can you read to the jury what you said as to why Lilly was entering the primary care market for Zyprexa?
A. One of several reasons on this page reads: "Zyprexa's success is crucial to corporate performance. PCPs represent last major untapped segment."
Q. Zyprexa's success is crucial to corporate performance was one of the reasons listed as to why Lilly was entering this market, right?
Sir?
A. The context for this document was that this was a sales organization audience and we were providing motivation for them to understand how they fit into the bigger picture.
Q. You were telling the truth to the sales reps, weren't you?
A. We were.
(Whereupon, Deposition Exhibit(s) 14 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Okay. And by the way, before I -- so Zyprexa's success is crucial to corporate performance. Let me hand you Bandick Exhibit No. 14, the 2000 Annual Report of Eli Lilly.
Have you ever seen that before?
A. I don't know if I've read it or not.
Q. Well, I don't need you to read the whole thing but there's a letter to the shareholders which is on the third page of this exhibit.

Q. Sir, on Page 3 of the 2000 annual report it says:

"To our shareholders, in keeping with our pledge to answer important questions I want to address one that I'm sure is on your minds.

For several years, we have been preparing for the expiration of the U.S. patents that have protected our exclusive rights to our top-selling product, Prozac. Due to uncertainty over the exact timing of this event, we have referred to it as Year X. In January '99, a federal district court had affirmed our 2003 Prozac patent. Last August" -- that means 2000 -- "we were very surprised when a federal appeals court reversed that ruling.

We strongly disagree with the ruling -- and we are making every effort in the court to secure our rights to the 2003 patent. At the same time, prudence dictates that we prepare and implement our plans with the assumption that Prozac will face generic competition in the United States in early August 2001."

Did I read that correctly?

A. So far you have.

Q. Now go over to the heading Strong Product Line Fuels Growth. Do you see where I am, sir?

A. Yes.

Q. It says here, the second paragraph: "Zyprexa exemplifies our growth opportunities."

Did I read that correctly?

A. Yes.

Q. Was Zyprexa a growth product or a niche product?

Michael Bandick (June 9, 2006)

A. I'm not seeing a list of growth products and a list of niche products.

Q. Sir, I didn't ask about that. I'm asking you, you're a marketing guy, I've read all your documents. You've, specifically, written down in a document, haven't you, sir, that Zyprexa was a growth product and not a niche product?

Michael Bandick (June 9, 2006)

A. It's possible. I don't recall it.

Q. Now I'm just asking you under oath, was Zyprexa a growth product or a niche product?

Michael Bandick (June 9, 2006)

A. If you're asking me if at this point in time if Zyprexa was considered to have considerable growth opportunity, I would say, yes, it was a growth product.

Q. Okay. Continuing reading: "Zyprexa exemplifies our growth opportunities. Initially introduced in 1996 as a treatment for schizophrenia, this molecule was approved in 2000 as a therapy for the manic phase of bipolar disease, a lifelong illness that affects as many as 34 million people worldwide."

Skipping down: "In 2000, our sales of Zyprexa were $2.3 billion, a 25 percent increase. During the fourth quarter, this neuroscience blockbuster surpassed Prozac as our top-selling product."

Did I read that correctly?

A. Yes.

Q. Back to Viva Zyprexa, the launch. Okay, are you there?

A. I am.

Michael Bandick (June 9, 2006)

Q. But anyhow, Mr. Bandick, the Viva Zyprexa document that you have, what exhibit number is it?

A. Thirteen.

Q. Okay. This was prepared for the launch in October of 2000 and we've just saw in the annual report for 2000 that Year X had arrived; is that correct?

A. Year X did occur in 2000.

Q. Was that the reason as reflected on Page 68 that Zyprexa's success was now crucial to corporate performance?

Michael Bandick (June 9, 2006)

A. At this point I believe Zyprexa was Lilly's largest product and I don't recall the exact rationale for why that bullet point was put on that slide.

Q. Okay. Go to the last page of the Viva Zyprexa document. It's the Viva Zyprexa song. I'm not going to sing it.

Michael Bandick (June 9, 2006)

Q. Sir, the Viva Zyprexa song, the first two lines: "The whole new purpose gonna set my soul, set my soul on fire."

Did I read that correctly?

A. Yes.

Q. There was a whole new purpose for Zyprexa in the fall of 2000?

Michael Bandick (June 9, 2006)

489:12 A. I didn't write the lyrics to the song, I don't know what the lyricist had in mind with "whole new purpose."
Q. Sir, by the way, you didn't write the lyrics but the Zyprexa, Viva Zyprexa document, Exhibit No. 12, had to go through the MLR committee we talked about at the very outset of the deposition, right?
A. There's a couple different ways for documents to be approved. If they're external it is through that MLR process. Some internal items like this would go through a different process that wouldn't necessarily be a MLR reviewed document.
490: 1 Q. This document -- what committee approved this document?
A. I don't recall who approved the lyrics to this song.
Q. Well, this was the major marketing campaign for every single sales rep in the country on Zyprexa, wasn't it?

Michael Bandick (June 9, 2006)

490: 9 THE WITNESS: I'm sorry?

Michael Bandick (June 9, 2006)

490:12 Q. Wasn't this launch for every single Zyprexa sales rep in the country?
A. No.
Q. For primary care physicians.
A. For primary care, that's correct.
Q. How many sales reps attended?
A. Approximately, 550.
Q. I'm going to skip down. It says "a whole new purpose going to set my soul." Was there a whole new purpose for Zyprexa in the fall of 2000?

Michael Bandick (June 9, 2006)

491: 2 A. I didn't look at it that way.
Q. So you don't think there was a whole new purpose?

Michael Bandick (June 9, 2006)

A. That's not how I would characterize it. We were launching the product into the primary care segment.

Q. Let's go down to the third versus: "Yeah, we're helping patients, Viva Zyprexa, many wonderful indications, Viva Zyprexa."

Did I read that correctly?

A. You did.

Q. Many wonderful indications. There was only two indications, weren't there, sir?

A. That's correct.

Q. Schizophrenia and manic, mania related to bipolar disorder disease, right?

A. That's correct.

Q. So there wasn't many wonderful indications, were there, sir?

A. I assume this had more to do with getting the right number of syllables into that line.

Q. You don't think it had something to do with mood, thought, irritability and anxiety?

A. I'm quite certain the person who wrote the lyrics to this song was not aware of our strategy or our promotional message.

Michael Bandick (June 9, 2006)

Q. Last, lyrics of the last stanza: "Can't rest now I've got to run, I'm gonna tell everyone, might tell a doctor 50 times, give a perfect message on every shot, keep Zyprexa at the top, Viva Zyprexa, Viva Zyprexa."

Did I quote from the lyrics correctly?

A. You left out a couple of lines in that stanza, but yes.

Q. "Might tell a doctor 50 times, give a perfect message on every shot, keep Zyprexa on top." Right?

A. As you just said, you left a few lines out of that stanza but the other lines were correct.

Q. Okay. By leaving the lines out did I misrepresent the song in any way?

A. I don't know how you intend to represent the song.

Q. Never mind, sir. Heck, you're smarter than me.

(Whereupon, Deposition Exhibit(s) 17 duly received, marked and made a part of the record.)

494:12 Q. -- Bandick Exhibit No. 17.
13 You know what this is, don't you?
14 Well, I'll tell the jury what
15 it is and see if you agree. This is the
16 June 2002 Zyprexa Primary Care Sales Force
17 Resource Guide, right?

Michael Bandick (June 9, 2006)

494:22 Q. What number is it?
23 A. It says 17.

Michael Bandick (June 9, 2006)

495:15 Q. Sir, I didn't ask you the
16 read every page. You recognize this as the
17 Primary Care Sales Resource Guide for
18 June 2002?
19 A. I'm taking a look through the
20 document because I was no longer in the
21 primary care role in June of 2002.
22 Q. I'll get you one from earlier
23 we have limited time.

Michael Bandick (June 9, 2006)

496: 9 Q. Can you turn to Page 77 of
10 the Primary Care Sales Force Resource Guide?
11 A. Yes.
12 Q. Exhibit 17. Who's the
13 patient profile No. 1?
14 A. It says Donna is a --
15 Q. No. Who's the patient
16 profile No. 1? Who?
17 A. I'm not sure what you mean.
18 Q. The person's name, patient
19 profile No. 1, who is that?
20 A. In this particular case the
21 patient profile is symbolized by the name
22 Donna.
23 Q. Right. Let's go ahead to
24 patient profile number on page 9, patient
497: 1 profile No. 2. Who's that?
2 A. This patient profile is
3 symbolized by the name Mark.
4 Q. Back to Donna, did she have
5 either schizophrenia or bipolar mania? On
6 Page 7.
7 Let me read: "Understanding
8 Donna's needs. Understanding needs. Donna
9 is a single mom in her mid-30s appearing in
10 your office in drab clothing and seeming
11 somewhat ill at ease. Her chief complaint is
12 I feel so anxious and irritable lately."
13 Did I read that correctly?

Michael Bandick (June 9, 2006)

497:17 Q. Did I read that correctly?
18 MR. HAMMERLE: Counsel, he

Michael Bandick (June 9, 2006)

498:22 Q. Sir, listen to my question,
23 listen to my question I withdraw the last
24 question. Sir, the fact of the matter is you
499: 1 at Lilly used illustrative metaphors, that's
2 what you called them, and you prepared --
3 A. No, I didn't.
4 Q. At Lilly, didn't you call
5 them illustrated metaphors?
6 A. No.
7 Q. You didn't?
8 A. I've not used that phrase
9 today and that's not a phrase I remember
10 using.
11 Q. Did anybody at Lilly use that
12 phrase?
13 A. I don't know.
14 Q. Okay. Do you recall
15 marketing to Donna, Mark and Martha?
16 A. You'd asked me that earlier
17 and I didn't know what you meant then and I'm
18 still not sure what you mean.
19 (Whereupon, Deposition
20 Exhibit(s) 15 duly received, marked
21 and made a part of the record.)
22 QUESTIONS BY MR. ALLEN:
23 Q. Okay, sir. By the way, we'll
24 get off that document.
500: 1 Bandick Exhibit 15, wasn't it
2 your goal in regard to the issue of weight
3 gain to minimize the liability of weight gain
4 while at the same time increasing the focus
5 on Zyprexa's superior efficacy. Wasn't that
6 your goal?
7 A. If you have a document that
8 you're reading from I'd like to take a look
9 at it.
10 Q. I'm just asking you first of
11 all, wasn't that your goal?
12 A. Well, if it's going to be
13 followed by reference to a specific document
14 I'd like the chance to review that document
15 before I answer your question.
16 Q. So you're telling me how to
17 ask questions now?
18 A. No, sir, I'm asking for a
19 chance to read the document.
20 Q. My question to you simply is,
21 without reference to any particular document,
22 sir, wasn't it Lilly's position to minimize
23 the liability of weight gain while at the
24 same time increasing the focus on Zyprexa's
501: 1 superior efficacy?

Michael Bandick (June 9, 2006)

501:10 Q. Sir, can you answer my
11 question?
12 A. I would like to take a look
13 at the document. There are a lot of ways to
14 interpret what you just read.
15 Q. Didn't Lilly try to, what was
16 the words here, minimize the risk and
17 accentuate the benefit?

Michael Bandick (June 9, 2006)

501:24 A. Those are very general terms
502: 1 so I can't answer the question the way you've
2 posed it.
3 Q. Without reading from a
4 document isn't it true that Lilly tried to
5 eliminate the risk of diabetes from the
6 risk/benefit equation?

Michael Bandick (June 9, 2006)

502: 9 A. No.
10 Q. No. Okay, sir.
11 (Whereupon, Deposition
12 Exhibit(s) 16 duly received, marked
13 and made a part of the record.)
14 QUESTIONS BY MR. ALLEN:
15 Q. Let me hand you what I have
16 marked as Bandick Exhibit No. 16. You
17 recognize that, don't you?
18 MR. ALLEN: I need one of
19 them back because I don't have one.
20 MR. FAHEY: Are you going to
21 mark 15?
22 MR. ALLEN: It's already
23 marked. I can mark them when I want
24 and introduce them when I want.
503: 1 QUESTIONS BY MR. ALLEN:
2 Q. Sir, you recognize the
3 Exhibit No. 16, Issue Management Planning on
4 Diabetes. Lilly Answers That Matter?
5 A. There are aspects of it that
6 are familiar. I'm not sure that I recall
7 this exact document.
8 Q. Okay. Why don't we go to
9 Page 2?
10 A. Okay.
11 Q. Diabetes. What is a
12 position, sir? A position as used in
13 marketing?
14 A. Well, in the context of this
15 document it would be similar to saying our
16 point of view.
17 Q. Okay. And isn't it, in
18 fact -- this document is a marketing
19 document, is it not?

A. This document would have come from a marketing source.
Q. Okay. Our position would be our point of view. "Our position: Diabetes hyperglycemia may appear in patients taking antipsychotics and/or mood stabilizers including Zyprexa at comparable rates with the possible exception of Clozapine."
Did I read that correctly?
A. Yes.
Q. We saw earlier today the consensus statement from April 2004, says that diabetes occurs in a greater rate in Zyprexa than it does in the other second generation antipsychotics, correct?
A. That is the conclusion that that group drew.
Q. Right. So right here your position in this document, Exhibit 16, is contrary to the consensus statement, correct?

Michael Bandick (June 9, 2006)

A. Well, this took place in 2000 and the consensus statement was three years later, but taken on its face, yes, they are in conflict.

Michael Bandick (June 9, 2006)

Q. I'm saying your position on diabetes in this document, Exhibit No. 16, is contrary to the consensus statement conclusions, correct?

Michael Bandick (June 9, 2006)

A. I would agree with that.
Q. Now, you know what as rationale is. Rationale means reason, correct?
A. Yes.
Q. So your position is, we've just read it: "Diabetes, hyperglycemia, may occur in patients taking antipsychotics and/or mood stabilizers including Zyprexa at comparable rates with the possible exception of Clozapine."
Skipping down: "To rationale for the position," which means reason for the position. You agreed with that, right?
A. I agree that rationale means reason.
Q. Okay. The reason for the position that's reported in your marketing document Exhibit 16 is as follows, follow along with me: "Showing that diabetes is a

common occurrence for all antipsychotics and not just Zyprexa will help reduce the perception that diabetes is linked to, specifically, to Zyprexa, and in turn, will help to eliminate this risk from the risk/benefit equation."
Did I read that correctly?
A. Yes, you did.
Q. So the reason that Lilly took the position that Zyprexa's risk of diabetes was comparable to other antipsychotics was in order to eliminate this risk from the risk/benefit equation, correct, sir?

Michael Bandick (June 9, 2006)

506:20 A. I didn't author this document.
Q. I didn't ask if you authored it? Isn't that the stated reason --

Michael Bandick (June 9, 2006)

507: 2 A. Which I'm using as a way to preface what I'm about to tell you.

Michael Bandick (June 9, 2006)

507: 6 THE WITNESS: Could you repeat your question?
MR. ALLEN: Yes, sir.
QUESTIONS BY MR. ALLEN:
Q. The stated reason in Exhibit 16 for stating that diabetes risk is comparable to other antipsychotics was in order to eliminate the diabetes risk from the risk/benefit equation?

Michael Bandick (June 9, 2006)

507:17 Q. Correct, sir?
A. No. I disagree with that.
Q. Doesn't -- the document says this will help eliminate this risk from the risk/benefit equation?
A. Yes, that document says that.
Q. And if the document is true -- is that document false, Exhibit 16?

Michael Bandick (June 9, 2006)

508: 3 Q. Is it false, sir?
4 A. It doesn't characterize the

way that I saw that issue nor the way that we worked with it in the years that I was in the marketplace management role.

The date of this document is about the time that I was joining that area. I did not author it, so I can't speak for what the author of this document had in mind.

Q. You can't read it and see the purpose and the reason and you can't interpret what that means as a marketing professional?

Michael Bandick (June 9, 2006)

508:19 A. You asked me if I agreed and
20 I disagreed with it.
21 Q. My question is: At least the
22 marketing document concerning Diabetes, Issue
23 Management Planning in November of 2001 was
24 that we will try to eliminate the risk of
509: 1 diabetes from the risk/benefit equation?

Michael Bandick (June 9, 2006)

509: 4 A. Again, I can't speak to what
5 the author of this document had in mind, so,
6 no, I can't answer the question.
7 Q. Why don't you read out loud
8 for the jury the rationale for the position.
9 Read it out loud.
10 A. In this document it says:
11 "Showing that diabetes is a common occurrence
12 for all antipsychotics and not just Zyprexa
13 will help reduce the perception that diabetes
14 is linked, specifically, to Zyprexa and in
15 turn" -- spelled wrong -- "will help to
16 eliminate this risk from the risk/benefit
17 equation."
18 Q. That's at least what the
19 author of the document in the marketing
20 department wrote?
21 A. That's correct.
22 Q. Issues Management Planning
23 Weight Gain, Exhibit 15, November 2001.
24 You've seen that document before, haven't
510: 1 you?
2 A. As with the last document
3 which was dated one day differently from this
4 one, I'm familiar with much of the content,
5 I'm not sure I recall the specific document.
6 Q. Okay. This is the Issues
7 Management Planning Weight Gain, Lilly
8 Answers That Matter. Our Position is on
9 Page 2. You following me?
10 A. Yes.
11 Q. Our position: Weight gain
12 can occur with Zyprexa as with other
13 antipsychotics and mood stabilizers. For
14 most patients this can be managed allowing

them to receive the overwhelming benefits Zyprexa offers."
Did I read that correctly?
A. Yes, you did.
Q. So it's your position that the benefits of Zyprexa overwhelmingly outweigh any alleged risk of weight gain, correct?

Michael Bandick (June 9, 2006)

A. No, I wouldn't interpret it the way that you just paraphrased.
Q. Okay. What is the rationale for the position as contained in this exhibit --
A. It says --
Q. -- No. 15?
A. In this document it says: "To minimize the liability of weight gain while at the same time increasing focus on Zyprexa's superior efficacy."
Q. At least as stated in Lilly's document produced in this case from November of 2001, the rationale for your position on weight gain was to minimize the liability of weight gain while at the same time increasing focus on Zyprexa's superior efficacy, correct?

Michael Bandick (June 9, 2006)

A. That is what I read in this document, yes.
Q. Okay.

Michael Bandick (June 9, 2006)

(Whereupon, Deposition Exhibit(s) 18 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. I'm going to hand you Bandick No. 18. You've seen this, haven't you? My question is you've seen this before, haven't you?
A. Not that I'm aware of.
Q. Let me read it out loud. What's the number again, 18?

Michael Bandick (June 9, 2006)

MR. FAHEY: Eighteen.
Q. Sir?
A. Eighteen.

Q. It's to Jack Jordan. That was your boss, right?
A. Yes, that's true.
Q. And it's dated February 14th, Valentine's day, 2000, right?
A. Yes, it is. And he was not my boss at that time.
Q. Okay. He was your boss at one time. From John Richards, who's John Richards?
A. John Richards was a member of the Zyprexa Brand Team in the U.S.
Q. Same team you were on, right?
A. That I later joined, yes.
Q. What were you doing in February 2000?
A. I was a sales manager.
Q. For what?
A. In the neuroscience group.
Q. Including Zyprexa?
A. That's right.
Q. Okay. So you were in the Zyprexa business in the marketing department, right?
A. No, that was in the sales organization.
Q. Sales organization, even better. Let's go back to Exhibit 18. From Jack, to Jack from John: "Jack, Attached as we discussed. As you can see we have been driving the depression story with Zyprexa in our DTP program since quarter three, 1998." Did I read that correctly?
A. Yes.
Q. What's DTP program?
A. DTP refers to direct-to-physician.
Q. Did you know that Lilly had been driving the depression story to physicians in the third quarter, since the third quarter of 1998?

Michael Bandick (June 9, 2006)

Q. Sir, did you know that?
A. I don't know the context of this specific e-mail but I do know that at that particular point in time there was data suggesting that use of Zyprexa in schizophrenia also had a corresponding effect on coexisting depression.
Q. Okay, sir. While my able associate is looking for another document, I'm going to mark this one.
You all marketed and sold Zyprexa to the elderly for dementia, didn't you?

Michael Bandick (June 9, 2006)

A. No.
(Whereupon, Deposition Exhibit(s) 19 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. What's Exhibit 19, do you recognize that? My question is do you recognize the document, sir?
A. No, I don't.
Q. You don't? Why don't we just turn to Page 7 of this document, okay? Page 7. Are you with me?
A. Yes, I am.
Q. Let me just read into the record -- by the way, the title of this document is Controlling Crisis Can Lead to Connection; is that right?
A. That's what it says on this document.
Q. It has an illustration, looks like a doctor and an older person, right?
A. It's a doctor, and from the sketch that could potentially be an older person, I'm not sure.
Q. Turn to Page 7, will you please, sir?
A. Um-hum, yes.
Q. And on Page 7 it says: "Zyprexa IntraMuscular olanzapine for injection. Safety in agitation associated with dementia in a clinical trial."
Did I read that correctly?
A. Yes.
Q. Then you go: "In patients up to 97 years old, mean age of 77, favorable adverse event profile, the most common treatment-emergent adverse event in dementia patients was somnolence 4 percent versus 3 percent with placebo."
Did I read that correctly?
A. Yes.
Q. Weren't you all marketing Zyprexa to dementia patients?

Michael Bandick (June 9, 2006)

Isn't it true Lilly marketed Zyprexa for dementia patients?

Michael Bandick (June 9, 2006)

A. No.
Q. Okay. Well let me ask you another question, isn't it true Lilly marketed Zyprexa for depressive symptoms related to dementia?

Michael Bandick (June 9, 2006)

519:10 A. Not that I'm aware.
11 Q. Isn't it true that Lilly
12 marketed Zyprexa for depressive symptoms
13 period?

Michael Bandick (June 9, 2006)

519:16 A. By themselves, no.
17 Q. Why don't you turn to
18 Page 18. What's the title of that page?
19 A. Improves depressive symptoms.
20 Q. Okay. Let's go to the page
21 20?

Michael Bandick (June 9, 2006)

521:13 Q. What's the title of Page 20?
14 A. Zyprexa Safely Stabilizes
15 Behavioral Symptoms.
16 Q. Zyprexa Safely Stabilizes
17 Behavioral Symptoms. That's what you just
18 said, right?
19 A. You asked me to read what was
20 at the top of the page.
21 Q. Didn't you market Zyprexa for
22 the treatment of symptoms?
23 A. No.
24 Q. Why don't you go down to the
522: 1 third section on this page where it says:
2 "Zyprexa IntraMuscular, olanzapine for
3 injection." You follow me?
4 A. Yes.
5 Q. Read out loud what it says
6 right there?
7 A. "First and only psychotropic
8 indicated for the treatment of agitation
9 associated with dementia."
10 Q. First of only psychotropic
11 indicated for the treatment of agitation
12 associated with dementia, right?
13 A. That's what it says.

Michael Bandick (June 9, 2006)

528: 8 Q. Sir, DTP programs, that means
9 direct-to-physician programs, right?
10 A. Yes.
11 Q. Didn't you at Eli Lilly
12 market directly to physician for the
13 treatment of depressive symptoms in relation
14 to Zyprexa?

Michael Bandick (June 9, 2006)

528:17 A. The only marketing to
18 physicians through DTP that I'm aware of that
19 included depressive symptoms were those
20 symptoms within the context of schizophrenia.

Michael Bandick (June 9, 2006)

528:24 Q. My only question to you was:
529: 1 Didn't Lilly market Zyprexa directly to
2 physicians for the treatment of depressive
3 symptoms?

Michael Bandick (June 9, 2006)

529: 7 A. We did not promote Zyprexa
8 for the treatment of depressive symptoms.
9 (Whereupon, Deposition
10 Exhibit(s) 22 duly received, marked
11 and made a part of the record.)
12 QUESTIONS BY MR. ALLEN:
13 Q. Can you read to the jury the
14 title of Bandick Exhibit No. 22?
15 A. It's entitled 1999 DTP
16 Programs.
17 Q. There's a little bit more of
18 the title, isn't there?
19 A. I'm sorry, Programs
20 Emphasizing Zyprexa's Efficacy for Depressive
21 Symptoms.
22 Q. And then it lists Programs
23 Emphasizing Zyprexa's Efficacy For depressive
24 Symptoms, does it not?
530: 1 A. Yes, that's what I just read.
2 Q. And are these Lilly programs?
3 A. I assume so.
4 Q. Are Doctors Keck or Shelton
5 or Zajecka, are they Lilly speakers, sir?
6 A. All three of them are
7 psychiatrists who did do speaking for Lilly,
8 among other companies.
9 Q. They were paid honoraria and
10 money by Lilly?
11 A. They were compensated for
12 their time and service.
13 Q. So the physicians listed here
14 on Exhibit 22 were paid money by Lilly to
15 participate and give the programs listed on
16 this exhibit; is that correct?
17 A. Yes.
18 (Whereupon, Deposition
19 Exhibit(s) 20 and 21 duly received,
20 marked and made a part of the
21 record.)
22 QUESTIONS BY MR. ALLEN:
23 Q. Bandick Exhibit No. 20, and
24 Bandick Exhibit No. 21, those are two
531: 1 speeches you gave, right? Or presentations,
2 whatever.
3 Let me rephrase the question.

Bandick Exhibit No. 20 and 21 are two presentations that you made in regard to Zyprexa, correct?

Michael Bandick (June 9, 2006)

Q. Simple question, those are presentations you made in regard to Zyprexa?
A. The exhibit entitled Bandick 20, it appears that I have some comments and then other members of the brand team are doing a role play. It's not clear to me if this is a draft or an approved document.
Q. Well, sir, let me tell you, I think I can help you there, doesn't it say they're videoing this presentation? Let me see where I can find that for you. I'll find it. At least that's what my recollection is.

Michael Bandick (June 9, 2006)

Q. What are we on Exhibit 20?
A. I'm on 20.
Q. Okay. Assume -- well, it appears to you to be a presentation you made at a Viva Zyprexa meeting, right?
A. No, I don't believe that's true.
Q. Well, what's the last word down there, "We deserve to win, Viva Zyprexa," correct?
A. That's correct.
Q. And then it says, it's Bandick introduction: "Thanks for taking the time to strengthen your Zyprexa product knowledge," and then it goes on.
Did I read that correctly?
A. That's what it says in this document.
Q. Are you denying that you gave this presentation on Zyprexa as reflected in Bandick Exhibit No. 20?
A. This does appear to be a script for either a video or audio tape. So I wouldn't characterize it as a presentation. As I mentioned, I'm not sure if this is a draft version or a final version.
Q. Why don't you look at the last page. Doesn't it appear this is notes that were taken by somebody at your presentation?
A. Not necessarily.
Q. Okay. Never mind.
Well, we'll agree at least at this juncture that Bandick Exhibit No. 20 is a script for an actual presentation or a draft for a script that is going to be given at a presentation, right?

Michael Bandick (June 9, 2006)

534: 6 A. Based on my read of this it
7 appears that it could be a script for a
8 presentation or a draft of a video or audio
9 tape.

Michael Bandick (June 9, 2006)

535: 4 Q. Let go to 21 and I'm going to
5 ask you. Let's go to 21, Bandick exhibit --

Michael Bandick (June 9, 2006)

535:13 Q. Bandick Exhibit No. 21. Are
14 you on to Bandick 21?
15 A. Yes.
16 Q. This is a presentation you
17 made, is it not? On my birthday. Do you
18 remember my birthday? You called me that
19 year and wished me happy birthday?
20 A. I don't recall that.
21 Q. Okay. Well, you didn't. We
22 never met each other until today, have we,
23 sir?
24 A. That's correct.
536: 1 Q. Anyhow, look at the first
2 page, Bandick, what exhibit number is this?
3 A. 21.
4 Q. 21. It says "Zyprexa Primary
5 Care Presentation, Mike Bandick, Zyprexa
6 Brand Manager, Eli Lilly National Sales
7 Meeting, March 13, 2001;" is that correct,
8 sir?
9 A. Yes, that's correct.
10 Q. This is your presentation, is
11 it not?
12 A. I was involved in this
13 presentation. There are other speakers who
14 followed me.
15 Q. We're in agreement. When
16 you're speaking this is you talking, right?
17 A. In the first part of the
18 document, that's right.
19 Q. Okay. It says by Mike. It
20 says: Mike: Good afternoon, Team Viva,
21 explanation point."
22 Did I read that correctly?
23 A. Yes.
24 Q. Go to Page 3. This is still
537: 1 you talking, isn't it?
2 A. Yes, it is.
3 Q. I'm going to start with the
4 presentation paragraph with just imagine.
5 You say here at the 2001 national sales
6 meeting on March the 13th: "Just imagine the
7 added impact that better sales messages,
8 competitive differentiation and peer-to-peer

activity will have on our future sales line.
Don't get me wrong, unit share growth is good, and what we have accomplished in that area has not gone unnoticed. But dollars pay the bills and boost the stock price so let's look at dollar growth. Again, we're redefining the market."
Did I read that correctly?
A. Yes.
Q. Go to Page 4. You know Bill Robinson?
A. Yes.
Q. I'm going to read what Bill Robinson says on Page 4. "Bill Robinson: Our timing is impeccable. This is for Year X, for Eli Lilly -- excuse me. "Our timing is impeccable. This is Year X for Eli Lilly, and the conventional wisdom is that companies just don't, quote, bounce back, close quote, from losing patent protection from their biggest product." Then it's redacted.
"We need to own this target because the affiliate needs our help."
Did I read that correctly?
A. Yes.
Q. Then you all had a Sweet Sixteen presentation to the sales representatives. You recall that?
A. Yes.

Michael Bandick (June 9, 2006)

Q. My only question, you recall the Sweet Sixteen presentation, right?
A. Yes, I do.
Q. Tell the jury what the Sweet Sixteen presentation was?
A. It was a recognition for individual sales representatives who had, who had shown the most growth in Zyprexa prescriptions.
Q. How much did you pay them for selling Zyprexa and reaching the Sweet Sixteen?

Michael Bandick (June 9, 2006)

Q. You gave them money, didn't you?

Michael Bandick (June 9, 2006)

A. I believe there was a bonus involved. I don't recall what the amount was.
Q. Okay, sir. Now you start talking again in this document on Page 10,

you see it says, "Mike", right? At the bottom?
A. Yes.
Q. Page 11 I'm going to read what you said. "We thrive on change, but there's a lot to be said also for continuity."
Did I read that correctly?
A. Yes.
Q. You said: "Our vision is unchanged. Our strategy unchanged. And our message is essentially unchanged." Right?
A. Yes.
Q. Go on to page 12. You say: "Don't get me wrong, you will see here in Dallas," so you're in Dallas, Texas, where this is taking place, right?
A. That's correct.
Q. "You will see here in Dallas many examples of our growth and evolution. But the foundation of who we are and why we're in primary care hasn't changed."
So you're talking about the primary care market, are you not?
A. I am.
Q. The next paragraph you say: "We intend, quite simply, to redefine the way PCPs treat mood, thought and behavioral disturbances." Right?
A. That's correct.
Q. You didn't say we intend, quite simply, to redefine the way primary care patients treat schizophrenia and mania related to bipolar disorder, did you?
A. That's correct.
Q. So you were intending for primary care physicians to use Zyprexa to treat mood, thought and behavioral disturbances, right?

Michael Bandick (June 9, 2006)

A. No, I disagree with that.
Q. So when you said: We intend, quite simply, to redefine the way PCPs treat mood, thought and behavioral disturbances," you didn't mean you were promoting Zyprexa to the sales force for promotion to doctors to treat mood, thought and behavioral disturbances?
A. That's correct. I did not intend for the sales force to promote under mood, thought and behavioral disturbances.
Q. Read your next comment in this paragraph. Don't you say: "We will continue to focus on symptoms and behaviors that PCPs see every day?"
A. Yes.
Q. "And we will tell that story through a mix of sales efforts, peer-to-peer activity and direct-to-physician marketing."

Did I read that correctly?
A. That's correct.
Q. Now, on Page 13, you said that one of your competitors, Geodon, this is you talking, you were going to squeeze the life out of Geodon because it was a dangerous little drug, right?
A. That's what it says.
Q. Why was it a dangerous little drug that you were going to squeeze the life out of?
A. The dangerous reference referred to its cardiotoxicity profile. And I don't recall what the rationale was for calling it "little."
Q. Okay. You were telling your sales force that Geodon, one of your competitors, was a dangerous little drug and you were going to squeeze the life out of it, right?

Michael Bandick (June 9, 2006)

Q. Right, sir?
A. That appears to be the second part of that comment. There is a part that's redacted.
Q. Okay. You continue on on Page 13. We're on Page 13, I'm skipping down. This is you talking, right? Sir?
A. Yes, I believe so.
Q. Page 13, this is what you say: "Let me call a time out and make one quick comment on Martha." Isn't that what you say?
A. Yes.
Q. I thought you told me earlier today when I asked whether or not Zyprexa was marketed to Martha you said, "Mr. Allen, I don't know what you're talking about?" Didn't you?

Michael Bandick (June 9, 2006)

Q. Didn't you say that?
A. I didn't understand what you meant by your question.
Q. Okay. This is you talking here back at the national sales meeting in Dallas, Texas, right?
A. Yes.
Q. And don't you say to the sales representatives: "Let me call a quick time out and make one quick comment on Martha." What did you mean?
A. Martha was one of the patient profiles that we had in our marketing material and was intended to portray a patient with late onset schizophrenia. We

never marketed to late onset schizophrenics. So when you said "did you market to Marthas," that didn't make any sense to me.

Q. But it made sense in the national sales meeting?

A. We're still not marketing to Marthas.

Q. This is your presentation at the national sales meeting, isn't it?

A. Yes.

Q. Let's just read what you said then as opposed to what you said now, okay?

Q. You want to read that?

THE WITNESS: Can you repeat your question?

Q. Let's see what you said back at the national sales meeting back in 2001. Let's start -- let me call out, okay? Are you there?

A. Go ahead.

Q. I want you to follow me and see if I read what you said correctly at the national sales meeting. "Let me call a time out and make one quick comment on Martha. What's the first thing you notice about Martha?"

You answer the question about Martha, "She's old. That does two things. First, it reinforces Zyprexa as a nursing home drug."

Did I read that correctly?

A. Yes.

Q. "Our mission is to build a primary care franchise, and let our long-term care team drive the nursing home business."

Did I read that correctly?

A. Yes.

Q. You go on, and I'm skipping down to talk more about Martha. You see when? You see it?

A. Yes.

Q. You say to the national sales meeting: "When you describe Martha, make her symptoms more prominent than her age."

Did you say that, sir?

A. Yes, I did.

Q. Then you said: "Zyprexa is extremely safe; note that Zyprexa has now been used to treat more than 6 million patients. Proven safety. Unsurpassed ease of use. No hassles, doctor."

Didn't you say that?

A. That's what it says in this document.

548:22 Q. Sir, let's move on. You said
23 "No hassles, doctor," didn't you?
24 A. That's what it says in this
549: 1 document.
2 Q. Just for the record, that's
3 not, I'm not asking what it says in this
4 document. These are your comments made to
5 the national sales force in Dallas, Texas, at
6 the national sales meeting, isn't it?

Michael Bandick (June 9, 2006)

549:13 Q. Are we communicating, sir?
14 This is the comments you, actually, made,
15 right?
16 A. What I'm indicating is that
17 this is a teleprompter script. If you ask me
18 if I made that exact comment, I don't recall
19 everything that came out of my mouth. I
20 don't know if this is a draft or the final
21 document. That's why I said it the way I
22 said it. I'm doing my best to answer your
23 questions.
24 Q. Yes. It's a teleprompter
550: 1 script for the national sales meeting, right?
2 A. In some form, yes.
3 Q. Okay. Let's go to Page 15.
4 Here's what you say going on. "Just safety
5 and broad symptom efficacy in a package
6 that's easy for you to prescribe and easy for
7 your patients to take."
8 Did I read that correctly?
9 A. Yes.
10 Q. Go down to the middle of the
11 page. You see you have QTc prolongation?
12 A. Yes.
13 Q. Let me read your comments.
14 "QTc prolongation. As you know, led to the
15 removal of Seldane, Hismina1 and Propulsid
16 from the market. Zyprexa's cardiovascular
17 profile is different from agents such as
18 Mellaril, which has a related black box
19 warning, and Geodon, a new antipsychotic with
20 a ten paragraph bolded warning regarding
21 QTc."
22 Right? Did you say that?
23 A. That's what it says.

Michael Bandick (June 9, 2006)

551:24 Q. Did you make this
552: 1 presentation that I just read to the national
2 sales force?

Michael Bandick (June 9, 2006)

553: 6 A. All I can tell you is this is

a teleprompter script. I don't know if it was the final or a draft version. This is what it says in this document.

Q. Now, continuing on Page 15, go down to the bottom. "During the first half of 2001, we on the brand team have focused on two key points of emphasis, peer-to-peer activity and competitive differentiation."

Did I read that directly?

A. Yes.

Q. Now peer-to-peer activity, when you're talking about that to the sales force, that means using your speakers bureau of Lilly to communicate with doctors, right?

A. That can be a part of it, yes.

Q. CME is another part, is that correct?

Michael Bandick (June 9, 2006)

A. That's not what I consider peer-to-peer.

Q. Lunch and learns?

A. Could be an example of peer-to-peer.

Q. Any other examples?

A. There can be audio conferences, there can be small groups that are invited to a dinner program. Not CME, though.

Q. Then you say, you talk about competitive differentiation and that's where you differentiate Zyprexa from your competition; is that correct?

A. That would be my definition of competitive differentiation.

Q. And one of the ways you did that was above, when you talked about the difference in other product's labels, right?

A. That is one example of competitive differentiation.

Q. So one of the ways you compete in the marketplace is you have your sales force compare your label on Zyprexa to the labels of the competitors, right?

A. Yes.

Q. So the label is not merely a conduit of information, it's utilized by the marketing department as a differentiator in the competitive marketing field; is that correct?

Michael Bandick (June 9, 2006)

A. By itself, the label conveys a significant amount of information. In comparison to other labels there may be other

information that you can get.
Q. But you, in the marketing department, used the differences in labels as a marketing tool, do you not?

Michael Bandick (June 9, 2006)

555:23 A. There are examples of that.
Q. And one of the examples is
556: 1 Page 16, I mean, excuse me, Page 15 of your
2 presentation to the national sales meeting in
3 March of 2001, right?
4 A. That's correct.
5 Q. Now, going to the bottom of
6 Page 15, you say: "Regarding peer-to-peer
7 we've just completed the second of two
8 speaker training programs, and have unleashed
9 more than 130 psychiatrists." Is that what
10 that's an abbreviation, sir?
11 A. Yes.
12 Q. So you say: "We've just
13 unleashed more than 130 psychiatrists and
14 PCPs who are chomping at the bit to help you
15 sell Zyprexa."
16 Did I read that correctly?

Michael Bandick (June 9, 2006)

558:15 Q. Sir, are the scripts you
16 prepared for presentations at national sales
17 meetings intended to convey accurate,
18 truthful information that the sales reps can
19 count on and convey to the doctors that they
20 detail?

Michael Bandick (June 9, 2006)

558:23 A. Not all of the content that
24 we would share at a national sales meeting
559: 1 would be appropriate for promotion to
2 physicians or verbatims.
3 Q. Would it be accurate and
4 truthful information that you gave the sales
5 representatives at a national sales meeting
6 as reflected in your presentation Bandick
7 Exhibit No. 21?

Michael Bandick (June 9, 2006)

559:10 A. I would expect to the best of
11 our ability that it would be accurate and
12 truthful, yes.
13 Q. Would it be fair and
14 balanced?

Michael Bandick (June 9, 2006)

559:18 A. I'm not sure how to evaluate
19 fair and balanced in that context.

Michael Bandick (June 9, 2006)

561: 2 Q. Do you remember who was on
3 the Board of Directors for Lilly Corporation
4 that was from Houston, Texas?
5 A. Yes, I do.
6 Q. Tell the jury who that was.
7 A. Ken Lay.
8 MR. ALLEN: Thank you, sir, I
9 have no further questions at this
10 time

Exhibit 2
Charles Beasley, M.D.

Charles Beasley, M.D. (July 26,2006)

26:10 Q. Good morning, Dr. Beasley.
11 Would you state your full name for the
12 record, please?
13 A. Yes, my name is Charles M.
14 Beasley Jr.
15 Q. And how old are you, sir?
16 A. I am 56.

Charles Beasley, M.D. (July 26,2006)

26:21 Q. Okay. And are you currently
22 employed by Eli Lilly?
23 A. Yes, I am.
24 Q. And what's your current job
27: 1 title?
2 A. My current job title is
3 Distinguished Lilly Scholar and Chief
4 Scientific Officer For Global Product Safety.

Charles Beasley, M.D. (July 26,2006)

31:18 Q. Okay. And you received your
19 medical degree in 1983 from the University of
20 Kentucky College of Medicine; is that
21 correct?
22 A. That's correct.

Charles Beasley, M.D. (July 26,2006)

32: 6 Q. Okay. And then you did a
7 three-year residency in psychiatry at the
8 University of Cincinnati in Ohio between 1984
9 and 1987; is that correct?
10 A. That would be correct. I
11 completed the residency in June of 1987.
12 Q. Okay. And I believe you
13 became board certified in psychiatry in 1988;
14 is that correct?
15 A. That would have been correct.
16 It's a two-step process and I believe that I
17 completed the second part in, I believe, it
18 was October of 1988.
19 Q. Okay. And you joined Eli
20 Lilly as an Associate Research Physician in
21 July of 1987; is that correct?
22 A. That's correct.
23 Q. Were you ever in private
24 practice in psychiatry after you completed
33: 1 your residency and before joining Eli Lilly?
2 A. No, I was not. I came
3 directly to Lilly from my residency.

Charles Beasley, M.D. (July 26,2006)

44: 7 Q. Okay.
8 I'm going to hand you what
9 has been previously marked Plaintiff's
10 Exhibit 1349.
11 (Whereupon, Deposition
12 Exhibit(s) 1349 previously
13 marked, was presented to the
14 witness.)

Charles Beasley, M.D. (July 26,2006)

45:18 By the way, for the record
19 this appears to be a PowerPoint
20 presentation. It's 24 pages. The
21 first page has a heading Human
22 Metabolism.
23 QUESTIONS BY MR. SUGGS:
24 Q. And I'd like to direct your
46: 1 attention to Page 5, if you would. And there
2 there's a heading entitled Development
3 Milestones. Do you see that page?
4 A. Yes, I do.
5 Q. Okay. And it indicates there
6 that the molecule olanzapine which was later
7 marketed under the trade name Zyprexa, was
8 first synthesized in April of 1982. Does
9 that square with your understanding?
10 A. That would be my
11 understanding.

Charles Beasley, M.D. (July 26,2006)

48: 7 Q. Okay. And in this case, the
8 first double blind placebo controlled dose
9 was given in November of 1991; is that
10 correct?
11 A. That's correct.
12 Q. And I believe you said you
13 started working with Zyprexa in 1991. Were
14 you involved in that very first clinical
15 testing?
16 A. Yes, I was. Although I did
17 not design those -- those clinical trials, I
18 took over responsibility for the supervision
19 of the molecule as those trials were
20 beginning.
21 Q. Okay. And then the document
22 indicates that the completion of core studies
23 occurred in February of 1995. And can you
24 describe for us what is meant by the term
49: 1 "core studies"?
2 A. Yes. These would have been
3 the studies that would have been included in
4 both the new drug application, the NDA in the
5 United States, as well as the regulatory
6 submissions in other countries.

Charles Beasley, M.D. (July 26,2006)

49:24 Q. Okay. And am I correct that
50: 1 the largest of the core studies that was done
2 was a study that was referred to as HGAJ?
3 A. That was the largest.
4 Q. And it had, approximately,
5 how many subjects in it?
6 A. It had 1,996 subjects.
7 Q. Okay. And was it the
8 largest, by far, of the various clinical
9 studies that were done in connection with the
10 drug?
11 A. It was.

Charles Beasley, M.D. (July 26,2006)

56: 4 Q. You've described various
5 testing that was done on Zyprexa before it
6 was -- went on the market. That testing was
7 done by Eli Lilly, correct?
8 A. I would characterize it as
9 being done by the -- by the investigators.
10 It was designed and administered by Lilly.
11 Q. Okay.
12 A. Now, I understand your --
13 Q. Okay.
14 A. The FDA didn't actually do
15 the studies or contract to have them done.

Charles Beasley, M.D. (July 26,2006)

72:16 Q. Am I correct that Lilly
17 employed an outside advisory panel with
18 respect to Zyprexa?
19 A. There was -- there was a --
20 there was both an international and a U.S.
21 advisory panel for the molecule during its
22 development that I'm familiar with.

Charles Beasley, M.D. (July 26,2006)

73: 5 MR. SUGGS: Let me show you
6 what's been previously marked as
7 Plaintiff's Exhibit 1586.
8 (Whereupon, Deposition
9 Exhibit(s) 1586 previously
10 marked, was presented to the
11 witness.)
12 MR. SUGGS: For the record
13 this is a document -- 30-page
14 document entitled Executive Summary,
15 The Third United States
16 Schizophrenia Advisory Panel Meeting
17 dated December 10, 1995, San Juan,
18 Puerto Rico.

Charles Beasley, M.D. (July 26,2006)

74:13 Q. Okay. And back at that time
14 in December of 1995, were you reporting
15 directly to Dr. Tollefson then?
16 A. Yes, I was.

Charles Beasley, M.D. (July 26,2006)

75:19 second paragraph -- actually, let's talk
20 about the first paragraph. It states, "The
21 third meeting of the U.S. Schizophrenia
22 Advisory Panel convened on December 10, 1995,
23 in San Juan, Puerto Rico, to discuss
24 olanzapine, the Eli Lilly and Company
76: 1 anti-psychiatric drug in development. Ten of
2 the 11 schizophrenia specialists who served
3 on the panel were present along with medical,
4 research, and marketing executives at Eli
5 Lilly and Company." Did I read that
6 correctly?
7 A. That's correct.
8 Q. And this would have been
9 about what, two, three months after the NDA
10 had been submitted to FDA?
11 A. I believe that's correct.
12 Because I think the NDA was submitted in
13 September.
14 Q. September. Okay. And then
15 the second paragraph it starts off by saying,
16 "The meeting began with first-time
17 presentation of efficacy and safety results
18 from HGAJ, the pivotal phase 3 trial by
19 Charles Beasley, Jr, MD, and a review of the
20 developmental history and update of the
21 integrated olanzapine database by Gary
22 Tollefson." Do you see that?
23 A. That's correct.
24 Q. And when it uses the phrase
77: 1 "the pivotal phase 3 trial" referring to
2 HGAJ, what does that mean?
3 A. That this was one of the
4 trials that was part of the NDA.
5 Q. Okay. And as we talked
6 before, it was not only one of the trials, it
7 was the largest trial, correct?
8 A. That's correct.
9 Q. Okay. If I could direct your
10 attention to Page 8. In the first paragraph,
11 in about the middle of that paragraph four
12 lines from the bottom it states, "For all
13 patients treated with olanzapine for any
14 amount of time, forty percent gained greater
15 than or equal to 7 percent body weight." Do
16 you see that language?
17 A. Let me just find it here.
18 Yes, I do.
19 Q. Okay. And it's generally
20 accepted that an increase in weight of
21 7 percent or more is clinically significant,

correct?
A. This has been a criteria established with the FDA for which the term is used potentially clinically significant.
Q. Okay. And that paragraph goes on to note that, "Patients who remained on olanzapine for 12 months gained an average of 24 pounds at the end of 12 months," correct?
A. That's correct.
Q. Okay. By the way, if 40 percent of the people who took the drug for any period of time had more than -- had equal to or more than 7 percent body weight that means that 40 percent of the people who took the drug for any length of time had potentially clinically significant weight gain, correct?
A. That's correct.
Q. Okay. And then there's a paragraph below that that's in italics which states quote, "Several advisors commented on the association of olanzapine with weight gain and encouraged Lilly to subject the data to a full analysis. Clinically significant weight gain is a risk factor for other conditions such as increased blood pressure, increased cholesterol and type II diabetes. The advisors also noted that Lilly has an opportunity to develop strategies to help manage the weight gain." Do you see that language?
A. Yes, I do.
Q. If we got 40 percent of the people who take the drug for any length of time having potentially significant weight gain, that means that those people are going to be at risk for those conditions that are referred to there, increased blood pressure, increased cholesterol and type II diabetes, correct?
MR. SEE: Object to the form.
A. That means that what they have is one risk factor for potentially developing these conditions.
Q. Um-hum. And you would expect in a population of people that if you enhance the risk by taking the drug that some people are, indeed, going to develop increased blood pressure, increased cholesterol, and type II diabetes as a result of using the drug, correct?
MR. SEE: Object to the form.
A. Individuals might or might not experience these phenomena either as a result of any number of things. And these would be appropriate for analysis.
Q. Well, you may not be able to predict which individual is going to actually contract any of those illnesses as a result of taking the drug. But if, in fact, the drug increases the risk of those adverse reactions as a population of people taking

the drug, you would expect that some people would, indeed, develop those adverse reactions as a result of using the drug, correct?

MR. SEE: Object to the form.

A. Individuals might or might not. And that's why it would be important to analyze the incidence of those things amongst patients taking the drug.

Q. But if you step away from the individuals and look at the population, it's a virtually certainty that if you increase the risk of an adverse reaction that some people within that group will, in fact, contract the adverse reaction as a result of using the drug, correct?

MR. SEE: Object to the form.

A. That is certainly the theory that would be intuitive and logical. What I am pointing out is that one would then need as, I think these advisors were doing, suggesting, scrutinizing our data and looking for whether or not those phenomena were observed.

Charles Beasley, M.D. (July 26,2006)

Q. With respect to the weight issue, your labeling did not inform physicians that for all patients treated with olanzapine for any amount of time 40 percent gained more than or equal to 7 percent of the body weight; is that correct?

MR. SEE: Object to the form.

A. Well --

Q. You got to answer that question "yes" or "no" or "I don't know?"

A. Well, it, specifically, did not. What our label did --

Charles Beasley, M.D. (July 26,2006)

Q. Your labeling also did not, specifically, inform physicians that patients who remained on olanzapine for 12 months gained an average of 24 pounds at the end of those 12 months, correct?

A. No, it did not.

Q. Okay. And on Page 8 at the bottom there's a -- in the last paragraph, there's a heading that says Laboratory Anolytes?

A. Yes.

Q. And what does that phrase mean?

A. This would refer to all of those things that are measured in blood or urine, specific measurements such as sodium, glucose, or white blood cells, that are

measured in a laboratory.
Q. And, in fact, the laboratory testing that was done on HGAJ subjects showed that there was a statistically significant increased incidence of high glucose and also high cholesterol; isn't that correct?
MR. SEE: Object to the form.
A. Again, without benefit of looking at the -- at the entirety of the data, my only recollection is with regard to a analysis of the, what we call the categorical incidence of elevated glucoses relative to haloperidol, based on what we call anytime data. I recall this number as being statistically significant. That is one number that needs to be appropriately put in the context of, actually, about nine analyses.
Q. You say "based on what we call anytime data I recall this number as being statistically significant." What was "this number" that you're referring to?
A. I believe it was the percentage of individuals who showed a shift from a normal glucose to what would be considered a high glucose.
Q. Okay. And you were aware of that at what point in time?
A. I don't know the specific. It would have been when the data were analyzed.
Q. It would be sometime between when the data was cutoff in February of 1995 and when it was submitted to FDA in September of 1995, correct?
A. That would have been correct.
MR. SUGGS: Okay. Let me show you a computer printout from that time. I'm handing you what's been previously marked as Plaintiff's Exhibit 1605.
(Whereupon, Deposition Exhibit(s) 1605 previously marked, was presented to the witness.)
MR. SUGGS: For the record this is a computer printout dated June 19, 1995. The title of it is Treatment-Emergent Abnormal,High, or Low Laboratory Values at Any Time, from the HGAJ Acute Phase.
QUESTIONS BY MR. SUGGS:
Q. Do you recognize this document, sir?
A. This would have been a printout, I believe, from the NDA that would have been part of the study report for the acute phase of study HGAJ.

94: 4 Q. Who was responsible for
5 having these types of analyses done and then
6 reviewed?
7 A. Okay. That would have been a
8 group of individuals, Dr. Tollefson, myself,
9 other physicians, senior statisticians that
10 would have been involved with the -- with the
11 project.
12 And I would think, also, we
13 would include the regulatory people who would
14 be involved with guiding us in terms of the
15 NDA preparation.
16 Q. Okay. Would it be fair to
17 say that if computer analyses were done of
18 the data from the HGAJ study back in June of
19 1995 that you and Dr. Tollefson would have
20 been aware of the results of those analyses?
21 A. Yes, we would have been.
22 Q. Okay. I'd like to direct
23 your attention to Page 11.
24 A. Yes.
95: 1 Q. Do you see there that there's
2 a heading for lab tests of Glucose,
3 Non-fasting?
4 A. Yes, I do.

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95: 9 In this study, HGAJ, there
10 were, actually, two groups of patients, some
11 of whom were taking olanzapine or Zyprexa the
12 other group was taking another drug referred
13 to as a first generation anti-psychotic drug
14 called Haldol or haloperidol; is that
15 correct?
16 A. That's correct.
17 Q. Okay. And what you were
18 doing in this study was comparing the
19 incidence of these different types of
20 laboratory anolytes between those folks who
21 took Zyprexa and those who Haldol, correct?
22 A. That's correct.
23 Q. On Page 11 here, this portion
24 of the printout regarding Glucose,
96: 1 Non-Fasting, shows a statistically
2 significant increased incidence of high
3 glucose in the Zyprexa group as compared to
4 the Haldol group, correct?
5 MR. SEE: Objection to the
6 form of the question.
7 A. Yes. I'm seeing a -- an
8 incidence of 2.6 percent high for olanzapine,
9 1.1 percent for haloperidol. And the P value
10 there, by this test, is .031 which is less
11 than .05, which is generally considered the
12 standard for statistical significance.

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99: 1 Q. Dr. Beasley, could I get you
2 to look at Page 12 of Exhibit 1605. And you
3 see at the top of the page there there's the
4 results of some laboratory testing on
5 cholesterol, correct?
6 A. Yes, I do.
7 Q. And it also shows a
8 statistically significant increased incidence
9 of high cholesterol, correct?
10 A. Yes, that's correct.
11 2.3 percent versus 0.8 percent.

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102:18 Q. And if I could direct your
19 attention back to the Executive Summary that
20 we looked at before, it's Exhibit 1586.
21 A. Yes.
22 Q. At the bottom of Page 8, I
23 believe it was.
24 A. Yes.
103: 1 Q. Under the section Laboratory
2 Anolytes, there is no mention in there of
3 there being statistically significant
4 increased incidences of either high glucose
5 or cholesterol, correct?
6 A. That's correct.
7 Q. Okay. And do you recall that
8 at that meeting that you had with the experts
9 in San Juan, Puerto Rico, in September
10 of 1995, that there was a transcript made of
11 that meeting?
12 A. I don't recall the -- the
13 specific of a transcript. There may well
14 have been one made.
15 Q. Do you recall that it was
16 often the case that transcripts of meetings
17 with experts would be made?
18 A. Yes, I believe that was the
19 case.
20 MR. SUGGS: Let me show you
21 what's been previously marked as
22 Plaintiff's Exhibit No. 1345.
23 (Whereupon, Deposition
24 Exhibit(s) 1345 previously
104: 1 marked, was presented to the
2 witness.)
3 MR. SUGGS: For the record
4 this is a 39-page document bearing
5 the title on the first page HGAJ
6 Data Presentation Charles Beasley,
7 Jr.
8 QUESTIONS BY MR. SUGGS:
9 Q. Correct?
10 A. Yes.
11 Q. And does it appear to you
12 that this is the transcript of the meeting
13 you had with the experts, your expert
14 advisory committee, in San Juan, Puerto Rico,
15 in December of '95?
16 A. It would appear to be, and

I'm reading the first page only, that this would be dealing primarily, specifically, with HGAJ.

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Q. Okay. If I could direct your attention now to Page 22. Actually, the bottom of Page 21 continuing on to Page 22, you point out to the group that "not everybody gained weight, but there are some patients who gained a substantial amount. In fact, that's the most consistent nontherapeutic physical finding you're talking about." Do you see that?
A. Yes, I do.
Q. Then there's a question from a Dr. Casey -- was that Dr. Daniel Casey?
A. Yes, it was.

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Q. Okay. But in any event, at this meeting in December of 1995, Dr. Casey asked you after you told him about the weight gain, he says quote, "Did any develop diabetes?" And I'm just going to read the interchange that goes on there. You responded by saying, "Very few people have developed type II diabetes during the time of this trial. We have over 400,000 patient days of olanzapine exposure, and the rate for diabetes, a couple of these cases I know are type I who got out of control. Treatment-emergent diabetes, does," and then you're interrupted by Dr. Potkin who asked, "Does that happen more often on olanzapine?" And then there's a response by Todd Sanger, who said, "I don't believe it did." Who is Mr. Sanger?
A. Dr. Sanger was the chief statistician for the project.
Q. Okay. And then you went on to say quote, "We don't have comparative data long term for haloperidol analyzed at this point. We need six-week data."
Then Todd Sanger jumped in and said, "We had 16 cases of treatment-emergent diabetes, which is .6 percent, of all 2500 patients. This is adverse event."
Then you jumped in and said, "Spontaneous adverse event."
And then Dr. Potkin -- by the way, he was another one of the outside consultants?
A. That's correct.
Q. Okay. And where was he from?
A. I believe he was from a

university in southern California, although I'm not sure which institution.
Q. Do you know if he's still there?
A. I'm not sure.
Q. Was he a psychiatrist or an endocrinologist?
A. He's a psychiatrist.
Q. Okay. Anyway, Dr. Potkin asked quote, "You were measuring glucose all along?" You see that question?
A. Yes.
Q. And then your response to him was, "And we don't see anything," correct?
A. That's correct.
Q. You made no mention of the results of that computer printout that we discussed some minutes before, correct?
A. No, I did not. This was a

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Zyprexa came on the market in 1996, in October, am I correct?
A. I believe that was the case, 13 months after the NDA filing.
Q. And the labeling that was in effect at that time when the product came out on the market, did not warn physicians that your clinical studies had found statistically significant increased incidence of high glucose in Zyprexa users, correct?
MR. SEE: Object to the form.
A. That is correct. But my

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Q. Do you recall that by 1998 Lilly had almost 200 reports of blood sugar elevation?
MR. SEE: Object to the form.
A. Are you speaking about spontaneous adverse event reports?
Q. Yes.
A. And the year was?
Q. 1998.
A. 1998. I cannot give you the specific number in 1998. But that would seem to me to be, approximately correct.

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For the record, this is a 26-page document bearing on the title page the title Census of Spontaneous Reports for Olanzapine During the First Two Years of

Marketing September 27, '96 to September 30, 1998.
It was apparently prepared by Ken Hornbuckle and Man Fung of the Worldwide Pharmacovigilance and Epidemiology Department at Eli Lilly and Company. And it is marked confidential.

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142: Q. Okay. And are you aware, sir, that it's generally estimated that only 1 percent, maybe 10 percent of the number of adverse events that, actually, occur in the use of a drug ever get reported?
MR. SEE: Object to the form.
A. The literature that I am familiar with estimated between 1 in 5 and 1 in 30 cases would be reported. This was in this time frame when I was more involved with doctors Funk and Hornbuckle. I believe that more recent literature has suggested it may be as low as one in a hundred.

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145: Q. If I could direct your attention to Page 14, and I'm referring to the bottom most number of Page 14.
A. Okay.

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146: Q. In any event, whoever prepared this report, well, Doctors Hornbuckle and Fung, have a bold heading there entitled Blood Sugar Elevation, correct?
A. That's correct.
Q. And then below that they have six different subcategories, including hyperglycemia, diabetes mellitus, diabetic acidosis, diabetic coma, ketosis, and glucose tolerance decreased, correct?
A. That's correct.
Q. And then below that they have another bold heading that says Unduplicated Reports, correct?
A. That's correct.

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147: Q. Okay. And it shows that if you looked at all four quarters of -- or I

guess eight quarters from '96 to '98 there were a total 194 unduplicated reports of what they had grouped together as blood sugar elevation, correct?
A. That's correct.
Q. Okay. And again, using the numbers we've talked about before, if we multiplied by -- well, the numbers we talked before in terms of what the range might be with respect to what's happening out in the real world. If we multiply the 194 by 5
148: that's almost a thousand and if we multiply by a hundred it would be almost 20,000 cases of blood sugar elevation, correct?
A. That is correct. As I said,

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149:12 With respect to Exhibit 988. The one you have there. It's marked confidential on every page. Was it standard drill at Eli Lilly to mark reports of adverse event reports as confidential?
MR. SEE: Object to the form.
A. Actually, I don't know whether all such reports would be so marked.

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150: 7 Q. Do you recall that by December of 1998, just a couple of months after the cutoff period for this report, Lilly was struggling about what to say regarding the link between weight gain and diabetes?
MR. SEE: Object to the form.
A. Again, in the -- I don't recall any specific information or discussion about what Lilly was going to say in any specific context in that time period.
MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 6890.
(Whereupon, Deposition Exhibit(s) 6890 previously marked, was presented to the witness.)
151: MR. SUGGS: For the record this is an e-mail from Mary Ann Adams to Michael Bandick, Charles Beasley, Dr. Alan Breier, Alan Clark, Annmarie Crawford, Charles Feehan, there may be another name that's cut off, and the subject is Agenda Zyprexa Medical Marketing Meeting.
QUESTIONS BY MR. SUGGS:
Q. And it's -- the agenda is dated December 9, 1998.

A. Yes.

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Q. Okay. Do you see that under the agenda there's several bullet points. The middle one is weight gain and link to diabetes, question mark, what does the data say and what is our action plan, question mark. Do you see that reference?
A. Yes, I do.
Q. And then there's a handwritten note at the bottom relating to weight gain, correct?
A. Yes, there is.
Q. By the way, do you recognize that handwriting?
A. No, I don't.
Q. The handwritten note says: "Weight gain and genetic vulnerability lead to hyperglycemia," correct?
A. Yes, it does.

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Q. Do you recall talking to people in the marketing department in December of 1998 about the issue of weight gain and diabetes?
A. I don't recall, specifically. I may well have done so in the process of trying to educate individuals that were specializing in neuroscience as opposed to diabetes care about sort of the basics of diabetes.
Q. Do you recall telling people in the marketing department back in December of 1998 that the use of antipsychotic drugs could result in weight gain and that people who gain weight may develop insulin resistance which can lead to hyperglycemia and diabetes?
A. I may have been explaining that -- that there are these associations.
Q. Okay. Was it your belief at the time, back in December of 1998, that the use of antipsychotic drugs could result in weight gain?
A. Yes. I think the data for that are rather clear as reflected in our package insert, specifically, for our drugs and I think the David Allison article that I think was published by this time, to which we'd contributed, looked at antipsychotics in general and suggested that.
Q. And was it your view back in December of 1998 that people who gain weight may develop insulin resistance which can lead to hyperglycemia and diabetes?

A. I would characterize it as a risk factor for developing.
Q. And if someone has a risk factors that means that they may develop that problem, correct?
MR. SEE: Object to the form.
A. That puts them at increased risk. To be very precise, that puts them at increased risk relative to patients or individuals without that risk factors.

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Q. Would you agree, sir, that if you have a group of people who are at increased risk of having some adverse event occur that it is more probable than not at the end of the day, that some of those people will, in fact, develop the adverse event as a result of using the drug that increased their risk?
MR. SEE: Object to the form.
A. All I can say is that there is increased probability among those individuals with that risk factor of developing the condition if they -- than if they did not have the risk factor.

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MR. SUGGS: Okay. Well, let's talk a little bit about the teams who were working on Zyprexa. I'm going to hand you what's been previously marked as MDL Plaintiff's Exhibit 8042.
(Whereupon, Deposition Exhibit(s) 8042 previously marked, was presented to the witness.)
MR. SUGGS: Which for the record is a November 29, 1999, e-mail from Michele Sharp to Gail Uminger, which then copies several other e-mails.
QUESTIONS BY MR. SUGGS:
Q. The first of which is an e-mail on November 28, 1999, from Edmundo Muniz to Michael Clayman, Timothy Franson with copies to Gregor Brophy, Kenneth Hornbuckle, Kenneth Kwong, correct?

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Q. Okay. And I believe you said earlier that Mr. Muniz -- am I pronouncing his name, right?

A. Muniz, Mr. Muniz, but yes.
Q. He was head of the pharmacovigilance department; is that correct?
A. That's correct.

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185:21 Q. And in his e-mail Dr. Muniz says, "Mike and Tim, below you will find the summary of issues discussed this week regarding hyperglycemia and Zyprexa. There
186: 1 are two types of initiatives," and then he lists what those two different types are, correct?
A. There are two types of initiatives, yes.
Q. And the first is a, what he refers to, as a cross-functional team -- pardon me -- cross-functional action team led by Alan Breier. Do you see that?
A. Yes, I do.
Q. And it states that the goal of this team is to bring to the same table all the groups and functions working to address the hyperglycemia issue, correct?
A. Yes.
Q. And the hyperglycemia issue was the fact that by November of 1999 there were published medical articles linking hyperglycemia with Zyprexa and you also had a number of adverse event reports linking hyperglycemia and Zyprexa, correct?
MR. SEE: Object to the form.
A. Yes, that would be correct.

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190:22 Q. Okay. And then Dr. Muniz states under that section, "while Val Simmons, Man Fung, Kenneth Kwong and Charles
191: 1 Beasley have been working closely together on this issue, it was felt that a broader involvement of regulatory pharmacovigilance Mike Clayman, Tim Franson, and Greg Brophy, and Edmundo Muniz, was needed to evaluate a short-term plan." Did I read that correctly?
A. Yes.
Q. Would it be fair to say, sir, that this memo reflects that in November of 1999 the hyperglycemia issue had -- with Zyprexa had become quite an issue, correct?
MR. SEE: Object to the form.
A. I think what this reflects is the company had very clearly intended to increase the resources, both number and level of resources, that were being brought to bear to assess the topic.

Q. Okay. It's pointed out by Dr. Muniz in the background section of this e-mail, that, "The discussion regarding hyperglycemia slash weight gain and antipsychotic drugs goes back as far as the early 1950s," and that, "For more than two decades, until the 1980s there was a large number of publications but the interest in the scientific community and the regulators decreased until very recently." Do you see that language, sir?

A. Yes, I do.

Q. And were you aware of that discussion of hyperglycemia and weight gain being linked with antipsychotic drugs going back to the early 1950s?

A. This was, actually, part of my residency training.

Q. Okay. And right below that section in Item B in the background, Dr. Muniz states, "Two regulatory agencies, EMEA and CANDA, have proactively asked questions about hyperglycemia and Zyprexa." Do you see that?

A. Yes.

Q. And were you involved in responding to those questions raised by the regulatory agencies and EMEA in Europe and Canada?

A. I certainly would have been involved, along with the pharmacovigilance people, who would have developed the primary response.

Q. And were the regulatory agencies in Canada and Europe concerned about hyperglycemia and being linked with Zyprexa?

MR. SEE: Object to the form.

A. They had certainly asked us to conduct specific evaluations of our post-marketing surveillance statement.

Q. And in fact, by this point in time, November of 1999, the European regulatory agencies had already requested that hyperglycemia be a precaution in the European label; isn't that correct?

A. I -- the European label does not make a distinction between warnings and precautions. There's one unified section. I don't have specific recollection of when they requested that it be included as a warning.

Q. If I were to suggest to you that it was requested in late 1998 and that Lilly finally added it to the warnings slash precaution section of the European labeling in July of 1999, would that refresh your recollection?

A. I could well believe that that was correct. Again, I don't remember the specific.

Q. Okay. You don't have any

reason to doubt those [illegible]es I stated there, do you?

MR. SEE: Object to the form.

A. No, I do not.

Q. And regardless of the precise month, you would agree with me that at least by this point in time, November of 1999, hyperglycemia had been added to the precaution slash warning section in Europe, correct?

A. That's correct.

Q. Okay. In fact, there's even a hand written note at the bottom of this e-mail saying precaution in Europe, correct?

A. Yes.

Q. Okay. And by this point in time, hyperglycemia was mentioned in the U.S. labeling but only in the adverse reaction section, correct?

A. Hyperglycemia, among other diabetic related terms, yes.

Q. In the adverse reaction section, not in the precaution section, not in the warning section, correct?

A. That's correct.

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Q. Okay. Now, you said you worked with the pharmacovigilance individuals and the team to produce a very detailed review of the spontaneous data and clinical trial data. Can you tell me which individuals those would have been?

A. Well, it would have -- for the pharmacovigilance side, it would have certainly been at the time Dr. Kwong and, probably, a number of other individuals that would have produced reports, summarized them. I don't know those -- the other individuals's names.

Q. Okay. And when you said in your earlier answer that, that group that you were working with was also going to do a very detailed review of the clinical trial data, was that existing clinical trial data?

A. That was existing clinical trial data. I think, by this time we had completed a very large number of studies.

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Q. This, as you referred to it, detailed review of the spontaneous data and the clinical trial data in 1999, was that for the purpose of addressing the hyperglycemia issue?

A. The topic of hyperglycemia, yes.

Q. Okay. And who was it that directed you to undertake that review?
A. No one, actually, directed that review to be undertaken, to the best of my recollection. It was Dr. Kwong in pharmacovigilance, his group, and myself that felt it would be appropriate to conduct a very, very thorough --
Q. Okay.
A. -- and comprehensive review. I believe that it began in early 1999.

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Q. Okay. In the Section 3 of the e-mail from Dr. Muniz, there's a reference to short term action plan. And there are a number of items listed below there, including continuing to strengthen the post-marketing safety surveillance of hyperglycemia, exploring the possibility of using GPRD to conduct database analysis, what's GPRD?
A. That is a database that, I believe, is available in the UK. So this was an intended epidemiologic study.
Q. Okay. And then Item D -- pardon me -- Item C rather, was "discuss Zyprexa label at a GPLC session and evaluate potential proactive regulatory strategies." Did I read that correctly?
A. Yes.
Q. Am I correct that GPLC stands for Global Product Labeling Committee?
A. That's correct.

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Q. And was the Zyprexa label the subject of a GPLC session in the weeks or months following this e-mail?
A. I don't recall.

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MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 990.
(Whereupon, Deposition Exhibit(s) 990 previously marked, was presented to the witness.)
MR. SUGGS: For the record this is a seven-page document, the first page of which is labeled Confidential, Do Not Forward, To be distributed only by Global

Operations Labeling Department, Indianapolis, Attachment E.
QUESTIONS BY MR. SUGGS:
Q. And, Dr. Beasley, if I could refer you to the second physical page of the document.
A. Um-hum.
Q. There is a heading towards the top of the page below the confidential label that says, "Olanzapine Labeling Change on Hyperglycemia For February 21, 2000, GPLC Meeting." Do you see that?
A. Yes, I do.

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Q. And if you could direct your attention to the last physical page, there is a box there referring to consultation process?
A. Yes.
Q. And it says "reviewed by," and it has, "Global Product Physician Charles Beasley," with the date of February 15, 2000?
A. Yes.
Q. And does that refresh your recollection that you would have seen this document or reviewed it back in February of 2000?
A. Oh, I'm very certain that I was very much involved in putting this document together. A technical correction, I was not the Global Product Physician, as I have explained. I was a consultant, not part of the team.

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Q. And regardless of whether you personally drafted the text that's in here, would it be fair to say you not only reviewed but approved this language?
A. Yes.

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Q. Okay. So your analysis, as reflected in this document, for the clinical trial data yielded results that showed that the frequency of hyperglycemia was common or frequent, correct?
A. Yes, by this nomenclature, absolutely.

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218:12 Q. Okay. And then there's a box
13 below that that says, "How Has this Proposal
14 Arisen?"
15 A. Yes.
16 Q. And then the language of that
17 says, "Recent review of random glucose levels
18 of patients in olanzapine clinical trials
19 revealed that the incidence of
20 treatment-emergent hyperglycemia in
21 olanzapine group, 3.6 percent, was higher
22 than the placebo group, 1.05 percent. For
23 common events, instances from clinical trials
24 provide more meaningful information." Did I
219: 1 read that correctly?
2 A. That's correct.
3 Q. Okay. Now, this recent
4 review that's being referred to there was the
5 review that you and Dr. Kwong had done on
6 your own initiative because you felt it was
7 important to do; is that correct?
8 A. That's correct.

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223:15 Q. And that incidence in the
16 olanzapine group was almost 3 and-a-half
17 times higher than the placebo group, correct?
18 MR. SEE: Object to the form.
19 A. The number is in excess of
20 three-fold.
21 Q. Almost three and-a-half,
22 correct?
23 A. Yes.
24 Q. Okay. Now, that language
224: 1 there could have been added to the label.
2 You could have suggested that that language
3 be added to the label, correct?
4 A. Yes, we could have.

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230:23 Q. Okay. If I could direct your
24 attention to the following page. You also
231: 1 indicate in here that there were a number of
2 literature reports published regarding
3 hyperglycemia and olanzapine, correct?
4 A. I'm seeing the literature
5 reports and I think these would have
6 reviewed, briefly, summarized such reports.
7 Q. Okay. And you also make
8 reference to Dr. Daniel Casey from Oregon
9 presenting a seminar at Lilly at the end of
10 1999 in that box, correct?
11 A. That's correct.
12 Q. Is this the same Dr. Daniel
13 Casey who was one of the expert advisors who
14 you spoke with at the December 1995 meeting
15 in Puerto Rico?
16 A. Yes, he was.

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232: 6 Q. Okay. Now, the section of
7 the document goes on to say that Dr. Casey,
8 "performed chart review of 136 veteran
9 patients who had been exposed to olanzapine
10 therapy for at least four months, with an
11 average of 1.4 years. Of the 39 patients who
12 had normal fasting glucose levels before
13 olanzapine therapy, seven or 18 percent had
14 fasting glucose levels of 126 milligrams per
15 deciliter or higher during olanzapine
16 therapy." And then it notes that that,
17 "threshold met the 1998 ADA diagnostic
18 criteria for diabetes," do you see that
19 language, sir?
20 A. That's correct.
21 Q. Now, the ADA refers to the
22 American Diabetic Association?
23 A. That's correct.

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233:17 Q. So what he found during that
18 review was that 18 percent of the people who
19 had normal fasting glucose levels before they
20 started using Zyprexa had thresholds that met
21 the 1998, ADA diagnostic criteria for
22 diabetes after they used Zyprexa, correct?
23 A. That's correct.

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234:18 Q. Okay. Well, you never warned
19 doctors in your Zyprexa labeling of
20 Dr. Casey's finding that 18 percent of people
21 who had used Zyprexa for at least four months
22 had fasting glucose levels that met the ADA
23 criteria for diabetes, correct?

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235: 1 is a retrospective chart. The answer to your
2 question is no.

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235:16 Q. And, sir, your company never
17 warned in your labeling that in your analysis
18 in February of 2000 you had found that the
19 incidence of treatment-emergent hyperglycemia
20 in patients treated with Zyprexa was

21 3.6 percent as compared to the placebo group
22 where the incidence was 1.05 percent,
23 correct?

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236: 1 A. No, but we did place the

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236: 6 Q. In fact, the label change
7 that ultimately came about within months
8 after your proposal here in February,
9 asserted that there was, essentially, no
10 change in glucose levels between patients who
11 used Zyprexa and those who were on placebo,
12 correct?
13 MR. SEE: Object to the form.
14 A. My recollection is that we
15 did report something close to 3.6 percent for
16 olanzapine.

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237: 1 Sir, maybe you don't remember
2 what your labeling, actually, said,
3 so let me show that to you. I'm
4 going to hand you what's been
5 previously marked as Plaintiff's
6 Exhibit 4858.
7 (Whereupon, Deposition
8 Exhibit(s) 4858 previously
9 marked, was presented to the
10 witness.)
11 MR. SUGGS: For the record
12 this is a May 9, 2000, letter to FDA
13 from Gregory T. Brophy with several
14 attachments.

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238: 7 Q. Okay. Now, it has in the
8 upper right-hand corner of the first page a
9 bold label that says, "Special Supplement
10 Changes Being Effected." Do you see it?
11 A. Yes, I do.
12 Q. And am I correct that there
13 is a provision of the FDA regulations which
14 permits a drug company to add a warning to
15 the labeling without prior FDA approval as
16 long as the label change strengthens the
17 warnings?
18 A. That's correct. Or provides
19 new information on safety, as I understand.

Charles Beasley, M.D. (July 26,2006)

239: 3 Q. Okay. In any event, this
4 label change which was made in May of 2000,
5 without prior FDA approval, had three
6 elements to it, correct?
7 A. I focused on the glycemic
8 numbers, but I believe it also had a change
9 to the MNS section, and then the term
10 diabetic coma was also added.

Charles Beasley, M.D. (July 26,2006)

242: 9 Q. The second numbered item in
10 this letter refers to the change that was,
11 actually, made regarding hyperglycemia, am I
12 correct?
13 A. It's with reference to the
14 laboratory findings of hyperglycemia.

Charles Beasley, M.D. (July 26,2006)

243:18 with respect to the language that was used in
19 the label change, did you tell doctors that
20 the incidence of hyperglycemia was common or
21 frequent? Did you use those words?
22 A. We did not use those words.

Charles Beasley, M.D. (July 26,2006)

244:17 Q. Can you -- would you read for
18 the jury the language that is used?
19 A. Yes. "In the olanzapine
20 clinical trial database, as of September 30,
21 1999, 4,577 olanzapine-treated patients begin
22 paren, representing, approximately, 2,255
23 patient-years exposure," end paren, "and 445
24 placebo-treated patients who had no history
245: 1 of diabetes mellitus and whose baseline
2 random plasma glucose levels were
3 140 milligrams per deciliter or lower were
4 identified. Persistent random glucose levels
5 greater than or equal to 200 milligrams per
6 deciliter," paren, "suggestive of possible
7 diabetes," end paren, "were observed in
8 0.8 percent of olanzapine treated patients,"
9 paren, "placebo 0.7 percent," end paren".
10 Transient," paren, "i.e., resolved while the
11 patients remained on treatment," end paren,
12 "random glucose levels greater than or equal
13 to 200 milligrams per deciliter were found in
14 0.3 percent of olanzapine treated patients,"
15 again, paren, "placebo, 0.2 percent, end
16 paren. Persistent random glucose levels
17 greater than 160"-- excuse me -- "greater
18 than or equal to 160 milligrams per deciliter

observed in 1.0 percent of olanzapine treated patients," begin paren", placebo, 1.1 percent," end paren. "Transient random glucose levels greater than or equal to 160 milligrams per deciliter but less than 200 milligram per deciliter were found in 1.0 percent of olanzapine treated patients," paren, "placebo, 0.4 percent," end paren.

Q. And that's the final language that went into the labeling, correct?

A. That's correct.

Q. And this is the language that came out of the end process that began with you and Kenneth Kwong suggesting a label change because your review of random glucose level of patients revealed an incidence of treatment-emergent hyperglycemia in the Zyprexa group of 3.6 percent as compared to 1.05 percent in the placebo group, correct?

A. And again, I believe what I have testified to is that the numbers that you have just quoted were, in fact, the result of the initial preliminary data analysis.

Q. And after you tortured the data for some period of time you came up with this language which, essentially, shows no difference between Zyprexa users and placebo users in terms of hyperglycemia, correct?

MR. SEE: Object to the form.

A. And again, I would disagree with your characterization of tortured. I would again refer to checking and double checking. There is a numerical deference with more on olanzapine but the numbers are certainly closer together.

Q. Is it your testimony that the change here that we see, from what was in the rationale for original proposal versus what came out of the end of the process, is because you checked your arithmetic and you found the numbers were wrong?

A. Well, it would not be appropriate to characterize it as arithmetic. It's the process of checking the computer programs that result in finding the results that you have.

Charles Beasley, M.D. (July 26,2006)

Q. So is it your testimony that this was just some computer error that takes the difference between Zyprexa and placebo users from three and-a-half times to virtually nothing?

MR. SEE: Object to the form.

A. And, again, I've characterized there continuing to be a slight numerical difference between drug and placebo with more on drug. And that is my understanding. The process of running these

programs, as I understand it, is quite complex.

Q. Well, sir, do you recall that you did later analyses in which you concluded that, "our continuous analyses showed that olanzapine does result in statistically significant mean increases in random glucose relative to placebo and haloperidol?"

A. I don't recall that specific set of analyses.

Q. Okay, well, we'll talk about that in just a minute. Let's finish up with this label change that you guys did in May of 2000. What happened, five months later, was that FDA came back and made you take it out -- made you take that language out of the label; is that correct?

A. That's correct.

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 195.

(Whereupon, Deposition Exhibit(s) 195 previously marked, was presented to the witness.)

MR. SUGGS: Which for the record is an October 11, 2000, letter from Russell Katz, the director of the Division of Neuropharmacological Drug Products at FDA to Gregory Brophy.

Charles Beasley, M.D. (July 26,2006)

Q. And if we just cut to the chase here, what happened was FDA five months after you made that label change on your own without prior FDA approval, FDA came back on October 11, 2000, and said you have to take that language out, correct?

A. That's correct.

Q. And the reason why they made you take it out is because the FDA said, this is on the second page of the document, "The descriptive data that is provided expresses a certain level of implied safety with respect to treatment emergent hyperglycemia." Do you see that language, sir?

A. Yes, I do.

Q. And in fact, that that was the case. The data that you reported in there, the statements that you had in the labeling showed that there was, essentially, no difference between hyperglycemia in Zyprexa users versus placebo patients. And the FDA concluded that that expresses a certain level of implied safety; is that correct?

MR. SEE: Object to the form.

A. I think you've asked me two questions. With respect to the FDA's

impression, that is correct. I view these

Charles Beasley, M.D. (July 26,2006)

In the proposed -- well, in the labeling that you guys actually put in in May 2000, when which the FDA made you take out five months later in October, there was no indication of any statistically significant differences in hyperglycemia between Zyprexa and other patients, correct?

A. There is clearly not in this information that was added.

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 5565.

(Whereupon, Deposition Exhibit(s) 5565 previously marked, was presented to the witness.)

MR. SUGGS: For the record this is a series of e-mails.

I'm going to be focusing on the one on the first page, Dr. Beasley, that you wrote to Ralph Dittmann with copies to Alan Breier, Patrizia Cavazzoni, Mark D. Millikan, Anna Thornton and Gary Tollefson.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. And you had received a request from Ralph Dittmann -- by the way, who was Ralph Dittmann?

A. Ralph Dittmann was a German -- he was a German psychiatrist in our German affiliate.

Q. And he was asking you for information on hyperglycemia, correct?

A. Let me see if I can --

Q. If you look at the top of the second page.

A. Yes.

Q. Okay. And you wrote back to him and you said, in part, "Our continuous analyses show that olanzapine does result in statistically significant mean increases in random glucoses relative to placebo and haloperidol." Did I read that correctly?

A. That's correct.

Charles Beasley, M.D. (July 26,2006)

MR. SUGGS: By the way. If I forgot to point out for the record the date of this e-mail is

February 22, 2001.
A. Right. These would have been analysis that were conducted subsequent to those that had been done as part of the review of data by myself and Dr. Kwong.
Q. So this -- would this have been -- would these analyses have been done before the May 2000 label change or after?
A. I think they would have been done afterward.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. I want to make sure I understand the time frame here. In February of 2000, a year before this e-mail, you and Kenneth Kwong do an analysis which finds an incidence of treatment-emergent hyperglycemia three and-a-half times higher in Zyprexa users versus placebo users, correct?
MR. SEE: Object to the form.
A. And again you've characterized that, I believe, as a final finding.
Q. I'm not characterizing as final, partial, whatever. You did an analysis that you thought was important enough and you felt confident enough in to submit to the Global Product Labeling Committee which said that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in Zyprexa users as compared to placebo users, correct?
A. That is correct and I'm

Charles Beasley, M.D. (July 26,2006)

Q. Three months later, you and others jen-up language that goes into the labeling under the special supplement changes being effected, which shows, essentially, no difference between the incidence of hyperglycemia in Zyprexa users versus placebo users. And five months after that, FDA makes you take out that language because they say it's -- it gives an implied sense of safety, correct?

Charles Beasley, M.D. (July 26,2006)

A. I agree with you with respect to the action of the FDA. In your question you characterized our actions in a certain fashion that I would disagree with.
Q. And then five months after the FDA makes you take out that language, which they said was expressing a certain

level of implied safety with respect to treatment-emergent hyperglycemia, you do another analysis which finds a statistically significant mean increase in random glucose for Zyprexa relative to placebo and haloperidol, correct?

A. That was my understanding at the time having not been involved in those analyses.

Q. And, sir, if I could direct your attention to the remaining language in that paragraph, you go on to state, "These increases are occurring as early as week one," correct?

A. Yes.

Q. That would be week one after beginning use of the drug?

A. That's correct.

Q. And you say "These changes are accounted for, in part but not entirely, by weight increase," correct?

A. I think you have excluded a parenthetical in the -- in this but -- that

261: states, "may not represent a true deterioration in glycemic metabolism but simply an increase in food intake since these are random and not fasting glucoses."

Q. And then you go on to say, "These changes are accounted for, in part but not entirely, by weight increase," correct?

A. That's correct.

Q. And then you say: Categorical analyses to values above a set of thresholds, 126, 140, 160, 200 milligrams per deciliter, do not reveal significant findings, but trends are there, except for the comparison of clozapine to olanzapine to the lower two thresholds, clozapine more, correct?

A. That's correct.

Q. And so, when you do categorical analyses like that, you are splitting the data up into different chunks, correct?

A. That's correct. We have been talking -- most of what we've been talking about so far has been categorical analysis.

262: Q. And when you --

A. You define a certain value that makes a distinction between normal and abnormal. At this time, 126 was the ADA criteria, so if you were 125 you would be considered normal, if you were 126 or above you would be considered abnormal.

Q. And describe for the jury what the difference is between a categorical analysis and a continuous analysis?

A. A continuous analysis is where you take averages, you have a certain number of individuals who have a baseline or a before treatment value, and each one of those patients has an individual value, and then they are observed to have multiple

values, because it's measured while they're on treatment. And each of those patients will then have a change at each point of the observation and those changes are taken as an average.

Q. And, sir, it was your continuous analysis that you're referring to here which showed that olanzapine does result in statistically significant mean increases in random glucose relative to placebo and haloperidol, correct?

A. That was my understanding of the work that had been done at that time, yes.

Q. Okay. And, sir, it was continuous analyses which your company's own outside experts recommended that you needed to be looking at, correct?

A. Yes. And I think that was the reason they were looked at.

Q. And let's talk about -- let's talk about that right now. Do you recall that in October of 2000, you and various representatives of Eli Lilly had a meeting with a group of outside experts in Atlanta?

A. Yes, I do.

Q. Okay. And those were -- those people that you met with, those outside experts, were an academic advisory board, correct?

A. That's correct.

Q. Now, Eli Lilly is a drug company which makes, not only psychiatric drugs, but also makes and distributes a number of drugs for the treatment of diabetes, correct?

A. That's correct.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. And do you recall that people in Lilly referred to these outside experts as being in the Who's Who of diabetes?

A. I don't recall that characterization but these were certainly a number of very, very prominent academic individuals.

Q. Okay. And so you and Chris Bomba and Patrizia Cavazzoni and Suni Keeling and Robert Baker, I went down there in October of 2000 to meet with them, correct?

A. That's correct.

Q. And did you give them a presentation?

A. I believe it was Dr. Cavazzoni that, basically, presented the results of the work that had been represented in what Dr. Kwong and I put together.

Would it be fair to say that the end result of the analysis and the research that you and Dr. Kwong put together, was what was reflected in the labeling that was implemented in May of 2000?

A. Yes.

Q. Okay.

A. That, certainly, that work that Dr. Kwong and I had performed, obviously, with a lot of assistance, led to the labeling change.

Q. Right. And fair to say that the results of your analysis, at the end of the day, were the numbers that we saw before that were stated in that labeling change that was made?

A. That's correct.

Q. Okay. That's the same labeling change that the FDA made you take out of the label five months later, correct?

A. That's correct.

Q. Okay. And, in fact, that letter that the FDA sent instructing you to take that language out of the labeling was dated October 11, correct, 2000?

It's in the upper right-hand corner.

A. There's a stamp here October 11, 2000.

Q. Right. And that was just days after you had the meeting with the outside experts in Atlanta, correct?

A. And again, I'm getting a bit confused on my.

Q. Well --

A. -- dates.

Q. Well, let me --

A. I think it was October.

MR. SUGGS: I apologize, I should have shown you this document before because it would have been a good record here of when exactly that meeting was. Let me hand you what's been previously marked as Exhibit 6998.

(Whereupon, Deposition Exhibit(s) 6998 previously marked, was presented to the witness.)

QUESTIONS BY MR. SUGGS:

Q. And for the record this is an e-mail dated October 9, 2000, from Robert Baker to Charles Beasley, Christopher Bomba, Alan Breier, Thomas Brodie, Patrizia Cavazzoni, James Gregory, John Holcombe, Jack E. Jordan, Suni Keeling, Michael Murphy, John Richards, Eugene Thiem, and Mauricio Tohen and Paula Trzepacz, correct?

A. Yes.

Q. And in this e-mail Dr. Baker states that -- in the first paragraph, "For

your information, the Lilly diabetes slash endocrine group held an academic advisory board meeting this weekend in Atlanta."

So that would have been days before October 9, correct?

A. Yes.

Q. Okay. And we know that on October 11, the FDA comes out and says you've got to take that label language out, right?

A. Correct.

Q. Okay. So within days after you meet with the outside experts, FDA tells you to take the label out, right?

A. Yes.

Q. Dr. Baker in Exhibit 6998, goes on in his e-mail to say, "They kindly allotted two hours for discussion of olanzapine's potential hyperglycemia risks and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic." Did I see that?

A. Yes, that's correct.

Q. Okay. In the second paragraph he goes on to state, "They were, however, concerned by our spontaneous AE reports." That's referring to adverse event reports, correct?

A. That's correct.

Q. "And quite impressed by the magnitude of weight gain on olanzapine and implications for glucose. Much of their input for helpful steps came back to addressing weight gain."

Did I read that correctly?

A. That's correct.

Q. And you had been warned about the weight gain problem by another panel of outside experts as we said -- as we talked about right at the beginning of your deposition back in December of 1995, correct?

A. That's correct. And this was something that we described and from my perspective, given Dr. Breier's efforts, we were attending to.

Q. And continuing on in his e-mail Dr. Baker said, "Citing methodological questions, at least the vocal members were not reassured adequately by our analyses, such that the finding that relative risk was not higher than comparative drugs. Disconcertingly, one member compared our approach to Warner-Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class." Do you see that language, sir?

A. Yes, I do.

Q. Were you familiar with what Warner-Lambert was doing with respect to

Rezulin?
A. No. I was familiar with the drug and I was familiar with the fact that it was, ultimately, withdrawn from the market.
Q. **Because of safety problems,** correct?
A. Because of the perception that it had a risk of hepatic dysfunction.

Charles Beasley, M.D. (July 26,2006)

274: Friday. Let me show you another e-mail regarding this meeting that you had with the outside experts in October of 2000. I hand you what's been previously marked as Exhibit 1449.

Charles Beasley, M.D. (July 26,2006)

276: Q. So I want to direct your attention first to that e-mail from Thomas Brodie to Robert Baker and Eugene Theim. It's on -- it starts in the middle of the first page. And first of all, who was Thomas Brodie?
A. I don't know who Mr. Brodie was.
Q. Do you know who Eugene Thiem was?
A. I think he was an individual involved in the marketing area in the U.S. Affiliate.
Q. Okay. And the subject is the meeting with endocrinologic consultants, correct?
A. Yes.
277: Q. And Mr. Brodie says, "Robert," referring to Robert Baker, "clearly this group of Endocrinologists, who spoke up and I would rate those who did speak up as the leaders of the pack, are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes. I can only hope that you and all of the team who attended the NADAB meeting are gaining the ear of senior leadership and articulating this finding. Although the board's recommendation is, probably, not the way Lilly, typically, does business, I do believe they made a very strong point that unless we come clean on this, it could get much more serious than we might anticipate." Do you see that language, sir?
A. Yes, I do.
Q. Okay. Now, you did, indeed, have the ear of senior leadership within the corporation, did you not?
A. Yes, I would characterize my

position as, at least, having their ear.

Charles Beasley, M.D. (July 26,2006)

Q. And the man that you had the ear of was Dr. Gary Tollefson, correct?
A. That's correct.
Q. And did you have the ear of any others who were -- would be regarded as senior leadership in the company?
A. I believe that I also was able to speak freely with Dr. Breier.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. And now, sir, if I could direct your attention to the third physical page. At the top of the page is an e-mail from Robert Baker to you, Alan Breier, Christopher Bomba, Patrizia Cavazzoni, Suni Keeling, again referring to the meeting with endocrinologic consultants, correct?
A. Yes.
Q. And in that e-mail Dr. Baker does two things, number one, he forwards to you and the others there that original e-mail that he'd gotten from Thomas Brodie, the one where he said that, "Although the board's recommendation is, probably, not the way Lilly, typically, does business, I do believe they made a very strong point that unless we come clean on this it could get much more serious than we might anticipate," correct?
THE WITNESS: Excuse me. I was looking at this and I believe that was on Page 1, as I recall.
Q. Well, sir, the language I just read was -- you're correct is in the e-mail at the bottom of Page 1. It's also in the e-mail that's at the bottom of Page 3, because on page -- what Page 3 does is reflect an e-mail that Robert Baker sent to you and others forwarding that e-mail from Thomas Brodie, correct?
A. Yes.
Q. And it was in that e-mail from Thomas Brodie that Mr. Brodie said that, "I can only hope that you and all of the team who attended the meeting are gaining the ear of senior leadership and articulating this finding," correct?
A. That's correct.
Q. And so, in fact, by Robert Baker sending this memo on to Alan Breier, he put this in the ear of senior leadership of the company, correct?
A. That's correct.
Q. So Alan Breier was informed in October of 2000, that these consultants

were saying that, "they made a very strong point that unless we come clean on this it could get much more serious than we might anticipate," correct?

A. That's correct.

Q. Okay. And then in his e-mail to Robert Baker -- pardon me -- in Robert Baker's e-mail to you and others at the top of this Page 3, he has -- he starts off by saying, "My take was that this board of academic endocrinologists was impressed enough by the magnitude of weight gain and the number of reports in the spontaneous adverse event database that they were predisposed to skepticism to any analysis that did not find hyperglycemia rates of olanzapine than comparators," correct?

A. That's correct.

286: Q. Then he goes on to have a message to you and also to Alan Breier, correct?

A. That's correct.

Q. And he says to you, "Do you think it appropriate to look at secondary analysis that does not exclude baseline abnormals and another looking at mean changes in glucose," correct?

A. That's correct.

Q. And the looking at mean changes in glucose is the continuous analysis that we referred to earlier, correct?

A. That's correct.

Q. And that's the one that when you did it, a couple months later, your understanding in February 2001 was that it did, indeed, show a statistically significant increase in random glucose for Zyprexa relative to placebo and haloperidol, correct?

A. That is my -- that was my understanding of those analysis at the time. I am not -- I have no knowledge of the ultimate outcome of what may have been

287: continuing analysis here.

Q. Okay. Because by that point you were out of it, right, you were gone?

A. I was transitioning out of it, yes.

Q. They took you out of the Zyprexa group and they sent you over to deal with Cialis, correct?

A. That's correct.

Q. Okay. Now, let's continue on with what Robert Baker was telling Alan Breier, one of the senior management at Lilly here in this e-mail of October 2000. Dr. Baker says, "Alan, I believe that what Tom is referring to as," quote, "not the way Lilly, typically, does business," end quote, "are suggestions to more vocally assert that olanzapine may have a problem on the glucose issue and rather than moving forward with our analyses turning all info over to an independent board for review, conclusions and

dissemination."
Do you see that language, sir?
A. Yes, I do.
Q. And so what Baker was telling Breier -- and by the way, Breier was not at the meeting, correct?
A. No.
Q. Okay. So Baker's telling Breier that these experts were saying that you should, actually, assert that Zyprexa may have a problem on the glucose issue, correct?
MR. SEE: Object to the form.
Q. Is that what he says?
A. That was apparently Dr. Baker's recollection at the time.
Q. Yeah. So he's saying that the experts are saying, "Hey, go out and tell doctors that Zyprexa may have a problem with glucose."
MR. SEE: Object to the form.
Q. Right?
A. Again, that was apparently Dr. Baker's recollection at the time.
Q. And that went over like a lead balloon, didn't it?
MR. SEE: Object to the form.
A. Again, I don't recall that being a -- I don't recall that as being emphasized or even discussed at the meeting. I do have my own recollections of what was discussed at the meeting.

Charles Beasley, M.D. (July 26,2006)

MR. SUGGS: Okay. I want to show you another e-mail, a series of e-mails, relating to this meeting in October of 2000. For the record, I'm handing you what's been previously marked Plaintiff's Exhibit 1453.
(Whereupon, Deposition Exhibit(s) 1453 previously marked, was presented to the witness.)

Charles Beasley, M.D. (July 26,2006)

Q. Sir, would you agree with me that the e-mail that's at the bottom of Page 3 of this exhibit is the same e-mail that we were just talking about in the prior exhibit?
A. I believe it is.
Q. Okay. And then what's above that, which actually starts on Page 2, is your e-mail response back to Dr. Baker?
A. I haven't read it yet but

that would appear to be -- the 9th at 3:42, the 10th at 8:33 -- he would have presumably sent that late in the afternoon and I would have seen it the next -- the next morning.

Charles Beasley, M.D. (July 26,2006)

Q. And in this e-mail you're giving your take on the situation, correct?
A. That's correct.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. And then in the second paragraph you say, "These guys were really concerned about the weight gain, not only because of the diabetes risk but all the other potential health risks. They initially thought it might simply be a response improvement in schizophrenia with a few outliers, a rather naive view, but they ain't shrinks. When they understood that this is seen in non-psychotic normals and animals on fixed diets, less concern with animals, and that olanzapine is the worst offender other than clozapine they advocated a different marketing strategy than we are taking. They believe we should," quote, "aggressively face the issue," end quote, "and work with physicians to address methods of reducing weight gain."

Did I read that correctly?
A. That's correct.
Q. Now, when you make a reference to nonpsychotic normals, am I correct that you're referring to clinical studies done by Lilly which showed that normal people, nonpsychotics, when they take Zyprexa have significant weight gain?
A. Yes.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. And when you refer to the animals on fixed diets in this e-mail, am I correct that that's referring to scientific studies conducted by Lilly which showed that animals on fixed diets also showed significant weight gain?
A. I don't recall the specific basis, at this point six years later, for this statement on my part. Again, Dr. Breier, on toxicology, were conducting studies with animals and studies had been previously conducted. So I cannot recall the specific studies that I was referring to.
Q. Okay. But if your e-mail is

correct, and you were the one that wrote this?

A. Right.

Q. That there were findings of significant weight gain in animals on fixed diets, that means you were seeing weight gain in animals whose diet was controlled, experimentally, so that they were not just free to feed as they wished, but they were given a fixed amount of food, correct?

A. That would be correct.

Q. Okay. So the weight gain that was shown by those animals would not be a result of, well, they were feeling more hungry so they ate more. Instead it would have to be because of some metabolic effect that the drug had on the animals, correct?

MR. SEE: Object to the form.

A. It could be due to a number of things. One thing that we've clearly observed is that animals given doses of this medication decrease their activity, so it could be simply a decrease in caloric expenditure.

Q. Which is a metabolic effect of one sort, correct?

A. Well --

Q. I guess it gets definitional.

A. It's -- yes. I mean, again, I would characterize it if you stop moving around, you stop having a certain amount of activity, therefore, you expend less calories.

Q. It wasn't like the experimental rats were going out to get Snickers or ice cream bars?

A. No, they didn't move around their cages as much.

Q. Okay. Now, did these experts give you any examples of what they meant when they said that Lilly should aggressively face the issue?

A. I can't recall any. Obviously, I have my impression that -- of what they meant.

Q. Okay. You go on to say at the bottom of that first paragraph that, again, talking about the weight gain "When you translate 1 to 2 percent gain of 40 plus kilos into the absolute number based on 5 million patients, the number is 50,000 to 100,000. 100,000 people putting on 90 pounds of weight is a lot."

A. And that was a speculation on my part as a possibility to underscore this to the people we communicated with.

Q. Okay. How did you arrive at that calculation?

A. My recollection is that we had -- a number of analyses had been done looking at weight gain in our clinical trials. I believe, that Dr. Kinon was, in fact, the primary individual running these --

running these -- having these analyses run.
And my recollection is that I would have seen listings that's would have shown percentages of patients with different amounts of weight gain who had been treated for various lengths of time.
Q. And, sir, do you recall writing a memo some months later in which you said it would be ludicrous to state that such a patient is not at long-term increased cardiac risk relative prior to gaining that weight, especially if in temporal relation with that weight gain, the patient developed an increase in fasting glucose and lipid levels?
A. I don't recall that specifically, but I may well have written that. Gaining body fat is clearly recognized as a risk factor for cardiovascular disease. I think I learned that in my first year physiology course.
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 6128, because I'd like to clear up that point about you writing that e-mail before I continue on with this other exhibit.
(Whereupon, Deposition Exhibit(s) 6128 previously marked, was presented to the witness.)
MR. SUGGS: For the record Exhibit 6128 is another series of e-mails.
QUESTIONS BY MR. SUGGS:
Q. If I could direct your attention to Page 3 of the document. That's an e-mail from Ernie Anand to Andrea Smith asking if there was a standby statement to clarify Lilly's position as to whether Zyprexa can cause cardiovascular complications due to weight gain and diabetes which are clinically recognized risk factors.
Do you see that, sir?
A. Yes.
Q. And then this gets forwarded on to you as reflected on Page 2 of the document, which is an e-mail from you to Andrea Smith with copies to Ernie Anand, Patrizia Cavazzoni, Margaret Sowell, Anna Thornton, in which you respond and say, "One thing that we can say definitively is that olanzapine causes weight gain and for, approximately, 50 percent of patients in trials who remained on the drug for more than six months, the amount of gain was more than ten pounds. Some patients, in clinical trials gained as much as 80 plus pounds. Lacking empirical data to the contrary, it would be ludicrous to state that such a patient is not at long-term, increased cardiac risk relative to prior to gaining

that weight, especially if in temporal association with that weight gain the patient developed an increase in fasting glucose and lipid levels."

Do you see that language, sir?

A. Yes.

Q. Do you recall writing that e-mail on or about March 15, 2001?

A. No. I mean, again, I do not recall.

Q. You don't dispute that you, indeed, did write that, though?

A. No, not at all.

Q. Turning your attention, if I could, sir, back to Exhibit 1453.

THE WITNESS: 1453.

MR. SUGGS: That's your October 10, 2000, e-mail to Alan Breier with copies to Robert Baker, Paul Burg, Scott Clark, John Holcombe, Roland Powell, Alvin Rampey and Roy Tamura.

THE WITNESS: That's correct.

Charles Beasley, M.D. (July 26,2006)

Q. Okay. You go on in your e-mail about ten lines down from there to say -- actually, 1, 2, 3, 4, 5, 6, 7, 8, 9 -- ten lines from the top, "The problem is the arbitrary nature of the cut point and the potential for big shifts depending on those cut points and the fact that we chose the cut points, not really they came from the ADA website. They specifically referred to the data as being tortured." Did I read that correctly?

A. That's correct.

Q. Do you know who it was that referred to the data as being tortured?

A. No, I do not.

Q. Dropping down to the next paragraph, in the second sentence you say, "They," referring to the outside consultants, "They want the continuous data, using all data, analyzed over time co-varying for both static, diabetic diagnosis, baseline, obesity, et cetera, and dynamic co-variants, weight gain, alteration in hyperglycemia dose. Similar to David Allison, one or two would be happy to take all our data and perform the correct analyses, like we don't have competent statisticians." Did I read that correctly?

A. That's correct.

Q. And apparently, you'd had some problems with the statisticians, as we've already discussed, because of that sequence of events that we talked about where you went to your original proposal of the

labeling change in February and the basis for that proposal then, and you came out with a much different label based on what you referred to as computer error?

MR. SEE: Objection to form.

A. I don't believe that our statisticians are incompetent or -- incompetent. There is a process of going through repeated analyses, performing them by multiple people until you are certain you get them correct, like adding a long column of figures.

Q. You go on to say towards the end of that paragraph, "I will say that I believe we should have a full time, dedicated, sophisticated, statistical resource that does nothing but hyperglycemia, no meetings, no surveys, zilch, until we have completely tortured the data." Did I read that correctly?

A. That's correct.

Q. And did you completely torture the data?

A. Well, and again, what I mean by torture the data here, in reference to the paragraph above where it was used in a positive context, that we thoroughly analyzed the data. Coming out of this meeting, we had the two individuals that were interested in working with us, we had Dr. Cavazzoni assigned full time, and I believe, although I could be incorrect, that Dr. Breier took steps to see that additional statistical resources were added.

We also increased the time commitment of the endocrinologist that was working with us on these matters.

MR. ALLEN: Objection, nonresponsive.

Q. And the additional statistical work that you did, at least your understanding of it, up until the time you left the Zyprexa project in later -- some months later in 2001, was that the continuous analyses that the outside consultants had asked for showed that olanzapine does result in a statistically significant mean increases in random glucose relative to placebo and haloperidol; isn't that correct?

A. And that was my understanding at the time of where those analysis stood. I do not know if those were the final analyses of those data.

Charles Beasley, M.D. (July 26,2006)

Q. I'd like to direct your attention to the last paragraph of your e-mail. It says, "With regard to the marketing side of this issue of impaired glucose tolerance slash diabetes, the message

was clear. Don't get so aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents until we are sure of the facts and sure that we can convince regulators and academicians. W-L with Rezulin was the example. Sounds like what, Dan" -- strike that. "Sounds exactly like what Dan Casey was saying." Did I read that correctly?

A. That's correct.

Q. Now, the W-L that's referred to is Warner-Lambert, correct?

A. I believe that would be correct.

Q. And we've talked about that Rezulin example before. And when you said that sounds exactly like what Dan Casey was saying, when had Dan Casey told Lilly that you shouldn't be too aggressive about denial, blaming it on schizophrenia, or claiming that Zyprexa was no worse than other agents.

A. Well, again, I don't recall, specifically, when Dr. Casey would have made those suggestions to us.

Q. Sir, in fact, despite these recommendations by your outside consultants, in fact, what Lilly did, for years after this, was to insist that the rate of hyperglycemia and diabetes with Zyprexa was comparable to other drugs, correct?

MR. SEE: Object to the form.

A. I do not have specific knowledge of the marketing materials that were put together over time and have been used over time. I did recall -- I did review one initial marketing piece that did present the data that was presented in our package insert.

Charles Beasley, M.D. (July 26,2006)

Q. Good afternoon.

A. Afternoon.

Q. Dr. Beasley, I'm Scott Allen and I'm from Houston. I represent the plaintiffs in this case also, you understand that?

A. Yes.

MR. ALLEN: I'm going to go over some areas that Mr. Suggs discussed with you so I could more fully understand them. And I've

Charles Beasley, M.D. (July 26,2006)

Q. Now, first of all, sir, I don't mean to be critical of you, but I have looked at your CV and I have read your qualifications and you have candidly told us

that your background, education, and training is in psychiatry; is that correct?
A. That is correct.
Q. You have also told us on this record today you are not a statistician?
A. That is correct. I have, probably, about 20-plus hours of statistic courses including some at the graduate level.
Q. Yes, sir. I took Spanish in high school, but I am not a translater, okay, and I took Spanish in college. My question is are you a qualified statistician?
MR. SEE: Object to the form of the question.
A. I have no degree in statistics and am not a member of the American Statistical Society.
Q. You are not an
316: epidemiologist?
A. No, that is correct.
Q. You are not an endocrinologist?
A. That is correct.
Q. You are not a diabetologist -- how do you pronounce that?
A. Diabetol -- have difficult as well -- diabetologist, I believe.
Q. You're not that either?
A. No.
Q. You did not take any specialized training, background, or education in hyperglycemia or diabetes, did you?
A. No, I did not.
Q. And, in fact, you, when you came to work for Eli Lilly there is a specific area of the company of doctors that are trained in endocrinology, is there not?
A. That is correct.
Q. You did not go work for that part of the company, did you?
A. No, I did not.
317: Q. And you've never worked for that part of the company, have you?
A. No, I have not.
Q. In fact, Eli Lilly and this area where Mr. Suggs was discussing with you the meeting in Atlanta of the endocrinology advisory board in October of 2000, you recall that?
A. Yes.
Q. Those individuals, that advisory board in Atlanta, was not a Zyprexa advisory board, was it?
A. No, it was not.

317:20 Q. In fact, these were the endocrinologists who raised the questions in October of 2000, that were the advisory board

to the endocrinology side of the company, the Diabetes Care side, correct?
A. That's correct.
Q. So when the information concerning Zyprexa was brought to the independent endocrinology board, that was not on the Zyprexa team, they're the individuals that raised the questions that Mr. Suggs discussed with you in October of 2000, isn't that right?
A. That's correct.

Charles Beasley, M.D. (July 26,2006)

(Whereupon, Deposition Exhibit(s) 1 duly received, marked and made a part of the record.)

Charles Beasley, M.D. (July 26,2006)

Q. This is the American Diabetes Association, and let me show that. The title's All About Diabetes. And it's put out by the American Diabetes Association, Cure, Care and Commitment. Do you see that?
A. Yes.
Q. And you've already told this jury that they're much more qualified than you to discuss issues concerning the seriousness or lack of seriousness of diabetes, right?
A. I think that would be the generally held opinion, yes.

Charles Beasley, M.D. (July 26,2006)

Q. This says, "Diabetes is a disease in which the body does not produce or properly use insulin. Insulin is a hormone that is needed to convert sugar, starches and other food into energy needed for daily life. The cause of diabetes continues to be a mystery" -- oh, let me see -- "continues to be a mystery, although both genetics and environmental factors such as" -- what, sir?
THE WITNESS: As -- you're asking me to read the --
Q. Yeah. Such as what?
A. "As obesity and lack of exercise appear to play roles."

Charles Beasley, M.D. (July 26,2006)

Q. You testified under oath that

diabetes is a known risk factor -- I mean, excuse me -- obesity is a known risk factor for diabetes, right?
A. That's correct.
Q. And in fact, you testified that the weight gain that you saw in Zyprexa -- I think -- you can correct me, because you'll probably get it -- you testified that 40 percent of patients who take Zyprexa have clinically significant weight gain within six months?
A. Actually, I think the best representation -- that's from the HGAJ study. I think the best representation is, actually, the combining of the data which would suggest it's 56 percent of individuals.
Q. Have clinically significant weight gain within six months?
A. Potentially, clinically significant defined as 7 percent or greater.
Q. Which would put them at an increased risk of developing hyperglycemia
345: and diabetes?
A. It would be a risk factor and might put them at risk.
Q. Sir, smoking's a risk factor for cancer, is it not?
A. Yes, it is.
Q. And so people tell people don't smoke because you want to decrease your risk for long cancer, correct?
A. That's correct.
Q. And if you continue to smoke you increase your risk for lung cancer, correct?
A. You are at an increased risk.
Q. Right. It's not -- when you go to the doctor, do they try to advise you to increase your risk for diabetes or decrease your risk for diabetes?
A. Oh, they would clearly suggest that you take steps to do those things that would decrease your risk.
Q. And you, certainly, then would agree with me that Zyprexa causes clinically significant weight gain which is a
346: risk factor for diabetes, correct?
MR. SEE: Object to the form of the question.
A. I have said that there is a strong association, and I believe that in some patients Zyprexa can cause weight gain. I've also testified that weight gain is a risk factor for diabetes.
Q. Right. Now, you've also taken -- and you certainly -- it's not a preferable thing to increase your risk factor for diabetes since diabetes is such a severe disease, is it not?
A. Well, again, one does not want to increase any risk factor that would put one at -- at increased risk of any disease, including diabetes.

Q. Right. And diabetes, we know, and hyperglycemia, itself, is a -- has numerous severe medical complications, does it not?

A. There are a number of complications that are associated with both hyperglycemia and, more importantly, diabetes.

Q. Right. Such as heart disease and stroke?

A. Yes. You've got a new page here.

Q. You, probably, don't need to read the page. You can just tell us, diabetes carries with it the risk of heart disease and stroke, kidney disease, eye complications including blindness, diabetic neuropathy, that's loss of feeling and sensation in your periphery, right?

A. Yes. It's -- actually, in diabetes, it's usually a painful sensation.

Q. Right. Nerve damage and foot complications, which I know from experience can lead to gangrene and amputations, right?

A. That's correct.

Q. Skin complications. Depression. It can cause depression in and of itself?

A. It has been associated with depression, yes.

Q. Right. Just, just so we're all communicating now, you and I will now both agree, and you can tell the jury under oath, that diabetes and hyperglycemia are serious medical conditions?

MR. SEE: Object to the form of the question.

Q. Are they not?

A. Okay. Diabetes clearly has very serious potential outcomes. The condition can, therefore, be considered clinically serious. Many cases would not meet the regulatory definition of seriousness.

Q. Well, how about when I say you can get amputations, heart disease, loss of vision, peripheral neuropathy, are you telling this jury that doesn't meet the FDA regulation definition of serious?

A. Those things that you just mention would meet the FDA criteria.

Q. Right. And aren't all those things as reported in this document, Beasley No. 1, secondary factors that occur following -- can occur following diabetes?

A. Can occur, yes, sir.

Charles Beasley, M.D. (July 26,2006)

Q. Okay, sir, I don't think you need to pull it out, it's Exhibit 1453, but

it is in that stack here. Just so the record is clear, this is your e-mail that you wrote on October 10, 2000, following -- this is No. 1453.

Charles Beasley, M.D. (July 26,2006)

knew that in the -- this is your words, I'll read it, "These guys," talking about after the meeting, "were really concerned about the weight gain, not only because of diabetes risk but all the other potential health risks."

So we have right here a statement that the people at the meeting were concerned about weight gain and diabetes, right?

A. You know, that is my recollection of their main topic of interest was the weight gain.

Q. Sir, and I'm not trying to argue with you. You didn't call it topic of interest. You said these guys were really concerned. Isn't that what you said? Not me?

A. Yes.

Charles Beasley, M.D. (July 26,2006)

Q. So the doctors in Atlanta, who talked about why they were concerned about weight gain were concerned because weight gain can lead to hyperglycemia, which is prediabetes, and diabetes can occur and all those risks such as peripheral neuropathy, amputations, and blindness are concerns, right?

MR. SEE: Object to the form of the question.

A. Those would be consequences or adverse outcomes of diabetes.

Q. Right. And these -- and that's exactly what these doctors were concerned about?

A. I think my reference here is to the other potential health risks such as cardiac disease and those things.

Charles Beasley, M.D. (July 26,2006)

Q. Thank you, sir. Let's go on. They initially thought it might simply be a response to improvement in schizophrenia with a few outliers. And you put this parenthetically, parens, "a rather naive view but they ain't shrinks."

A. See, I'm just a good old boy.

Q. Let's go back and continue to look at what you said on that day internally at your company. You said, "They were naive to think" -- by the way when you said it was a rather naive view you were saying the reason weight gain was occurring wasn't because people were getting better on schizophrenia, that's what you're saying here, right?

MR. SEE: Object to the form of the question.

A. Well, it was the issue with their belief -- and I'm not sure how they got this impression -- that it was a few outliers, that would influence the mean change.

Q. And you thought that was a rather naive view, correct?

A. That's correct.

Q. When they understood this is seen in nonpsychotic normals, which you told Mr. Suggs, we see weight gain in individuals who are not schizophrenic and psychotic, correct?

A. That's correct.

Q. And animals on fixed diets. "We see it on the animal model in testing when they have fixed food intake," correct?

A. That was clearly my understanding of preclinical studies at the time. I don't recall those studies sitting here today.

Q. But you would have tried to be accurate when you wrote this e-mail?

A. Yes.

Q. Okay. "That's concerned with animals and that olanzapine is the worst offender other than clozapine. They advocated a different marketing strategy than we are taking." Did I read that correctly?

A. That's correct.

Q. And that's a long way it took me to get there is what you were saying is Zyprexa, as opposed to other second generation antipsychotics such as Seroquel, Risperdal, Abilify, Geodon, Zyprexa is the worst offender concerning the issue of weight gain?

MR. SEE: Object to the form of the question.

Q. True?

A. And these are certainly the -- what I wrote here and what that characterizes is the fact that -- and again, I would come back to the David Allison analysis, it comes in number two. It's not necessarily far away from some of the other second generation.

Q. It's number two worst

offender behind clozapine for causing weight gain, correct?
A. That's correct.
Q. And that's certainly what you wrote in your e-mail, Exhibit 1453, on October 10, 2000, at 8:33 in the morning?
A. That's correct.

Exhibit 3
Charles Beasley, M.D.

Beasley, Charles M.D.(July 27, 2006)

445:23 Q. And it was February of 2001
24 when you had sent the e-mail saying "our
446: 1 continuous analysis shows there's a
2 statistically significant difference in blood
3 glucose levels comparing Zyprexa to placebo
4 and Haldol?"
5 A. That's correct.
6 Q. And then shortly after that
7 you're sent to Cialis, aren't you?
8 A. I was transitioned to Cialis
9 in 2001, in the middle of 2001.

Beasley, Charles M.D.(July 27, 2006)

447: 5 Q. Is that in the Central
6 Nervous System department?
7 A. No, it is not.
8 Q. And you had spent your entire
9 career since you started at Eli Lilly in the
10 CNS department?
11 A. That's correct.
12 Q. And you are the man that's
13 being asked the questions about the
14 continuous analysis, you give your answers,
15 and the next thing you know what department
16 do you ship to?
17 A. As I've stated, my
18 responsibilities were changed to Cialis.
19 Q. Who changed your
20 responsibilities?
21 A. I believe it would have been
22 Mike McDonald, who was the head of medical at
23 that time.
24 Q. Okay. How were you informed?
448: 1 A. I was asked to take on that
2 responsibility by Dr. McDonald.
3 Q. Right. You didn't request a
4 change, the company requested you to change?
5 A. That's correct.
6 MR. ALLEN: Thank you. Okay,
7 sir, we're on my last document, I
8 believe. It's 6128.

Beasley, Charles M.D.(July 27, 2006)

449: 7 Q. It's now March of 2001 when
8 you write this e-mail, isn't it?
9 A. Yes.

Beasley, Charles M.D.(July 27, 2006)

449:22 Q. You're intelligent. You know
23 how to use words and you know what words
24 mean, do you not?
450: 1 A. Yes.

Q. Ludicrous means crazy, doesn't it?
A. That's a rough approximation.
Q. Right. Ludicrous, as you use it and you used it in this e-mail, is it's crazy to think any different. It would be crazy, right?
A. Wouldn't be a good thing to think.
Q. Wouldn't be a good thing to think. If you think any different, and we're going to look at your e-mail, but if you think anything different than this you're crazy, right?
A. Essentially, yes.

Beasley, Charles M.D.(July 27, 2006)

Just to put us in setting, by March of 2001, this is a month after you've answered the question about is there a correlation between blood glucose and weight gain. Do you recall in the previous e-mail?
A. That's correct.
Q. And in March, you're asked the question, it's In Re: Olanzapine and cardiovascular risk. And here's what you say. "Unfortunately, I believe it will be a while before we have a clear, definitive position developed regarding hyperglycemia," correct?
A. That's not the entirety of the statement. "Hyperglycemia, hyperlipidemia, obesity, the metabolic syndrome and long-term cardiovascular risk and olanzapine."
Q. Yes, sir, I'm sorry, that is exactly correct. You said it will be a while before we have a clear, definitive position, correct?
A. That's correct.
Q. But from what we know in your internal e-mails you have clearly told everybody there is a statistically significant difference in our continuous data concerning blood glucose levels in Zyprexa patients compared to placebo and Haldol?
A. Those were based on my understanding of what I understood to be ongoing work and activity.
Q. But you had made that statement and you told them what the data said based upon your review?
A. At one point in time.

Beasley, Charles M.D.(July 27, 2006)

Q. My on the question, sir, was when you made the statement about

A. We have certainly agreed that weight gain is a risk factor for a number of adverse events.

Q. That's why when you go to the doctor they don't tell you, unless you're an anorexic, they don't tell you we'd like you to gain as much weight as possible. They don't tell you that, do they?

A. No, they don't.

Q. Why don't they tell you that? Just tell the jury, why do they tell you not to gain weight?

A. Well, they wouldn't tell you to gain weight because that is not considered a healthful thing to do.

Q. Right. It can put you at risk for cardiovascular disease?

A. Depending upon the amount that you gain it may well be a risk factor for cardiovascular disease.

Q. And what other thing, at least, diabetes?

A. Stroke.

Q. Heart attack?

A. That's cardiovascular disease.

Q. And diabetes?

A. And it is a risk factor for diabetes, as we discussed yesterday.

Exhibit 4
Alan Breier, M.D.

Breier, Alan M.D.(January 11, 2007)

19: 3 Q. Good morning. Would you
4 state you full name for the record, please.
5 A. Alan Breier.

Breier, Alan M.D.(January 11, 2007)

24:14 Q. And you are currently
15 Vice-president and the Chief Medical Officer
16 at Eli Lilly; is that correct?
17 A. That's correct.
18 Q. And you assumed that position
19 in August of 2003?
20 A. Yes.

Breier, Alan M.D.(January 11, 2007)

25:22 Q. And who do you currently
23 report to?
24 A. Steven Paul.
26: 1 Q. And what's his position?
2 A. He is president of Lilly
3 Research Laboratories.
4 Q. And to whom does he report?
5 A. He reports to Sydney Taurel.
6 Q. And Sydney Taurel is the
7 Chief Executive Officer and Chairman of the
8 Board of the company; is that correct?
9 A. Yes.

Breier, Alan M.D.(January 11, 2007)

26:21 Q. Okay. I'm going to be asking
22 a lot of questions about your activities
23 regarding Zyprexa, but before I do that, I'd
24 like to find out more about your background.
27: 1 Am I correct that your
2 received a Bachelor of Arts degree from the
3 University of Toledo in Ohio in 1975?
4 A. That's correct.
5 Q. And you received a Doctor of
6 Medicine degree in 1980 from the University
7 of Cincinnati School of Medicine?
8 A. Correct.
9 Q. And then you were a resident
10 in psychiatry from 1980 to 1984 at Yale
11 University School of Medicine; is that
12 correct?
13 A. Yes.

Breier, Alan M.D.(January 11, 2007)

29:12 Q. Okay. And before joining
13 Lilly, did you have any particular training

or expertise in the diagnose and treatment of diabetes other than what is generally provided in medical school?
A. I did not.
Q. Okay. Am I correct that you had not conducted any research regarding diabetes before joining Lilly?
A. No, I did not.
Q. And you had not published any scientific articles regarding diabetes before joining Lilly; is that correct?
A. That's correct.

Breier, Alan M.D.(January 11, 2007)

your background at Lilly. Am I correct that you started at Lilly in 1997 as a clinical research fellow?
A. That's correct.
Q. And what were your duties and responsibilities then?
A. A clinical research fellow at Lilly is a senior technical position.
Q. And which products were you working on at that time?
A. Zyprexa.
Q. What did you do with respect to Zyprexa at that time in 1997?
A. My focus was predominantly on schizophrenia.
Q. Were you conducting clinical trials, doing -- what were you doing with respect to that?
A. My primary responsibilities were designing and conducting clinical trials.

Breier, Alan M.D.(January 11, 2007)

Q. Who did you report to at that time?
A. Gary Tollefson.
Q. And who reported to you?
A. I had no direct reports.
Q. Am I correct that you became head of the Zyprexa Product Team in 1998?
A. Actually, I believe it was 1999.
Q. Okay. And do you recall what month that was?
A. I believe it was at the beginning of the year -- January.
Q. And did you still continue to report to Dr. Tollefson at that time?
A. Yes.

Breier, Alan M.D.(January 11, 2007)

58: 3 Q. As team leader of the Zyprexa
4 Product Team between 1999 and 2002, were you
5 responsible for both the medical and
6 marketing aspects of the Zyprexa Product
7 Team?
8 A. Yes, I was.

Breier, Alan M.D.(January 11, 2007)

64: 9 Q. Sir, isn't it a concern that
10 when you have medical and marketing people
11 working closely together in a drug company,
12 the medical people can get sucked into a
13 spinning mentality to gain a competitive
14 marketing advantage for the drug that their
15 company is promoting?
16 MR. BOISE: Object to the
17 form.
18 A. No.
19 MR. SUGGS: I'm going to hand
20 you what's previously been marked as
21 Plaintiff's Exhibit 9281.
22 (Whereupon, Plaintiff's
23 Exhibit(s) 9281, previously
24 marked, was presented to the
65: 1 witness.)
2 MR. SUGGS: For the record,
3 Exhibit 9281 is an e-mail that Alan
4 Breier wrote on February 6, 2004.
5 QUESTIONS BY MR. SUGGS:
6 Q. And do you recognize this
7 e-mail, sir?

Breier, Alan M.D.(January 11, 2007)

65:11 A. I see that, yes, I did write
12 this. I'm familiar with it.
13 Q. I was confused when I saw
14 this as to who this went to. It's addressed
15 in the e-mail to U.S. underscore medical
16 underscore medical U.S. Who was that or what
17 group was that?
18 A. At a minimum, it would be
19 medical personnel in the U.S. Quite frankly,
20 I'm not sure if this would have gone outside
21 of the U.S. or not based on just that header.
22 Q. And this would have been
23 written by you some, what, 16 months or so
24 after you'd taken over the position as chief
66: 1 medical officer?
2 A. That's correct.
3 Q. And how many people would
4 have been in that U.S. medical group?
5 A. I'm not sure.
6 Q. Are we talking dozens or
7 hundreds or thousands?
8 A. I would say hundreds.
9 Q. Okay. And I assume you gave
10 careful thought to the language that's in

this e-mail before you sent it out around to those hundreds of people; is that correct?
A. Yes.
Q. Okay. And in the middle of the first paragraph, pardon me, the middle of the first page, there's a paragraph that has a bolded title "Principles." Do you see that?
A. I do.
Q. And in that paragraph you stated, "Making medicine for people facing illness is a much different and higher calling than making consumer products for other markets. We do not sell soap. It therefore requires a different and higher code for conducting our business."
Do you see that language, sir?
A. I do.
Q. And I assume that no one ever came back and contradicted you about that; is that correct?
A. No.
Q. Okay. And if I could direct your attention to about the third line from the bottom, you state, "We are particularly challenged when it comes to presenting our data in a completely objective unbiased manner because of our passion for our molecules and the belief that spinning data is sometimes necessary to gain a competitive advantage. If we do not abandon the spinning mentality we will not restore confidence in our medical research and rebuild the public trust our industry has compromised."
Did I read that correctly?
A. You did.
Q. And the competitive advantage that you were referring to there would be a competitive advantage in the marketplace; is that correct?
A. Yes.
Q. Okay. And you clearly said that "If we do not abandon the spinning mentality we will not restore confidence on our medical research and rebuild the public trust our industry has compromised," correct?
MR. BOISE: Asked and answered.
A. That's correct.
Q. And "abandoned" refers to stopping something that was already being done, correct?
A. No.
Q. Would be what the word "abandon" means?
A. Leave behind.
Q. Okay. And when you talk about restoring confidence, you don't use that term "restore confidence" unless that confidence has already been compromised, correct?
A. That's correct.

Q. And when you talk about rebuilding the public trust, you don't use that phrase "rebuilding" something unless that public trust has already been broken, correct?

MR. BOISE: Object to the form.

A. I would agree with that.

Breier, Alan M.D.(January 11, 2007)

94:22 Q. Were you aware, sir, back when you were the head of the Zyprexa Product Team that FDA regulations require that the 95: 1 labeling shall be revised to include a warning as soon as there's reasonable evidence of an association of a serious hazard with a drug and that a causal relationship need not have been proved?

Breier, Alan M.D.(January 11, 2007)

96: 1 Q. My question to you is, were you aware of that when you were head of the Zyprexa Product Team?

A. Yes.

Breier, Alan M.D.(January 11, 2007)

100:21 MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 8562.

(Whereupon, Plaintiff's 101: 1 Exhibit(s) 8562, previously marked, was presented to the witness.)

MR. SUGGS: For the record this is a two-page -- take it back -- three-page document. It has a title at the top that says Zyprexa Business Processes.

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101:20 Q. Okay. I should note for the record also that when these documents are produced to us, Lilly also produces a computer database, and in some instances it shows a date, and in this particular instance, the 102: 1 Lilly-produced database shows that this document was dated August 27, 2001.

Sir, below that centered heading there's a side heading entitled "Zyprexa Key Decision Team." Do you see that?

A. Yes.

Q. Was this, in fact, a Zyprexa Key Decision Team in 2001 as noted in this document?
A. Yes.
Q. Okay. And does the document accurately describe the voting members of that key decision team?
A. I'm refreshing my memory from this document, but I must say that I don't recall specifically the voting members of this committee, but I accept what is on this piece of paper.

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104: to the types of decisions. The document lists the types of decisions to be made by the Zyprexa Key Decision Team, and they included, again, according to the document, clinical study priorities, label changes/modifications, publication priorities, key issues management, key marketplace decisions, IPP final submission Zyprexa marketing plan. Did I read that correctly?
A. You did.

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105: Q. Okay. Do you have any reason to doubt that those were the types of decisions made by the Zyprexa Key Decision Team?
A. Well, I mean, I know how these kinds of decisions ultimately got made, and, I mean, I could speak to that.
Q. Okay. Well, the document indicates that down in the process section, the third paragraph within there, that "Decisions were made on the basis of a group vote. Alan Breier retains the right to make a final decision if he's opposed to the group vote."
Did that accurately reflect how decisions were made within that team?
A. I don't recall. It's very

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109: Q. I'm trying to understand how your team worked and who within your team made decisions and how such decisions were made within your team. And within your team with respect to labeling, who was it that made
110: the determination as to whether or not a label change or modification would be

proposed or recommended by the Zyprexa Product Team?

MR. BOISE: Object to the form.

A. Again, that would be a cross-functional group of scientists who were working with the data. If the analysis of the data indicated that this was something that warranted a label change and would change what we call our core label, we would then take that information to GPLC, the group we talked about earlier. GPLC would look at it, determine, yes, this should be added to core or no it shouldn't.

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Q. Let me ask the question this way. You know how Harry Truman had a sign on his desk that said "The buck stops here?"

A. Yes.

Q. With respect to labeling decisions within the Zyprexa Product Team and whether a labeling change should be taken to the Global Product Labeling Committee for review, where did the buck stop in the Zyprexa Product Team for that type of decision?

MR. BOISE: Object to the form.

A. On the Zyprexa Product Team, the buck would stop with me. That

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Q. And would it be fair to say that while you were president -- pardon me -- while you were team leader of the Zyprexa Product Team, that you would have been aware of any proposal made by the product team to the Global Product Labeling Committee with respect to a label change?

A. Definitely.

Q. Okay. Would it also be fair to say that if a proposal was made by the product team to the Global Product Labeling Committee to change the Zyprexa label, not only would you have been aware of that proposal, but you would, in fact, have signed off on that proposal going to the Global Product Labeling Committee, correct?

A. I would be knowledgeable about it and I would endorse it going forward.

Q. Okay. And would it be fair to say that if something was taken to the Global Product Labeling Committee by your team, you would have wanted to make sure, in your own mind, that before that was done that the proposal was appropriate?

A. We would strive to get it right.
Q. Okay. And you would want to make sure that the basis for that proposal was well thought out and well analyzed before it was taken to the Global Product Labeling Committee, correct?
A. Ideally that is absolutely correct.

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MR. SUGGS: I'd like to go back in time, Dr. Breier, to November of 1999. And I want to hand you what's been previously marked as Plaintiff's Exhibit 8262.
(Whereupon, Plaintiff's Exhibit(s) 8262, previously marked, was presented to the witness.)
QUESTIONS BY MR. SUGGS:
Q. For the record, this is a string of e-mails. And the one I want to particularly focus your attention on is the one at the bottom of the first page which purports to be an e-mail from Alan Breier to a fairly lengthy list of people at Lilly dated November 9, 1999, the subject being Executive steering committee for olanzapine-associated weight changes and hyperglycemia.
Do you see this document?
A. I do.
Q. And do you recall writing this on or about the date indicated?
A. Yes, I do.

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Sir, I'm going to hand you what's been previously marked as Plaintiff's Exhibit 1605.
(Whereupon, Plaintiff's Exhibit(s) 1605, previously marked, was presented to the witness.)
MR. SUGGS: Which, for the record, is a computer printout from the HGAJ study dated June 19, 1995.
QUESTIONS BY MR. SUGGS:
Q. And if I could direct your attention in particular, sir, to Page 11. There is a reference on that page to glucose nonfasting?
A. Yes.
Q. And it indicates that -- by the way, in this HGAJ study, this was a study in which you had Zyprexa users and also

patients who were using another drug called Haldol, correct?
A. That's correct.
Q. And Haldol was a first generation antipsychotic drug, correct?
A. Yes.
Q. Okay. And in this particular computer printout it shows that the Zyprexa users had a statistically significant increased incidence of high glucose, correct?
A. That's correct.
Q. And is it your testimony that you were, in fact, aware of this back in 1999?
A. I'm going to presume that I was.

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123: Q. Do you also presume that the other medical members of the Zyprexa Product Team would have been familiar with the data from the HGAJ study, and in particular, this finding in June of 1995 that there was a statistically significant increased incidence of high glucose in the Zyprexa users?

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123:A. I can't speak for every physician or scientist on the team in terms of their knowledge of this particular finding because we had people working on, you know, vastly different themes. I would expect that scientists working, specifically, on this theme or on this particular trial would have been aware of it.

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125:Q. Well, let me ask this. If, in fact, the evidence shows that as of September 1998 there were 200 adverse event reports tallied by Lilly relating to blood glucose elevations, would you have been aware of that?
A. Again, I'm not recalling the exact number. I was clearly aware that there were adverse events reported in the database, I just don't recall the number.
Q. And adverse events relating to blood glucose and diabetes?
A. Yes.
Q. Okay. And I'm assuming that you were aware in November of 1999 that Lilly
126: 1 was required to discuss hyperglycemia and
2 diabetes in the special precautions and

special warnings section of the European label for Zyprexa; is that correct?

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126:13 A. Yes. We had a label change at that time on the topic that you're talking about in the European label.

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126:19 Q. Okay. And is it also fair to say that by November of 1999, Lilly's competitors were emphasizing the weight gain associated with Zyprexa and were at least claiming that that would put patients at greater risk for diabetes?
127: 1 MR. BOISE: Object to the form.
A. There was at that time what we refer to as counterdetailing where competitive companies will focus on potential side effects of competitor drugs.

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127:20 Q. Okay. And, in fact, you do admit that Zyprexa can cause weight gain; is that correct?
A. It certainly can cause weight gain in some patients.
128: 1 Q. Okay. With that background in mind, let's go back to Exhibit 8262, which is your November 9, 1999, e-mail.
And can you describe, generally, the people to whom your e-mail is addressed?
A. Yes. They are all scientists at Eli Lilly and Company. Many of them are some of our top scientists across the organization. There are other scientists here who are what I would call specific content experts.
Q. Okay. And in your first paragraph, you state, you start off by saying, "Olanzapine-associated weight gain and possible hyperglycemia is a major threat to the long-term success of this critically important molecule." Correct?
A. That's correct.
Q. And Zyprexa was critically important to the financial success of Lilly, was it not?
A. It was an important molecule.

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131:22 Q. After stating that
23 Zyprexa-associated weight gain and
24 hyperglycemia was a major threat, you went on
132: 1 to say, "In addition, it could be
2 argued that Eli Lilly with its strengths in
3 neuroscience, metabolism, endocrinology and
4 diabetology is better positioned than any
5 other institution to elucidate the mechanisms
6 and develop treatments for this side effect."
7 Do you see that language,
8 sir?
9 MR. BOISE: Object to the
10 form. You misread it.
11 QUESTIONS BY MR. SUGGS:
12 Q. Do you see the language?
13 A. I see the sentence.
14 Q. Okay. And why was it that
15 you thought that Eli Lilly could be better
16 positioned than any other institution to
17 elucidate the mechanisms and develop
18 treatments for this side effect?
19 A. Well, again, I think here
20 we're referring to weight gain, and our
21 company has strengths in the areas that I
22 articulate in that sentence, in
23 endocrinology, metabolism, and neuroscience.
24 So we had very deep expertise and, therefore,
133: 1 the potential to better understand this
2 phenomenon, potentially, then to explore,
3 examine, possible treatments.
4 Q. And, in fact, your company
5 had for many decades had a large portion of
6 its business the manufacture and sale of
7 drugs designed to treat diabetes, correct?
8 A. We still do, yes.

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136:13 Q. Okay. And then you go on to
14 say, "Success of this effort will contribute
15 to securing the future of olanzapine and the
16 financial health of our company and likely
17 spur the development of next generation
18 antipsychotic drugs, i.e., olanzapine without
19 the weight gain and drugs for obesity."

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136:23 financial health of our company," do you
24 recall what the sales of Zyprexa were at that
137: 1 point in time in November of '99?
2 A. I don't recall.

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137:12 Q. Okay. It was a very large

product, though, was it not, sir?
MR. BOISE: Object to the form.
A. It was a widely used medicine.
Q. Okay. And then later in your e-mail you refer to a meeting of this cross-functional team in a couple of weeks and state that "The purpose of the meeting was for the executive steering committee to review the ongoing work, future study plans, and resource needs, and to provide guidance for the scope of future activities;" is that correct?
A. You read it correctly.
Q. And did the members of that executive steering committee that are listed there, which is composed of yourself and a number of others, did they stay involved in this process?
A. Yes. We had been working with a number of them before this and had a number of activities, scientific activities, going on.

The purpose of the steering committee was to update a broader group of what we were doing, get their input, and then suggestions for future directions. Because we had already had cross-functional interactions with some of the key people, we decided that we would continue on as we had before; in other words, I would take responsibility for bringing in key people at appropriate times as opposed to, say, having a biweekly meeting or something like that with these people on a formal basis.

So the spirit of that was continued on, but not as a regular meeting of those key individuals, although I took, again, responsibility to keep them informed and to continue to get their input.

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Q. When did Lilly regard olanzapine-associated weight gain and possible hyperglycemia as a major threat to the long-term success of Zyprexa? Did it start -- did that perception start with your writing of this memo in November of 1999 or did it begin at some earlier point?

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A. If you would accept my characterization of excessive weight gain, my answer to your question would be day one.
Q. On the second page of your e-mail you refer to a meeting of the

cross-functional team on November 23, 1999; is that correct?
THE WITNESS: I'm sorry, were you in the last paragraph?
MR. SUGGS: Yes.
A. Yes.
Q. And the very next day you wrote an e-mail to the top levels within the company about Zyprexa and its associated weight changes; do you recall that?
A. I don't recall that now.
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 918.
(Whereupon, Plaintiff's Exhibit(s) 918, previously marked, was presented to the witness.)
MR. SUGGS: For the record, this is an e-mail from Alan Breier dated November 24, 1999, and addressed to Gerhard Mayr, Gino Santini Lorenzo Tallarigo, Albertus van den Bergh with copies to himself, John Lechleiter, Roland Powell and Gary Tollefson.
QUESTIONS BY MR. SUGGS:
Q. Do you recall writing this memo on or about November 24, 1999?
A. I do.

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Q. Who were the recipients of your November 24, 1999, e-mail?
A. The addressees were leaders in sales marketing.
Q. Okay. You start off your e-mail by saying, "John asked me to overview the topic of olanzapine associated weight changes." You refer to that as OWC, correct?
A. Yes.
Q. Okay. And who was the John, was that John Lechleiter?
A. Yes.
Q. You go on to say, "I want to emphasize to you that OWC has been and continues to be a top priority for the Zyprexa Product Team. Although it is a significant issue for us, perhaps our only/major clinical Achilles heel, and our competitors have robustly focused on it reminiscent of anxiety" -- and something is blanked out -- "the fact is Zyprexa offers the best combination of efficacy and safety and ease of use of any available treatment for psychosis and acute mania."
Do you see that language, sir?
A. Yes.
Q. And do you know what would

have been X'd out there.
A. No.
Q. Okay. Would it be fair to say, sir, that Lilly always emphasized the efficacy of Zyprexa to outside physicians?
MR. BOISE: Object to the form of the question. Vague.
A. We emphasized the data. So that would be, that would include efficacy, safety, other important datasets associated with the molecule.

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153:13 Q. Okay. Then I'd like to
14 direct your attention to the next section of
15 your e-mail. It's in the Market Research
16 section. And you have a number of bulleted
17 points below there, correct?
18 A. Um-hum.

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154:12 Q. Okay. And you say in your
13 e-mail here, "Outliers are the main concern
14 for physicians; 20 pound increase is viewed
15 as threshold for concern." And then you have
16 in parentheses, "Fact: Two-thirds of
17 olanzapine-treated patients gain less than
18 20 pounds."
19 Do I read that correctly?
20 A. You do.
21 Q. But it was also a fact that
22 there were some patients who gained
23 considerable amounts of weight from Zyprexa,
24 correct?
155: 1 A. That's correct.
2 Q. In fact, some people gained
3 as much as 80 pounds, correct?
4 A. Is that possible? Yes.

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155:11 Q. We'll go over that later. If
12 I could direct your attention to the
13 following bullet point that states:
14 "Olanzapine is viewed to have more associated
15 weight gain than risperidone, seroquel and
16 traditional neuroleptics."
17 The term "neuroleptics" is
18 another word for antipsychotic drug, correct?
19 A. It's generally reserved for
20 the traditional or first-generation
21 antipsychotic drugs.

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156: 1 Q. And then in parenthesis state
2 "Fact: The order of weight gain among
3 antipsychotics is: Clozapine greater than
4 olanzapine greater than seroquel greater than
5 risperidone greater than traditional
6 neuroleptics."
7 Did I read that correctly?
8 A. You did.

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158:13 attention back to the e-mail. Olanzapine,
14 that's referred to next in there in that chain
15 or in that ordering of weight gain,
16 olanzapine is just another name for Zyprexa,
17 correct?
18 A. That's correct.

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160: 6 Q. Okay. And so the first part
7 was the market research telling you that
8 olanzapine was viewed by physicians to have
9 more associated weight gain than risperidone,
10 Seroquel and traditional neuroleptics and the
11 fact was that that was true?
12 A. Correct. So those clinical
13 observations that were captured in the market
14 research was compatible or consistent with
15 the known literature.

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162:23 Q. Okay. And then in your next
24 bullet point you say, "Blanket detailing will
163: 1 be damaging since many physicians do not see
2 OWC as an issue."
3 Did I read that correctly?
4 A. You did.

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163:10 detailing. In the pharmaceutical business,
11 the process of a sales representative calling
12 on physicians and discussing the product with
13 the physician is often referred to as
14 detailing, correct?
15 A. That's correct.

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164:11 Q. And what you say here is

blanket detailing will be damaging since many physicians do not see olanzapine weight change as an issue, correct?
A. That's what it says.

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Sir, do you recall that within a couple of months after that e-mail, the Zyprexa Product Team and Pharmacovigilance at Lilly recommended a label change that was triggered by an analysis showing that Zyprexa users had a three and-a-half times higher incidence of treatment-emergent hyperglycemia?
MR. BOISE: Object to the form.
A. I'm familiar with the analysis that you're speaking about.

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MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 990.
(Whereupon, Plaintiff's Exhibit(s) 990, previously marked, was presented to the witness.)
MR. SUGGS: For the record, this is a multi-page document, the first page of which has a big bold heading at the top which says Attachment E and then attaches an Olanzapine Labeling Change and Hyperglycemia for the February 21, 2000, GPLC meeting.
QUESTIONS BY MR. SUGGS:
Q. Do you recognize this document, Dr. Breier?
A. I've seen it before.

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Q. Okay. If I could direct your attention to the top of the page, there's a box that has the title "Proposal of the Product Team and PhV." Do you see that?
A. Yes.
Q. And the product team in this case would be Zyprexa, correct?
A. That's correct.
Q. And PhV stands for pharmacovigilance, correct?
A. I believe that's correct.
Q. And as we said before, you were the head of the product team, correct?

A. Yes.

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Q. If I could direct your attention to the middle box on the first page, it says "How has that proposal arisen?" It states, "Recent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment emergent hyperglycemia in olanzapine group, 3.6 percent, was higher than that in the placebo group, 1.05 percent."

Do you see that language?

A. I do.

Q. And the phrase "treatment-emergent hyperglycemia" refers to hyperglycemia occurring during the context or after a person's been exposed to the drug in a clinical trial; is that correct?

A. I would characterize it as data coming from a clinical trial.

Q. And these would be in people who did not have hyperglycemia before they started taking the drug, correct?

A. I don't know that that's the case.

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Q. Well, apparently, though, your product team and pharmacovigilance group thought this finding of treatment-emergent hyperglycemia in the olanzapine group warranted a revision to the label, correct?

A. I don't know all or who was involved in this particular analysis because, as I noted before, I don't have recollection of it, but whoever put this table together suggested that it go into the label.

Q. Well, we know that at least according to the first page of the document this was the proposal of the product team, correct?

A. That's what it says, and Pharmacovigilance.

Q. And Pharmacovigilance.

Now, when they refer to the treatment-emergent hyperglycemia in the olanzapine group being 3.6 percent and that the incidence of a placebo group was 1.05 percent, the rate of treatment-emergent hyperglycemia in the Zyprexa group was three and-a-half times higher than in the placebo group, correct?

A. I would agree that 3.6 percent is three and-a-half times greater than 1.05 percent.

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192:10 Q. Sir, did you tell physicians
11 at any time that analysis of clinical trial
12 data from Lilly's own studies showed that the
13 existence of treatment-emergent hyperglycemia
14 was three and-a-half times higher than in the
15 placebo group?
16 MR. BOISE: Object to the
17 form of the question.
18 Q. Yes or no?
19 A. We did not.

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195:18 Q. Okay. Were you informed that
19 after that Global Product Labeling Committee
20 meeting, someone on that committee let your
21 boss, Dr. Tollefson, know that they were
22 concerned about this analysis which found a
23 three and-a-half times higher incidence of
24 treatment-emergent hyperglycemia?
196: 1 MR. BOISE: Object to the
2 form. Foundation. Vague.
3 A. I'm not aware of that.

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196:10 Q. If I could direct your
11 attention to the third physical page or,
12 actually, Page 4 numbered in the bottom
13 right-hand corner. There's a reference to
14 literature reports in the second box down
15 from the top.
16 A. Yes.
17 Q. And in the second paragraph
18 in that box there's a reference to a
19 Dr. Daniel Casey that states, "Daniel Casey
20 from Oregon presented in a seminar at Lilly
21 at the end of 1999."
22 Did you know Dr. Casey?
23 A. Yes.

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197: 4 Q. Okay. And was Dr. Casey a
5 consultant to Lilly back in 1999 and 2000?
6 A. Yes.

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198: 1 Q. Okay. That seminar that's

referred to there at Lilly at the end of 1999, did you attend that seminar?
A. Yes.
Q. Okay. And I assume Dr. Casey was, must have been invited to come and give a presentation, correct?
A. I invited him.
Q. Okay. And at that seminar, according to this document, "He," referring to Dr. Casey, "performed chart review of 136 veteran patients who had been exposed to olanzapine therapy for at least four months, average of 1.4 year. Of the 39 patients who had normal fasting glucose levels before olanzapine therapy, seven, or 18 percent, had fasting glucose levels of 126 milligrams per deciliter or higher during olanzapine therapy." And then in parentheses it says, "threshold that met the 1998 ADA diagnostic criteria for diabetes."
Do you see that language?
A. I do.
Q. And the ADA that's referred to there is the American Diabetes Association, correct?
A. Yes.
Q. Okay. And so in this review of charts that Dr. Casey did of patients who had normal fasting glucose levels before they started using Zyprexa, 18 percent of them had fasting glucose levels that exceeded the criteria for diabetes after they had used it for at least four months; is that correct?
A. You are reading this correctly.

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199:18 Q. Okay. When Dr. Casey came to
19 Lilly and gave that presentation in which he

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199:20 said that 18 percent of people with normal
21 blood levels had diabetic blood levels after
22 using the drug for four months or more, did
23 that come as a surprise to you at that point,
24 or were you aware of his findings before he
200: 1 came to give the seminar?
2 MR. BOISE: Object to the
3 form of the question.
4 A. I don't recall if he and I
5 talked about the data before he came or not.
6 Q. Do you recall who else was at
7 that seminar where Dr. Casey said that
8 18 percent of the people who use Zyprexa
9 after four months had diabetic blood levels?
10 A. I don't recall, sitting here
11 at this moment, who else was at the seminar.

Q. Okay. The very term "seminar" makes me think, and I could be wrong, that there was a group of people there. Is that a fair assessment?
A. I think that's a fair characterization.
Q. And would you have expected the majority of people from the Zyprexa Product Team to be there?

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200:21 A. I, again, don't recall who
22 was in attendance. Typically, when we have a
23 seminar with an outside speaker, we advertise
24 it fairly broadly within the company. It's
201: 1 an open-door policy, so those interested in
2 this particular area were invited.
3 Q. Okay. And it's fair to say
4 that, also, isn't it, sir, that Lilly never
5 advised prescribing physicians in the
6 labeling of Dr. Casey's findings, did it,
7 sir?
8 MR. BOISE: Object to the
9 form.
10 A. No, we didn't, because this

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202: 7 Q. Sir, this proposal to change
8 the label that was reviewed by the Global
9 Products Labeling Committee did not go
10 forward in February of 2000, correct?
11 MR. BOISE: Object to the
12 form.
13 A. These data were not included
14 in the label.
15 Q. Now, you did make a label
16 change several months later in May of 2000,
17 correct?
18 A. That's correct.
19 Q. And we've seen the document
20 where that was done, Exhibit 4858. If you
21 can find that in the pile. That was the
22 May 9, 2000, letter?
23 A. Yes.
24 Q. And this May 9, 2000, letter
203: 1 is from Gregory T. Brophy in the U.S.
2 Regulatory Affairs Department in Eli Lilly to
3 the FDA on May 9, 2000, correct?
4 A. Yes.
5 Q. And it informs the FDA that
6 Lilly has already revised the package label
7 for Zyprexa in three respects, correct?
8 A. Yes.
9 Q. And Dr. Brophy notes in his
10 letter of May 9, "Effective immediately we
11 will be implementing this change," correct?
12 It's on the second page,

second to the last paragraph, last sentence.
A. Yes.
Q. And so this label change was made without prior FDA approval, correct?
A. That's correct.

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Q. Okay. And then the other change that was made was item No. 2 in the adverse reaction section, there was some additional language added regarding the laboratory changes section and findings of data from the olanzapine clinical trial database with respect to random plasma glucose levels, correct?
A. Yes.

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Q. Thank you. And would you agree with me, sir, that essentially that language is indicating that there was really not much, if any, difference in blood glucose levels between the patients who used Zyprexa and those who were on placebo?

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A. The overall -- I mean, there's a number of different placebo/olanzapine comparisons described here. Overall, there is relatively little difference between the placebo-related values and the olanzapine-related values.

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Q. Okay. I'll represent to you that we've had deposition testimony from Dr. Beasley and Dr. Kenneth Kwong that the analysis which formed the basis for this May 2000 label change was later expanded into a lengthy submission to FDA in July of 2000 and was also the basis for a paper for publication. Does that square with your recollection as well?
A. Yes.
Q. Okay. And you were one of the authors listed on the paper that was prepared; isn't that correct?
A. Yes.

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Q. It was submitted to the "Journal of Biological Psychiatry" and rejected due to methodological concerns; isn't that correct?
A. I recall it being submitted to "Biological Psychiatry" and rejected. I do not recall all of the reasons it was not accepted.
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 1440.
(Whereupon, Plaintiff's Exhibit(s) 1440, previously marked, was presented to the witness.)
MR. SUGGS: For the record, this is a November 3, 2000, fax from "Biological Psychiatry" referring to Manuscript No. 5380 entitled Incidence and Rate of Treatment-emergent Potential Glucose Impaired Glucose Tolerance (Igt) and Potential Diabetes with Olanzapine Compared to Other Antipsychotic Agents and Placebo by Charles M. Beasley, Jr., Kenneth Kwong, Paul H. Berg, Cindy C. Taylor, Jamie Dananberg and Alan Breier.
QUESTIONS BY MR. SUGGS:
Q. Was that the title of the paper that was prepared and submitted?
MR. BOISE: Object to the form.
A. Yes.

Breier, Alan M.D.(January 11, 2007)

Q. Okay. And it would appear that this document that we have before us, Exhibit 1440, is a copy of the reviewer's comments from the biological psychiatry journal, correct?
A. Yes.

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attention to the first paragraph. By the way, there are several reviewers comments here, correct?
A. There were three.
Q. And they're, actually, referred to as referees, correct?
A. That's correct.

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219:20 Q. Okay. Let me direct you to
21 the comments on Page 2. He states, "The
22 authors present a highly curious dataset.
23 Since their own work has shown that
24 olanzapine is associated with a clinically
220: 1 and statistically pertinent increase in
2 weight compared to both haloperidol and
3 placebo. They seem to be suggesting that
4 olanzapine exerts a sizable antidiabetic
5 power. It is estimated by the American
6 Diabetic Association that a 1-pound increase
7 in adipose tissue is associated with a
8 4 percent increase in the risk of diabetes.
9 Given that olanzapine induces significant
10 weight changes and the authors believe and
11 report that it does not increase the risk of
12 diabetes, olanzapine appears to be in the
13 enviable position of eliminating the known
14 risk of glucose" tolerance "associated with
15 weight gain."
16 MR. BOISE: You misspoke.
17 MR. SUGGS: On what word?
18 MR. BOISE: Intolerance.
19 MR. SUGGS: What did I say,
20 "glucose tolerance"?
21 MR. BOISE: I heard "tolerance"
22 but the record will speak.
23 MR. SUGGS: You're right. I
24 did misspeak.
221: 1 I don't want to read the
2 whole thing again.
3 MR. BOISE: You did it so
4 well almost.
5 QUESTIONS BY MR. SUGGS:
6 Q. Bottom line, this reviewer is
7 saying that these findings that you had there,
8 he regarded at least them as being very
9 curious, correct?
10 A. "Highly curious" is the
11 phraseology.
12 Q. Because you were finding,
13 yes, Zyprexa causes weight gain but, no, it
14 doesn't cause diabetes or increase the risk
15 of diabetes, correct?
16 MR. BOISE: Object to the
17 form.
18 A. That's the data.
19 Q. And this reviewer didn't
20 believe that, did he?
21 MR. BOISE: Object to the
22 form.
23 A. I wouldn't interpret curious
24 as disbelief.

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272: 5 can refresh your recollection. Let
6 me show you what's been previously
7 marked as Plaintiff's Exhibit 6998.
8 (Whereupon, Plaintiff's
9 Exhibit(s) 6998, previously

marked was presented to the witness.)

MR. SUGGS: Which, for the record, is an October 9, 2000, e-mail from Robert Baker to Charles Beasley, Christopher Bomba, Alan Breier, Thomas Brodie, Patrizia Cavazzoni, James Gregory, John Holcombe, Jack Jordan, Suni Keeling, Bruce Kinon, Michael Murray, John Richards, Eugene Thiem, Mauricia Tohen and Paula Trzepacz.

QUESTIONS BY MR. SUGGS:

Q. If I could direct your attention, sir, to the first paragraph. It states, "FYI: The Lilly diabetes/endocrine group held an academic advisory board meeting this weekend in Atlanta. They kindly allotted two hours for discussion of olanzapine's potential hyperglycemia risks, and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic."

Do you see that language, sir?

A. I do.

Q. And does that refresh your recollection that members of your Zyprexa Product Team had a meeting with outside consultants in October of 2000?

MR. BOISE: Object to the form.

A. I recall this message, and I recall that consultation. Just to be

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Q. Okay. So the diabetes side of the company which deals with diabetes all the time has this group of outside consultants, outside experts that they deal with. And some of your folks dealing with Zyprexa went down there to attend the meeting and presented the data to them, correct?

A. That's correct.

Q. Okay. And the data they presented to them was essentially the same data that was reflected in your May 2000 label change and in the presentation to FDA in July of 2000 and in the paper that was submitted for publication to the "Journal of Biological Psychiatry." Isn't that correct, sir?

MR. BOISE: Object to the form of the question. Foundation. Compound.

A. What I recall is that the

categorical glycemic d[illegible] that we discussed earlier was presented. I believe also other data as well, including weight gain data and data of that nature.

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277: Q. It goes on to say, "They were however concerned by our spontaneous AE reports, and quite impressed by the magnitude of weight gain on olanzapine and indications for glucose."

And when they're referring there to "spontaneous AE reports," am I correct that that stands for adverse event reports?

A. Yes.

Q. Okay. And these would be reports made to the company or to the FDA by either treating doctors or patients, or, frankly, could be anybody recording an adverse event that occurred to a patient while they were using the drug, correct?

A. Typically, the treating physician.

Q. Okay. And continuing on in

278: that paragraph dropping down a couple of lines, it says, "Citing methodological questions, at least the vocal members were not reassured adequately by our analyses, such as the finding that relative risk was not higher than comparative drugs. Disconcertingly, one member compared our approach to Warner Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class."

Do you see that language, sir?

A. Um-hum.

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278:15 Q. Are you familiar with the reference to Warner Lambert and Rezulin at that time?

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278:20 A. To the extent that my understanding is that there were similar comparative claims presented on Rezulin.

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279:21 Q. Dr. Ba[illegible] found that
22 reference to Warner Lambert and the arguments
23 that they had been making with respect to
24 Rezulin, he found that disconcerting,
280: 1 correct?
2 A. Yes.
3 Q. Okay. If I could direct your
4 attention next to Plaintiff's Exhibit 1453.
5 (Whereupon, Plaintiff's
6 Exhibit(s) 1453, previously
7 marked, was presented to the
8 witness.)
9 MR. SUGGS: This is another
10 string of e-mails. The very first
11 one of which -- well, it's the first
12 at the top of the first page of the
13 document -- is from Robert Baker to
14 Charles Beasley dated October 10,
15 2000.

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281:24 Q. The subject of this e-mail is
282: 1 the meeting with endocrinologic consultants.
2 And it goes on to state, "Robert,
3 clearly this group of endocrinologists who
4 spoke up, and I would rate those who did
5 speak up as the leaders of the pack, are very
6 concerned with the approach Lilly is taking
7 towards the issue that Zyprexa leads to
8 diabetes. I can only hope that you and all
9 of the team who attended the NADAB meeting
10 are gaining the ear of senior leadership and
11 articulating this finding. Although the
12 board's recommendation is probably not the
13 way Lilly typically does business, I do
14 believe they made a very strong point that
15 unless we come clean on this it could get
16 much more serious than we might anticipate."
17 Do you see that language,
18 sir?
19 A. I do.
20 Q. And you were informed of that
21 language, were you not?
22 A. I was informed of the
23 meeting.
24 Q. Well, and you were informed
283: 1 of this particular, these statements by
2 Mr. Brodie, correct?
3 A. I have to trace the string of
4 e-mails. I'm looking at this particular
5 e-mail. I really have no idea what he was
6 talking about. I mean, we --
7 Q. Well, if you can turn to the
8 prior page, it would appear, and we've had
9 prior testimony on this subject as well, that
10 the e-mail just before that was from Robert
11 Baker to Charles Beasley and you with copies
12 to Christopher Bomba, Patrizia Cavazzoni, and
13 Suni Keeling. And as you can see, at the top
14 of the next page it says "forwarded by Robert

Baker."

It appears that Robert Baker took that e-mail from Thomas Brodie and he forwarded it on to you and Charles Beasley with copies to those other folks; isn't that correct?

A. That appears to be the case.

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285:20 Q. Okay. And when you saw the language in there that this group of endocrinologists "are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes" and "I can
286: 1 only hope that you and all of the team who attended the NADAB meeting are gaining the ear of senior leadership and articulating this finding," did you, in fact, communicate this to your superiors, this feedback that you'd received from endocrinology consultants?

MR. BOISE: Object to the form of the question.

THE WITNESS: So the question is what?

MR. SUGGS: Did you pass on, did you contact your superiors about this information you received from Dr. Baker?

A. Well, first of all, I think that I would be considered senior leadership. So, for the mere fact that it was being brought to me would be getting the ear of senior leadership.

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287:12 Q. Sir, when you received this information in this e-mail that this group of endocrinologists was telling you that Lilly needed to come clean on this and that he hoped that those who attended the meeting are gaining the ear of senior leadership and articulating this finding, did that cause you any concern?

MR. BOISE: Object to form.

A. The "come clean" comment to me -- I have no idea what that person was thinking about.

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290: 4 Q. You talked to Dr. Tollefson about this information you received, correct?

A. We talked nearly daily when we were both in the office. I can't recall

sitting down with Dr. [redacted]ilefson and having an exact conversation about this topic. I assume we did because these are the kinds of things we talked about in our frequent communications.

Q. Okay. Directing your attention to the e-mail preceding the one from Mr. Baker, pardon me, the one from Mr. Brodie, the one at the bottom of Page 3 which starts off by saying, "FYI: My take was that this board of academic endocrinologists was impressed enough by the magnitude of weight gain and number of reports in the spontaneous adverse event database, that they were predisposed towards skepticism to any analysis that did not find higher hyperglycemia rates on olanzapine than comparators."

I read that correctly, right?

A. Yes.

Q. And that's, essentially, the same kind of concern or lack of belief that was expressed by one of the reviewers of your paper. Do you recall that?

A. I recall that. But I again

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Q. Can I direct your attention to Page 2. This is an e-mail in the same chain from Dr. Beasley to you with copies to Robert Baker, Paul Berg, Scott Clark, John Holcombe, Roland Powell, Alvin Rampey and Roy Tamura, correct?

A. Yes.

Q. And in his second paragraph he says, "These guys were really concerned about the weight gain. Not only because of a diabetes risk but all of the other potential health risks."

Do you see that language?

A. Yes.

Q. And what other potential health risks are there as a function of weight gain?

A. Well, one would first have to qualify weight gain as excessive weight or obesity as opposed to mere weight gain. If we're talking about obesity, then there are other health risks, cardiac, et cetera.

Q. Well, when you got this e-mail from Dr. Beasley where he said these guys are really concerned about the weight gain not only because of diabetes but all the other potential health risks, did you have anything in your mind as to what Dr. Beasley was referring to?

A. I'm not quite sure. I don't understand the question.

Q. Or were you scratching your

head when you got this e-mail from Dr. Beasley where he talked about all the other potential health risks or did you know what he was talking about?

MR. BOISE: Object to form.

A. Maybe I misunderstood your previous question. I thought you were asking me what are the other possible health risks of weight gain, and I qualified that to obesity, and I mentioned that there were other health concerns.

Q. Let's go on in Dr. Beasley's e-mail. He says, "They initially thought it might imply be a response to improvement in schizophrenia with a few outliers. A rather naive view but they ain't shrinks. When they understood that this is seen in nonpsychotic normals and animals on fixed diets, less concerned with animals, and that olanzapine is the worst offender other than clozapine, they advocated a different marketing strategy than we are taking."

Do you see that language?

296: A. I do.

Q. And did you inform Dr. Tollefson of that?

A. Again, we had frequent and ongoing discussions about this topic.

Q. So you believe you would have told Dr. Tollefson about that?

A. Yes.

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296:23 bet-the-farm comment, when you get comments
24 from outside experts that are experts in the
297: 1 field of diabetes and they're telling you
2 that you ought to be using a different
3 marketing strategy than what you're engaged
4 in, and this is one of your top selling
5 drugs, wouldn't you expect that Dr. Tollefson
6 would have informed the top levels of the
7 company about that?

MR. BOISE: Object to the form of the question. Calls for speculation.

A. There was broad knowledge across the company of the weight gain profile of Zyprexa.

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299: 2 Q. Okay. Let's go on in the
3 e-mail from Dr. Beasley. He says, "They
4 believe we should aggressively face the issue
5 and work with physicians to address methods
6 of reducing weight gain."
7 Do you see that language,
8 sir?

A. Yes.
Q. And, in fact, Lilly was telling physicians, outside physicians, that weight gain with Zyprexa was manageable; isn't that correct?
A. Again, we had many, many, different channels of communication on weight gain to the prescribing community.

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302: Did Lilly tell physicians that weight gain with Zyprexa was manageable for most patients?
MR. BOISE: Object to the form of the question.
A. I don't recall that exact phrase.

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302:Q. If I could direct your attention back to Dr. Beasley's e-mail. Three lines up from the bottom he says, "There does not seem much to say about scientific analyses of weight gain. We know it's a weighty problem. When you translate 1 to 2 percent gain of 40 plus kilos into the absolute number based on 5 million patients, the number is 50 to 100,000. 100,000 people
303: putting on 90 pounds of weight is a lot." Were you aware of that type of calculation before Dr. Beasley mentioned it in this e-mail to you?
A. I knew there was a distribution of weight gain. And knew, again we talked about the tails of a bell-shaped curve.
Q. And you recall this morning I asked you whether you were aware that Dr. Beasley had done calculations indicating that there were some people who gained 80 to 90 pounds of weight and you said you didn't recall that?
MR. BOISE: Object to the form.
A. I'd need to refresh that transcript.
Q. Okay. Well, does this refresh your recollection that Dr. Beasley, had, in fact, calculated on the order of 50 to 100,000 people gaining 90 pounds of weight while using Zyprexa?
A. I don't doubt the statistics.

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309:16 Q. If I could direct your
17 attention to Page 3. At the very top of the
18 page it starts off by saying "On the diabetes
19 side the concern was about the use of
20 categorical analyses."
21 And I believe you told me
22 that you weren't sure who had suggested the
23 use of categorical analyses of your blood
24 glucose data; is that correct?
310: 1 A. Again, my assumption would be
2 that Charles Beasley working with
3 endocrinology colleagues.
4 Q. Okay. And then if you could
5 drop down about two-thirds of the way through
6 that paragraph there's a sentence that says,
7 "They specifically referred to the data as
8 being 'tortured'." And the word tortured is
9 in quotation marks. Do you see that? The
10 word tortured is at the far left margin.
11 A. I see it, um-hum.
12 Q. And the "they" who are
13 referring to the data being tortured were the
14 outside consultants, correct? That was your
15 understanding?
16 A. Um-hum.
17 Q. Did that surprise you when
18 you learned from Dr. Beasley that the outside
19 consultants felt that the data was being
20 tortured?
21 MR. BOISE: Object to the
22 form.
23 A. I don't recall having any
24 particular reaction.

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312: 8 The last paragraph of
9 Dr. Beasley's e-mail states, "With
10 regard to the marketing side of this issue of
11 impaired glucose tolerance/diabetes the
12 message was clear, don't get too aggressive
13 about denial. Blaming it on schizophrenia or
14 claiming no worse than other agents, until we
15 are sure of the facts and sure that we can
16 convince regulators and academicians. WL
17 with Rezulin was the example. Sounds exactly
18 like what Dan Casey was saying."
19 Do you see that reference?
20 A. Yes.
21 Q. And the reference to "WL" is
22 Warner Lambert; is that correct?
23 A. I assume so, yes.
24 Q. Okay. And this Dan Casey
313: 1 that's referred to there, is that the same
2 Dr. Casey who back about a year earlier in
3 November of 1999 presented data showing that
4 18 percent of people who used Zyprexa had
5 diabetic levels of blood glucose that
6 previously had been normal after using the
7 drug for four months?
8 MR. BOISE: Object to the

form.
Q. **Is it the same doctor?**
A. I believe it's the same doctor but I can't accept the statement that you made of the 18 percent.
We -- I already commented on that dataset and qualified it as not being a dataset that we could draw those kinds of conclusions.

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314:15 Q. **When Dr. Beasley here is saying "Sounds exactly like what Dan Casey was saying," was Dr. Casey also saying don't get too aggressive about denial?**
A. What I recall Dan Casey saying, and what I agree with in this paragraph, is be sure, get it right, don't go out with data or messages that are not substantiated by the data, and be cautious. That to me is the Lilly way.
315: 1 Q. **So, clearly you were under the impression these outside consultants were saying don't be too aggressive, correct?**
MR. BOISE: Object to the form.
A. Don't get too aggressive about denial.
Q. **"Blaming it on schizophrenia or claiming no worse than other agents until we are sure of the facts."**
A. So the aggressive piece here, according to Charles, was don't get too aggressive about denial. I think that being energetic, he liked the word "aggressive." In terms of the science and the analyses is something I suspect they would support.
Q. **In fact, sir, Lilly was very aggressive about marketing Zyprexa after October of 2000, correct?**
MR. BOISE: Object to the form of the question.
A. Again, as I stated earlier, I didn't perceive any difference in our approach to Zyprexa before versus after that
316: 1 time period.
Q. **You were equally aggressive both before and after that meeting with the consultants, correct?**
MR. BOISE: Object to the form.
A. I wouldn't characterize it as being aggressive.
MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 4968.
(Whereupon, Plaintiff's Exhibit(s) 4968, previously marked, was presented to the witness.)

MR. SUGGS: For the record, this is a multi-page document entitled "Zyprexa Diabetes Update." I'll also represent to you that the database produced to us by Eli Lilly dates this document as February 9, 2001.

QUESTIONS BY MR. SUGGS:

Q. And if I could direct your attention to Page 3, sir. The title at the top of that page is Hyperglycemia/diabetes U.S. Situation Analysis.

Do you see that page?

A. Yes.

Q. And in the middle of that page there's a heading with two bullet points under it that says "Lilly Actions in 2000."

Do you see that?

A. Yes.

Q. And it states, "DTP efforts across 4K consultants triple DTP spend."

I'm going to translate that from Lilly language to plain everyday English. DTP stands for direct-to-physician, correct?

A. I believe that's what it refers to.

Q. And 4K refers to 4,000, correct?

A. I would also agree with that.

Q. And the consultants that are referred to there are consultants that Lilly would hire to make presentations regarding Zyprexa, correct?

MR. BOISE: Object to the form.

A. I don't know that that's what it's referring to.

Q. Wasn't that what the direct-to-physician -- what was your understanding of what DTP or direct-to-physician marketing entailed?

A. Quite frankly, don't know what direct-to-physician means.

Q. Sir, isn't it a fact that that involved hiring outside physicians to speak to other physicians at presentations and seminars about Zyprexa?

A. I've heard the term, but I don't know what it is.

Q. In your Zyprexa Product Team, at least through 2002 or up to 2002, you had responsibility for supervising both the medical side and the marketing side, correct?

MR. BOISE: Object to the form.

A. We had on the Zyprexa Product Team a global marketing component and a R&D component.

Q. And you're telling us that you don't know what DTP meant?

A. That's correct.

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Q. Let me direct your attention to the following page, Page 4.

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Q. At the top of the page it says, "'Comparable rate,' slides in all DTP programs (SCC, CME advisory, et cetera) consistent with Accelerate Zyprexa/Blunt Pfizer strategy." Do you see that language, sir?

A. I do.

Q. And "comparable rates" refers to the message that the rate of hyperglycemia with Zyprexa was comparable to the rates of hyperglycemia with other atypical drugs, correct?

A. That's correct.

Q. Okay. And that was the position that Lilly was taking in 2000 and 2001, correct?

A. Yes. And at that time, that was the best interpretation of the data.

Q. And Lilly was stating that position despite the fact that the outside consultants in October of 2000 were saying "don't get too aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents," correct?

A. Again, what I took from that consultation was to don't stop looking. Keep -- do the recommended additional analyses. And we accepted their recommendations and conducted those.

So what I heard them say was, you know, there may be more to this story, continue to look, consider different analyses, et cetera, and that's what we did.

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Q. Sir, I'd like to explore some more with you about what the company was telling doctors about weight gain and diabetes.

MR. SUGGS: I'm going to hand you what has previously been marked as Plaintiff's Exhibit 1110, and also Plaintiff's Exhibit 1111.

(Whereupon, Deposition Exhibit(s) 1110, 1111, previously marked, was presented to the witness.)

MR. SUGGS: And I'll represent to you that these

documents are dated in the database that was provided to us by Lilly as November 2001 -- actually, Exhibit 1110 is dated 11/29/01 and Exhibit 1111 is dated 11/28/01.

And I'll also represent that these documents came, again according to the database, from the files of Matthew Pike.

QUESTIONS BY MR. SUGGS:

Q. Do you know who Matthew Pike is, sir?

A. I don't recall Matthew Pike.

Q. Matthew Pike, I'll represent that he was in the Issues Management group that reported to Denice Torres. Does that ring any bells?

A. I'm not recalling that name.

Q. In November of 2001, Denice Torres reported to you in the Zyprexa Product Team; is that correct?

A. Yes.

Q. If I could direct your attention first to Exhibit 1110, the one on weight gain. In particular, the second page. There are several headings there. The first one is "Issue" and the second one is "Our Position." And under "Issue," the first bulleted point states, "Weight gain remains the No. 1 liability of Zyprexa and is leading to many of the new issues surrounding the drug -- diabetes, lipids, et cetera."

Do you see that?

A. Yes.

Q. And were you aware in November of 2001 that weight gain remained the No. 1 liability of Zyprexa?

A. I wouldn't necessarily use those terms, but that was a significant side effect for some patients, and it was an area of substantial focus.

Q. And then below that issue is a heading titled "Our Position." And Our Position was, "Weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers. For most patients, this can be managed allowing him to receive the overwhelming benefits Zyprexa offers."

Do you see that language?

A. Yes.

Q. And were you aware that that was Lilly's position in 2001?

MR. BOISE: Object to the form of the question. Foundation.

A. You know, I'm reading the words on this page. I don't know precisely what was intended or meant here. We were heavily investing in management approaches to weight gain and getting data that some of them were successful for some patients, and this may well have been referring to that work.

Q. Sir, this statement in the

physician section here that, "For most patients this," referring to weight gain, "can be managed allowing them to receive the overwhelming benefit Zyprexa offers."

That was just spinning the data, wasn't it?

MR. BOISE: Object to the form. Argumentative.

A. No.

Q. If I could direct your attention to the second page, pardon me, the following page on Page 3. There's a section in there about "Marketplace Feedback" and some bulleted items. And in the middle is a quote stating, "It is laughable when Lilly comes in and tries to talk about weight gain."

Do you see that?

A. I do.

Q. Were you informed that the market research was that doctors were saying it was laughable when Lilly comes in and tries to talk about weight gain?

MR. BOISE: Object to form. Foundation.

A. This sounds like the quotation of one individual. It was not my impression that that was generally held. We, again, were quite active in our transmission of data on this particular topic. My general sense was that people were impressed with the work that we were doing.

Q. If I could get you to direct your attention to Page 4. There's a heading towards the bottom saying "What We Don't Know." The last bullet point in that section states, "Knowing that weight loss programs only work approximately 5 percent of the time in normal volunteers, does Lilly want to provide a program where if it doesn't work it may be looked at as another 'laughable attempt?'"

Do you see that language, sir?

A. Um-hum.

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Q. Sir, if weight gain -- if weight loss programs only work approximately 5 percent of the normal time in volunteers, how could weight gain for most patients be managed?

MR. BOISE: Object to the form. Argumentative.

A. I'm not prepared to accept this 5 percent. I don't know who authored this document. I don't know what the resource was or their knowledge base. I'm familiar with the studies that we conducted on interventions. Again would state that for

some patients the interventions were quite helpful and for other patients they were not.

Q. Sir, for most patients they were not, correct?

MR. BOISE: Objection to form. Foundation.

A. We'd have to look at each study one at a time.

Q. If I could direct your attention to Exhibit 1111. This is the one that has the title "Diabetes." In particular, if I could direct your attention to Page 4. There's a heading at the bottom that says "What We Don't Know." And the second point there of "What We Don't Know" was "How to effectively deal with the weight gain associated with Zyprexa."

Do you see that?

A. I'm reading the page.

A. I see that.

Q. Sir, if you didn't know how to effectively deal with the weight gain associated with Zyprexa, then it would be a falsehood to tell doctors that for most patients weight gain's manageable; isn't that correct?

MR. BOISE: Object to the form of the question. Foundation. Argumentative.

A. I'd have to raise the same concern with this document that I raised with the weight gain document. I don't know who authored this, I don't know what the source of the information was, I don't know -- for example, is this an early draft, is it one person's opinion, or what it was.

I will again indicate that we had a number of different interventions for weight gain. For some patients they were helpful, for other patients they were not.

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Q. Those two statements are mutually incompatible, correct?

MR. BOISE: Object to the form of the question.

A. I mentioned earlier today that I did not know and cannot confirm that Lilly was telling doctors that weight gain could be managed for most patients.

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Q. Sir, are you going to deny to the jury that Lilly told doctors that weight gain was manageable for most patients? Wasn't that, in fact, a central part of your marketing pitch in 2000, 2001, 2002, 2003?

MR. BOISE: Object to the form of the question. Foundation. Argumentative.

A. Again, I'll say that I don't know that that was the case. I can speak, again, to the data. I've already reiterated that.

There were a number of different studies that were conducted to look at interventions, and some of them were effective and some of them weren't.

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Q. If I could direct your attention to the second page of Exhibit 1111.

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Dropping down to the next heading there regarding Our Position. It states, quote, "Diabetes/hyperglycemia may occur in patients taking antipsychotics and/or mood stabilizers including Zyprexa at comparable rates with the possible exception of clozapine."

Do you see that, sir?

A. Yes.

Q. And you were aware and, in fact, endorsed that as Lilly's position, correct?

MR. BOISE: Object to the form. Mischaracterizes his testimony.

A. This is an accurate statement of the data.

Q. And you endorsed that position, correct?

MR. BOISE: Object to the form.

A. Yes.

Q. Okay. And then below that at the very bottom of the first page is the "Rationale For Position" and it states, "Showing that diabetes is a common occurrence for all antipsychotics and not just Zyprexa will help reduce the perception that diabetes is linked specifically to Zyprexa and, in turn, will help to eliminate this risk from the risk/benefit equation."

Do you see that, sir?

A. I do.

Q. And were you informed that at least the marketing department viewed that as a rationale for the position?

MR. BOISE: Object to form. Foundation.

A. I am, again, going to say that this is an isolated point. I don't know

where it came from. There's elements of this statement that are not something I would agree with and are not consistent with my view of the data.

Breier, Alan M.D.(January 11, 2007)

345:11 Q. I'd direct your attention to
12 Page 4 of this exhibit. There's a heading
13 there entitled "What We Know." First bullet
14 point says, "Olanzapine does cause modest
15 elevations in mean random glucose."
16 Do you see that language?
17 A. Um-hum.
18 Q. And physicians were never
19 told that, were they, sir?
20 MR. BOISE: Object to the
21 form. Foundation.
22 A. Again, this is misleading,
23 it's not accurate, and I can't -- I can't
24 support it.
346: 1 Q. And you would agree with me,
2 sir, that treating physicians were never
3 warned by Lilly that "Olanzapine does
4 cause modest elevations in mean random
5 glucose," correct?
6 A. There is no data to support a
7 cause-and-effect relationship.
8 Q. Sir, again, that's not
9 responsive to my question. I need a direct
10 answer to my question.
11 Lilly never told
12 prescribing physicians that
13 "Olanzapine does cause modest elevations of
14 mean random glucose." Whether you think
15 that's true or not, the fact of the matter is,
16 Lilly never told doctors that, correct?
17 MR. BOISE: Object to the
18 form of the question.
19 A. Our marketing message
20 followed the scientific understanding of the
21 data.
22 MR. SUGGS: Sir, can you
23 please just listen to my question
24 and answer it directly.

Breier, Alan M.D.(January 11, 2007)

347: 9 Q. Sir, Lilly never told
10 treating doctors that olanzapine does cause
11 modest elevations of mean random glucose?.
12 MR. BOISE: Object to the
13 form of the question.
14 Q. True or not?
15 A. Correct.

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Q. If you go to the third bullet point, it states, "Glucose elevation partially accounted for by weight gain."
Do you see that language?
A. I see it.
Q. Physicians were never advised of that, were they, sir, by Lilly?
A. It's not supported by the data. Again, we looked at that very carefully. So I -- we talked about this earlier today, and those data are not supported.
Q. Well, sir, isn't it true Dr. Beasley wrote you a memo in February of 2001 in which he specifically said these increases, pardon me, these changes are accounted for in part but not entirely by weight increase? Do you recall that?
MR. BOISE: Object to the form. Mischaracterizes the document.
A. I'd have to look at it.
Q. Well, independent of the document, before I hand it to you, do you recall that?
A. No.
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 5565.
(Whereupon, Plaintiff's Exhibit(s) 5565, previously marked, was presented to the witness.)
MR. SUGGS: For the record, this is a string of e-mails. The one I'm particularly concerned with, sir, is the one in the middle of the page, of the first page, from Charles Beasley to Ralf Dittmann with copies to you, Patrizia Cavazzoni, Mark Millikan, Anna Thornton and Gary Tollefson, Subject: Olanzapine and hyperglycemia, et cetera.

QUESTIONS BY MR. SUGGS:

Q. Do you recall receiving this e-mail from Dr. Beasley back in February of 2001?
A. I do.

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Q. And in this e-mail Dr. Beasley wrote starting in the third sentence, "Our continuous analyses show that olanzapine does result in statistically significant mean increases in random glucoses relative to placebo and haloperidol. No significant difference relative to Risperidone but power is small. Clozapine is associated with a larger

olanzapine versus haloperidol and a significant increase compared to haloperidol. These increases are occurring as early as week one. May not represent a true deterioration in glycemic metabolism but simply an increase in food intake since these are random and not fasting glucoses. These changes are accounted for in part but not entirely by weight increase."

Do you see that language, sir?

A. Yes.

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And my question is: Does this now refresh your recollection that Dr. Beasley told you that? That's my question.

A. And I would say yes at this one point in time, but in order to give you

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Q. I'd like to direct your attention to Page 6. There's a table there entitled Desired Evolution. Are you familiar with that?

A. I've not seen this before, no.

Q. It lists as an action step: "Drive in the minds of our customers that risk of developing diabetes is no different on Zyprexa than other agents."

You were certainly aware of that, weren't you?

A. Well, I was aware of the data that indicated that there were comparable rates among all atypical antipsychotic drugs.

Q. And the desired outcome for that action step was to "Lower the percentage of customers that directly linked Zyprexa with diabetes." Do you see that, sir?

A. Yes.

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Q. Sir, at least the language as stated in this document indicates that whoever wrote this, their desire was to get doctors so they didn't even think about diabetes with Zyprexa, and, in fact, took it out of the risk/benefit calculation; isn't that correct?

MR. BOISE: Object to the form. Compound.

A. No, that's completely inconsistent with our approach. We were very clear about the data. We were clear that there was a higher rate of diabetes in schizophrenic and bipolar patients. We had medical letters, slide sets, publications.

What I'm trying to address in this point is what is most critical is that prescribers have an accurate understanding of the information, and through multiple different approaches we strove to achieve that.

Q. Sir, you just denied that it was the approach of Lilly to have physicians take diabetes out of the risk/benefit calculation. Can I direct your attention to Page 2 of this document? And you see at the bottom of that page there's a Rationale For Position?

A. Um-hum.

Q. Can you read that aloud for the jury, please?

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A. "Showing that diabetes is a common occurrence for all antipsychotics and not just Zyprexa will help reduce the perception that diabetes is linked specifically to Zyprexa, and in turn, will help to eliminate this risk from the risk/benefit equation."

Exhibit 5
Alan Breier, M.D.

Q. Doctor, do you recall in 2002 the Japanese regulatory authority required Lilly to drastically change their warning and issue an emergency safety information letter to Japanese physicians warning of the risk of diabetes with Zyprexa?

A. In April of 2002, there were label changes to the Japanese label for Zyprexa that included a warning and a letter to doctors.

MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 320.

(Whereupon, Plaintiff's Exhibit(s) 320, previously marked, was presented to the witness.)

MR. SUGGS: For the record this document has a cover page which states Appendix Six, Japanese Dear Doctor Letter.

QUESTIONS BY MR. SUGGS:

Q. And, sir, do you recognize this as a translation of an emergency safety information letter that Lilly issued to Japanese physicians in April of 2002?

A. Yes.

Q. Okay. And in the actual letter, am I correct that the border that appears to be black on this black and white copy is, in fact, red?

THE WITNESS: In Japan?

MR. SUGGS: Yes. In the original letter that went to Japanese physicians.

A. Yes, that is their practice.

Q. Okay. And the heading at the top of the letter says "Important" in the upper left-hand corner and then in big bold letters right at the top says "Emergency Safety Information," correct?

A. Yes.

Q. This is definitely designed to get the attention of physicians in Japan, correct?

A. Yes. That's the purpose of a communication to prescribers.

Q. And in fact, it did definitely get the attention of physicians in Japan, correct?

MR. BOISE: Object to the form.

A. Physicians in Japan were aware of this warning and of the data.

Q. And Zyprexa sales went dramatically down after physicians in Japan received this label; isn't that correct?

A. I don't recall the sales trends after this was issued.

Q. Sir, don't you recall writing a memo about those sales trends to

Mr. Lechleiter?
A. Sitting here today, I don't recall that.
Q. Okay. We'll go into that in some more detail later.
Let's talk about this "Dear Doctor Letter" or this Emergency Safety Information Letter that went out. This was done at the order of the Japanese regulatory authorities by Lilly, correct?
A. Yes.
Q. Thank you. This was not something Lilly wanted to do. Lilly was ordered to do this by the Japanese regulatory authorities, right?
MR. BOISE: Object to the form of the question.
A. The issue of wanting or not wanting is not relevant. The Japanese regulatory authorities directed us to send this letter out, and we complied with that direction.

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Q. You objected to having to do this, and the regulatory authorities listened to what you had to say and then directed you to issue this letter to physicians in Japan, correct?
A. On the merits of the small number of cases that they were citing, the fact that those cases were confounded and an extensive worldwide literature, we felt that this action was not warranted. They disagreed, and we complied with their direction.
Q. And at this point in time in Japan there had been nine serious cases including two cases of death with hyperglycemia, diabetic ketoacidosis, and diabetic coma that had been reported in Japan. Correct?
A. That is correct.

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Q. And worldwide, Lilly was aware of hundreds of reports of hyperglycemia and diabetes by April of 2002; isn't that correct?
A. There were a number of spontaneous adverse event reports of a variety of different occurrences similar to the ones that we're talking about here that were, again, thoroughly reviewed, assessed for confounds, and presented to all the regulatory agencies around the world, including the Japanese regulatory agency.

Q. In the middle of the first page of this emergency safety information letter is a black box. Well, it appears to be black. Was it also bordered in red or was it actually in black, if you recall?

A. I don't recall.

Q. Okay. It has in some rather large font and bold print three principle points; is that correct?

A. There were three numbered points in the box.

Q. Okay. And the first one states "Do not administer to patients with diabetes mellitus and those who have a history of diabetes mellitus," correct?

A. That's correct.

Q. And in the United States, at least, Lilly was not taking the position that Zyprexa should not be used with patients having diabetes, correct?

A. Our view of the science was that the science did not support a contraindication for diabetes.

Q. You used the term there "contraindication." That's a term of art in the pharmaceutical industry, correct?

A. In the regulatory, in the regulatory world.

Q. Okay. And basically what it means is if there is a contraindication in the label, it means do not use this product for this particular type of patient or this particular type of illness or whatever, correct?

A. That's correct. Whatever is specified in that contraindication, you're correct.

Q. So, the Japanese regulatory authority was making diabetes a contraindication for the use of Zyprexa, correct?

A. Correct.

Q. Okay. Diabetes was not a contraindication in the United States, correct?

A. It was not a contraindication at this time, nor is it a contraindication today, and, frankly, I'm not aware of there being a contraindication for diabetes any other place in the world.

Q. Okay. Point No. 2 in the Japanese Emergency Safety Information Letter was "During administration of this product" -- this is an English translation -- it says, "observe sufficiently with such as measurement of blood glucose." And I realize it's --

MR. BOISE: Those are your words, Mr. Suggs.

MR. SUGGS: Well, actually, it's whoever translated this for Lilly.

Q. Was it your understanding that the Zyprexa label in Japan instructed physicians to conduct glucose blood testing of patients who were using Zyprexa?

A. Yes. They were directing physicians to monitor for the occurrences of potential diabetes and to do so with blood monitoring.

Q. And did it specify a schedule for conducting such testing?

THE WITNESS: Let me take a look further into the document.

A. I don't see an exact schedule here. I'll share with you my recollection, but I'm sure there would be a way to refresh this if I'm not completely accurate.

What I recall was that there was direction to monitor that would include but was not exclusive of blood monitoring.

I recall there being recommendations to take a blood glucose at the initiation of treatment, but I don't recall there was specificity around the frequency or the number of blood draws that would occur after treatment.

I also recall that Lilly partnered with the agency to assess this topic following these directions to try to refine guidance on blood monitoring. And that's my best recollection.

Q. Okay. It's fair to say that the situation with respect to the Zyprexa label in April of 2002 was as follows then: In the European labeling there was discussion of diabetes and hyperglycemia in the special precautions and special warnings section of the labeling and such discussion had been there since July of 1999; is that correct?

A. The European label does not have a separate warnings and a separate precautions, it's all inclusive so there's warnings and precautions. And you're correct that in 1999 there was information put into that section.

Q. And then we also had the warnings in Japan that we've just discussed, correct?

A. That's correct.

Q. But in the U.S. there was no language in either the warnings or the precautions section about diabetes or hyperglycemia, isn't that correct, in April of 2002?

A. At that time that is correct.

Q. Okay. Now as the head of the product team, did you have discussions within the company after the Japanese label change in April of 2002 as to whether or not Lilly should voluntarily change the U.S. label to include a warnings or precautions section

about the risk of diabetes?
A. Because the approach to labeling varies from country to country, there's different practices and philosophies of labeling, we felt confident that we were accurately labeled in the U.S. at that time.
I will say that part of our practice was continual assessment of regulatory issues, labeling issues, multiple different issues. So that we would be having discussions about, and challenging ourselves was part of the practice on the team. But I can tell you as head of the team at that time we were confident that we were appropriately labeled in the U.S.

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question first. What's the policy committee at Lilly?
A. There's a number of different governance committee and committees that work on policy.
THE WITNESS: I will assume that you're referring to the corporate policy committee; is that correct?
MR. SUGGS: Yes.
A. If that's the case, that would be the primary governance committee in the company.
Q. **And who are the members of that policy committee?**
A. The chair of the committee is Sydney Taurel, and depending on what time period we're talking about, there would be different representation.
Q. **Say, April of 2002?**
A. I will attempt to give you my recollection of the membership at that time, understanding that at certain points people retire and other people assume positions.
At that time, I would -- my recollection is that John Lechleiter would have been a member, Gus Watanabe, perhaps Gerhard Mayr, Ms. Goss, Pedro Granidio, and there may have been a few more and I'm not recalling them at this moment.

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MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 4051.
(Whereupon, Plaintiff's Exhibit(s) 4051, previously marked, was presented to the witness.)
MR. SUGGS: For the record

this is a four-page document. The cover page states Policy Committee Meeting April 12, 2002, Zyprexa Safety Overview. And it has some handwritten notes on the front page.

QUESTIONS BY MR. SUGGS:

Q. First of all, do you recall, sir, that there was a policy committee meeting which was given a Zyprexa safety overview in April of 2002?

A. Prior to looking at this document, I don't recall that specific date.

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Q. And was Sydney Taurel, the chief executive officer, was he usually present at these policy committee meetings?

A. Yes.

Q. And was John Lechleiter usually present at those policy committee meetings also?

A. Yes.

Q. Okay. And at these policy meetings, was it the usual practice to give a presentation regarding the safety of Zyprexa when Zyprexa was discussed?

MR. BOISE: Object to the form of the question.

A. The topics would vary. So it would depend on the particular theme that the policy committee was either interested in or we felt was important to present to them.

Q. Okay. And who would give the presentation to the policy committee regarding Zyprexa?

A. The format of that meeting was a relatively brief preread. And then --

Q. Can I interrupt you for a second? What do you mean by "preread"?

A. A short text of the topic at hand.

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Q. Okay. With that background in mind, if I could direct your attention to Exhibit 4051, and does this appear to be a preread that you referred to?

A. It appears to be.

Q. Okay. And who would have prepared the Zyprexa safety overview?

A. I don't have a recollection of who prepared this particular document. Given the nature of the document, I'm going to venture that it was likely physicians that worked on Zyprexa, scientists that worked on Zyprexa, members of the Zyprexa Product Team, perhaps other scientists as well.

Q. Okay. Who were the likely candidates for having a hand in that?
A. At this time myself, Patrizia Cavazzoni, Charles Beasley, are people who likely could have worked on this.
Q. Okay. I'm presuming that since this -- the members of the policy committee were all upper level executives, correct?
A. Yes.
Q. I'm assuming that in the preparation of these types of prereads that you would take care to make sure that things were stated accurately, correct?
A. Strive to do that.

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Q. Okay. If I could direct your attention to the second page. In the introduction section, in the second to last sentence it states, "A side effect that is associated with Zyprexa is weight gain and the sequelae of weight gain."

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Q. Okay. And what, the word sequelae is a medical term, is it not?
A. It is used in medicine.
Q. And when it's used in medicine it means the results of or the effects of something, correct?
A. I would say may be associated with.

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Q. Okay. If I could direct your attention to the section on clinical data. There's a section there for weight gain that says, "Five atypical antipsychotic agents are associated with more weight gain than most traditional neuroleptic agents in the following order, most to least, Clozaril greater than Zyprexa greater than Seroquel greater than Risperdal." And then below that it says, "Zyprexa weight gain is roughly twice that of Risperdal;" is that correct?
A. You've read that correctly.
Q. And was that conclusion on the basis of studies that had been conducted by Lilly or was that an analysis of other data?
A. This would represent a combination of the available data at the time. So that would include Lilly data, but

10 it would also include other sources of data.

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425:21 Q. "It also notes that Pfizer's
22 Geodon and aripiprazole --
23 MR. SUGGS: Is that how you
24 pronounce it? Probably, not. You
426: 1 can pronounce it.
2 THE WITNESS: Aripiprazole.
3 QUESTIONS BY MR. SUGGS:
4 Q. "Aripriprazole appear to have
5 less metabolic issue than other atypicals."
6 Have I stated that correctly?
7 A. You've read those words
8 correctly.
9 Q. And that's a reference to
10 other atypical antipsychotic drugs, correct?
11 A. The term "atypicals" is
12 referring to other atypical antipsychotic
13 drugs, that's correct.
14 Q. And Geodon and aripiprazole
15 are two other atypical antipsychotic drugs,
16 correct?
17 A. That's correct.
18 Q. And they had less weight gain
19 than the four drugs that were listed above,
20 and they had, appear to have, less metabolic
21 issues than those drugs, correct?
22 MS. JOBES: Object to
23 foundation.
24 A. My assumption, what's been
427: 1 referred to by metabolic issues is weight
2 gain because it's under a section called
3 Weight Gain and the available data on these
4 newer drugs was, primarily, related to weight
5 gain.

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428:11 your opinion, I'm asking for fact. The
12 Zyprexa label did not inform physicians that
13 Zyprexa weight gain was roughly twice that of
14 Risperdal, correct?

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428:22 as regarding to the label, you are correct.

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429:14 Q. If I could direct your
15 attention to the next section in this
16 document that pertains to diabetes. And
17 there are a number of bullet points below

that heading. And in particular, I direct your attention to the third bullet point. You see where I'm indicating, sir?

A. Yes.

Q. Okay. And the first sentence there states, "Results of two Lilly epidemiology studies, analysis of AdvancePCS and GPRD databases, indicate that the risk of DM is increased in patients treated with antipsychotics including Zyprexa."

And the DM that's referred to there is diabetes mellitus, correct?

A. That is correct.

Q. Okay. So Lilly had conducted two epidemiological studies which showed that the risk of diabetes is increased in patients treated with antipsychotics including Zyprexa, correct?

A. You've read that sentence correctly.

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Q. It is true, is it not, that Lilly's label in 2002 did not inform physicians in the warnings or the precautions section that results of two Lilly epidemiological studies showed that the risk of diabetes is increased in patients treated with antipsychotics including Zyprexa?

Yes or no?

A. The answer is no. And the

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Q. Dr. Breier, I'd like to direct your attention back to Exhibit 4051. In the bullet point just below the one we were talking about it states "FDA FOI Database of reports of DM cases: Clozaril 542, Zyprexa 434, Risperdal 244, Seroquel 57."

We need to do some translation of that into English.

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Q. "FDA," obviously, is the FDA, but FOI stands for freedom of information; is that correct?

A. Yes.

Q. And the reports of DM cases refers to report of diabetes, correct?

A. Yes.

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435:18 And then the number behind
19 the names of the various drugs there are the
20 number of diabetes adverse events that were
21 contained in the FDA's freedom of information
22 database; is that correct?
23 MS. JOBES: Object to
24 foundation.
436: 1 A. I believe you've read that
2 correctly.
3 Q. Okay. And did Lilly have
4 someone who would periodically check the FDA
5 database for adverse event reports of not
6 only Zyprexa but also other drugs as well?
7 A. Yes. And additionally, we
8 had our own before department that was
9 serving the environment as well.
10 Q. And part of the
11 pharmacovigilance department's function was
12 to do that type of accessing of the FDA's
13 database on adverse event reports?
14 MR. BOISE: Object to the
15 form.
16 A. They would have been doing
17 that as well.
18 Q. Okay. And this shows that
19 for Clozaril there were 542 reports of
20 diabetes, correct?
21 A. Yes.
22 Q. Okay. And Clozaril had been
23 on the market for some years longer than
24 Zyprexa, correct.
437: 1 A. Yes.
2 Q. Okay. Zyprexa had 434
3 reports of diabetes, and Risperdal had only
4 244, correct?
5 A. Correct.
6 Q. And Risperdal had also been
7 on the market longer than Zyprexa, correct?
8 A. That's correct. They were
9 registered at different times.

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437:15 Q. Am I correct that it's
16 generally assumed that the number of adverse
17 events that are reported are only a fraction
18 of what actually occurs because of
19 underreporting?
20 MR. BOISE: Object to the
21 form of the question.
22 A. You're correct in that all of
23 the cases that occur are not always reported.

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438:15 Q. It's often said the number of
16 events that are actually reported are only
17 the tip of the iceberg, one to ten percent,

in that range, correct?
MR. BOISE: Object to the form of the question.
A. Again, it's quite variable depending upon the condition, the drug. They may change over time depending on the kinds of information, for example, that might be in the public domain. So there's a variety of different factors that would impact reporting trends.

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There was no change in the U.S. label to add any warnings or precautions regarding diabetes or hyperglycemia in the United States in 2002, correct?
A. Correct.

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let me back up a second. Who is Bert van den Bergh?
A. Bert van den Bergh is an executive at Eli Lilly.

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Q. What was his position back in July of 2002?
A. He was President of Neuroscience and my boss.
Q. Okay. And do you recall traveling to Japan for four days in June of 2002 with Mr. van den Berg?
A. I do.
Q. And when you came back, you wrote a memo, you and Mr. van den Bergh wrote a memo to Dr. Lechleiter and Gerhardt Mayr and with a copy to Mr. Mascarenhas; is that correct?
A. I'm not recalling that specific, a specific message. When we returned from visiting Japan, we communicated notes about our trip. But I can't say I'm recalling a specific e-mail to the people that you mentioned.
MR. SUGGS: Okay. Let me show you a document that we'll have marked as Breier Exhibit 5.
(Whereupon, Deposition Exhibit(s) 5 duly received, marked and made a part of the record.)
MR. SUGGS: For the record, this is a three-page document dated July 1, 2002. It appears to be a

memo from Ber[illegible]van den Bergh and
Alan Breier to Dr. Lechleiter,
Mr. G. Mayr and Mr. A. Mascarenhas,
and it has beginning Bates No.
ZY203332491.
QUESTIONS BY MR. SUGGS:
Q. And did you, in fact, prepare this memorandum with Mr. van den Bergh on July 1, 2002?
A. I'm not recalling the preparation of this specific message. I see both of our names at the bottom, so I'm assuming that we both worked together on this communication.
Q. Okay. And I'm assuming that you and your boss, when you prepared this memorandum for Dr. Lechleiter and Mr. Mayr, would have taken care to be accurate in your reporting on your trip to Japan, correct?
A. We'd strive to be accurate.

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It appears that you went to Japan with Mr. van den Bergh from June 23 to June 27, 2002, correct?
A. That's correct.

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Q. And in the first paragraph of your memo you state in the second sentence, "It is clear that the impact of the label change in Japan has been very profound. We concluded that we have lost substantial ground and trust in our relationships with the MHLW."
And am I correct that MHLW are the initials for the Japanese regulatory authority?
A. You are correct.
Q. And your memo continues on to state, "Market research shows that we have also lost quite a bit of credibility with prescribers and opinion leaders. Basically they felt left in the dark with what they perceive as the late sharing of safety information. As a result, there has been a 75 percent drop in new patients who are being put on the drug and a continuing fairly high drop-out rate."
Did I read that correctly?
A. You've correctly read the words in the e-mail.
Q. And I'm assuming that that market research was conducted by Lilly, correct?
A. That would also be my assumption.

Q. Okay. And then if you could drop down to the third paragraph on the first page you state, "A further issue is team motivation and turnover in the sales organization and lack of trust, both from a sales force and a customer level. We have recommended, in line with the affiliate's proposal, to adjust promotional strategy to reflect the reality of the new label in Japan, enhance confidence by our message for the appropriate use of the product within the label, and point out how to specifically address concerns about hyperglycemia and the potential use of the product in patients with diabetes."

Do you see that language, sir?

A. I do.

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445:17 Q. And my question was, what did
18 you mean by use of the phrase "use of the
19 product within the label"?
20 A. The label had just been
21 changed to include a warning on hyperglycemia
22 and diabetes, as we had discussed. This then
23 would require the company to approach
24 customers in a different way, customers
446: 1 meaning, primarily, psychiatrists, in a
2 different way. And therefore, it was
3 essentially adapting the sales force approach
4 to psychiatrists with the new information.
5 So, how were they going to
6 present the new label change? What will that
7 mean for using the product? We talked about
8 blood monitoring, et cetera. So this
9 essentially was referring to the
10 implementation of the new label change.
11 Q. Well, when you use the
12 expression there message -- "enhance
13 confidence by our message for the appropriate
14 use of the product within the label," did
15 that mean that your sales force was going to
16 go out to the doctors and point out the
17 information that was in that letter that had
18 sent around and say, "Hey, docs, we're saying
19 here do not administer to patients with
20 diabetes mellitus and those who have a
21 history of diabetes mellitus, just as is in
22 the black box in the letter. And also,
23 during the administration of this product do
24 blood glucose testing. And also, you know,
447: 1 explain sufficiently to the patient and the
2 family members what the, about the possible
3 occurrence of serious adverse reactions
4 relating to diabetes."
5 Is that what you meant by the
6 message for appropriate use of the product
7 within the label?
8 MR. BOISE: Object to the

form of the question.
A. Yes. The sales force got specific direction to carry the new label language into the doctor's office to make sure the doctors were aware and understood the new directions in the label, the new content of the label. And at the same time, what this phrase was referring to is that yes, this is new information in the label, it's important that doctors understand it and respond accordingly, but at the same time to still be able to express confidence in the molecule. It's still an efficacious drug and has an important place in the care of schizophrenic patients.
Q. Okay. Now if I could direct your attention to the last page. About four lines up from the bottom of that last paragraph there, there is language which states, "There appears to be a decrease of glycemic AEs since the label changes."
Am I correct that AEs refers to adverse events?
A. You are correct.
Q. Okay. So by -- if the label change went into effect at the beginning of April of 2002, only April, May, June, three months would have expired between the time of the label change and the time you wrote this memo, correct?
A. Two months, something like that.
Q. Okay. Well, all of April, all of May, and all of June, three months, correct? And already --
A. I'm going to have to refresh my memory on precisely when the label change, when in April was the label change made and when was the actual communication of the label change to physicians.
I know it was April, but I don't recall if it was the end of April or the beginning, the middle of April and when the sales force actually began to carry the document out. But in that time frame.
Q. Okay. In any event, whether it was the beginning of April or end of April, we're still talking about a fairly short time period from when the label change was made to the time of your memo, correct?
A. It was approximately two months, two and-a-half months.

Even in the short span of time between when the Japanese label change was made and the date of your writing of this memo it appeared that there was a decrease in the number of hyperglycemia adverse events, correct?

MR. BOISE: Object to the form.
A. You've reflected that sentence accurately.
Q. Okay. And you, after stating that to Mr. Lechleiter, you then went on to say, "Again, we will make every effort through promotional efforts and physician-to-physician and medical communications to ensure that we promote the use of the drug within the label, which would by design dramatically reduce the number of events."
Did I read that correctly?
A. You did.
Q. And the events that are being referred to there were also adverse events, correct?
A. Yes.
Q. Okay. So it was your expectation that if your sales force went out and promoted the use of Zyprexa within the new Japanese label and told physicians "don't give this to patients with diabetes, test people's blood glucose, and explain this issue sufficiently to the patient and family members," that that would, by design, dramatically reduce the number of adverse events, correct?
MR. BOISE: Object to the form.
A. That is correct. And the

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Q. Do you recall being informed in June of 2002 that a clinical study by Lilly indicated that high nonfasting glucose in Zyprexa users was probably causally related?
MR. BOISE: Object to the form. Foundation.
THE WITNESS: I'm not understanding the question. Could you repeat it?
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 7802.
(Whereupon, Plaintiff's Exhibit(s) 7802, previously marked, was presented to the witness.)
MR. SUGGS: Which, for the record, is a one-page document Listing of Treatment Emergent Abnormal Lab Findings in Olanzapine-Treated Patients. This is from study HGFU.
QUESTIONS BY MR. SUGGS:
Q. Are you familiar with study HGFU?

A. I'm recalling that to be a bipolar trial that looked at olanzapine plus mood stabilizers.

Q. And if you could direct your attention to the laboratory value for glucose nonfasting. It shows that 2.2 percent of the people who got olanzapine had high glucose and 0 percent had, of the placebo group, had high glucose; isn't that correct?

A. Yes. What I'm reading is 185 patients on olanzapine plus mood stabilizer, of the 185, four, or 2.2 percent, is on the glucose nonfasting high line. And that then looks like it's being contrasted with 97 patients with mood stabilizer plus placebo with zero cases or 0 percent.

Q. Um-hum. And to the right on that line there's some letters, A -- you see those letters A?

A. I do.

457:1 Q. And if you could drop down to the bottom of the page there's a little legend describing what those letters mean. Could you read what it says for letter A aloud?

A. "Category: A equals event probably causally related."

Q. And did anyone inform you of that conclusion with respect to study HGFU?

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457:12 A. No. And I was, actually,

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458:16 Q. Did you know a Dr. Simeon Taylor?

A. I have a recollection of that individual.

Q. And what's your recollection of that individual?

A. My recollection is that he was an endocrinologist who joined Lilly. Worked at Lilly, I'm recalling, for a

459:1 relatively brief period of time and then left the company.

Q. And endocrinologists are types of doctors who specialize in the treatment of diabetes, correct?

A. They certainly can. Diabetes could be one of the conditions.

Q. An endocrinologist doesn't have to specialize in diabetes, but if somebody is specializing in diabetes, they're probably in the field of endocrinology, correct?

MR. BOISE: Object to the form.

A. I think that's a reasonably fair description.
MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 8666.
(Whereupon, Plaintiff's Exhibit(s) 8666, previously marked, was presented to the witness.)
MR. SUGGS: For the record this is a June 27, 2002, e-mail from Simeon Israel Taylor to a number of individuals.
QUESTIONS BY MR. SUGGS:
Q. And I would direct your attention in particular, sir, to the last two lines of -- well, actually, the last two sentences in the first paragraph of Dr. Taylor's e-mail in which he says, "However, I feel that we need to deal with the scientific facts, whatever they are. Ultimately, I expected a fair-minded, scholarly evaluation of the available data is likely to support several conclusions: 1, Zyprexa, like other members of the class causes weight gain; 2, like other causes of weight gain, Zyprexa-induced weight gain probably increases the risk of diabetes."
Do you see that language, sir?
A. Yes.
Q. And were you ever informed that Dr. Taylor had expressed those views?
A. I'm not recalling this specific e-mail.

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(Whereupon, Plaintiff's Exhibit(s) 995, 9201, previously marked, was presented to the witness.)
MR. SUGGS: And for the record, Exhibit 995 is a memo to the policy committee from Alan Breier, Jack Jordan, Mike Bandick, dated July 7, 2003. And Exhibit 9201 appears to be a letter by Dr. Alan Breier, the addressee is not listed there but we'll go over that.
QUESTIONS BY MR. SUGGS:
Q. Turning your attention first to Plaintiff's Exhibit 995. Do you recall

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was: Do you recall preparing this memorandum to the policy committee on or about July 7, 2003, as indicated?

A. I don't recall the preparation of this document. The content, however, of the document is information that I do recall.

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478:17 the -- well, direct your attention to the
18 bottom paragraph on the first page. It says,
19 "Our goal is to influence key stakeholders,
20 (clinicians, Lilly sales representatives,
21 patients, Wall Street, the media, Lilly
22 senior management, caregivers and thought
23 leaders) with the facts about diabetes
24 relative to the seriously mentally ill,
479: 1 Zyprexa, and other typical agents. Our
2 message." And then there are seven items
3 listed there, correct?
4 A. Yes.

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479:22 this way: Included in your message was the
23 Point No. 4 that "Data do not support a
24 causal link between Zyprexa and diabetes;
480: 1 while the scientific literature is mixed
2 there does not a appear to be significant
3 differences among atypicals." Correct?
4 A. You read that correctly, and

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480:10 Q. When you stated there that
11 there does not appear to be consistent
12 differences among atypicals, that was
13 referring to differences in rates of
14 hyperglycemia and diabetes, correct?
15
16 MR. BOISE: Object to the
17 form of the question.
18 A. That's my reading of that
19 item.
20 Q. And on the second page under
21 the heading Corporate Response Letter it
22 states, "On July 11 customers will begin to
23 receive the corporate response letter,
24 Attachment 1, a letter targeted to
481: 1 clinicians, delivered by their Lilly sales
2 representative. The letter is written on
3 behalf of Lilly and signed by Doctor Alan
4 Breier. Market research on the letter was
5 conducted July 2-3 and was very positive."
6 And my question to you, sir,
7 is Exhibit 9201 a copy of that letter that
8 was referred to in Exhibit 995?
9 THE WITNESS: Take a look at
10 this.
A. It appears to be the case.

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Q. Did you come up with the first draft of this letter?
A. My recollection is that I sent a voicemail that touched on some of these themes, but for internal use, and that that particular message was found to be helpful and that that then began sort of the thinking that perhaps then a different document or another document might be helpful.
So, as I recall, that was the genesis of this document. I don't recall if I actually wrote the first draft of this specific document.
(Whereupon, Plaintiff's Exhibit(s) 3909, previously marked, was presented to the witness.)
MR. SUGGS: Let me hand you what's been previously marked as Exhibit 3909, which is an e-mail dated -- well, it's an e-mail string but you started it off with one dated May 6, 2003, which then got forwarded on to Alan, pardon me, to Denice Torres, who then sent it to -- I'm assuming that's some marketing group within Lilly.

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Q. Is this e-mail that you're referring to here, is this that genesis that you were referring to?
A. Again, my recollection is that I sent a voicemail attempting to summarize some facts on this topic. I believe this might have been a transcript of that voicemail.
Q. Oh, okay.
A. And that then was found to be helpful in terms of particular context.
I think then that activity then led to some thinking that maybe a different kind of communication that also looked at important questions might be helpful for the external environment.

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Q. You made some gestures with your hands, and I want to track through and make sure I understand the process.
It's your recollection and understanding that you initially left a

lengthy voice mail discussing the issue of Zyprexa and diabetes. That, somehow that got converted into this e-mail that's reflected in Exhibit 3909?
A. I'm not a hundred percent sure, but that's my recollection.

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Q. Okay. And then the exhibit, the material that's in Exhibit 3909 became the basis for or the genesis for what then turned into the letter which we see reflected in Exhibit 9201; is that correct?
MR. BOISE: Object to the form.
A. What I'm recalling is that the approach I took in what I believe was a voicemail of posing a specific question, providing the scientific information, was found to be helpful. And that led to then the thought that a similar kind of format might be helpful to the external, to clinicians who might be having the same kinds of questions.

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Q. Okay. The letter, though, was clearly intended for marketing purposes. Because as you said, it was going to be distributed by sales reps to physicians out in the field, correct?

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MR. SUGGS: Exhibit 9201.
A. This was intended for doctors. It was intended to raise questions that we understood were on some of their minds and then provide scientifically-based answers to those questions.
Q. Okay. The format of your letter, Exhibit 9201, is, after the introductory paragraph, there are other paragraphs that lead off with a question in bold and then your response to that, to those questions, correct?
A. Yes.

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You start off in the initial paragraph of your letter, Exhibit 9201, by stating at the end of that paragraph,

"We believe it's in the best interest of patients to set the record straight." Correct?
A. You've read that correctly.
Q. And you intended for physicians to believe that what you were stating in here was the truth, the whole truth, and nothing but the truth, correct?
MR. BOISE: Object to the form.
A. I would state that these were facts. That they were expressed in an honest, straightforward and clear manner.
Q. With no spinning, correct?
MR. BOISE: Object to the form.
A. Correct.

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490:15 Q. In the letter that went out to the doctors, Exhibit 9201, the second question there is, "Does Zyprexa cause diabetes?" And the answer starts off by saying, "The available data do not establish a causal link between diabetes and Zyprexa -- or any other antipsychotic, for that matter."
Is that correct?
A. Yes, it does.

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493:12 Q. My question was, you knew and told other people at Lilly that the weight gain caused by Zyprexa could push some patients over in becoming diabetic, did you not, sir?
MR. BOISE: Object to the form of the question.
A. That's an important hypothesis to examine. There's no data that confirms that relationship, and we looked very, very, carefully and very, very hard at that exact point, and the data available does not prove that point.

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494:21 Q. Sir, do you deny that the weight gain caused by Zyprexa can push some patients over into becoming diabetic?
495: 1 MR. BOISE: Object to the form of the question.
A. We have no data to support that.

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Q. Okay. Directing your attention back to Exhibit 3909, the first numbered paragraph says, "1. Does Zyprexa cause diabetes?" And your first part of your response says, quote, "The most straightforward answer is we do not think so. Why do I not say Zyprexa definitively does not cause diabetes? In part, because it is very difficult to prove a negative. When anyone develops diabetes in the general population it is often impossible to say definitively why they developed diabetes."

Do you see that language, sir?

A. I do.

Q. And then you go on in point two to say, "Why do I say no direct link as opposed to any link at all?" And then you wrote, quote, "We know and have well characterized that Zyprexa and all antipsychotics causes weight gain and weight gain is an established risk factor for diabetes. Thus in some patients the weight gain of Zyprexa could predispose them to diabetes, particularly if those patients have other risk factors for diabetes. However, and this is very important, most people who gain weight do not develop diabetes. Diabetes is an illness with multiple pathways leading to and contributing towards its development. Thus a patient who gains weight on Zyprexa or other antipsychotic drugs and mood stabilizers is probably, like anyone else who gains weight, the general population. For the vast majority of individuals their pancreases are healthy and the weight gain will not precipitate diabetes. For those in the minority whose pancreases are functioning suboptimally, weight gain could push them over to diabetes."

Do you see that language, sir?

A. I do.

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A. Um-hum.

Q. And then numbered Item 3 states, "Okay, then how can I tell if a patient's pancreas is functioning suboptimally?" And your answer was, "The most efficient and practical way to get a handle on this is easy, just get a fasting glucose level."

Did I read that correctly?

A. You did.

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Q. The Japanese regulatory authority made Lilly tell physicians in Japan to get a blood test for glucose before a patient started on Zyprexa, correct?
MR. BOISE: Object to the form.
A. The part of the label language were to get a blood glucose prior to starting treatment.
Q. Okay.
A. That's correct.
Q. And those, that language that we just talked about here that was in Exhibit 3909 is not contained in the letter 9201 that went out to physicians in the U.S. that was distributed by Lilly sales representatives, isn't that correct, sir?
A. You are correct.

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Q. Dr. Breier, who was it that made the decision not to include that language that was in 3909 in the internal e-mail, in the letter that went out to the public in Exhibit 9201? Who made that decision?
MR. BOISE: Object to the form of the question.
A. I'm the author of both. I take responsibility for both.

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Q. Yes, sir. Dr. Breier, my name is Scott Allen, and I'm from Houston, Texas. Other than this deposition, you and I have never met before; is that correct?
A. That's correct.

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Q. You were the Zyprexa product team leader, correct?
A. I was.
Q. Who assigned you to that task?
A. That decision would have been made by key members of upper management, including John Lechleiter.

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508:10 head of the Zyprexa Product Team, on the
11 Zyprexa Product Team were people that were
12 physicians and people that were marketers,
13 correct?
14 A. In addition, among all the
15 other people that I indicated.
16 Q. **Yes, sir. And on the**
17 **marketing side, as you've indicated, there**
18 **was a global marketing team and that was**
19 **headed up by Denice Torres, correct?**
20 MR. BOISE: Object to the
21 form. Time period?
22 A. When I began as product team
23 leader at the beginning of 1999, Roland
24 Powell was the medical director for two
509: 1 years. Denice Torres then assumed the
2 position when Roland Powell rotated into a
3 new position.

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509:11 Q. **When you say "Roland Powell,"**
12 **you meant he was Marketing Director and then**
13 **Denice Torres took over?**
14 A. That's right.
15 Q. **Since Lilly appointed her to**
16 **be local marketing director, that would**
17 **involve issues involving marketing?**
18 A. That's correct.
19 Q. **And she would know,**
20 **obviously, those things that could affect**
21 **marketing of a product. She would know those**
22 **things, that would be her job?**
23 A. Her background was in
24 marketing, and she had an expertise in
510: 1 marketing, correct.

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511: 8 Torres. As an expert, she testified to me --
9 and I want to see if it was your
10 understanding of this, too -- she testified
11 to me under oath that it was common knowledge
12 that a warning on a drug product could affect
13 sales. Were you aware of that?

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511:21 Q. **First of all, yes, were you**
22 **aware she held that view?**
23 MR. BOISE: Object to form.
24 A. I don't recall discussing
512: 1 that with her having that, knowing of that
2 view.

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let me ask this: Did you understand as Zyprexa Product Team leader that a warning on drug products can affect the sales of the drug?

MR. BOISE: Object to the form. Foundation.

A. My best answer to that is I think it would depend on what the warning was. I think, ultimately, what's going to affect the sales of a product would be the overall attributes, which includes potentials for warning, other situations, as well as the efficacy of a product, and then the degree of unmet need that it has to address.

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Q. But of course, in this case in this setting with Zyprexa, you know for a fact, not just as a matter of opinion, you know as a matter of a fact that a warning on diabetes, blood monitoring, and diabetic ketoacidosis, those things would have affected the sales of a product? You know that as a fact?

MR. BOISE: Object to the form of the question. Compound. Foundation.

A. No.

Q. Didn't you have facts in your possession, your own personal possession, that a warning about diabetes, diabetic ketoacidosis, blood monitoring, would have a very profound effect on the sales of Zyprexa?

MR. BOISE: Object to the form.

A. I would say that it's very difficult to predict what would or would not have a bearing. And it would relate to the other factors that I talked about.

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Q. Didn't you have actual evidence, empirical evidence by the summer of 2002, you, that a warning about diabetes and blood monitoring would for certain have a very profound effect on the sales of Zyprexa?

A. Again, I'm going to answer no.

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I'll hand you what I've marked as Breier Exhibit No. 6 and one for your counsel.

(Whereupon, Deposition Exhibit(s) 6 duly received, marked and made a part of the record.)

MR. ALLEN: This is the summary of the Japan trip that you took over to Japan from June 23rd to 27th with Dr. Lechleiter.

QUESTIONS BY MR. ALLEN:

Q. You've seen this earlier in the deposition. You've already read it, correct?

A. Yes.

Q. And you've seen earlier that by this time the Japanese label had changed, you discussed that with Mr. Suggs, and it warned of diabetes, diabetic ketoacidosis, death, and also advised to do blood glucose monitoring in the warning. And the warning or the new label in Japan also suggested that for patients with diabetes, or who were at risk for diabetes, should not be prescribed Zyprexa, correct?

MR. BOISE: Object to the form.

A. One part I'm going to refresh my memory, on your last point, if you had a diagnosis of diabetes, then Zyprexa was contraindicated by the label language, I don't recall risk for diabetes as being a contraindication.

Q. Thank you, sir. Other than with that modification, you agree with what I said?

MR. BOISE: Same objections.

A. Yes.

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Q. And I know without a doubt, because in my job, in any job, and the jury will understand, that when you're reporting to your superior concerning a trip to Japan, you're going to try to be as accurate and as truthful as you possibly can be so your superior will have true and accurate information upon which to make his or her decision that needs to be made, right?

MR. BOISE: Objection. Asked and answered.

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A. We would convey our impressions as accurately as possible.

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524: 2 impressions as accurately as possible.
3 Q. And you told us at least one
4 of the reasons you went to Japan was to
5 assess how the affiliate was doing in Japan
6 after the label change, right?
7 MR. BOISE: Objection. Asked
8 and answered.
9 A. That's correct. We wanted to
10 assess their implementation of the

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524:11 guidelines.
12 Q. Yes, sir. And if you look at
13 Paragraph 1, and I will read it into evidence
14 so it will be easier than making you read it.

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525: 6 Q. "It is clear that the impact
7 of the label change in Japan has been very
8 profound. We concluded we have lost
9 substantial ground and trust in our
10 relationship with the MHLW."
11 That's the Japanese
12 equivalent of the FDA, correct? Sir?
13 A. Yes.
14 Q. "Market research shows we
15 have also lost quite a bit of credibility
16 with prescribers and opinion leaders.
17 Basically, because they felt left in the dark
18 with what they perceived as the late sharing
19 of safety information. As a result, there
20 has been a 75 percent drop in new patients
21 who are being put on the drug and a
22 continuing fairly high drop-out rate. That's
23 going to lead to a significant performance
24 impact. Probably, over and above the
526: 1 10 percent assumed on the sales line in the
2 short term. Although we think we will be
3 able to stem the tide and turn this around."
4 Did I read that correctly?
5 A. Yes.

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528:22 with what you just said, but also there was
23 on the team people who were specifically
24 assigned in what they call the Marketplace
529: 1 Management. You know who the Marketplace
2 Management people are? You know that
3 department?
4 MR. BOISE: Object to form.
5 Q. Matt Pike and Cassandra
6 Mehlman and others?
7 A. I'm not a hundred percent
8 clear on the term "Marketplace Management" or

how that's being referred.
Q. Okay. Well, tell me how you're not clear because I think -- I want you and I to communicate, and I'm doing the best job I can, and I'd like you to help me and the jury. I've also heard it referred as Issues Management. Does that help you at all?
A. For a period on the team we had a group called an Issues Management team.
Q. Right. Thank you. And one of the main things the Issues Management team had to do was address the issue of hyperglycemia?
A. One of the topics for this team was to examine information around hyperglycemia.

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understand, I'm going to hand you Breier Exhibit No. 7.
(Whereupon, Deposition Exhibit(s) 7 duly received, marked and made a part of the record.)
MR. ALLEN: Which is a document from Denice Torres's deposition. You do not need to read the whole thing, you just need to turn to the second page and go to the top where the name Mr. Mike Bandick is listed at the top of the second page.
QUESTIONS BY MR. ALLEN:
Q. You see where it says "Mike Bandick will assume the role of Director, Marketplace Management"?
Do you see that?
A. I do.
Q. Does that help you help me and help the jury understand what Marketplace Management is? Marketplace Management was one of the people on the Zyprexa Product Team, correct?
MR. BOISE: Object to the form.
A. I, in terms of -- obviously, seeing the sentence they refer to, I don't doubt that that was the title that Mr. Bandick assumed.
A Marketplace Management team or a Marketplace Management organization is something that I'm not familiar with.

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Q. Okay. Back when you were head of the Zyprexa Product Team, you knew

Mike Bandick. Mike Bandick was a friend of yours professionally?

MR. BOISE: Object to the form.

A. No.

Q. You never dealt with Mike Bandick?

MR. BOISE: Object to the form.

A. You had two parts of your question: One, did I know Mike Bandick? The answer to that is yes. The second part of your question was were we friends.

Q. Professional friends.

A. No.

Q. Okay. How did you know Mike Bandick when you were head of the Zyprexa Product Team?

A. He joined as a member of the team.

Q. Tell the jury what he did for your team that you were head of?

A. Mr. Bandick, his background in marketing, he joined as part of Denice's team in the marketing area and was focused on issues management.

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Why did Mr. Bandick get fired?

MR. BOISE: Object to the form. Foundation.

A. My understanding, he was separated from the company because of inappropriate activities with a vendor or vendors.

Q. Tell me what those are.

MR. BOISE: Object to the form.

A. I don't know.

Q. Mr. Bandick was on the Zyprexa Product Team. We've seen him described in the document I gave you as Marketplace Manager. He was, actually, also the brand manager at the time of the Zyprexa primary care physician launch, right?

A. Yes.

Q. Mr. Bandick worked on your Zyprexa team. And we know he was fired. And you're telling this jury you don't know why he was fired --

MR. BOISE: Object to form.

Q. -- other than, quote, "some inappropriate activity with vendors?"

MR. BOISE: Object to the form.

A. My understanding is he was separated from the company because of inappropriate activities with a vendor or vendors.

Q. Tell the jury, help the jury understand, help me understand, what would be some examples of inappropriate activities with vendors?
MR. BOISE: Object to the form.
A. I don't know.

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558:15 where did you learn that Mr. Bandick was
16 fired because of inappropriate activities
17 with vendors?
18 MR. BOISE: Object to the
19 form.
20 A. I had -- it occurred after I
21 left the team. I had heard after the fact.
22 And I was notified by a person in the human
23 resource department.
24 Q. Who?
559: 1 A. Diedre Connolly.

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561: 2 Q. Nevertheless, Ms. Connolly
3 picked up the phone and called you in your
4 office to give you this information, right?
5 MR. BOISE: Object to the
6 form.
7 A. She called me and gave me
8 that information.
9 Q. Right. I bet -- this is
10 Scott Allen thinking, you tell me if I'm
11 wrong. I bet she didn't call -- did she call
12 you Alan or did she call you Dr. Breier?
13 A. Calls me Alan.
14 Q. And you call her Diedre?
15 A. Yes.

Alan Breier, M. D. (January 12, 2007)

562: 9 Q. It went like this, "Alan,
10 this is Diedre. I'm calling to tell you Mike
11 Bandick has been separated from the company
12 for some activities with vendors. Got to go
13 now," and hung up?
14 MR. BOISE: Objection to the
15 form. It's been asked and answered
16 two times.
17 A. I don't recall any other
18 content.

Alan Breier, M. D. (January 12, 2007)

566: 1 Q. You know as a fact that Mike

Bandick's separation from the company, and I'm going to call it a firing, occurred due to his activities surrounding Zyprexa. You know that?

MR. BOISE: Objection. Asked and answered.

A. My knowledge of what happened was that there was some inappropriate behavior with vendors. I don't know the details of it beyond that. It occurred when I was no longer on the team. And that's the extent of my knowledge.

Exhibit 6
Clewell, Pharm. D.

Jerry Clewell-Pharm.D.(October 5, 2006)

31:19 Q Would you state your full name for the
20 record name, please?
21 A Jerry Dean Clewell.

Jerry Clewell-Pharm.D.(October 5, 2006)

31:24 Q And what's your occupation?
25 A Pharmacist.
32: 1 Q And by whom are you presently employed?
2 A Abbott Laboratories.
3 Q And what's your job title?
4 A Regional Clinical Executive.
5 Q And can you briefly describe what you do in
6 that position?
7 A My responsibility is to provide information
8 upon request to payor customers and also listen to
9 any feedback that they may have with the Company.
10 Q Okay. And who do you regard as payor
11 customers?
12 A Those would be health plans, Medicaid
13 organizations, people that purchase pharmaceuticals.
14 Q Okay. And it's my understanding that you
15 used to be employed by Eli Lilly and had some
16 responsibilities for a drug called Zyprexa when you
17 were with Lilly; is that correct?
18 A That's correct.

Jerry Clewell-Pharm.D.(October 5, 2006)

40:24 Q Okay. And can you describe just very
25 briefly the various positions you held at Lilly
41: 1 between 1999 and 2006?
2 A I had the same position essentially --
3 Q Okay.
4 A -- through the whole course. The title
5 changed slightly, but the job was the same.
6 Q And what was the job?
7 A I was an Outcome Liaison.
8 Q Can you explain to us what an Outcomes
9 Liaison person does?
10 A An Outcome Liaison is a person who responds
11 to questions from payors, health plans, as described
12 before; and also is the person that's responsible
13 for receiving some feedback or communications from
14 the payor customers and providing those back into
15 Lilly.
16 Q Okay. And, typically, what type of
17 questions would you get from the payors?
18 A Um, questions around health outcome matters.
19 Like quality of life, cost, spending, health
20 economics.
21 Q Okay. Would it be fair to say that the
22 questions that you would get would range from the
23 efficacy of the drug, to the safety profile, to the
24 cost, and all aspects of using the drug?
25 A Those are -- yeah, three broad categories
42: 1 that would -- that would be --

Q Okay.
A -- within that.

Jerry Clewell-Pharm.D.(October 5, 2006)

Q Okay. Do you recall when you first had any responsibilities as an Outcome Liaison with respect to Zyprexa?
A Uh, yes.
Q And when was that?
A When I was hired.
Q Okay. So right from the outset you were dealing with Zyprexa?
A Yes.
Q Okay. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 9543 and this is a series of E-mails. The one at the top of the first page is from Cassandra Mehlman to Vickie Poole Hoffman dated September 16, 2002. Um. But, as you look through this, I think you can see that there are several E-mails in here to and from you, Mr. Clewell. And, actually, I'd like to start -- go through these from -- from back to front because I think that represents the chronological sequence.
A Okay.
Q And the first e-mail is from Robert Brown on page 4. You'll see on the bottom right-hand corner there's page numbers --
A Okay.
Q -- page 4 of 5.
A Okay.
Q And Mr. Brown's E-mail is to you and a lot of other folks as well dated September 13th, 2002 and he is forwarding an E-mail from Patrick Toalson to a number of individuals regarding label changes related to hyperglycemia.
A Okay.

Jerry Clewell-Pharm.D.(October 5, 2006)

Q (By Mr. Suggs) If I could, sir, have you turn to page 3. And on page 3 is an E-mail -- at the bottom is an E-mail from you to Dr. Brown dated the same day about 20 minutes after you got his E-mail.
A Okay, I see that.
Q Okay. And the text of your E-mail, first couple of sentences say: "Hi, Bob and Pat, thanks for forwarding this. It's very important for us to know what the regulatory agencies are thinking. But is there any discussion of sending out a dear doctor letter that lays all the facts i.e., epidemiologic and clinical information. I ask because at the end of the day there's a credibility concern among many in the medical community that the FDA has not moved fast enough or aggressive enough with drug safety issues, i.e., Rezulin."
Do you see that language, sir?
A I do.

Q First, can you explain to the Jury what a dear doctor letter is? Is that a term of art in the pharmaceutical industry?
A Um, yeah, I've come to learn that.
Q Okay.
A Um, it can be used as a term of art.
Q Okay. And what was -- how were you using that phrase in that E-mail to Dr. Brown?
A I am using that phrase in this E-mail to Dr. Brown to propose an idea. And that idea is in response to what we believe was largely our -- our competitors' external way that the information on this subject matter was being used. And my feeling was simply that we needed to get out more information in addition to, um, you know, existing information that our customers were receiving from our competitors. We needed to give out information on all of the epidemiologic data known to date.
Q And all this hadn't -- with -- with respect to hyper -- the issue of hyperglycemia and diabetes and antipsychotic drugs; is that correct?
A That's correct.
Q Because at this point in time by September of 2002, there had been a lot of discussion in the industry and, as you said, by competitors as to whether or not antipsychotics in general were linked with the development of diabetes and in particular whether Zyprexa had a higher incidence of that than other drugs; is that correct?

Jerry Clewell-Pharm.D.(October 5, 2006)

Q (By Mr. Suggs) Those were the issues that were being discussed in the marketplace.
A Whether there was a link between antipsychotics and diabetes?
Q Right.
A Is that what you're asking me?
Q That was one thing that was being discussed; correct?
A In the marketplace in general, yes.
Q Okay. And then there's also the issue of whether particular antipsychotics had a higher incidence than others; correct --
MR. BRENNAN: Object.
Q -- that was also another issue that was being discussed in the marketplace?

Jerry Clewell-Pharm.D.(October 5, 2006)

A Is there -- yeah. Yeah.
Q (By Mr. Suggs) Okay. And you point out here that in your E-mail that you said that there was -- there's a credibility concern among many in the medical community that the FDA hasn't moved fas -- fast enough or aggressive enough with drug safety issues, i.e. Rezulin.
Could you explain to the Jury what you meant by that?

A There was a general perception going back, you know, anybody could pick up a New York Times article and the like going back to, really, the mid '90s what we would hear from time to time as well from people in the medical community around, um, you know, what the FDA is doing and how the FDA is shaping and -- and monitoring drugs on -- on safety issues.

Q Okay. And did you hear from your payor customers that you dealt with expressions of concern that the FDA wasn't moving fast enough on safety issues?

A Not commonly.

Q Okay.

A But, you know, occasionally you would -- you would, you know, hear it. I can't point to a particular instance I heard it from a payor customer, no.

Q Okay. But you said in your E-mail that there was concern among many in the medical community that the FDA hasn't moved fast enough; correct?

A Yeah, again, that reflects what I would see in, you know, professional journals and the lay press for that matter.

Q Okay. And at this point in time September of 2002 were you aware that European regulatory authorities had required label language for Zyprexa over in Europe that put a discussion of hyperglycemia in what was referred to as a special precautions and special warnings section of the European label. Were you aware of that?

A No.

Q Okay. Were you aware in September of 2002 that the Japanese regulatory authorities had required a much stronger warning about hyperglycemia and the risk of diabetes with the use of Zyprexa that was in effect in the US labeling?

Jerry Clewell-Pharm.D.(October 5, 2006)

A I was aware that there was a label change in Japan, the -- the level of detail on that label change, I don't recall knowing.

Q (By Mr. Suggs) Okay. Were you aware that the Japanese label change contraindicated use of Zyprexa in patients with diabetes?

Jerry Clewell-Pharm.D.(October 5, 2006)

A I don't recall that level of detail.

Q (By Mr. Suggs) Okay. Do you recall that the Japanese label required monitoring of patients for their blood glucose levels?

Jerry Clewell-Pharm.D.(October 5, 2006)

51:16 A I don't recall that.
17 Q (By Mr. Suggs) Okay. Were you aware that
18 the Japanese government required a dear doctor
19 letter to go out to all Japanese physicians?

Jerry Clewell-Pharm.D.(October 5, 2006)

51:21 A No.
22 Q (By Mr. Suggs) Okay. Let me show you what's
23 been previously marked --
24 A Not that I recall.
25 Q -- as Zyprexa MDL Plaintiff's Exhibit No.
52: 1 320. For the record, this is an English translation
2 of the dear doctor letter that the Japanese
3 regulatory authorities required be sent out. And on
4 the second page is the beginning of that English
5 translation and I'll represent to you, sir, that --
6 if you could direct your attention back to the
7 second page.

Jerry Clewell-Pharm.D.(October 5, 2006)

52:11 Q I'll represent for the record that the first
12 page of the document has the title: Appendix 6
13 Japanese Dear Doctor Letter. We've established
14 through the testimony of other witnesses already
15 that page 2 is the dear doctor letter and at the
16 bottom of the dear doctor letter it notes that we
17 also report the revisions made to the warnings,
18 contraindications and precautions as shown on the
19 back of this overleaf and there then follow English
20 translations on the rest of the Japanese label.
21 And if I could direct your attention, sir,
22 to page 2 of this exhibit which was the -- which
23 you're on.
24 A This one.
25 Q Were you aware that the Japanese dear doctor
53: 1 letter -- in here we see it looks like it has a
2 black border, but in actual fact, it was a bright
3 red border. Were you aware that a letter with that
4 type of red border had gone out?
5 A No, not to my knowledge.
6 Q Okay. And could you hold the second page up
7 to the video camera so the camera can see what the
8 heading says there?
9 MR. SUGGS: Can you focus on that?
10 VIDEOGRAPHER: Got it.
11 Q (By Mr. Suggs) Okay. Were you aware that
12 the dear doctor letter that the Japanese government
13 required be sent out in April of 2002 bore that big
14 bold heading described as Emergency Safety
15 Information?

Jerry Clewell-Pharm.D.(October 5, 2006)

53:17 A This is the first time I've seen this
18 document.

Q (By Mr. Suggs) Okay. It would be fair to say that at least no one at Lilly provided you with a copy of this document back in -- in 2002; correct?
A If they did, I don't recall seeing it.
Q Okay. Do you recall whether you received questions from your payor customers about the Japanese label change?
A I can't recall a specific question on it.

Jerry Clewell-Pharm.D.(October 5, 2006)

Referring back again to Exhibit 9543 in that same paragraph that we were discussing before, after pointing out that there was concern among many in the medical community that the FDA wasn't being aggressive enough with drug safety issues, you then went on to say and I quote: It would seem to me that a summary of the actual science would go a long way in educating prescribers on the facts and help alleviate any concerns that clinicians and customers have that Lilly may not be acting in the most forthcoming matter to help them now and understand the actual evidence. In other words, it's not uncommon for us in the field to hear from customers that they perceive Lilly is dodging the issue or hiding the truth rather than giving them the answers that matter on how to act or react to concerns."
Did I read that correctly, sir?
A Yes, you did.

Jerry Clewell-Pharm.D.(October 5, 2006)

Q (By Mr. Suggs) That's fine. And you would agree, sir, that it is absolutely essential that prescribing physicians know the facts about safety issues that may be involved with the drugs they prescribe to their patients; correct?
A Yes.
Q Okay. And then -- well, let me back up for a second. You noted that it was not uncommon for us in the field to hear from customers that Lilly is dodging the issue or hiding the truth. Who -- what customers were you hearing that from?
A Occasionally, personally from my perspective, probably, you know, two or three times, um, payor customers that were, um, on P&T Committees and the like.
Q What's a P&T Committee?
A Pharmacy & Therapeutics.
Q Well, what does a Pharmacy & Therapeutics Committee do?
A A Pharmacy & Therapeutics Committee is the committee that selects and approves the availability of drugs for a formulary for health plans.

Jerry Clewell-Pharm.D.(October 5, 2006)

57:20 Q What's the formulary?
21 A It's a list of drugs that the health plan
22 has selected to be available at some level or
23 another.
24 Q What do you mean "at some level or another"?
25 A It may be, uh, available without restriction
58: 1 or with some type of restriction. It may be
2 available with a certain co-pay.

Jerry Clewell-Pharm.D.(October 5, 2006)

58:12 Q And what is that Pharmacy & Therapeutics
13 Committee's involvement with the formulary?
14 A They do the reviews of the drugs.
15 Q Okay. And it was your testimony before that
16 you had had two or three people on such committees
17 tell you that they had concerns about whether Lilly
18 was dodging the issue or hiding the truth with
19 respect to hyperglycemia and Zyprexa; is that
20 correct?
21 A The situation, um, that I'm describing in
22 this E-mail is -- is simply one where, you know,
23 it's my job to relay, as I stated earlier, that
24 information I heard back from our payor customers.
25 Q Uh-huh.
59: 1 A And, you know, it was my job to listen to
2 them.
3 Q And what were you hearing --
4 A And so I would occasionally hear that and
5 was relaying that sentiment back.
6 Q I understand. And was it your understanding
7 that others in your position who were also
8 interacting with different payor customers were
9 hearing that from their customers as well?
10 A Um, again, you know, on occasion.

Jerry Clewell-Pharm.D.(October 5, 2006)

59:19 Q Okay. I'm going to show you what's been
20 previously marked as Plaintiff's Exhibit 1605. For
21 the record, this is a computer printout dated
22 June 19, 1995. And the description of the printout
23 at the top of the first page is:
24 "Treatment-Emergent Abnormal, High, or Low
25 Laboratory Values at Any Time Regarding the Acute
60: 1 Phase of the HGAJ Study".
2 And, sir, I'll represent to you that we've
3 had prior testimony from Dr. Beasley and others that
4 study HGAJ was the largest clinical study done by
5 Lilly in support of its new drug application. I'll
6 also represent to you that this date of June 19,
7 1995 was more than a year before Zyprexa went on the
8 market. And if I could direct your attention, sir,
9 to page 11. If you turn it so it's oriented
10 lengthwise, the numbers are in the -- that corner
11 over there -- and it's the second to the last
12 physical page. And if I can direct your attention
13 to about the middle of the page there's a reference
14 to lab test for glucose non-fasting. Do you see

that, sir?
A Yes, I do.
Q And do you see that it's broken out into high and low?
A Yes, I do.
Q And do you see that there is -- that this was a comparative test between olanzipine or Zyprexa and haloperidol?
A I assume that's what those two columns are.
Q Okay. And I'll represent to you that we've had prior testimony that indeed that was what the nature of the study was.
A Okay.
Q And do you see also in the last column, in the field of data there is referring to a p-Value?
A Yes.
Q Okay. And you're familiar, are you not, sir, that a reference -- a p-Value is a measure of statistical significance; correct?
A That's my understanding.
Q Okay. Is it your understanding also that a p-Value less than .05 is what's referred to as statistically significant?
A That's one possibility.
Q Okay. And I'll represent to you, sir, that -- well, if you can direct your attention to the p-Value for the high glucose, it is .03; correct?
A You've read that correctly.
Q Okay. And, sir, did anyone ever tell you while you were working at Lilly with respect to Zyprexa that before the drug even went on the market that their clinical study had found a statistically significant increased incidence of high glucose --

Jerry Clewell-Pharm.D.(October 5, 2006)

Q (By Mr. Suggs) -- in Zyprexa users as compared to haloperidol?

Jerry Clewell-Pharm.D.(October 5, 2006)

A I don't recall hearing that.
Q (By Mr. Suggs) And, in fact, haloperidol is another antipsychotic drug, is it not?
A Yes, it is.
Q Okay. I'm going to show you what's been previously marked as Zyprexa MDL Plaintiff's Exhibit No. 990.

Jerry Clewell-Pharm.D.(October 5, 2006)

Q For the record, Exhibit 990 is a seven-page document. It's been used as an Exhibit in the depositions of Dr. Beasley, Dr. Kinon, Dr. Baker. And in the second page of the document, it indicates that it is a olanzipine labeling change on

hyperglycemia for a February 21, 2000 GPLC meeting. Do you see that reference, sir?
A I see that.
Q And did you have an understanding when you were at Lilly that the initials "GPLC" stood for Global Product Labeling Committee?
A No.
Q Okay. If I could direct your attention to the last physical page. It indicates that this proposed labeling change was reviewed by Dr. Charles Beasley and Dr. Kenneth Kwong. Did you know either of those individuals?
A No.
Q Okay. If I could direct your attention to the middle of the first page, there's a box that has the bold heading: "How has this proposal arisen". And the next that box states, quote: Recent review of random glucose levels of patients in olanzipine clinical trials reveal that the incidence of treatment-emergent hyperglycemia in olanzipine group 3.6 percent is higher than that in the placebo group 1.05 percent." Do you see that language, sir?
A I see that.
Q And the difference between 3.6 percent and 1.05 percent is a three-fold difference; correct?

Jerry Clewell-Pharm.D.(October 5, 2006)

A I don't know if it's a three-fold dif -- difference.
Q (By Mr. Suggs) Well, you can divide 1.05 into 3.6 and the result of that is going to be more than three; correct?
A If you take those two numbers and make that division, that would be correct.
Q Okay. And, sir, did anyone from Eli Lilly ever tell that you back in 2000 they had reviewed the data from their clinical trials and found that the incidence of treatment-emergent hyperglycemia was three times higher in the olanzipine group than it was in the placebo group?

Jerry Clewell-Pharm.D.(October 5, 2006)

A I don't recall that.
Q (By Mr. Suggs) Okay. And so, obviously, sir, if you had received questions from your payors about what data Eli Lilly had about the incidence of hyperglycemia in Zyprexa users as compared to placebo users, you would not have been capable of giving them this information because you simply wouldn't have it; correct?
A Um, this is the -- to my knowledge, this is the first time I have seen this information and I don't know how to interpret it.
Q Okay. Sir, I'm going to show you what -- next what's been previously marked as Plaintiff's Exhibit 5565. For the record, this is a series of E-mails. I'm going to be directing your attention,

sir, just to the E-mail that's on page 1. Actually, the second E-mail that's on page 1, which is a February 22, 2001 E-mail from Charles Beasley to Ralf Dittman with copies to Allan Breier, Patrizia Cavazzoni, Ralf Dittman, Mark Millikan, Anna Thornton, and Gary Tollefson.

Do you see with what I'm referring to there, sir?

A Yes, I do.

Q Okay. Now I think you previously said that you did not know who Dr. Charles Beasley was; correct?

A Correct.

Q Okay. Did you know Dr. Alan Breier or know who he was?

A I know that he was the Medical Director for Eli Lilly.

Q Okay. And you would characterize that as a high-level executive, would you not?

A I kind of characterize as a mid-level executive.

Q Okay. Did you know Dr. Gary D. Tollefson?

A No.

Q Okay. I'll represent to you that he was a Vice-President of the Company and that Dr. Breier reported to him. Are you familiar with that?

A No.

Q Okay. If I could direct your attention to the second -- actually, I guess, it's the third sentence in Dr. Beasley's E-mail.

A The third --

A The third sentence of Dr. Beasley's?

Q (By Mr. Suggs) Right. It starts out: "Our continuous", do you see where I'm at?

A Okay.

Q Okay.

A I see that.

Q It states: "Our continuous analyses show that olanzipine does result in statistically significant mean increases in random glucoses relative to placebo in haloperidol. No significant difference relative to Risperidone, but the power is small. Clozapine is associated with a larger and significant increase compared to haloperidol."

Do you see that language, sir?

A I see the language. I don't think you read it all, but I see the language.

Q What part did I not read?

A Is there -- did you skip over the olanzipine versus haloperidol, or did I just not hear that?

Q Oh, in the parenthesis?

A Yeah.

Q I -- I perhaps didn't. Let me read it again just so we're straight here on the record. His third and fourth and fifth sentences in his E-mail state: "Our continuous analyses show that olanzipine does result in statistically significant mean increases of random glucoses relative to

placebo in haloperidol. No sig difference relative to Risperidone the power is small. Clozapine is associated with a larger (OLZ versus haloperidol) and sig increased compared to haloperidol."

Did I read that correctly, sir?

A Yes.

Q Okay. Did anyone advise you back in February of 2001 or at any other time that continuous analyses of Lilly's own clinical data showed that there was a statistically significant mean increase in random blood glucose for Zyprexa users as compared to placebo in haloperidol?

Jerry Clewell-Pharm.D.(October 5, 2006)

67:23 A In 2001?
24 Q (By Mr. Suggs) At any time, sir.
25 A At any time?
68: 1 Q Yeah.
2 A Um. Did anyone at Lilly tell me --
3 Q Yes.
4 A -- that there was a difference in the continuous -- if I understand your question.
5 Q Okay. Let me -- let me restate the question --
6 A Okay.
7 Q -- so it's clear. At any time, sir, did anyone at Lilly tell you that the data from Lilly's own clinical studies showed that a continuous analysis of that data indicated that Zyprexa had a statistically significant increase in random blood glucose relative to placebo or haloperidol?
8
9
10
11
12
13
14

Jerry Clewell-Pharm.D.(October 5, 2006)

68:16 A I do not recall hearing that.

Jerry Clewell-Pharm.D.(October 5, 2006)

69:16 Q (By Mr. Suggs) For the record, Exhibit 7802 is a document bearing the title "Listing of treatment-emergent abnormal lab findings in olanzipine treated patients. Placebo controlled FID-MC-HGFU Studies 1 and 2 combined."
17
18
19
20
21 I'll also represent to you that when Lilly produces documents to us, that they often had a date in the database that's associated with it and that the database that was provided to us states that this document was generated June 24, 2002, which would have been several months before your E-mail that was Exhibit 9543 that we've been discussing for a while.
22
23
24
25
70: 1
2
3
4 Sir, if I could direct your attention to the clinical chemistry section of this document. Do you see where there's a listing for the glucose non-fasting high?
5
6
7
8 A I see that.

Q And do you see that there are columns of data for olanzipine subjects and also for placebo subjects?
A I see "OLZY plus MS and PLB plus MS" --
Q Correct.
A -- columns.
Q And do you see that the percent of olanzipine subjects with high glucose is 2.2 percent?

Jerry Clewell-Pharm.D.(October 5, 2006)

70:19 A Wouldn't that be the olanzipine plus MS column?
Q (By Mr. Suggs) Correct.
A I don't know what "MS" is.
Q Okay.
A But, I see the 2.2 percent on the line you're pointing to, I believe.
71: 1 Q Okay. And that for the placebo plus MS, the incidence of glucose was 0 percent; correct?

Jerry Clewell-Pharm.D.(October 5, 2006)

71: 4 A If -- if you're asking me if the 0 percent is in that column, placebo MS, yes.
Q (By Mr. Suggs) And you see how there's some columns labeled "Current Oral Category" and "Category for New Events from HGFU, Acute Phase Database and/or Upgrade"?
A I'm sorry, where are you pointing to?
Q Pardon me. The columns, the second and third ones past the column that we were just looking at before.
A Okay. So the last two columns in the table?
Q Right. The ones that have A's in them.
A Okay.
Q And do you see that down at the bottom of the document there is a description of what the A's and the B's and the C's mean?
A Yes, I do.
Q Okay. And do you see the Category A equals event probably causally related?
A I see that.

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72:12 Q Okay. Did anybody at the Company tell you that their own -- that the Company's own clinical studies showed that high glucose was probably causally related by use of the drug --

Jerry Clewell-Pharm.D.(October 5, 2006)

72:17 Q (By Mr. Suggs) -- Zyprexa?

A No.
Q Okay. Let me show you what's been previously marked as Plaintiff's Exhibit No. 8666. For the record, this document is also a series of E-mails. I'm just going to be asking you about an E-mail on the first physical page, which is a June 27, 2002 E-mail from Siemon Israel Taylor to a number of individuals. And, sir, this E-mail dated
73: 1 in June 2002 is several months before your E-mail to
2 Mr. Brown; correct?
3 A Refresh my memory, when was the E-mail to
4 Mr. Brown --
5 Q September 13 --
6 A -- because I don't remember?
7 Q -- 2002.
8 A Okay. And so this is 6/27/2002?
9 Q Several months before that.
10 A Okay.
11 Q Directing your attention to the cc list of
12 Dr. Israel's E-mail. There's a John Holcombe and a
13 Margaret Sowell and a Gary D. Tollefson listed
14 there. Did you know any of those individuals?
15 A No.
16 Q Okay. So you wouldn't -- you would not be
17 knowledgeable of the fact that they were working on
18 the issue of hyperglycemia in the medical department
19 with respect to Zyprexa; correct?
20 A No. Correct.
21 Q Okay. If I could direct your attention
22 to -- well, let me back up for a second. Did you
23 know that Dr. Simeon Israel Taylor was an
24 endocrinologist who was also working on the
25 hyperglycemia issue?
74: 1 A I did not know that.
2 Q Okay. If I could direct your attention to
3 the first sentence in the first paragraph of
4 Dr. Taylor's E-mail and then to the first two bullet
5 items or two numbered items below that Dr. Taylor
6 says: "Ultimately, I am expect that a fair-minded,
7 scholarly evaluation of the available data is likely
8 to support several conclusions: One, Zyprexa, like
9 other members of the class, causes weight gain.
10 Two, like other causes of weight gain,
11 Zyprexa-induced weight gain probably increases the
12 risk of diabetes".
13 Do you see that language, sir?
14 A I see that language.
15 Q Did anyone tell you in 2002 or at any other
16 time that physicians within the Company who were
17 working on the issue of hyperglycemia with the use
18 of Zyprexa had concluded that Zyprexa-induced weight
19 gain probably increases the risk of diabetes?

75:24 A I am not aware, nor do I recall being told
25 that information.
76: 1 Q Okay. And you were one of the people whose
2 job responsibility it was was to field questions
3 from payors who had questions about not only the
4 efficacy, but also the safety of the drug and relay

information back to them; correct?
A Correct.
Q Okay. But you weren't given this information so you could not -- if you had been asked a question like that by one of your payors, does -- does Zyprexa-induced weight gain probably increase the risk of diabetes, you would not have been able to inform them that your own medical people had -- had reached that conclusion; correct?
A I don't know that they reached that entire conclusion. I know that this is one E-mail in a bunch of conversations, I would suspect.

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77: 3 Q (By Mr. Suggs) Dr. Clewell, if I could refer
4 you back to Exhibit 9543, which was your E-mail to
5 Dr. Brown.

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77: 9 response -- well, let me back up for a second. As
10 we pointed out before, you had written to Dr. Brown
11 asking whether or not there had been a discussion of
12 sending out a dear doctor letter and then at the top
13 of that page, he writes back and says "I have not
14 heard of any such plans"; correct?
15 A That is what he responded.
16 Q Okay. And then if we back up a page, we see
17 what appears to be another E-mail from you to
18 Dr. Brown with copies to Matthew Pike, Patrick
19 Toalson, Patrizia Cavazzoni, Robert Baker, Vickie
20 Poole Hoffman. And the subject of that is
21 "hyperglycemia AJHP response, help needed". Is that
22 correct?
23 A Yes. This is a separate issue from the
24 previous E-mails that you discussed.
25 Q That's exactly what I wanted to establish.
78: 1 Why was it that you addressed this E-mail to those
2 individuals?
3 A Um. As I best recall, those were colleagues
4 over in the US Medical Department, not in Outcomes
5 Research other than Dr. Brown, that might be
6 interested in the AJHP article.
7 Q And when I saw that you had written to those
8 individuals, it led me to believe that you might
9 have an understanding that Patrizia Cavazzoni and
10 Robert Baker, at least, were dealing with the
11 hyperglycemia issue with respect to Zyprexa, is
12 that -- would that be a fair assumption?
13 A I honestly don't recall if they -- if I knew
14 they were interested in that specific area, but I
15 know they were on the medical team --
16 Q Okay.
17 A -- at Lilly.
18 Q Okay. And in the text of your E-mail, you
19 start off by saying: "Bob and others knowledgeable
20 of hyperglycemia issues", that's how you start it;
21 correct?

A Uh-huh.
Q So, assuming that --
A Yeah, okay.
Q -- that you believed that those other folks probably were knowledge about the hyperglycemia issues; correct?
A Correct.
Q Okay. And you then continue on: "In this month's issue of Am J and Health Syst Pharmacists, (AJHP) there's a supplement sponsored by Lilly on "Managing" psych drug therapy across the continuum of care." Did I read that correctly?
A Yes.
Q And what is the "AJHP"?
A American Journal of Health System Pharmacists.
Q And is it a peer reviewed journal?
A I honestly don't know --
Q Okay.
A -- if it is or not.
Q This supplement, you said was sponsored by Lilly. Was that just an article that was in there?
A I don't recall if it was the supplemental or the article.

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Q Okay. But, you note that on page 21 the following is written, quote: The mechanism for

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Quote: The mechanism for antipsychotic-induced diabetes mellitus is not completely understood and most of the available data come from research related to clozapine and olanzipine." And then in bold language there's the following sentence: "With these agents, there is an increased rate of hyperglycemia and hyperinsulinemia". Line -- it goes back to regular text. It says: "It is not known if the hyperinsulinemia is merely a response to the increased glucose levels, or if it is secondary to a direct effect of the drug on insulin release. Alternatively, it may be due to resistence to insulin at the tissue level, end quote. Did I read that correctly?
A Yes.
Q Now in the beginning sentence there when they were referring to the mechanism for antipsychotic-induced diabetes mellitus, there was clearly the implication that antipsychotics had a causal relationship with the development of diabetes; correct?

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A The first sentence of the quote?

81: 1 Q (By Mr. Suggs) Yes.
2 A Says that the mechanism is not completely
3 understood.
4 Q But it refers to antipsychotic-induced.
5 What does the word "induced" mean?

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81: 7 A Um. I assume that it means, you know, it
8 occurs afterward or it's related to it.
9 Q (By Mr. Suggs) Well, it's something -- if I
10 induce you to do something, doesn't that mean that I
11 had a causative role in making that happen?

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81:13 A I don't know if that's always true.
14 Q (By Mr. Suggs) Okay. In any event, you go
15 on to say: "My understanding of the literature is
16 that the bolded statement is not known to be true.
17 The OL's understanding of existing data do not
18 support that there is a difference among APs in the
19 incidence of hyperglycemia."
20 What is the meaning of the phrase "OL" or
21 the word "OL"?
22 A Outcomes Liaisons.
23 Q Ah, so that would be you and the other folks
24 that you worked with; correct?
25 A Yes.
82: 1 Q Okay. And the difference among APs? What's
2 "APs" antipsychotics?
3 A Antipsychotics.
4 Q Okay. So in your second sentence, sir, you
5 were saying that the Outcome Liaisons' people
6 understanding of existing data do not support that
7 there is a difference among antipsychotics and the
8 incidence of hyperglycemia --

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82:10 Q (By Mr. Suggs) -- would that be a fair
11 reading of that sentence if we translate out those
12 words?
13 A It says: "The OL's understanding of
14 existing data do not support that there is a
15 difference among APs in the incidence of
16 hyperglycemia."
17 Q Okay. And then you go on to say: "Beyond
18 uncontrolled case reports, is their data supporting
19 this assertion that I/we may not be aware of."
20 Is that correct? Did I read that
21 correctly?
22 A Yes, you did.
23 Q Okay. But, as we pointed out before, you
24 were not aware of the computer printout from 1995
25 showing that there was a statistically significant
83: 1 increased incidence of hyperglycemia or high glucose

in Zyprexa users as compared to haloperidol; correct?

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Q (By Mr. Suggs) That was Exhibit 1605, you were not aware of that data; correct?
A That's the first time I recall ever seeing that piece of paper.
Q Okay. And you were also not aware of the information contained in Exhibit 990 that there was a three-fold higher incidence of treatment-emergent hyperglycemia in the Zyprexa group of clinical subjects as compared to placebo; correct?

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A Let me look at that one again --
Q (By Mr. Suggs) Sure.
A -- if you don't mind. Again, the numbers are as -- as you've stated earlier, but I don't know that that is a three-fold difference. If it was truly a three-fold difference.
Q Okay. And you were not aware of that data; correct?
A Not to my knowledge.
Q Okay. And you were also unaware of Dr. Beasley's statement in his February 2001 E-mail that the continuous analyses shows that olanzipine does result in statistically significant mean increases in random glucoses relative to placebo and haloperidol --

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Q (By Mr. Suggs) -- right? That's from Exhibit 5565.
A If you're asking me if I have seen that E-mail before?
Q Yeah.
A The answer is, no.
Q Okay. And, sir, are you familiar that there was in 19 -- in the fall of 2003, the American Diabetes Association and the American Psychiatric Association, as well as some other medical associations, convened a consensus group meeting to analyze the -- whether there was a difference in the incidence of hyperglycemia and diabetes among antipsychotics. Are you familiar with that?
A I'm aware that there was a publication.
Q Okay. The publication that came out, actually came out in early 2004 --
A Okay.
Q -- is that what you're referring to?
A That's what I'm aware of.
Q Okay. And, indeed, that consensus statement did conclude that both clozapine and Zyprexa had a

higher incidence of hyperglycemia and diabetes as compared to other antipsychotics; correct --

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Q (By Mr. Suggs) -- that was a conclusion that they made?
A I don't recall the specific conclusions of that entire consensus statement, there was a lot of things in that --
Q Do you --
A -- document.
Q Do you recall that conclusion?
A Um. I recall there being some notation of olanzipine being different.
Q Okay.
A But I don't recall their exact conclusion.
Q Okay.
A It's been a while since I read that.
Q Okay. When you read those conclusions of the consensus statement in early 2004, did you dispute the conclusion?

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Q (By Mr. Suggs) Or did you dis -- dispute any of the conclusions?
A With whom?
Q With anyone?
A Not that I -- I mean, I remember talking about the conclusions of needing to, you know, monitor people -- everybody on an antipsychotic regardless of drug.
Q Okay. Referring back to your E-mail in September 16, 2002, you concluded by saying: "We in the field who are talking with customers and physicians have to know how to respond if / when someone asks us about this publication. I can see where a customer could interpret it to mean that Lilly believes there to be an increased rate of hyperglycemia and hyperinsulinemia with olanzipine because that is what it says in a Lilly-sponsored publication". That's what you wrote; correct?
A That is what I wrote.
Q Okay. And then if you could direct your attention to the proceeding page, which is actually page 1 of this exhibit. There are two E-mails on that page 1 from Vickie Poole to Kathryn Armington and Cassandra Mehlman and the other one from Vickie Poole to Cassandra Mehlman?
A Okay.
Q Actually, I guess I misspoke. The one on the top, the last one in time is actually from Cassandra Mehlman back to Vickie Poole Hoffman. You were not indicated as receiving copies of those. But, in Vickie Poole Hoffman's E-mail to Kathryn Armington and Cassandra Mehlman she says: "Kathy and Casey, do you know anything about this publication? Was it really sponsored by Lilly? I

would like to make sure that the group that supported the publication is aware of this so they can provide feedback to the vendor".
Were you ever made aware that Vickie Poole Hoffman had concerns about that publication?

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87:14 A You know, this is the first time that I can recall seeing this, so I can't really --
Q (By Mr. Suggs) Okay.
A -- comment.
Q Do you recall getting any feedback from the E-mail that you sent that we looked at before that was on page 2?
A Not that I recall.

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87:24 Q (By Mr. Suggs) Okay. Sir, Lilly did not send out a dear doctor letter about diabetes, as you
88: 1 suggested, in one of your E-mails that we looked at in either 2002 or 2003; is that correct?

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88: 4 A Um. Not that I'm aware of in the context of having all of the epidemiologic -- published epidemiologic trials in one spot.
Q (By Mr. Suggs) Okay. But you were involved, yourself, in having a third party send out a letter to 30,000 doctors which said that there was no causal relationship between Zyprexa and diabetes, were you not?
A Not that I recall epidemiologic.

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88:18 Q (By Mr. Suggs) For the record, this is a string of E-mails that -- the one on the top of the first page is dated May 14, 2003 from Eric Schultz to Daniel Janochoski with copies to Eric Klein, Jerry Clewell. The copy of this document has the Bates numbers cut off and I'll represent that the very first page of this document has the Bates No. ZY203647283.

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89: 5 Q (By Mr. Suggs) Okay. And, sir, I'd like to direct your -- again, we'll work through this document from back to front, because I believe that sequentially in time that's the way things work on

this one. So if I could direct your attention to page 2?
A Okay.
Q There is an E-mail from Daniel G. Janochoski -- did I pronounce that correctly, do you know?
A I believe it's Janochoski.
Q Jaochoski, okay. To Louann Cash, Eric Schultz with copies to Paula McCain. Did they work

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Q Okay. And Mr. Janochoski's E-mail, by the way, it's dated 5 -- May 12, 2003. He states: "Eric and Louann, during the week starting April 28, 2003 Express Scripts began mailing the attached letter on the hyperglycemia issue to the top 30,000 physicians who prescribe antipsychotics. Initially, Lilly and ESI developed a service agreement to support this mailing with $150,000. However, ESI changed their policy toward Pharma Service Agreements and decided to go forward with this letter without Pharma funding. Therefore, this letter was sent by Express Scripts without funding support from Eli Lilly.
Eric, you may want to use -- may want to forward this on to the appropriate field personnel as a heads up for the sales representatives. It would need to be water marked for, quote -- pardon me -- for not for use in detailing". And then there's a letter attached.
A Okay.
Q And you used to work for Express Scripts before you went to work for Lilly; correct?
A Correct.
Q Okay. And do you recall working with Express Scripts in the drafting of this letter?
A No.
Q Okay. Let me direct your attention to the E-mail immediately preceding that which is from Eric Schultz to Jack Bailey, Robert Baker, Michael Bandick, Thomas Hardy, Jack Jordan, Glyn Parkin, Bill Robinson, Joshua Smilely. With copies to Louann Cash, yourself, Daniel Janochoski and Paula McCain and Cassandra Mehlman. Do you see that E-mail?
A Okay.
Q Okay. And it was your understanding, was it not, that Michael Bandick, Jack Jordan, Glyn Parkin, Bill Robinson were all in the -- and Cassandra Mehlman were all people who dealt with the marketing of Zyprexa?

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Q (By Mr. Suggs) Did you have that understanding?
A No.
Q Okay. In his E-mail, Eric Schultz responds

24 to Mr. Janochoski's E-mail by saying: "Outstanding!
25 The benefits of a collaborative working relationship
92: 1 (at least 150,000). Kudos to Dan and Paula for
2 their relationship with this customer. Another
3 third-party communication aligned with Lilly data on
4 this issue reaching 30,000 prescribers." And then
5 it goes on to talk about how the field communication
6 should be dealing with that.
7 And then I want to direct your attention
8 next to the E-mail immediately preceding that which
9 is from Daniel Janochoski to Eric Klein and you in
10 which he notes in the second paragraph: "I also
11 want to recognize Jerry Clewell for his work with
12 ESI assisting them with data and research as they
13 wrote this letter. Jerry spent a significant amount
14 of time helping ESI feel comfortable with the data
15 available on this topic through conference calls and
16 follow-up meetings with this key customer. Jerry's
17 understanding of the data and ability to explain the
18 data was a key factor in ESI developing a comfort
19 level to produce this letter for their physicians."
20 Did I read that correctly?
21 A Yes, you did.

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94: 8 Q Do you recall what information you gave to
9 ESI so that they could put this letter together that
10 went out to 30,000 doctors?

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94:19 Q (By Mr. Suggs) My question was: Did you
20 recall what you gave them?
21 A Specifically?
22 Q Yes.
23 A Uh, I recall providing a presentation in
24 oral form of the -- an overview of all of the
25 epidemiology information.
95: 1 Q Do you recall whether you would have given
2 them a presentation on either what we marked earlier
3 as Exhibit 1 or Exhibit 2?
4 A I don't recall if this is the specific
5 presentation I provided to them or not. You know --
6 Q I'm sorry, your answer is?
7 A I don't -- I don't recall if this is the
8 presentation I gave to them or not.
9 Q Okay. Was it a PowerPoint presentation that
10 you did give to them?
11 A Yes.
12 Q Okay. Would you have been the one that told
13 them -- well, let me back up for a second. If you
14 can direct your attention to the letter. In the
15 second paragraph of the letter, it says: "The
16 purpose of this letter is to provide updated
17 information regarding the link between antipsychotic
18 medications and the risk of hyperglycemia, glucose
19 intolerance and diabetes mellitus in patients with
20 schizophrenia."

Did I read that part correctly?
A Yes.
Q And then in the next paragraph it says: "Zyprexa/olanzipine manufactured by Eli Lilly and Company is on the Express Scripts formulary, (inclusion under individual health plans formularies may vary)".
Did I read that correctly?
A Yes, you did.
Q And then below that there's a heading: "Clinical information". And then there are a number of bulletted points below that; correct?
A Correct.
Q And the second one, second bullet point state, quote: A number of recent case reports and studies have noted the association between specific atypical antipsychotic medications including clozapine, olanzipine, quetiapine, risperidone and ziprasidone, and the development of either hyperglycemia or diabetes in patients with schizophrenia. However, a definitive causal relationship between the use of these agents and the diabetes has not been established."
Did I read that correctly?
A Yes, you did.
Q And would you have been the one that told the ESI people that definitive causal relationship had not been established?
A I don't recall specifically telling them that.
Q Do you recall generally telling them that?
A No.
Q And you would not have been able to give them any of the exhibits that we referred to before relating to hyperglycemia and Zyprexa that had not been provided to you because if you didn't have that information, you couldn't have told them that information; correct?

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A If you're asking me if I had seen those other documents before, as previously testified, I don't recall seeing those documents before.
Q (By Mr. Suggs) Okay. And you certainly never told them that Dr. Taylor had concluded that Zyprexa-induced weight gain probably increases the risk of diabetes; correct?

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A Say that again.
Q (By Mr. Suggs) I said: You certainly never told them that Dr. Taylor had concluded that Zyprexa-induced weight gain probably increases the risk of diabetes; correct?
A Not to my knowledge.
Q Okay. Can I direct your attention next to Plaintiff's Exhibit 3223. For the record, this is

another string of E-mail, the one on the first page is dated January 14, 2004 from Jerry Clewell to a long lest -- well, to Virginia Stauffer with ccs to a long list of individuals. The subject line is "Re: Annals of Pharmacotherapy Recent Articles of interest 2004". And have you had a chance to just briefly see what this E-mail is about, sir?

A Very briefly. If you don't mind, I'd like another minute to --

Q Sure.

A -- scan it through.

Q Do you recall whether you reviewed this in preparation for your deposition?

A This is -- as I best recall the first time I've seen this since --

Q You wrote it?

A Yeah, I would have written it.

Q Okay.

A Okay.

Q Your E-mail on the first page is -- of this exhibit is the last in the E-mail chain discussing an article by Denise Sprauge, which was interpreted by others in the E-mail chain as saying that all antipsychotics have equal efficacy so that drug selection should be based on side effects. Would you agree with that general description?

A I did not get that out of it.

Q Okay. Let me -- maybe I can help you with -- if you can direct your attention to the bottom of page 3.

A Okay.

Q And over on the top of page 4 there's an E-mail from Vickie Poole to Thomas Hardy, Ilya Lipkovich, Patrick Toalson and a fair number of other folks in which she says: "Below is an abstract from the Annals of Pharmacotherapy February issue. It appears to say that all antipsychotics have equal efficacy so drug selection should be based on side effect profile."

Did I read that correctly?

A Yes.

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Q Virginia Stauffer replied to Vickie Poole Hoffman and the other folks that had been on the prior E-mail. And then your E-mail which begins on page 1 was the last of that E-mail chain; is that correct?

A My E-mail is the last on the chain, yes.

Q Okay. In the first part of your response you say: "Jenny, et al., I too would like to offer a couple of observations from the payor world relative to these studies and the environment."

And what did you mean by the phrase "payor world"?

A Um. Those would be the customers that the Outcome Liaisons interact with.

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102: 3 Q Okay. Directing your attention back to your
4 E-mail, you go on to state: "It cannot be
5 understated that the annals as well as AJHP are very
6 widely read pharmacy journals that influence
7 clinicals pharmacists and their recommendations at
8 the patients and P&T Committee levels."
9 And I believe you testified earlier that
10 the P&T Committee levels stood for Pharmacy &
11 Treatment?
12 A Therapeutics.
13 Q Therapeutic Committee. Okay. And those are
14 the committees that review the drugs that are listed
15 in the formulary; correct?
16 A Correct.

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103: 1 Q Okay. And you go on to say: "These
2 reviews, especially in addition to this month's
3 publication on the consensus guidelines for
4 schizophrenia published in AJHP can provide powerful
5 arguments for P&T Committee members to restrict
6 access to olanzipine on the basis of, one, perceived
7 parity or near parity and efficacy in light of, two,
8 the perceived 2 X cost differential between
9 olanzipine and risperidone."
10 Did I read that correctly?
11 A Yes, you did.
12 Q And the consensus guidelines that you're
13 referring to there, are those the guidelines that we
14 discussed briefly that came out of the American
15 Diabetic Association and the American Psychiatric
16 Association?

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104:10 Q Okay. And then continuing on in your E-mail
11 you have an Item No. 1 and it has a heading:
12 Selection of atypical antipsychotics for the
13 management of schizophrenia - Dennis Sprauge. This
14 is referring to the Sprauge article; is that
15 correct?

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104:22 A Um, I would assume so.
23 Q Okay. And you stated quote: Payors have
24 already expressed to me just yesterday that they
25 view this information as confirming their

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105: 1 interpretation of the data that there is very little
2 clinical difference between olanzipine and

risperidone."
Did I read that correctly?
A Yes.
Q Do you recall which payors had expressed to you that view?
A Which payor?
Q Yes.
A Specifically?
Q Yes.
A No.
Q Do you recall that there was more than one who did?
A Uh, yes.
Q Okay. Was that -- at that point the consensus view among payors that there was very little clinical difference between olanzipine and risperidone?
MR. BRENNAN: Objection to the form.
A I'm not aware of it being a consensus view.
Q (By Mr. Suggs) Okay.
A But we would hear that.
Q You did hear it, okay. Continuing on in your E-mail you then have a heading entitled "what can / we do in reaction to these perceptions"? You continue on by saying: "I believe this means that we have to step up all publications and communication efforts to educate decision-makers and their consultants (thought leaders, PBMs, etc.) on a long-term effectiveness (relapse prevention and medication persistence) of olanzipine. We were specifically criticized yesterday by a large Medicare payor consultant for not being able to provide more peer reviewed publications supporting an argument for long-term effectiveness."
Did I read that correctly?
A Yes.

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Q Okay. In the following paragraph you go on to say: "As a company we all need to do a much better job of proactively listening to payors (and other customers) concerns and proactively communicating important information such as adverse effective label changes without the tone of minimizing their importance (e.g. weight gain, diabetes, CVA)."
Did I read that sentence correctly?
A Yes, you did.

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Q And had you gotten feedback from -- from customers that the adverse effect label changes had been communicated with the tone of minimizing their importance?
A Not directly.
Q Okay. How did you -- did you hear about that indirectly?

A Yes.
Q And how did you hear about it indirectly?
A Um. I think my account executives that I worked with.
Q And who are those? Were these people within Lilly --
A Yes.
Q -- or--? Do you recall any people in particular?
A I had an account executive, yes, that I recall.
Q And what did this person communicate to you on that issue?
A Um. In a -- in a general sense, I don't recall the details. In a general sense it was more mannerisms of hearing from the competitors about, you know, side effects of Zyprexa and then them not being as open and interested, necessarily, of hearing it from Lilly by the time they had heard it from four other competitors they were convinced and they didn't feel like we were, you know -- they felt we were a lone wolf out there, I guess.
Q Well, in your E-mail you said that there was a tone of minimizing their importance referring to the safety label changes; correct?
A That was my impression.
Q Okay. And do you know who within the Company would have determined the tone of communicating adverse effect label changes?

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109:21 A No.

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110: 4 Q (By Mr. Suggs) Okay. You go on to say in your E-mail quote: Payors and clinicians have clearly articulated that this is an area where Lilly has lost its scientific integrity and therefore exposed us to great skepticism and we need to communicate the positive benefits of our products."
Did you read that correctly?
A Yes.

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110:23 Q Okay. And how was it that -- that you learned that payors and clinicians had articulated that Lilly had lost its scientific integrity?

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111: 2 A I think that's a paraphrase of my impression and the specifics of what generated that, sitting

here today, I couldn't tell you the specific --

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Q But that was the sense that you had back in early 2004 was that your customers, the payors and also clinicians were saying that Lilly had lost its scientific integrity and -- in dealing with adverse effect label changes; correct?

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A No. My -- my sense -- are you asking me what my sense of the --

Q (By Mr. Suggs) Well, let me -- let me restate the question because what I'm trying to figure out. When you say "Payors and clinicians have clearly articulated that this is an area where Lilly has lost its scientific integrity", what's the "this"?

A Um. I would assume that "this" relates to the above sentence.

Q And the above sentence had to do with communicating information about adverse effect label changes with the tone of minimizing their importance; correct?

A That's what the above sentence says, yes.

Q Okay. And you note that because of the perception that Lilly had lost its scientific integrity you were then exposed to great skepticism when you need to communicate the positive benefits of your products; correct?

A That's what this sentence says.

Q Okay. After you sent this E-mail, did you get any written response back from any of the -- well, let me back up for a second. It looks like you sent this E-mail to quite a few individuals. I haven't done a count, but it looks like there's probably a couple dozen people that you sent this to; correct?

A Um. It looks to me like I used the -- the group E-mail.

Q From the prior E-mails, you were basically replying to the people --

A Yeah.

Q -- who had been on the E-mail chain?

A Yeah. It looks like I hit reply to all to that effect to me.

Q And, like I said, there's probably, what, a couple dozen people who were listed there as receiving this; correct?

A I suppose so.

Q Do you recall whether you ever got any written response back saying anything about your E-mail?

A Did I get a written response back?

Q Yes.

A Not that I recall.

Q Did you get an oral response back from

anybody?
A Not that I recall.
Q Okay. So, when you sent this E-mail out saying that payors and clinicians have clearly articulated that this is an area where Lilly has lost its scientific integrity, nobody came back and challenged that -- that view at all either orally or in writing; correct?
A I don't know if they didn't or if you just don't have any responses or that I just don't recall an oral discussion.
Q Well, you certainly don't recall any oral or verbal -- pardon me -- any oral or written discussion about that; correct?
A I do not recall.
Q Okay. Let me show you what's previously been marked as Plaintiff's Exhibit 9281. For the record, this is an E-mail from Dr. Alan Breier to US Medical dated February 6th, 2004 which would have been about a month or three weeks, I guess, after your E-mail in which you noted that clinicians are saying Lilly has lost its scientific integrity. And, Mr. Clewell, do you recall receiving this E-mail from Dr. Breier?
A I do not.

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Q Okay. I'm going to direct your attention to the third paragraph of his E-mail that's in the paragraph with the bold heading "principles". Do you see that paragraph?
A Yes.
Q In particular, I'd like to direct your attention to four lines up from the bottom with the sentence that starts off by saying "we are", do you see where I'm at?
A Yes.
Q Okay. And, by the way, it was your understanding that Dr. Breier was the Medical Director of Lilly; correct?
A Yes.
Q Was it your understanding that he was then the top medical person within the Company?
A Um, I believe so --
Q Okay.
A -- but I'm not certain.

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Q (By Mr. Suggs) Okay. Well, in that paragraph I directed your attention to and in particular the sentence I drew your attention to, he says, quote: We are particularly challenged when it comes to presenting our data in a completely objective unbiassed manner because of our passion for our molecules and the belief that "spinning", data is sometimes necessary to gain a competitive advantage. If we do not abandon the spinning

mentality, we will not restore confidence in our medical research and rebuild the public trust our industry has compromised."

Do you see that language, sir?

A Yes, I do.

Q And having now read that particular sentence, do you recall receiving this E-mail?

A No.

Q Okay. Do you see any parallels between what Dr. Breier was saying here when he was talking about the need to abandon the spinning mentality and your E-mail a month -- or three weeks earlier when you noted that payors and clinicians have articulated that Lilly has lost its scientific integrity?

MR. BRENNAN: Objection to the form.

A I don't know if there's a parallel there or not, sir. I see those two documents there as they're read.

Q (By Mr. Suggs) Do you recall being advised by payors and clinicians that they believe that Lilly was spinning the data?

A I recall talking with payors, sometimes they were also clinicians, I don't specifically recall hearing that we were spinning data.

Q They just told you that they thought you had lost your scientific integrity; correct?

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A Again, that may be my -- my paraphrase of a couple of comments I had heard.

Q (By Mr. Suggs) And if, in fact, Lilly had been en -- engaged in a policy of spinning the data, that would indeed lead people to believe that Lilly had lost its scientific integrity, wouldn't it?

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A I can't speculate on that.

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Q (By Mr. Suggs) Okay. I'm going to show you what's been previously marked as Plaintiff's Exhibit No. 9165. For the record, this is another series of E-mails. The one in the very first page is dated June 11, 2004 from Woodie Moore Zachry to Haya Ascher-Svanum with copies to a number of other individuals. And, again, Mr. Clewell, I want to proceed with this from back to front. Because I think it's chronologically that's how it came about. So, if I could direct your attention to page 6 --

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118: 6 Q -- which I believe is the beginning of the
7 E-mail chain. There is a little bit down from the
8 top an E-mail from Haya Ascher-Svanum to us, under
9 score, usmdor, under score, zys yol.
10 A Okay.
11 Q Do you know what that is?
12 A That is the Outcomes Liaison Group. My
13 peers in the field in counter facilities.

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118:22 Q Okay. In Ms. Ascher-Svanum's E-mail, she is
23 forwarding an E-mail that Bruce Kinon had originally
24 written to Eric Schultz and the copies to others
25 earlier that day; correct?
119: 1 A It would appear that way.
2 Q Okay. And in Dr. Kinon's E-mail he says:
3 "Dear Eric, as we briefly discussed today, I would
4 appreciate your guidance in generating a list of the
5 top ten reasons for payors to keep Zyprexa as second
6 line APD (after RIS failure), end quote.
7 What does "APD" stand for?
8 MR. BRENNAN: Objection to the form.
9 A Um, you'd probably have to ask Bruce Kinon
10 to be certain.
11 Q (By Mr. Suggs) Did you understand it to mean
12 antipsychotic drug?
13 A It probably is.
14 Q Okay. And the "RIS failure" would be
15 referring to a failure with using the drug
16 risperidone; correct?
17 A Um, probably so.
18 Q And would you agree with me, sir, that we
19 can interpret that first sentence of Dr. Kinon's as
20 asking for guidance in generating a list of the top
21 10 reasons for payors to keep Zyprexa as a second
22 line antipsychotic drug to be used after there has
23 been a failure with the use of risperidone?

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119:25 A Um. I read it the same as you. I
120: 1 appreciate your guidance in generating the list of
2 the top 10 reasons, etc., etc.
3 Q (By Mr. Suggs) Okay.
4 A If that's what you're asking me.
5 Q Yes. And then the second sentence states:
6 "These reasons would help us to generate CSFs for an
7 OLZ Time to D/C versus Comparators study."
8 Can you translate that into lay, non-Lilly
9 speaking language?

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120:11 A I actually can't. I do not know what CSFs
12 are.
13 Q (By Mr. Suggs) Okay. And then he goes on to

say: "These should be reasons that you generally wish to have when arguing before state pharmacy boards that are dying to PA Zyprexa."
Did I read that correctly?
A Yes.
Q Do you have an understanding what the expression "PA" means?
MR. BRENNAN: Objection to form.
A Um. I -- I can guess.
Q (By Mr. Suggs) And would your guess be the

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120:24 "PA" stands for prior authorization?
25 A That would be a guess.
121: 1 Q That was my guess, too. So what he's saying
2 there is these should be reasons that you generally
3 wish to have in arguing before state pharmacy boards
4 that were dying to put Zyprexa on a list of drugs
5 where you had to have prior authorization, is that
6 how you interpreted this when you saw it?
7 A Um. I interpret this as Dr. Kinon seeking
8 field feedback from people that interact with
9 payors. If that's what you're asking me, then the
10 answer is, yes.
11 Q Okay. And Mr. Allen just showed me a page
12 from what we had previously marked as Exhibit 1
13 where you, yourself, had used the initials PA for --
14 to stand for prior authorization.
15 A Yes.
16 MR. BRENNAN: What page are you showing him?
17 Q (By Mr. Suggs) Page 2.
18 MR. ALLEN: So it's not a guess.
19 A Yes.
20 Q (By Mr. Suggs) Okay. And can you explain
21 what's involved when prior authorization is
22 required?
23 A It means that the payor has to approve use
24 of the drug.
25 Q Okay. And was that prior authorization
122: 1 required as to all antipsychotics or any
2 antipsychotics?

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122: 4 A I'm not sure I understand that question.
5 It's very broad.
6 Q (By Mr. Suggs) Okay. Well, when Dr. Kinon
7 says: These should be reasons that you generally
8 wish to have when arguing before state pharmacy
9 boards that are dying to put Zyprexa on a --
10 Zyprexa -- pardon me -- on a prior authorization
11 list, was Zyprexa already on prior authorization
12 lists in some states?
13 A In 2004? I'm not aware of any.
14 Q Okay. Did their subsequently --
15 A There may have been one.
16 Q Okay. Did -- was Zyprexa subsequently put
17 on prior authorization?

A It's my understanding that one state did it, but I don't recall when.
Q Okay.

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123: 6 Q (By Mr. Suggs) Okay. Mr. Clewell, after
7 Ms. Haya Ascher-Svanum received Dr. Kinon's E-mail
8 asking for the top 10 list, she then forwarded that
9 on to the folks in the Outcomes Liaison group and
10 said: "During the Monday teleconference, it would
11 be helpful if you were to help generate a few items
12 to construct a list of the top 10 reasons for payors
13 to keep Zyprexa as second line APD (after RIS
14 failure)." Correct?

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123:19 A Okay.
20 Q (By Mr. Suggs) So basically she forwarded on
21 Dr. Kinon's E-mail to your group --
22 A Correct.
23 Q -- in Outcome Liaison? And then you on the
24 very same day, just a couple hours later, respond
25 back with what you saw as the top five reasons for
124: 1 payors to keep Zyprexa as a second line APD after
2 RIS failure; correct?
3 A My response is listing five reasons, if I
4 were to adopt the hat of a payor.
5 Q Okay.
6 A I'm paraphrasing what a payor might say,
7 so...
8 Q Okay. And I just want to go through those.
9 The first of your top five was -- it states, quote:
10 The "real" No. 1 reason is almost always cost/RX
11 relative to competitors. But among decision-makers
12 who are intent on moving Zyprexa to second or later,
13 it is generally stated to be due to some other
14 reasons."
15 Now, when you say that the real No. 1
16 reason is almost always cost/RX relative to all
17 competitors, that's just basically talking about the
18 cost of the drug prescription; correct?
19 A Cost per RX would be cost per prescription.
20 Q Okay. And you go on to state in that
21 paragraph: This is begin decision-makers must
22 publicly, A, evaluate drugs on safety and efficacy
23 before cost and; B, have solid arguments to convince
24 mental health state holders to agree with their
25 decisions who would otherwise be in opposition."
125: 1 Did I state that correctly?
2 A Yes.
3 Q And that was your perception based on -- at
4 that point in time you had had, what, five years of
5 experience in that job dealing with payors?
6 A Excuse me, about that.
7 Q Okay. And do you recall what the cost per
8 prescription of Zyprexa was as compared to
9 competitors?

A Not specifically.
Q Do you recall generally?
A If you look at the cost per prescription, again, their perception without adjusting for differences in populations, which is critical to understanding that data, they would assume that it was about twice.
Q Okay. And you go on in your second point to state, quote: Diabetes and the assoc -- association of diabetes to weight gain in the general population is the most common clinical rationale for moving Zyprexa to second line. For example, Dr. John Newcomer has been meeting with the advocacy community asking them to back off on their opposition to open an equal access because of "Zyprexa safety concerns around metabolic issues".

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128:10 Q Okay. And how was it that you became aware
11 that diabetes and the association of diabetes to
12 weight gain in the general population was the most
13 common clinical rationale for moving Zyprexa to
14 second line?
15 A That was -- that was what we were hearing,
16 um, you know, people out in the field. Either, you
17 know, account managers or, you know, as I think
18 about it those are the people that I had heard that
19 from the most, I think.
20 Q Okay. I'd like to move on to your next
21 point, which is three: "The entire market
22 (clinicians, decision-makers, thought leaders, etc.)
23 deeply believes that efficacy is the same across all
24 ages. The market does not -- also does not
25 distinguish between efficacy and effectiveness."
129: 1 And then it continues on with some more language
2 there. But that issue of whether or not efficacy
3 was the same across all agents is something that we
4 also saw being discussed in your earlier memo back
5 in January of 2004; correct? The one that was
6 Exhibit 3223.
7 A Can I see that again?
8 Q Sure.
9 A I don't remember with all the documents.
10 Are you refer -- referring to the last sentence?
11 Q Well, the E-mail generally, yes.
12 MR. BRENNAN: Objection to form.
13 A You know, I honestly am not reading that --
14 that same concept in here.
15 Q (By Mr. Suggs) Okay.
16 A Oh, okay. Very little clinical difference
17 between olanzipine and risperidone is what you're
18 referring to?
19 Q Yes.
20 A Okay.

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130: 8 Q Okay. If I could direct your attention to

the next numbered item in your E-mail. You say: "Lilly has a very negative image in the minds of many decision-makers and thought leaders over the Company's business practices."

That's the first sentence in that section; correct?

A Yes.

Q And how is it that you learned that Lilly had a very negative image in the minds of any decision-makers and thought leaders?

A Again, you know, I would say that that's a characterization I had heard through other people at Lilly.

Q Okay. And what were the Company's business practices that had led these decision-makers to have a very negative image of the Company?

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131:

A Uh. Can you restate that?

Q (By Mr. Suggs) Sure. What were the Company's business practices which had led these decision-makers and thought leaders you were referring to to have a very negative image of the Company?

A I think specifically the thing that stands out is not willing to provide supplemental rebates.

Q Okay. You go on to say in the second sentence: "Even some of our greatest clinical and business allies are willing to make very negative public comments regarding issues related to our pricing and other business practices while continuing to believe in the need for open access."

Did I read that sentence correctly?

A Yes, you did.

Q Now, the issues relating to your pricing, that would be the rebates that you were talking about; correct?

A Uh. It would be related to that.

Q Okay. And what were the other business practices that you were getting very negative comments about?

A Well, I mean, pricing and rebating and supplemental rebating are all business practices --

132:

Q Okay.

A -- if that's what you're asking me.

Q Okay.

A They're related but different.

Q Okay. And then -- pardon me. You then went on to say: "Unfortunately, I'm seeing rapid erosion of support for open/equal access from those who would have been supported just 12 to 18 months ago." Correct?

A Correct.

Q Okay. So, apparently this was an issue that was picking up steam at this point; is that correct?

A Um. Yeah, I suppose I was seeing or hearing more of it.

Q Okay. And then finally your -- the last in your top five list says, quote: Lilly has a credibility problem over the way that it

historically dealt with weight gain because some customers feel that the Company was not responsive in helping clinicians address the issue of weight gain, they do not trust Lilly to help them with diabetes issues. See point No. 2."

And point No. 2 is: The issue about diabetes and the association of diabetes to weight gain. Correct?

133: A Correct.

Q Okay. Now, how is it that you learned that Lilly had a credibility problem over the weight -- it had dealt with weight gain?

A Again, I would listen to the feedback of our customers, it's not something that I agreed with. I know you could usually correct it with, you know, a discussion of all the data.

MR. ALLEN: Objection, non-responsive.

Q (By Mr. Suggs) Did the payors that told you that they had a problem with Lilly's credibility, did they bring that up on your own or did you actively ask them whether there was a credibility problem?

A It was more subtle than that.

Q Okay. And how was it more subtle?

A Um. They wouldn't specifically say you have a credibility problem --

Q But when you met --

A -- and it was an impression --

Q Okay. And you had interactions with these --

A -- that I -- that I would hear.

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135: Q Okay. And do you recall anyone ever coming back and saying, no, Jerry, you got it wrong, these top five just aren't, you know, we're not buying that?

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135: A I don't think I heard anybody say we are or aren't.

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187: Q All right. Exhibit No. 2 has your name on it and I assume you prepared Exhibit No. 2?

MR. BRENNAN: You want to see my copy?

A Sure.

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189: Q What's Exhibit 2 for the Jury, please?

A A PowerPoint presentation.

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189: know it's a PowerPoint presentation. Can you tell the Jury -- try to assist the Jury in understanding what Exhibit No. 2 is, can you do that for me, please?
A It is a PowerPoint presentation on the subject entitled: Antipsychotics and Diabetes: An Evidence Based Approach.
Q You just read the title, did you not?
A Yes.
Q Okay. Now that you've read the title, can you tell the Jury what the purpose -- why was this PowerPoint presentation, which you've now read the title, why was it put together and who was this PowerPoint presentation for?

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190: Q Yes. Who was this PowerPoint presentation prepared for and why?
A This was prepared in response to a question from the coalition of Community Mental Health Centers in Missouri.
Q What question did they ask you?
A For an update on the information related to antipsychotics and diabetes.
Q What year?
A Uh, probably 2004.
Q Why were they asking?

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190:14 A My understanding as to why they were asking --
Q (By Mr. Allen) Yes.
A -- was with the label changes on the products they wanted to better understand it.
Q And is all the information -- so you were asked by these coalition of -- mental health facilities, did you say?
A Coalition of Community Mental Health Centers.
Q Is that an actual name of an organization?
A Yes.

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191: Q Who from this organization asked you?
A Kathy Carter.

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191:12 Q Was she a customer?
13 A Yes.

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192: 2 I'll ask you again later. So Exhibit No. 2 was
3 prepared by this lady -- at the request of this
4 lady, the coalition lady in Jefferson City; right?
5 A Yes.
6 Q She asked you to prepare it. And the
7 question was she wanted a complete update on the
8 relationship between Zyprexa and hyperglycemia?
9 A No.

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192:12 A Antipsychotics and diabetes.
13 Q Okay. So all antipsychotics and diabetes;
14 is that correct?
15 A Yes, sir.
16 Q Is hyperglycemia relative to diabetes or do
17 you know?
18 A Hyperglycemia can be relevant.
19 Q How?

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192:21 A I mean, it's one of the symptoms of
22 diabetes.

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192:23 Q (By Mr. Allen) It certainly is. It's
24 actually a sign, is it not, as opposed to a symptom.
25 Do you know the difference --
193: 1 A Yes.
2 Q -- between a symptom and a sign?
3 A Yes.
4 Q It's a sign, not a symptom, isn't it?
5 A Yes.
6 Q Okay. So, hyperglycemia is a sign of
7 diabetes, is it not?
8 A Yes.
9 Q By the way, obesity, is that in any way
10 related to diabetes?
11 A It's one of the risk factors for diabetes.
12 Q It's an established risk factor?

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193:14 Q (By Mr. Allen) Is it not?
15 A Yes.
16 Q It's a well-established risk factor;

correct?
A Yes.
Q Okay. In fact, in your presentation, if you look back -- on it looks like on slide 12, you see slide 12?

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193:25 Q (By Mr. Allen) I mean slide 12.
194: 1 A Okay.
2 Q Are you with me, sir?
3 A Yes.
4 Q Are you with me?
5 A Yes. Yes.
6 Q What -- you list here established risk
7 factors for diabetes in the general population.
8 A Yes.
9 Q And one of those is being overweight, is it
10 not?
11 A Yes.
12 Q So now let me ask this. Isn't it an
13 established fact that Zyprexa causes weight gain?
14 A Yes.
15 Q And it's an established fact that being over
16 weight is a risk factor for diabetes; correct?
17 A Being obese, defined as a BMI greater than
18 25. Body Mass Index for the Jury's.
19 Q Thank you. So it's established, as you said
20 right here: Established risk factor for diabetes is
21 being obese -- your term is overweight, BMI greater
22 than or equal to 25; correct?
23 A That would be the American Diabetes
24 Association's term as is cited there --
25 Q Sir?
195: 1 A -- overweight greater than 25 -- BMI greater
2 than 25.
3 Q Sir, this is a slide show you prepared in
4 answering the questions. Remember you said you did
5 that; right?
6 A Based on evidence that's published, and
7 information that's published.
8 Q Right. And you said you state facts, not
9 opinions; right?
10 A Yes.
11 Q Okay. So it's an established fact, using
12 your word, being overweight, BMI greater than or
13 equal to 25 is an established fact, it's a risk
14 factor of diabetes; right?
15 A For patients that have a BMI greater than
16 25, they would be overweight and that is an
17 established risk factor for diabetes. If that's
18 what you're asking, the answer is yes.
19 Q And it's also a fact -- it's also an
20 established fact that Zyprexa causes weight gain;
21 correct?

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195:23 A Yes.

Q (By Mr. Allen) It's also an established fact that Zyprexa causes statistically significant weight gain; correct?
A Yes.
Q It's also an established fact that hyperglycemia is a sign of diabetes, correct? You just told us that.
A Yes.
Q And it's also an established fact that Zyprexa causes statistically significant elevations in blood glucose levels; correct?

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A Um, I don't think that that's an established fact.
Q (By Mr. Allen) Is there any evidence for that fact?
A There's evidence for and against, as I understand it.
Q Have you been provided all the evidence for the fact -- let me ask this question. Let me be very clear.
Do you think you've been given all the evidence by your bosses at Eli Lilly about the fact that Zyprexa can cause statistically significant increases in blood glucose levels?

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A To the best of my knowledge --

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A -- I've been provided the data that is necessary to evaluate that.
MR. ALLEN: Objection, non-responsive. I didn't ask you that question, I asked you a different question.
Q (By Mr. Allen) Do you think your bosses at Eli Lilly have provided you all of the information they have -- they have concerning whether or not Zyprexa causes statistically significant increases in blood glucose levels?

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A I don't know.
Q (By Mr. Allen) You don't know, do you?
A That's what I just said.
Q Right. So, if you don't know -- if your bosses or your superiors don't give you information -- it's just like a computer you can only get -- give it as much good information as you have inputted; right?

A Sure.
Q So if you're not told information, there's no way you can relate it to the third-party payors or the customers; isn't that correct?
A That would be true.
Q And isn't it a fact, by the way, that Eli Lilly has known since 1999 -- about the time you started, they've known since 1999 that Zyprexa caused greater weight gain than other second generation antipsychotics other than clozapine?

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Q (By Mr. Allen) Isn't that a fact?
A Some others.
Q No, all others. They've known since 1999, haven't they?

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A In 1999 Eli Lilly, if you're asking me if in 1999 Eli Lilly knew that compared to some of the other antipsychotics it caused statistically significantly more weight gain, the answer is, yes.
Q (By Mr. Allen) Than other second generation antipsychotics?
A Yes.
Q Including Risperdal?
A Yes.
Q Including Seroquel?
A Yes.
Q Later including Geodon?
A Yes.
Q Okay. So they've known that since 1999; right?
A That's my understanding.
Q Where is that letter? I'm looking for the letter that came from your department or the medical department to the third-party payors or the doctors as of 1999 saying we want you to know that Zyprexa causes greater weight gain than Risperdal, Seroquel, and the other second generation antipsychotics, where is that letter?

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A I don't know.

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A I understand there was a medical letter on the subject of weight gain available. But the details of what that was, I don't know because it re -- that resides in another department.
Q Didn't you, in fact -- I thought you told

Mr. Suggs this morning -- well, let me -- let me -- we'll get to that in a second. So you heard there might be a letter, but you've never seen this letter; is that right?
A On weight gain, just to be clear, you're discussing weight gain?
Q That's what I said.
A Okay.
Q Right?
A That's my understanding.
Q Okay. But if -- if Eli Lilly was being fair and honest and open and not spinning data, they would have had to say by 1999 that Zyprexa causes statistically significant weight gain greater than that of Seroquel, Risperdal, and the other second generation antipsychotics other than clozapine; is that correct?
MR. BRENNAN: Object to the form.
A To the best of my knowledge, that's what Eli Lilly was saying in 1999.
MR. ALLEN: Objection, non-responsive.
Q (By Mr. Allen) I didn't ask you what you think they were saying. I said if they were being fair and honest they would have to say that our product causes statistically significant weight gain greater than that of other second generation antipsychotics other than clozapine; correct?
A To be fair -- let me paraphrase your question back to make sure I understand it.
Q Uh-huh.
A To be fair and honest, Lilly would have to state that it caused significantly -- olanzipine caused significantly more weight gain --
Q Yes, sir.
A -- than other second generation antipsychotics?
Q Yes, sir.
A As I said, we were stating that. So, I think we were fair and honest, yes.
MR. ALLEN: Objection, non-responsive. I didn't ask you for an opinion. Okay. I didn't ask you for what you claim they said or what you said they did. I just asked you whether or not this is a true statement. Answer my questions. Mr. Bill over there -- Mr. Bill --
MR. BRENNAN: Brennan, just so you know.

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question is: If Eli Lilly was being fair and honest, they would be telling people as of 1999 Zyprexa causes statistically significant weight gain greater than the other second generation antipsychotics, including Seroquel and Risperdal; correct?

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A They were.

MR. ALLEN: Objection, non-responsive.
A Yes.
Q (By Mr. Allen) The answer to my question is what, sir?
A Yes.

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Q (By Mr. Allen) Okay. Look at slide 24. Atypical, you with me, sir?
A Yes.

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Q What -- what in this slide 24, what product did you-all say has a relative risk highest for diabetes between Zyprexa, Risperdal or Seroquel?
A This isn't what we said. This is what the publication found or the study found.
Q I understand. I'm just asking you what you -- what you published when you were asked a question by this lady in Jefferson City which product did you say that carried with it the greatest risk of diabetes?
A They actually are the same.
Q They are?
A Yes.
Q Didn't you have Seroquel as a greater risk here?
A No.
Q Okay. So you -- did you try, you and your Company, did your Company try to say that the risk of diabetes, hyperglycemia was comparable among the second generation antipsychotics?
A I don't recall using that exact word, but they're similar.
Q So, it was your Company's position, Zyprexa caused statically greater weight gain but did not cause a statistically greater incidence or risk of diabetes; is that correct?

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A It is my understanding that there are statistically greater weight gain observed. There is statistically greater weight gain observed amongst olanzipine treated patients, but there is not statistically greater observation amongst atypicals with respect to diabetes in all studies.
Q (By Mr. Allen) In all studies. But, of course, it's also your understanding as an established fact that being overweight or at least a BMI greater than or equal to 25 puts you at an increase risk of diabetes; right?

204: 7 A Again, it's one of many risk factors.
8 Q (By Mr. Allen) Did -- is this part of --
9 sir, when I ask you whether or not Zyprexa carries a
10 greater risk of diabetes and you've already told me
11 it carries a greater risk of being overweight, but
12 not necessarily diabetes, are you dodging and
13 spinning?
14 A No, sir.
15 Q Would it be wrong to dodge and spin?
16 A I suppose so.
17 Q Are you hiding the truth?
18 A No, sir.
19 Q Okay. Those were problems at Eli Lilly,
20 though, weren't they?

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204:22 A Again, hearing from customers on occasion,
23 that's something that was voiced to me.

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206:25 Q You know, I was sitting here listening to
207: 1 your testimony and your E-mails today. Did you
2 prepare your E-mails to be truthful and accurate at
3 the time you prepared them?
4 A To the best of my knowledge.
5 Q Okay. You were trying -- you were not
6 trying to hide facts from those individuals to whom
7 you wrote the E-mails, were you?
8 A Not to the best of my knowledge.
9 Q You were trying to accurately relay to them
10 the state of affairs that existed around at Eli
11 Lilly; isn't that right?

Jerry Clewell-Pharm.D.(October 5, 2006)

207:13 Q (By Mr. Allen) As you knew it?
14 A I was relaying on to Eli Lilly what I and
15 occasionally some of my other colleagues in the
16 field would hear.

Jerry Clewell-Pharm.D.(October 5, 2006)

284: 2 Q Okay. Can you hold that exhibit,
3 Exhibit 01110 up for the Jury, please. You see it
4 says: "Issues Management Planning Weight Gain". At
5 the bottom it says: "Lilly Answers That Matter".
6 Did I read that correctly?

Jerry Clewell-Pharm.D.(October 5, 2006)

284: 8 Q (By Mr. Allen) Can you hold that back up?

Jerry Clewell-Pharm.D.(October 5, 2006)

284:10 Q (By Mr. Allen) Okay. Now, "answers that
11 matter", that's something you're familiar with;
12 right?
13 A I've heard that.
14 Q As a matter of fact, you used it in your
15 September 13th, 2002 E-mail, did you not?
16 A Yes.
17 Q In fact, in your September 13th,
18 2002 E-mail, you said: "In other words, it is not
19 uncommon for us in the field to hear from customers
20 that they perceive Lilly is dodging the issue or
21 hiding the truth rather than giving them answers
22 that matter" --

Jerry Clewell-Pharm.D.(October 5, 2006)

284:24 Q (By Mr. Allen) -- is that your words?

Jerry Clewell-Pharm.D.(October 5, 2006)

285: 1 A I'll presume you read this correctly.
2 Q (By Mr. Allen) That's your words?
3 A Yes.
4 Q Because Lilly's slogan has always been that
5 when they give answers, the answers will matter;
6 isn't that correct?
7 A Their slogan has always been answers that
8 matter.
9 Q Right. And you personally --
10 (phone dialing)
11 MR. BRENNAN: Is anybody still on? All
12 right.
13 Q (By Mr. Allen) You personally have written
14 in your own E-mail that it was your perception that
15 Lilly wasn't giving answers that mattered; right?
16 A It's my perception that -- oh, Lordy, let's
17 go back to that sentence then.
18 Q September 13th, 2002.
19 MR. ALLEN: Here it is. You can have it.
20 MR. BRENNAN: Thanks. Okay. Thank you.
21 A Okay. Could you re-ask the question?
22 Q (By Mr. Allen) Yes. All I'm trying to say,
23 sir, we're on exhibit now No. 01110, the Issues
24 Management Planning and we were on the Lilly slogan
25 answers that matter; right?
286: 1 A Okay, yes.
2 Q And I was trying to relate it back to your
3 own personal E-mail of September of 2002 where you
4 said Lilly was not getting answers that matters;
5 right?
6 A No. What I was saying is it's not uncommon
7 from us in the field to hear from customers that
8 their perception was that we weren't giving answers

sir

that matter.
Q Yeah. And my question to you then is, you found the sentence. Why did you use that phrase we're not getting answers that matter?
A Probably because that was a common phrase used --
Q By?
A -- at Lilly.
Q At Lilly, that's what I thought.
A Yes.
Q That's all I meant to ask.
A Yes.
Q So when you wrote your September 2002 E-mail, you in fact -- you, in fact, were reflecting on your own Company slogan that we need to give answers that matter; right?
A Yes.
Q And so when you wrote that E-mail and you were talking about your customer's perceptions the phrase "answers that matter" is not something that Scott Allen created, it's something that you, your Company created, isn't that true?
A True.
Q And isn't it true that your Company -- and can you hold this up for the Jury again, so we can get back in context of Exhibit 01110.
A This one?
Q Yes, sir. Your Company promises that when it gives answers, the answers are going to matter; right?
VIDEOGRAPHER: Got it.
A I don't know if it's promising that, but it says that Lilly is a Company that has answers that matter.
Q (By Mr. Allen) Okay.
A That's what I understand from the slogan.
Q So illy -- Lilly is telling its customers, be it payors or doctors or patients, that when you hear from us on a topic, our answers matter and we're telling you the truth, isn't that true?
MR. BRENNAN: Objection to the form.
A Yeah, it says that their answers will matter. And I presume it would be that we're telling you the truth.
Q (By Mr. Allen) Right. And as part of your process when you talk to customers, it was your own belief that customers thought Eli Lilly was minimizing the issue of weight gain, right?
MR. BRENNAN: Objection to the -- asked and answered.
A It was my belief that customers would give me the feedback on occasion and to my colleagues, other OLs, that we weren't always being as upfront, yes, whatever language that's been in that E-mail that we've talked.
Q (By Mr. Allen) Okay. Look at the second page and hold it up for the Jury. The issue is weight gain, isn't it not?
A That is what's titled on the page, yes.
Q Right. This is an Issues Management Planning document; correct?
A That's how it's labeled. I don't know what an Issues Management Planning document is, but

that's how it's labeled.
Q You're -- yes, sir. Okay. Now, what is the issue -- thank you.

Jerry Clewell-Pharm.D.(October 5, 2006)

289: Q (By Mr. Allen) What is the issue -- the first bullet point, what's the issue? Can you read it out loud for the Jury, please?
A It says: "Weight gain remains the No. 1 liability of Zyprexa and is leading to many of the new issues surrounding the drug, i.e., diabetes, lipids, etc."
Q Do you agree that weight gain was the No. 1 liability of Zyprexa and was leading to many new issues including diabetes and lipids?
MR. BRENNAN: Objection to the form.
A I don't know what they mean by "leading to". It was a common question for us to get. I mean, not uncommon, I'll put it that way. I can't say it's common, but it's not an uncommon question for us to get questions on weight gain.
Q (By Mr. Allen) Okay. Now, you told -- if you look under the second bullet point, it talks about our position. Do you see that?
A Yes.
Q Can you read the first sentence out loud for the Jury, please, about our position Eli Lilly's position on the issue of weight gain?
A It says: "Weight gain can occur with Zyprexa as with other antipsychotics and mood
290: stabilizers."
Q Okay. So the stated position in this document is weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers; is that correct?
A That's what it says.
Q It doesn't say our position is Zyprexa causes more weight gain than other second generation antipsychotics, does it?

Jerry Clewell-Pharm.D.(October 5, 2006)

290:12 A That's not what it says.
Q (By Mr. Allen) Right.
A You're right.
Q Okay. What's the stated rational in this document for your Company's position that weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers?

Jerry Clewell-Pharm.D.(October 5, 2006)

290:20 A What is their position, I'm sorry, was that your question?
Q (By Mr. Allen) What is the rational listed for this that position?

24 A I don't know, I didn't write it.

Jerry Clewell-Pharm.D.(October 5, 2006)

291: 2 A I've never saw this document.
3 Q (By Mr. Allen) I didn't ask whether you'd
4 ever seen it before, sir. What is the stated
5 rational for this position in this document? You
6 see the rational for our position?
7 A No, I just say our position. I didn't see
8 the word "rational".
9 Q Yes. If you look at the bottom of the page,
10 it has rational for our position.
11 A I'm sorry, I was look at our position.
12 Okay.
13 Q Can you tell me -- this is Eli Lilly's
14 words, the rational for your position on weight
15 gain. Read it out loud, please.
16 A This document says: "Rational for position
17 to minimize the liability of weight gain while at
18 the same time increasing focus of Zyprexa's superior
19 efficacy."
20 Q Okay. This document states the rational for
21 Eli Lilly's position on weight gain is to minimize
22 the liability of weight gain; correct?
23 A That is what this document says.
24 Q Okay. Now, assuming that this is an Eli
25 Lilly document and Eli Lilly followed their position
292: 1 on this issue and minimized the liability for weight
2 gain. Okay, you with me so far?
3 A No.

Jerry Clewell-Pharm.D.(October 5, 2006)

292: 4 Q Do you have --
5 A Assuming that it's a Lilly document, I got
6 that.
7 Q Well, you agree it's a Lilly document, isn't
8 it?
9 A It appears to be a Lilly document. What was
10 the second part of the statement, I'm sorry.
11 Q Yes. When you have said under oath that the
12 dodging the issues and we're hiding the truth and
13 we're losing credibility concerning the issue of
14 weight gain, isn't it possible it's because of what
15 Eli Lilly is doing on the issue of weight gain?
16 A I don't know.
17 Q Well, if Eli Lilly is trying to minimize the
18 liability of weight gain maybe that's why they're
19 losing credibility, is that possible?

Jerry Clewell-Pharm.D.(October 5, 2006)

292:21 A I don't know. Again, it's my experience
22 that we weren't minimizing the liability of weight
23 gain.
24 Q (By Mr. Allen) Well, didn't you try --

didn't Eli Lilly try to eliminate the risk of diabetes from the risk benefit equation for doctors and payors?

Jerry Clewell-Pharm.D.(October 5, 2006)

Q Sir, I'm going to hand you what's been marked as Plaintiff's Exhibit 16, it's marked 01111, you can hold this up for the Jury: Issues Management Planning on Diabetes; is that correct?

Jerry Clewell-Pharm.D.(October 5, 2006)

A It says: Issues Management Planning Diabetes.

Jerry Clewell-Pharm.D.(October 5, 2006)

A Can I have a second to look over it, if you're going to ask me about --
Q I'm just going to ask you about one thing -- I'm going to ask you about one thing. You see on the first page of that document the rational for your Company's on diabetes?
A On the first page of this document.
Q Yes, sir.
A It see a bullet point states rational for position, yes.
Q Can you read out loud to the Jury what Eli Lilly stated rational for their position on diabetes is?
A This document states: "Showing that diabetes is common occurrence for all antipsychotics and not just Zyprexa will help reduce the perception that diabetes is linked specifically to Zyprexa and in turn will help to eliminate the risk from the risk benefit equation."
Q The last part says "will help to eliminate this risk from the benefit risk equation"; is that correct?
A "Will help eliminate this risk from the benefit risk equation", okay, that's what it says.
Q Okay. Now, you've told us were not in the sales force; isn't that correct?
A That's correct.
Q You said you weren't part of the sales trainers; is that correct?
A That's correct.
Q You said you didn't go out and talk to physicians; is that correct?
A Not as prescribers.
Q Okay.
A Only if they were on a P&T Committee.
Q But you know that prescribers talk to patients; right?
A Yes.
Q You know that prescribers have to evaluate

the risk of a product; isn't that correct?
A Yes.
Q You know that prescribers have to give the best information that they get from the drug Company, they can get the best information they get from the drug company to their patients; right?
A From all sources they give the best information they can.
Q Right. And if the drug company is trying to eliminate a risk from the risk benefit equation, what does that mean, eliminate a risk from the risk benefit equation?

Jerry Clewell-Pharm.D.(October 5, 2006)

295:15 A I honestly don't know what that means.

Jerry Clewell-Pharm.D.(October 5, 2006)

295:16 Q (By Mr. Allen) Do you know what a risk benefit equation is?
A I know that conceptually it's a -- you know, which is greater, the risk or the benefit. Beyond that, that's the best I can explain it.
Q Did your Company, Eli Lilly, try to involve themselves into effecting the risk benefit equation?

Jerry Clewell-Pharm.D.(October 5, 2006)

295:24 A I don't know. Not to my knowledge.

Exhibit 7
Jack Jordan

Jack E. Jordan (October 26, 2006)

21:24 Q. Can you tell the jury your
22: 1 name, please, sir?
2 A. My name's Jack E. Jordan.

Jack E. Jordan (October 26, 2006)

22:10 Q. And for whom do you work?
11 A. I do several things. I'm an
12 Associate Professor at the School of Business
13 at Indiana University of South Bend. And I
14 do other activities on the side.

Jack E. Jordan (October 26, 2006)

24: 3 Q. You said you're an Associate
4 Professor in the School of Business at the
5 University of Indiana South Bend. Is there
6 any particular course you teach?
7 A. Two courses: I teach
8 Strategic Marketing and I teach a management
9 course.
10 Q. Can you briefly describe for
11 the jury, please, what is Strategic
12 Marketing?
13 A. The conceptual framework I
14 use is I go through a conceptual framework of
15 analyzing the market environment, coming up
16 with a marketing strategy, and then
17 determining a marketing mix from that
18 strategy and, ultimately, customer retention.
19 So that's kind of the semester framework.

Jack E. Jordan (October 26, 2006)

24:20 Q. Any particular textbook you
21 use?
22 A. There is. It's called
23 Strategic Marketing. I can't remember the
24 authors of the book.
25: 1 Q. The title of it is Strategic
2 Marketing?
3 A. It is, yes.
4 Q. Now if I wrote this down
5 right, and I may not have and you help me, I
6 asked you what is strategic marketing? I
7 believe is what you said, you correct me if
8 I'm wrong, that you determine a market?
9 A. You assess the marketing
10 environment.
11 Q. What's that mean?
12 A. It's an assessed quantitative
13 and qualitative assessment of customers,
14 competition, context, and competition.
15 Q. What's "context" mean?
16 A. The regulatory environment,

the political environment, social issues, et cetera.

Q. Okay. Then you said after you determine -- you assess the marketing environment, you determine the marketing mix, I think is the next thing I wrote down.

A. No. It's the marketing strategy.

Q. Okay, good. I wrote that down just in reverse order. What's that mean?

A. That's where you segment the market. Basically, segment, target, and position. So you segment the market, target your customers, and position your product vis-a-vis those customers.

Q. You say you "segment the market," and I'm just trying to use layman's terms, if I was a student in your class -- I took a marketing class probably, in 1978 -- to segment the market, I think what you're saying is for a particular product you may have more than one market segment that you market that product to; is that right?

A. Yes.

Jack E. Jordan (October 26, 2006)

Q. You have a truck to sell, a Ford truck, is that a good example of a product?

A. I drive a Ford truck, yes.

Q. But -- okay. You may want to sell it to farmers and ranchers, right?

A. Yes.

Q. People that live in the city?

A. Yes.

Q. And maybe mothers of children, potential market?

A. Yes.

Q. Okay. And so while you have one product, you have different segments of the market that you're trying to get to utilize your product?

A. Yes.

Q. Okay. And then you said you define the market segments. That's what you do first?

A. Um-hum.

Q. Is that yes?

A. Segment, yes.

Q. Okay. And then you said you target the segment. Is that what I heard you say?

A. Yes.

Q. And tell the jury, please, what you mean by "target the segment?"

A. So, for example, using the Ford truck analogy, you might segment the market into farmers, and use the term. A mother with kids, you, probably, wouldn't

focus a pickup truck on the mother with kids, you'd focus it on the farmer.
So you pick your segments, who you're going to really focus on. In that case you target farmers and not the mother with kids.
Q. Okay. But wouldn't you try to engage in communication of your product position and messaging to all the target segments?
A. You may or you may not, depending on your strategy.

Jack E. Jordan (October 26, 2006)

Q. And you said once you segment the market, define your targets, you position your product?
A. Yes.
Q. Tell the jury what you mean by "position your product?"
A. Positioning is ultimately how you want your customers to think about your product. So, for example, staying with the Ford truck analogy, it would be that if you drive this truck you're tough, could be a positioning. I'm Ford tough. That's part of what they're trying to have their customers think about their product.

Jack E. Jordan (October 26, 2006)

Q. In product positioning you said you determine how you want your customers to think about your product; is that correct?
A. Yes.
Q. And that is a critical part of marketing, is it not?
A. It is, yes.
Q. Now I'm trying to figure out how you go about getting your customers to think what you want them to think. I'm sure there's some things you need to do to do that, right?
A. There are, yes.
Q. Can you tell the jury, please, what you teach and what you know about how you get your customers to think what you want them to think?
A. Ultimately, that gets into the marketing mix, which is the next step. And most of that revolves around your promotional activities.
Q. Okay. So you would agree with me as of this juncture, as a person who's in the field of marketing, who worked in the field of marketing at Eli Lilly; is that correct?

A. For part of my time there, yes.
Q. Yes, sir. We're going to take a lot about that today. But we're now just talking about your understanding of marketing and what you teach to your students and so the jury understands what marketing is.
You have told us that once you determine, once you assess the marketing environment, you determine a marketing strategy. We're up there so far?
A. Yes.

Jack E. Jordan (October 26, 2006)

As part of your strategy you determine how you want your customers, how you want your customers to think about your product, right?
A. Yes.
Q. Okay. And when you determine how you want your customers to think about the product, you said we go to this next step which is called the marketing mix; is that right?
A. Yes.

Jack E. Jordan (October 26, 2006)

explain again for this jury, please, as you did previously, what it is, what is a marketing mix?
A. The marketing mix are the four Ps of marketing: Product, what the product is; what the price is for that product; what promotion you're going to do around that product; and then the fourth P is place. Kind of the distribution channel or the place that you're going to sell that product.
Q. And I want to focus on this issue of how you want your customers to think, one of your goals, and you said that deals with the marketing mix. Is there any particular P of the four Ps, or more than one P, of the marketing mix which allows you as a marketer to have your customers think what you want them to think?
A. Well, it ultimately starts with the product. The -- what the product is. And then using promotion to reach your customers, which could be a variety of initiatives.
Q. Okay. So your product and your promotion of the product is the marketing mechanism that enables you to get your customers to think what you want them to think?

A. Yeah. Yes, mostly, yes.
Q. Yes, sir. And that's a fair answer. And as a lawyer a lot of times when people tell me "mostly" is there something else I'm missing about how to get people to think what you want them to think?
A. You can use the place, and price influences that, so that's what I was referring to.
Q. So all the Ps can come into play, right?
A. Yes.
Q. Okay. And I want to talk about this issue of promotion. I think you said, and I remember this and I can, actually, tell from the documents that I've reviewed in this case, that there's many ways, and many channels, I think, market channels, in which you promote your product; is that right?
A. In most industries, yes.

Jack E. Jordan (October 26, 2006)

Q. Assume I'm not a senior. Assume I'm a freshman, all right, and I've never taken a marketing course before. And I'm a student and I raise my hand and I say, "Professor, tell us about promotion and how you promote a product. Tell us the mechanisms." Can you do that for me, please?
A. Yes. There are -- the major division is sales force versus nonsales force promotions. And then under nonsales force promotions, just in general in most industries, you have mailings, there are advertisings, there are Internet things you can do. And so those, just a whole variety based on the industry.
And then on sales force promotion, those are face-to-face interactions. And again, in most industries, they're company-hired people but you could outsource it to joint ventures with other sales forces, et cetera.
Q. So in this -- by the way, is this strategy, this, or when you told me assessing the marketing environment, determine a marketing strategy, determine a marketing mix, and customer retention, isn't that the four things that you told me that --
A. Yes.
Q. Are these essential to good marketing?
A. I believe they are, yes.
Q. And is it essential to good marketing to get your customers to think what you want them to think?
A. I believe it is, yes.
Q. And I'm on the topic of getting your customers to think what you want

them to think. And you told us that all four Ps can come into play but you agreed with me that promotion is the primary way that you get your customers to think what you want them to think, correct?

A. Between the product and promotion, those have the most influence, yes.

Jack E. Jordan (October 26, 2006)

38: 7 told the jury -- by the way you do know
8 you're testifying before a jury right now?
9 A. That is my understanding.
10 Q. You understand the reason the
11 camera's here is because the jury who hears
12 these cases will listen to your testimony,
13 and you understand that?
14 A. I do, yes.
15 Q. Okay. Now under the issue of
16 promotion you said there's a sales force
17 promotion as one category and nonsales force
18 promotion is the other category; is that
19 right?
20 A. That's one way to divide it.
21 That's how I divide it, yes.
22 Q. Is it a good way to divide
23 it?
24 A. That's how I teach my
39: 1 students, yes.
2 Q. Okay. Is that also based not
3 upon just your teaching but your practical
4 experience at working at Eli Lilly, for
5 example?
6 A. Yes, it is.
7 Q. And the sales force promotion
8 you said, and these are just things I jotted
9 down, you can have face-to-face promotion,
10 right?
11 A. Yes.
12 Q. You said you can have joint
13 ventures with other sales forces; is that
14 correct?
15 A. You could, yes.
16 Q. And is there something else
17 I'm missing or --
18 A. No.
19 Q. Okay. Now the nonsales force
20 promotion, your list could not have been
21 exhaustive, I understand. You're saying
22 there's just various mechanisms that you're
23 able to promote your product not in the sales
24 force, but some examples you gave us were
40: 1 advertisings, Internet, mailings, and things
2 of that nature, right?
3 A. Yes.
4 Q. But you, as a company, if
5 you're a marketer for a company, you can be
6 involved in, not only sales force promotion
7 but nonsales force promotion, right?
8 A. Yes.

Q. Which has as its ultimate goal getting your customers to think what you want them to think; is that right?
A. Yes.
Q. And your real ultimate goal, if you get your customers to think what you want them to think, is you create action; is that correct?
A. You do want them to buy your product, yes.

Jack E. Jordan (October 26, 2006)

41: 1 Q. What does create action mean,
2 sir?

Jack E. Jordan (October 26, 2006)

41: 9 A. The example would be, with
10 the Ford truck, would be for a, it might be,
11 the action you might want is to actually have
12 a farmer go to the Ford dealer, that could be
13 part of it, or it could be to have him or
14 her, actually, buy the truck.
15 Q. Right. And I would think,
16 and I don't know, I mean, obviously, you
17 want, when you see an advertisement on TV,
18 you want the person to be interested in the
19 product, right?
20 A. You'd want your target market
21 to be interested in the product, yes.
22 Q. Well, you'd hope maybe even
23 that other people that are not your target
24 market might get interested, right?
42: 1 A. You might. But you mostly
2 focus on your target market.
3 Q. Let's just focus with the
4 target market. Creating action. You want
5 them to be interested, that's created some
6 action, did it not?
7 A. That is one step, yes.
8 Q. And then the next step you
9 said you want them to go to the Ford
10 dealership, right?
11 A. That might be a goal of
12 promotional effort, yes.
13 Q. But the ultimate goal of
14 marketing is to do what, sir?
15 A. It's, ultimately, for your
16 target customer to buy your product.
17 Q. Right. I mean, all this
18 marketing is not to try to get somebody to go
19 to a dealership, for example, it's to try to
20 get your market to buy your product; is that
21 correct?
22 A. It is, yes.
23 Q. Okay. And what you have told
24 this jury, and what you want us to understand
43: 1 as an Associate Professor of Business at the

University of Indiana in South Bend, and as a former employee of Eli Lilly, that a key point, a purpose, or goal of marketing is to get your customers to think what you want them to think so that they will purchase your product, correct?

43:14 THE WITNESS: Can you repeat
15 it, I'm sorry?
16 MR. ALLEN: Yes, sir.
17 QUESTIONS BY MR. ALLEN:
18 Q. As an Associate Professor of
19 Business, and as a former brand leader at Eli
20 Lilly for Zyprexa, the ultimate goal of
21 marketing is to get your customers to think
22 what you want them to think so they will
23 purchase your product, correct?
24 A. Yeah, you want them to
44: 1 appropriately think about your product and,
2 ultimately, purchase it for the target
3 market.
4 Q. Now, we went from assessing
5 the market, to marketing strategy, to
6 marketing mix. Is there anything else --
7 have we done a fair job for the jury, a fair
8 job for the jury of discussing marketing mix
9 or is there some other essential things that
10 you think are important to talk about for the
11 jury?
12 A. No, I think we've covered it.
13 Q. Okay. Now the last part of
14 marketing that I wrote down is customer
15 retention; is that the last thing?
16 A. Yes.
17 Q. For the jury, can you explain
18 for us, please, why customer retention is
19 important?
20 A. If an individual buys a Ford
21 truck, you, obviously, want him or her to be
22 satisfied with that Ford truck. And the next
23 time they make a purchase, when they need to
24 haul stuff, you would hope they'd buy a Ford
45: 1 truck for their needs.
2 Q. So you want, not only to
3 initially create action to get a person to
4 buy your product, you want them to continue
5 to use your product and/or repurchase your
6 product again in the future; is that correct?
7 A. Yes.
8 Q. How do you go about that in
9 marketing?
10 A. The most important part is
11 that they're satisfied with your product.
12 Q. Yes, sir. Go ahead. Is
13 there anything else about customer retention,
14 how you get your customer's retention?
15 A. Well, that they be also
16 satisfied with the company, also, yes.
17 Q. Well, don't you also utilize

sales force and nonsales force mechanisms to assure customer retention?
A. Yes.
Q. Okay. So just for the jury's benefit, and let's talk about Eli Lilly and marketing. By the way, are the marketing principles that you have discussed with me today exclusive to Ford trucks or are they marketing principles that are used across this country for all products?
A. They're general marketing principles used across most industries.
Q. Right. Now on customer retention, you said you use sales force and nonsales force mechanisms; is that right?
A. Yes.
Q. Tell this jury, please, the sales force and nonsales force mechanisms one would use to assure or to try to assure customer retention.
A. You would want to have competent sales people that share useful information with your customers. That's, probably, the most important thing.
Q. So the most important thing that you can identify for this jury on customer retention is to have competent sales force personnel; is that right?
A. Sharing useful and good information.
Q. Sharing useful and good information; is that correct?
A. Yes.
Q. Now, if I'm trying to think, for the jury and for me, if I'm trying to have competent sales force to share good and useful information, I'm wondering where the sales force is going to get their good and useful information that they can share with the customer. Do you understand what I'm saying?
A. Yes.
Q. Can you tell the jury, please, where the sales force gets this good and useful information that they can share with their customers in order to assure or try to assure customer retention?

Jack E. Jordan (October 26, 2006)

A. It would be through, in most industries it's through the engineering specifications, if it's a specific product, that are various studies about that product, and then synthesized through the marketing group for the target customer.
Q. Right. The sales force, to get this good and useful information for whatever product, as a general marketing principle to go out to talk to the customers, the sales force is going to have to get this

good and useful information to share from the company who is manufacturing and selling the product; is that correct?
A. Yes.
Q. And as you said, the company who's manufacturing and selling the product has to synthesize information for the sales force so they can share it with the customer; is that correct?
A. Yes.
Q. Okay. And in the Eli Lilly context, which you're very familiar with, right?
A. I am.
Q. And, in fact, I think you just testified a minute ago that the synthesization -- is that a word by the way, synthesis?
A. I do not know.
Q. Okay. Well, it, probably, isn't. But when you said when you synthesize information you said that comes from the marketing department. I heard you say that, right?
A. That is one of the roles.

Jack E. Jordan (October 26, 2006)

49:24 Q. You said that where the sales
50: 1 force gets this information that's
2 synthesized comes from the marketing
3 department, correct?
4 A. Yeah. It ultimately comes
5 from the medical department but it goes
6 through a process and then marketing rolls it
7 out to sales within Lilly, yes.

Jack E. Jordan (October 26, 2006)

51:17 We're trying to get the sales
18 force, right, to give good and useful
19 information to the customer. That's our
20 goal, right?
21 A. It is.
22 Q. You said the way the sales
23 force gets the good and useful information is
24 they get that information from the company
52: 1 who manufactures and sells the product,
2 right?
3 A. No.
4 Q. Okay. Well, tell me where
5 they get it.
6 A. Some of the data might be
7 studies done by other entities, might be
8 government studies. So the information can
9 come from company studies, external studies.
10 So there's a number of ways to quote/unquote
11 get the information.
12 Q. Yes, sir. And you said,

though, that the marketing department synthesizes this information and passes it on to the sales force, right?

Jack E. Jordan (October 26, 2006)

A. The process is that the medical group gets the studies, gets the data, analyzes it, and determines, along with the regulatory group, what's medically useful and what's in the context of Lilly's label, and passes that information off to marketing to make materials to communicate with customers through various venues, one of which is the sales force.

Q. Okay. So -- and you used the term, and I'm just trying to find out when you used the term, the record will reflect you used the term "synthesize the data and information." You recall that? Synthesization? Synthesize them?

A. I did use that term and I want to be clear on the process. It's the medical department, along with the regulatory group, that does the analysis, determines what the data's actually saying, and leads the marketing department on what's appropriate to communicate to physicians. So I just want to make sure the process is clear.

Q. Yes, sir. I apologize. And I thank you for your help.

You said the medical and regulatory take the information and give it to the marketing department to determine what's proper to communicate to the physicians?

A. No. There's a whole process that determines what's proper to communicate to physicians. It's called a, it's called, actually, it's a standardized process, it's called the ELMR process, which stands for --ELMR process.

Q. Can you spell that for me?

A. E-L-M-R. It's an acronym for the editor, legal, medical and regulatory.

Q. What's the E stand for, I'm sorry?

A. The editor.

Q. Okay. Go ahead, I'm sorry. Go ahead.

A. Editor, legal, medical and regulatory approve everything that goes out. And then the marketing department takes that approved information for promotional items and communicates it to customers.

Q. And the marketing department also takes this approved information and communicates it to the sales force to help train them so they can appropriately communicate, as you said, good and useful

information to the customer?
A. Yes. It goes through the process and is approved and, for promotional activities through the sales force, yes.
Q. You used the term "promotional activities." Is that a term of art?
A. No.
Q. Okay. What do you mean by "promotional activities?"
A. In the pharmaceutical industry there are two communication, ways to communicate with customers: One is promotional, and there are nonpromotional activities.

Jack E. Jordan (October 26, 2006)

59:18 Q. And you worked for Eli Lilly from 1988 until when, sir?
A. Until April of 2004.

Jack E. Jordan (October 26, 2006)

60:18 left off with your career at Eli Lilly. I believe, you had told this jury you worked at Eli Lilly from 1988 to April 2004?
A. Yes.
Q. What was your title at the time you left Eli Lilly in April of 2004?
A. I was a sales director for
61: 1 the northeast part of the country.
Q. And prior to being -- and when did you become sales director for the entire northeast part of the country?
A. For one division.
Q. What division?
A. It was the Gamma Division.
Q. What's the Gamma Division?
A. We sold Strattera Adult --
Q. Tell me -- go ahead, I'm sorry.
A. We sold Strattera Adult, Cialis, and Evista.
Q. Prior to the time you were Sales Director for the Gamma Division for the northeastern portion of the United States, what was your job at Eli Lilly?
A. I was the Brand Leader for Zyprexa.
Q. You were the Brand Leader for the drug Zyprexa for Eli Lilly from when to when?
A. From May of 1998 until about August of 2003.
62: 1 Q. We will, of course, explore it in some detail, but can you tell us as an executive, as a Brand Leader for Zyprexa from May of 1988 until August of 2003, can you

tell this jury in layman's terms what it means to be a brand leader in that position?
A. It's really two areas of responsibility: One was to be responsible for the marketing strategy for the U.S., and the second area was to make sure there was alignment across the organization around that strategy.
Q. And when you said "alignment across the organization," is that correct?
A. Yes.
Q. Tell this jury what you mean when you say "alignment across the organization?"
A. To make sure that those folks that are responsible to communicate data, such as the sales organization, such as, such as the -- we had business-to-business people who would communicate clinical data to customers, we had organizations that would do promotional mailings out to customers -- to make sure that they were aligned with our strategy and with the approved data for that strategy.
Q. There's a lot more than that, though. Didn't you, also, when you're aligning your strategy across the organization, you're dealing with the sales forces, right?
A. We did, yes.
Q. The various levels of the marketing department, correct?
A. I did, yes.
Q. The medical department, correct?
A. I worked with the medical department, yes.
Q. You dealt with -- well, let me tell you, I'm going to ask this. I've seen in the documents I reviewed in this case that it was your job to focus, align, and motivate the entire organization around Zyprexa; is that true?
A. To make sure we were focused on the priorities, yes, to make sure we were aligned around those priorities, yes, and to make sure people are motivated around their objectives, yes.
Q. Yes. And so if the job description or descriptions on your job reflected in the documents produced in this case say that Mr. Jack Jordan's responsibilities were to focus, align, and motivate the entire Lilly organization around Zyprexa, that would be accurate?

Jack E. Jordan (October 26, 2006)

A. No.
Q. You can't answer my question?
A. No. The answer's "no" to

your question.
Q. Okay. It was not your job to focus, align, and motivate the entire organization around Zyprexa?
A. It was not, no.
Q. Okay. Whose job was it to focus, align, and motivate the entire organization around Zyprexa?
A. It would be the Global Product Leader, Alan Breier, Dr. Alan Breier.
Q. He was the global product leader?
A. I believe that was his title, yes.
Q. Is that to whom you reported?
A. I did not, no.
Q. To whom did you report?
A. I reported to various people at various times.
Q. Okay. Let's get back to your job title; it was Brand Leader for Zyprexa, is that correct, from May of 1998 to August of 2003?
A. They would change back and forth between that and Marketing Director for Zyprexa for the U.S.
Q. Okay. So, just so the jury understands who we're talking to today, we're talking to Mr. Jack Jordan, the Brand Leader or the Marketing Director for the entire United States of America for the product Zyprexa from Eli Lilly from 1998 till August of 2003; is that correct?

Jack E. Jordan (October 26, 2006)

A. That was my title, yes.

Jack E. Jordan (October 26, 2006)

Q. Was your job responsibility, your area of responsibility, did it include the marketing strategy for the United States of America?
A. It was -- it was -- part of it was, yes.
Q. Okay. And the marketing strategy, you've already explained to us earlier today in your discussion of general marketing principles, is to segment the market, determine your targets, position your product, determine a marketing mix, try to get customer retention, those things, right?

Jack E. Jordan (October 26, 2006)

A. The one caveat on that is the

global product team was responsible for the global strategy, which the U.S. needed to align with that. So it's not right that I quote/unquote owned what you just stated.

Q. Owned? Did I use the word "owned?" You said what I stated. I just want to know, did I use the word "owned?"

A. I don't know.

Q. Okay. So your area of responsibility included the marketing strategy of the United States. And you had to align that marketing strategy with Eli Lilly's global marketing strategy around the world; is that right?

A. Yes.

Q. Okay. And so we can see whatever you did in the United States of America has to be aligned with the global marketing team; is that right?

MR. GOLD: Objection to form.

A. Yes.

Q. Can you explain why, or the importance of aligning the marketing strategy here in the United States with the global marketing strategy?

A. It was mostly for consistency around the world.

Q. And why does Eli Lilly want to be consistent around the world when it comes to marketing Zyprexa around the world?

A. The -- well, you want the colors to be the same. You want physicians, if they travel to other countries, to recognize the product branding, et cetera.

Q. I would hardly think that the most important reason to be consistent in your marketing strategy around the world is color. Is that the most important reason?

Jack E. Jordan (October 26, 2006)

69:16 A. No.

Jack E. Jordan (October 26, 2006)

71:12 Q. We're talking, according to you, you talked about the importance of aligning the U.S. marketing strategy with the global marketing strategy, you follow?

A. I understand that, yes.

Q. Yes. In fact, I didn't say that, you told us it was, you didn't own, in your words, you didn't own the marketing strategy in the United States, you had to align it with the global marketing strategy, correct?

A. The positioning needed to be aligned. The one caveat I would say is around the world there are different

regulatory agencies, and so all efforts had to comply and be consistent with that specific country's regulatory agency requirements.

Jack E. Jordan (October 26, 2006)

72: 9 Q. Now you indicated that you
10 wanted to align the U.S. marketing strategy
11 with the global marketing strategy. Tell the
12 jury the importance of that and why that
13 needed to be done.
14 A. The most important reason is
15 so customers would not be confused if they
16 saw different positionings from different
17 countries.

Jack E. Jordan (October 26, 2006)

74:12 rephrase the question. Why is it important
13 to position the product universally with the
14 global and United States marketing strategy
15 in order, in your words, to avoid confusion?
16 Why is that important?
17 A. There was, again, two guiding
18 principles: One is consistency at
19 positioning, we never wanted customers
20 confused; and the second guiding principle is
21 to align with each country's regulatory
22 requirements.
23 Q. And where are these guiding
24 principles written down, sir?
75: 1 A. It's part of Lilly policy.
2 The global marketing -- I forget what it's
3 called -- the global marketing group
4 identified alignment around positioning
5 worldwide was one of the stated goals. And
6 part of Lilly Red Book is always to ensure
7 that we comply with the regulatory
8 requirement in each specific country.
9 Q. You said the Lilly Red Book.
10 And I had that actually here in my questions,
11 the Lilly Red Book. Can you tell the jury
12 what the Lilly Red Book is?
13 A. Yes.
14 Q. Please do so.
15 A. In general, the most general
16 terms, it's Lilly's guiding principle on how
17 we would act with integrity, respect for
18 people.
19 Q. The Lilly Red Book, though,
20 is a book, is it not?
21 A. It was. I think it's now on
22 line, but yes.
23 Q. Okay. The Lilly Red Book is
24 a written document. The Lilly Red Book is a
76: 1 written document.
2 A. It is.
3 Q. And the Lilly Red Book

contains the guiding principles for marketing?
A. No. For the ethical behavior of the company.
Q. Of the entire company?
A. It is, yes.
Q. Including marketing?
A. Yes.
Q. Including brand leadership?
A. Yes.
Q. Including product promotion?
A. Yes.
Q. Including sales force activities?
A. Yes.
Q. Including nonsales force promotion?
A. Yes.
Q. Including the brand leader's -- the brand leader's conduct, correct?
A. Yes.
Q. Including the brand manager's conduct, right?
A. Yes.
Q. Did you, sir, in your job as Marketing Director and/or Brand Leader for Zyprexa from May of 1998 to August of 2003, align the U.S. marketing strategy with the global marketing strategy for Zyprexa?
A. I did.
Q. And did you, as Marketing Manager and Brand Leader for Zyprexa in the United States from May of 1998 till April of 2003, take a consistent product position for Zyprexa with that also of the global marketing team?

Jack E. Jordan (October 26, 2006)

A. With the two stated goals of the high level positioning aligned with the global positioning, and complying with the regulatory requirements in the U.S., yes.
Q. And you said you aligned, you said "high level positioning" with the global positioning. Did I hear you use that term, sir?
A. Yes.
Q. What did you mean, for the jury, please, when you use the term "high level positioning?"
A. For Zyprexa, specifically, it was, there was a positioning of dependability to help our customers help their patients. However, each country had different indications and different labels. So at that level, we would align with the U.S. regulatory requirements.
Q. Okay. The term "high level positioning," is that a term of art in the

16 marketing business?

Jack E. Jordan (October 26, 2006)

78:18 MR. ALLEN: Yes, sir, I
19 apologize. I will tell you I
20 couldn't find the document now if I
21 wanted. I bet we'll stumble across
22 it today. But I have seen documents
23 in the marketing files, from the
24 files that have been produced and
79: 1 represented to be your documents,
2 using the term "high level
3 positioning," and you just used it
4 in your testimony.
5 QUESTIONS BY MR. ALLEN:
6 Q. With that as background is
7 high level positioning a term of art?
8 A. I've never heard the term
9 "term of art," so I don't know what that
10 means.
11 Q. Well, and I apologize, maybe
12 I didn't do a good job there. When I use
13 "term of art," is it something used in your
14 trade, a marketing term, high level
15 positioning?
16 A. It's a term I've heard used
17 in a number of marketing venues, yes.
18 Q. Yes, sir. And, in fact, you
19 used that term in your testimony and I'd like
20 the jury to understand what the term "high
21 level positioning" means.
22 A. It's at the -- it's your
23 positioning at the most basic level.

Jack E. Jordan (October 26, 2006)

80: 8 Q. All right, sir. Is there a
9 difference between the Red Book and the Good
10 Promotion Practices Manual?
11 A. There is, yes.
12 Q. Okay. I guess, tell this
13 jury in as shortest term as possible that
14 will do a good job of explaining, because we
15 want the jury to understand the differences
16 between or the difference between the Red
17 Book and the Good Promotion Practices Manual?
18 A. The Red Book was a, our
19 corporate, Lilly's corporate commitment to
20 ethical business practices. And as a part of
21 that, the Good Promotional Practices are
22 those things that align with Red Book and
23 align with the specific regulatory agency for
24 the U.S., which is the Food and Drug
81: 1 Administration.
2 Q. And I take it as brand leader
3 for Zyprexa for Eli Lilly between May of 1998
4 until August of 2003, that all of the
5 promotional activities and marketing

activities for Zyprexa were consistent with the rules, regulations and guidelines contained in either the Red Book or the Good Promotion Practices Manual; is that correct?

Jack E. Jordan (October 26, 2006)

81:12 A. Yes.
13 Q. Okay. So we, when the jury
14 looks at --
15 MR. ALLEN: Yes, sir, you
16 have something to add?
17 A. The one exception is if there
18 was anybody -- sales rep, marketing person --
19 that violated those, they would, in most
20 instances, be terminated from the company.
21 Q. Why was Mr. Bandick
22 terminated?
23 A. I don't know.
24 Q. He was terminated?
82: 1 A. I don't know.
2 Q. Okay. Well, he was a Brand
3 Manager for Zyprexa, wasn't he?
4 A. At one point he was, yes.

Jack E. Jordan (October 26, 2006)

82:15 Q. Was Mr. Bandick a Brand
16 Manager for Zyprexa for a long time?
17 A. He was a Brand Manager for, I
18 think a year, year and-a-half, in the U.S.
19 affiliate.
20 Q. What years?
21 A. From, approximately, June of
22 2000. I don't know when he got promoted to
23 the product team. It was about a year, year
24 and-a-half, I believe. It was about a year,
83: 1 year and-a-half. I just can't remember.
2 Q. He was Brand Manager for
3 Zyprexa and after he was Brand Manager he got
4 promoted to the product team; is that
5 correct?
6 A. He did. No, he, actually,
7 went over to work on the Strattera brand for
8 a few months and then went over to the
9 Zyprexa Product Team.

Jack E. Jordan (October 26, 2006)

84:16 Q. You were Mr. Bandick's
17 superior, were you not?

Jack E. Jordan (October 26, 2006)

84:20 A. When he was the Zyprexa Brand

Manager for that year, year and-a-half, he did report to me, yes.
Q. And did all of Mr. Bandick's conduct comply with the guidelines, rules, regulations of the Red Book and Good Product Practices?
A. Yes.
Q. Now, are you, were you a senior manager in the corporation of Lilly?
A. I was not, no.
Q. How would you describe your level? We know you're a marketing director, we know you're a brand leader, right? Right?
A. Yes.
Q. How would you describe that, if you can?
A. Well, I was two levels above the sales rep and, depending on the time, five or six levels below the Chief Executive Officer. So, I guess, lower level manager.
Q. So Eli Lilly put a lower level manager in charge of the U.S. marketing of Zyprexa?

Jack E. Jordan (October 26, 2006)

85:23 A. The level is what it is.

Jack E. Jordan (October 26, 2006)

86:16 Q. Eli Lilly, according to your testimony, put a lower level manager in charge of marketing for Zyprexa?
A. Again, I was U.S. So in the U.S. I was a director in the U.S. for marketing. So I don't know how to characterize that.
Q. Sir, you characterized your level just a few minutes ago as lower level manager. Do you recall that testimony?
A. I do.
Q. Okay. Is that testimony accurate?
A. It's difficult -- I mean, it's accurate insofar as it's difficult to characterize what level that was in an organization. I mean, it just was what it was.
Q. Yes, sir. And that's -- my teenager says "it is what it is" but you understand we're under oath here today, you understand that?
A. I do.
Q. You understand your testimony's very important.
A. I do.
Q. You understand you took an oath from this court reporter to tell the truth, the whole truth, and nothing but the

truth?
A. I do.
Q. Will you agree to do that?
A. I am.
Q. Have you done so up to this point?
A. I have.
Q. When you testified you were a lower level manager was that testimony accurate or inaccurate?
A. It was me struggling to identify what -- how it compares to other organizations. So it was -- I was a director of marketing so.
Q. Okay. Would you like to change your testimony concerning the fact you were a lower level manager?
A. No. It just -- I was what I was, yeah.

Jack E. Jordan (October 26, 2006)

Q. As a lower level manager in the United States were you responsible for the United States marketing of Zyprexa?
A. I was.
Q. Thank you, sir.
Was there anybody -- and who did you report to, sir?
A. Different people different times.

Jack E. Jordan (October 26, 2006)

can ask. Let me rephrase the question, do the very best you can for this jury in telling us the names of the people to whom you reported and what their title was from May of 1998 until August of 2003 when you were Zyprexa Brand Leader.
A. I, initially, reported to Andrew Hodgekiss, who was Executive Director of Marketing for Neuroscience. It's not precisely right but approximately.
And that was for just a few months.
Then I reported to Dan Hasler.
Q. Can you spell that for the jury, please?
A. A-S-L-E-R.
Q. Dan Asler?
A. Hasler.
Q. Hasler?
A. Yeah, H-A-S-L-E-R.
Q. That's what I thought you said.
A. He was Vice-president of Marketing for the U.S.

Then I reported to Newt Crenshaw. He was vice-president, but I don't know what -- it was Sales and Marketing, I believe.

Then I reported to Bill Robinson, who is Vice-president of Sales and Marketing for Neuroscience in primary care.

Then I reported to Glyn Parkin, who, the last, his last title was Vice-president of Neuroscience, I believe.

And then I reported to Jo Taylor, J-O not J-O-E, Jo Taylor, and I don't, I was just transitioning out so I don't know what her title was. They reorganized.

Q. When you say "transitioning out" you mean out of your role as Director of Marketing and Brand Leader for Zyprexa?

A. Yes.

Q. Okay. I've written -- is there anyone else? You've done your very best at this point?

A. I have.

Q. Okay. Andrew Hodgekiss you said was very few months. So that, I take it was sometime in May of '98 until a few months later, approximately?

A. Toward the end of the year. May have been six months.

Q. That's all I need to know, sir.

We then move to Dan Hasler, Vice-president of Marketing in the United States. For how long did you report to Mr. Hasler and can you give the jury your best testimony of from when to when?

A. Probably, six months. Maybe not -- yeah, three to six months.

Q. So by your testimony, the best estimation we have, sometime in the beginning of 1999 until the middle of 1999?

A. Boy, I think maybe Andrew was three months and Dan Hasler was three months because at the beginning of '99 was Newt Crenshaw.

Q. Okay. And there's memos in the case with this Crenshaw slash Jordan meetings. Did you and Mr. Crenshaw have regular meetings with the marketing team for Zyprexa?

A. As my direct supervisor I did meet with him frequently, yes.

Q. Yes. And, in fact, though, didn't you and Mr. Crenshaw jointly put out marketing memoranda following the Crenshaw/Jordan meetings?

A. I'm not sure what you're referring to.

Q. We'll look at examples today. Nevertheless, you reported to Newt Crenshaw, Vice-president of Sales and Marketing for Eli Lilly; is that right?
A. I believe that was his title, yes.
Q. Yes. Your best -- and was Mr. Crenshaw, Vice-president of Sales and Marketing, that would include not just Zyprexa but all of the pharmaceutical products?
A. No. He didn't have all of them; he had neuroscience and some primary care drugs.
Q. Neuroscience and primary care drugs. By the way, Zyprexa was a primary care drug, was it not?
A. We did launch into primary care, yes.
Q. So the chief marketing person solely responsible for Zyprexa in the United States was you, Jack Jordan; is that correct?
A. Yes.
Q. And you reported to Newt Crenshaw, Vice-president of Sales and Marketing for Neurosciences and some Primary Care products; is that correct?
A. I believe so, yes.

Jack E. Jordan (October 26, 2006)

Q. When did you begin reporting to Newt Crenshaw?
A. I believe it was January of 1999.

Jack E. Jordan (October 26, 2006)

Q. You reported to Mr. Crenshaw beginning in January of 1999 until, approximately, when?
A. The first -- I believe, it was the first part of 2000.
Q. And what happened to Mr. Crenshaw then?
A. He was moved to -- it was like an IT job, a small entrepreneurial arm that we started, that focused on how we can use technology to help the corporation.
Q. And, I apologize, because I want to make sure we're communicating, we're going to talk about acronyms in a minute. IT, is that Internet technology? Intellectual property? I don't know --
A. I'm sorry. It had to do with Internet, had to do with technology in general. How we could use it to help the company.
Q. Did his leaving have anything

to do with his job performance in regard to Zyprexa?
A. No. I think it was considered a promotion.
Q. Okay. Then you began reporting, I guess, in January of 2000, or, approximately, January of 2000, to Mr. Bill Robinson?
A. Yes.
Q. And how long did you report to Mr. Robinson?
A. Probably, six to 12 months.
Q. From, approximately, according to -- six to 12 months, is that what you said?
A. Yeah. There was an extended transition between Bill Robinson and Glyn Parkin. So, just, I can't remember when that transition timeline was.

Jack E. Jordan (October 26, 2006)

Q. Why, if you know, or have you heard, why Mr. Robinson left the job that he held after six to 12 months superior to you, why did he leave that position?
A. Oh, he, they reorganized, and so he took on broad responsibility. And then he, Glyn Parkin, was put into a new job, and so Bill Robinson was two levels above me then with broader responsibility.
Q. Okay. And I think your testimony earlier was it was your best recollection that Mr. Robinson's title at the time he was your superior, on the issue of the marketing of Zyprexa, he was Vice-president of Sales and Marketing for Primary Care?
A. And Neuroscience, yes.
Q. So he, basically, just took over Newt Crenshaw's position?
A. Yeah. But they reorganized, and I just can't remember what additional responsibilities.
Q. Right. And after the six-to-12 month period that Mr. Robinson, you reported to him, Vice-president of Sales and Marketing Primary Care and Neurosciences, Mr. Glyn Parkin became your supervisor or your chain of command reporting? The person you reported to?
A. Yes.
Q. Glyn is spelled G-L-Y-N?
A. I believe so, yes.
Q. Parkin, P-A-R-K-I-N?
A. Yes.
Q. And what was his title and position?
A. He was Business Unit Head for Neuroscience.
Q. Did that include more

products than just Zyprexa?
A. He was responsible for the Zyprexa Brand Team along with the Neuroscience Sales Force.
Q. So the answer is it did or did not contain more products than Zyprexa?
A. On the sales side there were more products than Zyprexa.
Q. So you reported to Mr. Parkin, approximately, according to my notes and your best estimate, beginning in 2001?
A. I believe so.
Q. And you reported to him until sometime in the summer of 2003?
A. Yes.

Jack E. Jordan (October 26, 2006)

you -- let me back up there. During the time that you reported to Mr. Parkin, you told us he was responsible for other products besides Zyprexa, correct?
A. I was the only marketing group -- well, Prozac Weekly Brand Manager reported to him. And then on the sales side, the sales organization carried various Neuroscience products.
Q. So Mr. Parkin was responsible for other products other than Zyprexa?
A. He was, yes.
Q. So during the time you reported to Mr. Parkin, you were the head individual at Eli Lilly who was solely responsible for the marketing of Zyprexa?
A. The marketing responsibilities, yes.
Q. Thank you.
And then you said he transitioned out, Jo Taylor came in. And was that at or near the time you left?
A. It was a few months I reported to her and went to a sales director job, yes.
Q. A what, sir?
A. A sales director job.
Q. Jo Taylor's title was what, sir?
A. I don't know what. It was during a reorganization, and I don't remember what her title was.
Q. Was this reorganization that occurred in the summer of 2000, where Mr. Parkin moved out and Ms. Taylor moved in, was that a result of any of the problems that were then being faced with Zyprexa?

Jack E. Jordan (October 26, 2006)

102: 5 A. I don't recall problems with
6 Zyprexa. So -- it was a result of dividing
7 up Sales and Marketing.
8 Q. So during the entire time
9 that you were Brand Leader and Marketing
10 Manager for Zyprexa you recall no problems
11 with Zyprexa in the summer of 2003?

Jack E. Jordan (October 26, 2006)

102:14 Q. In your role as Marketing
15 Manager and Brand Leader?
16 A. There were no problems.
17 Q. Thank you, sir.
18 Now you, during this time
19 period from 1998 to 2003, where were you
20 physically located in your job -- here in
21 Indianapolis?
22 A. I was, yes.
23 Q. At the Indianapolis Corporate
24 Center?
103: 1 A. No. I was, it's a building
2 called -- the Lilly Technology Center South,
3 I believe, is the building it was called.
4 Q. You had to walk in there
5 every day. I bet you had some idea. Is it
6 Lilly Technology Center South?
7 A. I know it was Lilly
8 Technology Center, I just --
9 Q. Okay. Were Mr. Crenshaw,
10 Mr. Robinson, Mr. Parkin, and then Ms. Taylor
11 also located in that facility?
12 A. They were, yes.
13 Q. Okay. Were you on the same
14 floor as those individuals?
15 A. Most of the time, yes. The
16 only individual that would have ever been on
17 a different floor was Jo Taylor during the
18 transition; she was one floor below me.
19 Q. So during the entire time you
20 were brand manager -- Brand Leader. You were
21 not brand manager you were Brand Leader,
22 correct?
23 A. That's correct.
24 Q. That's senior to a brand
104: 1 manager, obviously?
2 A. It is.
3 Q. Okay. During the entire time
4 you were Brand Leader for Zyprexa you were
5 always physically, physically located on the
6 same floor in the same facility with your
7 superiors or your reporting chain of command,
8 either Mr. Hasler, Mr. Crenshaw, Mr. Robinson
9 or Mr. Parkin?
10 A. Yes. We were all relatively
11 close.
12 Q. Yes, sir. And so you worked
13 closely with those gentlemen during the time
14 you were responsible as the Marketing
15 Director and Brand Leader for Zyprexa?

Jack E. Jordan (October 26, 2006)

104:18 A. I did.
19 Q. And they were certainly aware
20 of, and you made them aware of, your
21 activities, and your marketing strategies,
22 and marketing mixes, and promotional
23 activities, concerning Zyprexa?

Jack E. Jordan (October 26, 2006)

105: 2 A. Yes. Lilly's a very
3 consensus environment, and so the activities
4 we undertook were always known by my senior
5 management as well as other teams, yes.

Jack E. Jordan (October 26, 2006)

105: 6 Q. Right. Your activities
7 concerning the marketing of Zyprexa were
8 known by senior management and senior
9 executives and it was done on a consensus
10 environment, on a consensus basis?

Jack E. Jordan (October 26, 2006)

105:15 A. It was, yes.
16 Q. Thank you, sir.
17 During the entire time you
18 were Brand Leader and Marketing Director for
19 Zyprexa, from 1998 until 2003, were you ever
20 reprimanded, disciplined, in any regard for
21 any of your activities as Marketing Manager
22 or Brand Leader for Zyprexa?

Jack E. Jordan (October 26, 2006)

106: 1 A. No.
2 Q. And I take it, at least, that
3 you received -- did you receive reviews every
4 year? Every quarter? How did -- when did
5 you get your reviews?

Jack E. Jordan (October 26, 2006)

106: 8 A. We had annual reviews.
9 Q. And who was responsible for
10 your annual review?
11 A. Whoever I was reporting to.
12 Q. Okay. So the individuals you
13 listed already, that would be Mr. Hasler,

Mr. Crenshaw, Mr. Robinson, and Mr. Parkin, are the individuals responsible for your yearly annual review?
A. Yes.
Q. Were you ever given any poor performance reviews by any of those gentlemen for your -- in your role as Brand Leader and Marketing Manager for Zyprexa?
A. No.
Q. Okay. Did they give you -- I would take it that they rate you, you know, from some scale. Some scale is used, isn't it?

Jack E. Jordan (October 26, 2006)

A. There was.
Q. I mean, we've all had jobs, and the jury has jobs, we understand there's a rating scale. How were you rated in your role as Brand Leader and Marketing Director for Zyprexa from 1998 until 2003?

Jack E. Jordan (October 26, 2006)

A. Most years was exemplary.
Q. Okay. And was that, was your exemplary status as Brand Leader and Marketing Director across the board?

Jack E. Jordan (October 26, 2006)

A. It was not, no.
Q. Okay. Did you have any areas in which you did not receive exemplary ratings?

Jack E. Jordan (October 26, 2006)

A. I believe, 1999 was successful as opposed to exemplary. And, I believe, 2002, was successful as opposed to exemplary.

Jack E. Jordan (October 26, 2006)

review. You told me that in '99 and 2000, you believe your rating was successful?
A. No. I don't think that's what I said. I think --
Q. Satisfactory?
A. I think '99 and 2003 it was successful and the other years were

exemplary.
Q. Okay. So your job rating was exemplary the other years. '98 it was exemplary, 2000 it was exemplary, 2001 it was exemplary, and 2002 it was exemplary?
A. No. '98 was a -- I'm sorry, was a transition year. So if you're in a job for less than six or nine months it's successful. So '98 was successful, also.
Q. Okay. So '98 successful, '99 successful, 2000 was exemplary, 2001 was exemplary, 2002 was successful; is that correct?
A. I can't remember 2002. I just can't remember.
Q. Is successful the level below exemplary or is there some level in between?
A. There's, basically, three levels: Unsuccessful, I think it was called or unsatisfactory, and then the middle is successful, and then the top is exemplary.
Q. During the entire time you were Brand Leader and/or Marketing Director your job performance rating was either successful and/or exemplary?
A. It was, yes.
Q. What was your job rating as -- let's talk about this Marketing Director term. You used it, and so I want to make sure we're communicating and the jury understands, is there a difference between Brand Leader and Marketing Director for Zyprexa?
A. No, it was just a change in title.
Q. Okay. When did that title change occur?
A. I believe when I went into the job it was Marketing Director. Then after six months it changed to Brand Leader, and then, I believe, approximately the last year it turned back to Marketing Director.
Q. Okay. During the entire time you were Brand Leader or Marketing Director your job performance was exemplary or successful for Zyprexa?
A. It was, yes.
Q. Now, 2003, what was your job rating for 2003 as Marketing Director and/or Brand Leader for Zyprexa?
A. It was successful.
Q. Now was there a particular reason that you can recall in 2003 why your rating was successful as opposed to exemplary?
A. No. I don't recall a reason, no.
Q. You don't?
A. I don't, no.
Q. Now did you, actually, have a meeting when you got your job reviews or would you get a piece of paper with your job review, or both?

A. Most years you'd have a meeting.
Q. And who would your meeting be with?
A. It would be my supervisor at that time.
Q. Right. And you've identified those individuals for us, have you not?
A. I have, yes.
Q. Were there any other people besides your supervisor that you were involved with when you got your job review every year?
A. No. Not, normally, no.
Q. And did they also, in addition to meeting with you, did they also provide you with a written assessment in your
113: job review?
A. Not always, no.
Q. Okay. Sometimes they did, sometimes they didn't?
A. Yes.
Q. Thank you. Now from 1998 to 2003, you've told us your title regarding Zyprexa. Were you responsible for the marketing or brand leadership of any other Lilly products during that time period?
A. During that time period, I did have responsibility for a period of time for the Symbyax, the Symbyax marketing team.
Q. And can you spell Symbyax for the jury and for the court reporter, please?
A. I don't know exactly how to spell it. S-Y-M -- I'm somebody that needs to write B-Y-A-X, I believe. I'm sorry, I've got to see things in writing.
MR. ALLEN: I'm the same way. Same exact way. I've got to write it down. I'm a bad speller, also.
QUESTIONS BY MR. ALLEN:
Q. Symbyax for the jury, tell
114: the jury what that product was?
A. Symbyax was and is a combination of Zyprexa-olanzapine, and Prozac-fluoxetine.
Q. Right. So from 1998 to 2003, you were Marketing Director and/or Brand Leader for Zyprexa and/or the combination of Zyprexa and Prozac -- Symbyax?
A. Yes. For a short period of time.
Q. Yes, sir. And when were you Brand Leader or Marketing Director for Symbyax?
A. It was during the 2003 time frame.
Q. And when was Symbyax launched?
A. It was never launched while I was responsible for it.
Q. When was it introduced onto the market?
A. I believe it was, it had to

be after I leave, so late 2003, 2004, I just don't recall.
Q. Right. You were Marketing Manager and Brand Leader for Symbyax, but the product did not come on to the market until after you left the brand leadership marketing job for Zyprexa?
A. Yes.

Jack E. Jordan (October 26, 2006)

Q. From May of 1998 until August of 2003, the only Eli Lilly drug product that was then on the market that you were Marketing Director for and/or Brand Leader was Zyprexa?
A. Yes.
Q. Okay. That was -- so Zyprexa was your sole job during that time period?

Jack E. Jordan (October 26, 2006)

A. Yes.

Jack E. Jordan (October 26, 2006)

Q. How many hours a day, on average, from May of 1998 till August of 2003, did you work on Zyprexa in your job?
A. Mostly, ten-to-12-hour days.
Q. And how many days a week, on average?

Jack E. Jordan (October 26, 2006)

A. Most of the time Monday through Friday but there was weekend travel at times.

Jack E. Jordan (October 26, 2006)

Q. And, generally, then you worked at least about a 60-hour week or a 50-hour week?

Jack E. Jordan (October 26, 2006)

A. Yes.
Q. And you worked 50 weeks a year?
A. No.

Q. How many weeks?
A. Probably, 46 or 47 weeks a year.
Q. I guess the bottom line is you spent many thousands of hours per year working on Zyprexa?

Jack E. Jordan (October 26, 2006)

A. I did.
Q. And not only that, you worked, not only in your office, but you would get calls and memoranda and e-mails at home, also, would you not?

Jack E. Jordan (October 26, 2006)

A. No. I rarely got, rarely would work from home.
Q. Okay. And your job also included travel?
A. It did.
Q. And why did you need to travel, generally, in your job? Tell the jury why the Marketing Director or Brand Leader for Zyprexa would need to travel in his job?
A. For market research I would travel, to spend time in various meetings, both internal to the company and external to the company, meetings, conferences.
Q. Did Eli Lilly conduct market research on Zyprexa?
A. They did, yes.
Q. Did they use third parties to assist them in the market research?

Jack E. Jordan (October 26, 2006)

Q. Third-party companies or individuals?
A. Yes, most of it was.
Q. Tell us the individuals and/or companies whom Eli Lilly utilized for Zyprexa during the time you were Brand Leader in the marketing research?
A. That was the responsibility of the Market Research Group, and I don't recall who we used. I can see the faces but I don't recall the companies.
Q. So it's your best testimony under oath, as we sit here in October of 2006, that you cannot remember the name of one marketing research company and/or individual that with whom you worked during the time you were Brand Leader?

120: 1 A. I can remember faces. I just
2 don't remember the specific -- yeah, I
3 apologize.
4 Q. You don't remember any
5 marketing companies?
6 A. I don't remember the titles
7 of the company, no.
8 Q. Okay. Did you work with any
9 advertising agencies during the time you were
10 Brand Leader or Marketing Director? Or
11 utilize their services?
12 A. We did use a company that
13 part of their responsibility was advertising.
14 Q. They would be whom, sir?
15 A. It was -- the gentleman's
16 name was Mark Frank and he worked with -- I'm
17 sorry, I can't remember the name of the
18 company he worked for.
19 Q. Did you use any PR firms,
20 public relations firms, or press relations
21 firms during the time -- let me finish the
22 question -- during the time you were Brand
23 Leader for Zyprexa?
24 A. We did.
121: 1 Q. Tell the jury those that you
2 remember, please.
3 A. Well, the communications
4 group used a number of vendors. The one I
5 remember is Nichols-Dezenhall.
6 Q. Excuse me?
7 A. The one I remember was
8 Nichols-Dezenhall.
9 Q. You know, I'm sorry, it may
10 be my fault. I couldn't hear you at first
11 and I couldn't understand you the second.
12 Could you slow down so the court reporter can
13 hear and the jury can hear? Nichols who?
14 A. Dezenhall.
15 Q. Okay. Can you spell that for
16 us?
17 A. Nichols is N-I-C-H-O-L-S
18 slash Dezenhall is D-E-Z-E-N-H-A-L-L.
19 Q. And where are they located,
20 sir?
21 A. Out of D.C.
22 Q. And did they help among other
23 things -- what did they do? What did
24 Nichols-Dezenhall do, that you can recall,
122: 1 for you in the marketing department?
2 A. Well, most of their work was
3 in the communications department. And so I'm
4 not familiar with all they did for our
5 communications department. I'm just familiar
6 with the interaction I had with them.
7 Q. Okay. Was the communications
8 department in the marketing department?
9 A. No. They were part of a
10 different group.
11 Q. Okay. Did you work regularly
12 with them?

A. Regularly -- I'd interact with them, maybe, weekly.
Q. Okay. And what other departments -- and I use the term "regularly," and I apologize to you and the jury if you think that's vague or in any way difficult to understand -- but you would say in your role as Brand Leader or Marketing Director you worked with the Communications Department, would that be accurate?
A. Yeah, it was part of my interaction, yes.
Q. What other departments did you work with?
A. I had frequent interaction with the Medical Group, with the Product Team, with the Regulatory Group, with the Legal Group, with the Business-to-Business Group, with the Sales Organization, with the Market Research Group, the PR Department, with the Health Outcomes Department, with the Medical Liaison Group, the Health Outcomes Group, and there's a number of others. At one point I had 20 or 30 groups.
Q. Why as Brand Leader or Marketing Manager would you work with these various groups you've identified for the jury?
A. It would be different reasons for each group.
Q. I understand that, sir. But why in your role would you need to work with all these groups? Why did your job responsibility require that?
A. Because most of these groups had some sort of responsibility around Zyprexa.
Q. And you, as Marketing Director, would have to interface -- I've seen that word used -- interface, talk to, communicate, with all of these groups in order to gather the necessary information in your role as Marketing Director and/or Brand Leader to effectuate your marketing strategy; is that true?

Jack E. Jordan (October 26, 2006)

A. No, that wasn't. For some groups yes, for some groups no.
Q. Okay. So in your role, in your desire to do the very best job you could as Marketing Director and Brand Leader, you interacted with those groups in order to assist you in your job performance?

Jack E. Jordan (October 26, 2006)

Q. Is that correct, sir?

A. That's part of the reason, yes.
Q. Yes, sir. And, in fact, you had testified previously that part of your responsibility for, as Brand Leader, was for the marketing strategy and alignment across the organization; is that correct, sir?

Jack E. Jordan (October 26, 2006)

A. Yes. Part of it was to make sure there was organizational alignment around what we were trying to accomplish, yes.
Q. So that's why you would have to interface, talk to or communicate with these various departments in order to achieve that necessary alignment, sir?

Jack E. Jordan (October 26, 2006)

A. That was one of many reasons.
Q. Yes, sir. Thank you.
Now you left Zyprexa Brand Leadership and Marketing Director in August of 2003?
A. It was, again, most transitions weren't -- it was the August-ish time frame.
Q. Okay. And you said that you then went to -- I'm looking for my notes, but you could tell us -- the Sales Director for the northeast; is that right?
A. For the Gamma Division Northeast, yes.

Jack E. Jordan (October 26, 2006)

Q. Okay. From the time of your graduation and the time you went to Eli Lilly, did you live anywhere else but Indiana?
A. I did, yes.
Q. Okay, where did you live?
A. I lived in New Jersey as a sales rep at one point.
Q. For Eli Lilly?
A. I did.
Q. From what year to what year, approximately?
A. From September of '89 through the first part of '92.
Q. Were you a representative for Prozac?
A. I was not, no.
Q. After you were a sales representative in New Jersey till '92, what

did you do then?
MR. ALLEN: I'm sorry, I --
QUESTIONS BY MR. ALLEN:
Q. After you were a sales rep, you said till '92 in New Jersey, what did you do next for Eli Lilly?
A. I went into the Health Outcomes Group, which is part of the Public Policy area.
Q. Where was that?
A. That was in Indianapolis.
Q. From '92 till when?
A. I did that for about a year.
Q. After that, what did you do for Eli Lilly?
A. I was in the Public Policy Group; just a general associate.
Q. Where was that, here in Indianapolis?
A. Indianapolis, yes.
Q. After that, what did you do for Eli Lilly?
A. After that I went to Market Research.
Q. Where was that?
A. It was in Indianapolis.
Q. And after that job what did you have for Eli Lilly?
A. Then I went into Business Development.
Q. Where was that?
A. Indianapolis.
Q. And after that what did you do for Eli Lilly?
A. Then I became the General Manager of Control Diabetes Services.
Q. What years were that, approximately?
A. '94 through '98, I believe.
Q. You were the General Manager for Control Diabetes Services for Eli Lilly from 1994 to 1998?
A. Yes.
Q. And was it after that job that you took over the Brand Leader and Marketing Director for Zyprexa?
A. It was, yes.
Q. Okay. What is General Manager of Control Diabetes Services, what does that mean?
A. It was a company that we acquired in 1994, that provided diabetes education to patients and contracted with managed care companies to provide that service.
Q. You were involved in diabetes education?
A. I was, yes.
Q. Was that here in Indianapolis?
A. No, it wasn't.
Q. Where was your job?
A. Dallas, Texas.

131: 1 Q. So from 1994 to 1998 you
2 lived in Dallas?
3 A. I did not; I commuted.
4 Q. You flew out on Sundays and
5 came back on Fridays?
6 A. Most weeks, yes.
7 Q. And your family lived in
8 Bremen, Indiana?
9 A. No, they lived in Zionsville,
10 Indiana.
11 Q. And Control Diabetes Services
12 was a company wholly owned by Eli Lilly?
13 A. It was a wholly owned
14 subsidiary of Lilly, yes.
15 Q. And you were the general
16 manager of that outfit?
17 A. I started out as the director
18 of business development for them and then
19 within a couple months took over general
20 manager.

Jack E. Jordan (October 26, 2006)

132: 6 Q. Yes. And then when '98 was
7 up you came back to Indianapolis or the
8 surrounding communities and you worked in
9 your role that we're here to discuss today as
10 Brand Leader and Marketing Manager for
11 Zyprexa, right?
12 A. For the U.S., yes.
13 Q. For the United States.
14 What's the largest market,
15 individual country, for Zyprexa sales at the
16 time you were Brand Leader and Marketing
17 Manager?
18 A. It was the United States.
19 Q. So you were the Marketing
20 Director and the Brand Leader for the single
21 largest market for Zyprexa in the entire
22 world?

Jack E. Jordan (October 26, 2006)

133: 1 A. Yes.
2 Q. Thank you, sir.
3 Now, after you were Marketing
4 Director and Brand Leader for the single
5 largest market for Zyprexa in the entire
6 world, you took another position in August of
7 2003, with Eli Lilly?

Jack E. Jordan (October 26, 2006)

133:10 A. I did, yes.
11 Q. And that was Sales Director
12 for the Northeast for what, sir?
13 A. The Gamma Division.

Q. The Gamma Division. The northeast consisted of what states -- New Jersey?
A. It was all the way from Maine, as far west as Pennsylvania, and as far south as Virginia.
Q. Okay. We could look at a map and we can determine that but that would probably be states like Virginia, West Virginia, Pennsylvania, Delaware, New Jersey, Rhode Island, Connecticut, New York, Vermont, New Hampshire, and Maine?
A. Very good.
Q. Is there any other ones?
A. Actually, not that I recall.
Q. I did a pretty good job, didn't I?
A. Yes.
Q. Okay. So you went from the Marketing Director and the Brand Leader for Zyprexa for the single largest market in the world to the Gamma Division for the Northeast and the states I mentioned; is that right?
A. Yes.
Q. And what did the Gamma Division sell or do?
A. That division was responsible for Strattera for the adult indication.
Q. Strattera. Tell the jury what that is, please?
A. Strattera is for attention deficit disorder.
Q. Okay.
A. We were responsible for Evista.
Q. What product is that?
A. It's for osteoporosis.
Q. And any other products?
A. And Cialis.
Q. And Cialis. They put on a golf tournament?
A. They have sponsored golf tournaments.
Q. Yes. The Cialis Western Open.
But, nevertheless, you were the Gamma Division Sales Director; did I get your title right?
A. Yes.
Q. How many sales representatives are in the Gamma sales division at that time?

A. For the country there were 500, 510, something like that.
Q. 510. I didn't understand?
A. For the country, there were, approximately, 500 sales reps.
Q. Yes. For the Gamma Division,

right?
A. For the whole division, yes.
Q. I'm asking for the northeast.
A. Oh, I'm sorry, is was a quarter of that -- 125-ish.
Q. At its heighth, at its heighth during the time you were Brand Leader and Marketing Director for Zyprexa in the United States, how many sales representatives were involved in the promotion and representation of Zyprexa?

Jack E. Jordan (October 26, 2006)

136:15 A. We had, approximately, a couple thousand sales reps.
Q. And a couple of thousand. And then you leave Zyprexa and are the Sales Director of the Gamma Division which contained 125 sales representatives?
A. Yes.
Q. Okay. And the sales division -- was there different sales forces in Eli Lilly?
137: 1 A. Yes.
Q. Sigma Sales Force?
A. Yes.
Q. The -- and, of course, we know, and you would agree and tell this jury, the Sigma Sales Force promoted Zyprexa, correct?

Jack E. Jordan (October 26, 2006)

137:10 A. They were the launch sales force for primary care, yes.
Q. Then you have a Neuroscience Sales Force; is that correct?
A. Yes.
Q. And that's a separate sales force from the Sigma Sales Force; is it not?
A. Yes.
Q. And they were, the Neuroscience Sales Force had job responsibilities for promotion and detailing of Zyprexa, do they not?
A. That was part of their responsibility, yes.
138: 1 Q. Then you had a Long-Term Care Sales Force, did you not?
A. We did, yes.
Q. And that was a separate sales force from the Sigma Sales Force and the Neuroscience Sales Force, correct?
A. Yes.
Q. And they had responsibilities for the promotion and detailing of Zyprexa, didn't they?
A. That was part of their

responsibility, yes.
Q. And then you had an Institutional Sales Force, did you not?
A. We did, yes.
Q. And that's a separate sales force from Long-Term Care, Sigma, and Neuroscience Sales Force?
A. Yes.
Q. And the Institutional Sales Force had responsibilities for the promotion and detailing of Zyprexa, correct?
A. That was part of their responsibility, yes.
Q. And then you had other sales forces, such as the Alpha Sales Force, the Beta Sales Force and the Gamma Sales Force; is that correct?
A. I believe that's correct, yes.
Q. Yes. And all of those sales forces had responsibilities for the marketing and detailing and promotion of Zyprexa, did they not?

Jack E. Jordan (October 26, 2006)

A. I don't know if all of them did.
Q. Do you remember Project Four, Increase In Voice, of March the 1st, 2002?
A. I do not, no.
Q. Do you remember that the Alpha, Beta and Gamma Sales Forces were added on to the sales forces marketing and detailing Zyprexa?
A. I don't remember that Gamma was added. I thought we only added two sales forces. I apologize, I don't remember the third one.
Q. So you do agree that the Alpha and the Beta, at least your recollection, sales forces were added on to the marketing of Zyprexa?

Jack E. Jordan (October 26, 2006)

A. I believe those were the two. I know -- I thought it was -- my recollection was it was two sales forces.
Q. And those would be Alpha and Beta?
A. I'm just not sure which ones they were.
Q. We know in 2003, when you went to Gamma, you were not promoting or detailing Zyprexa, were you?
A. No, I was not.
Q. You know two were added. You believe two were added. We can eliminate

Gamma because you didn't detail or promote Zyprexa in Gamma, did you?

Jack E. Jordan (October 26, 2006)

A. Again, the sales forces only did it for, the two additional sales forces only did it for a period of time and then they didn't have it anymore. So I just don't remember if Gamma had it for a period of time.

Q. What kind of sales force is the Alpha Sales Force?

A. I don't recall.

Q. What about the Beta Sales Force?

A. I don't recall.

Q. Which of the sales forces -- well, we've now looked at several sales forces, the Neuroscience Sales Force, the Sigma Sales Force, the Long-Term Care Sales Force, the Institutional Sales Force, the Alpha Sales Force and the Beta Sales Force; is that right?

A. The Sigma Sales Force.

Q. And the Sigma Sales Force, correct?

A. Yeah. I'm just not sure on the Alpha Beta.

Q. Okay. Do you know any other sales forces that detailed or promoted Zyprexa?

A. I don't recall any other, no.

Q. Why did -- these different sales forces have different roles. Did they promote to different key players or different customers?

Jack E. Jordan (October 26, 2006)

A. Sometimes, yes.

Q. And you, obviously, know what a key player and a customer is, do you not?

A. Key player and a customer. No, I'm not. I need to see what context you're talking about.

Q. Have you ever heard the term "key player?"

A. I have heard the term "key player."

Q. Tell the jury what you know what a key player is, what your definition is.

A. I'd have to see the context.

Q. Without seeing the context you could not identify for us the term "key player."

A. It's just a general term. I'd have to see.

Q. Okay. Does the term "key player," did you utilize that term in your role as Zyprexa Marketing Director or Brand Leader?
A. I might have. I just, I'd just have to see the context.
Q. Okay. All right, sir. Did you go directly -- let me ask this: When you went to the Gamma Sales Force Director, where were you located? Where was your headquarters?
A. It was Conshohocken, Pennsylvania.

Jack E. Jordan (October 26, 2006)

Q. Is Conshohocken, Pennsylvania, a suburb of Philadelphia?
A. I believe it's considered a suburb, yes.
Q. Yes, sir. Do you remember the day you left Zyprexa?
A. The day -- no, I don't, actually.
Q. Had you had some weeks or month's notice prior to the time of your leaving your job as Marketing Director and/or Brand Leader for Zyprexa?
A. For several months I was working with Bill Robinson to, to get a sales director position.
Q. And my question to you is: Did you know several weeks or several months before you left Zyprexa that you would be leaving Zyprexa?
A. Yes.
Q. Okay. Tell the jury when you knew you would be leaving Zyprexa.
A. I don't remember. It was, probably, July/August time frame.
Q. And was there a particular reason given why you left Indiana and moved to Pennsylvania?
A. Yes.
Q. Can you tell the jury what that is, please?
A. There were two reasons.
Q. Yes, sir.
A. The first reason was to become a general manager at Lilly you need a sales leadership position, which I had never had.

And the second reason was my wife, her father was ill on the east coast and so she wanted to be close to him during his passing.
Q. You said to be a general manager at Eli Lilly you needed to hold a sales director position?
A. Yes. It's very rare that anybody gets a general manager position

within the corporate environment without a sales leadership position.
Q. Of course, you'd been a general manager from 1994 to 1998 in Dallas, had you not?
A. With a small operation, yes.
Q. But you have held the title of General Manager, even before you were Zyprexa Brand Leader and Marketing Manager?
A. I had, yes.
Q. Okay. So was any of the reason that you left Zyprexa related to any job dissatisfaction on behalf of the company with your performance?
A. No.
Q. Was any of the reason you left your role for Zyprexa due to any insatisfaction or dissatisfaction that you had with the company and Zyprexa?
A. No.
Q. So we can tell this jury, and you can testify under oath, that you were completely satisfied and comfortable with what had took place within the organization of Eli Lilly in general, and the marketing department in particular, concerning the marketing and sales of Zyprexa from 1998 to 2003?

Jack E. Jordan (October 26, 2006)

A. Absolutely.
Q. You have no -- do you have any regrets or believe that there's any conduct that you are personally aware of when you were Brand Leader or Marketing Manager, is there any conduct of any individual that you are aware of surrounding Zyprexa that you believe was incorrect, improper, or wrong, that you can identify for this jury between '98 and 2003?

Jack E. Jordan (October 26, 2006)

A. There were a couple sales reps that were identified for doing inappropriate things and were dismissed from the company, but beyond that, no.
Q. Okay. Besides a couple of sales reps who were dismissed from the company, between 1998 and 2003, as Marketing Director and Brand Leader, you were completely satisfied with the conduct and activities surrounding the promotion, marketing, and sales, of Zyprexa on behalf of Eli Lilly?

Jack E. Jordan (October 26, 2006)

148:23 A. Yes.
24 Q. Thank you, sir.
149: 1 Why did you leave your
2 position as Director of Sales of the
3 Northeast for the Gamma Sales Force?

Jack E. Jordan (October 26, 2006)

149: 6 A. I decided to leave the
7 company.

Jack E. Jordan (October 26, 2006)

149:18 Q. Did you make the move into
19 the Gamma Sales Director's job knowing that
20 at some point very soon thereafter you would
21 be leaving Eli Lilly?
22 A. No.

Jack E. Jordan (October 26, 2006)

150: 1 Q. Okay. Was there anything
2 that happened in your role as Sales Director
3 for the Northeast in the Gamma Sales Force,
4 anything that happened there that made you
5 want to leave Eli Lilly?
6 A. No.
7 Q. Were you fired from Eli
8 Lilly?
9 A. I was not.
10 Q. Did you resign from Eli
11 Lilly?
12 A. I did.
13 Q. Did you do so in writing?
14 A. I did.
15 Q. Did you -- are you under any
16 kind of current contract from Eli Lilly?
17 A. No.
18 Q. Are you currently compensated
19 by Eli Lilly?
20 A. I am not, no.
21 Q. When is the last time you
22 received any funds from Eli Lilly, either
23 directly or indirectly?
24 A. They have reimbursed my
151: 1 expenses associated with this travel.
2 Q. From Bremen, Indiana, to
3 Indianapolis, Indiana?
4 A. Yes.
5 Q. During the time that you
6 worked at Eli Lilly, including but not
7 limited to your time period as Marketing
8 Director and Brand Leader, did you obtain
9 stock options?
10 A. I did, yes.
11 Q. Did -- do you own stock in

Eli Lilly?
A. I do.
Q. How many shares of Eli Lilly stock do you own, either directly or indirectly, as a part of your direct ownership or through any trust or any other indirect ownership?
A. I don't know how many shares. I don't know how many shares.
Q. Approximately, for the jury, please.
A. I think about a thousand shares.
Q. Okay. Did you exercise any stock options? Were you granted yearly stock options in your role as Brand Leader or Marketing Director for Zyprexa?
A. I was, yes.
Q. How many stock options were you granted every year during that time period?
A. I don't know.
Q. Approximately.
A. Boy, I don't know.

Jack E. Jordan (October 26, 2006)

Q. All right. Can you give this jury, under oath, any estimation, whatsoever, on the number of stock options you were granted during the time you were Brand Leader and Marketing Director for Zyprexa?

Jack E. Jordan (October 26, 2006)

A. I don't know.

Jack E. Jordan (October 26, 2006)

Q. Okay. How much money did you make as Marketing Director and Brand Leader for Zyprexa?

Jack E. Jordan (October 26, 2006)

A. It was about a hundred, $120,000, depending on what year.
Q. So your base salary was between 100 and $120,000 a year as Brand Leader or Marketing Director, right?
A. As I recall it, yes.
Q. And did you then get incentive bonuses or anything of that nature?
A. No incentive bonuses, dollar bonuses, no.

Q. Did you have means and mechanisms by which you could increase your annual compensation during the time you were Brand Leader or Marketing Director?
A. There were stock options offered, yes.
Q. Okay. So your two primary elements of compensation -- sir, go ahead.
A. And performance awards.
Q. And performance awards. That's what I meant by incentive but I --
A. Okay, I'm sorry.
Q. So you had three areas of compensation. A base salary, correct?
A. Yes.
Q. Stock options?
A. Yes.
Q. And performance awards?
A. Yes.
Q. And you could take the stock options and your performance award and, obviously, increase your annual compensation.
A. Yes.
Q. And were the stock options based upon your performance or just a set amount of stock options that were granted every year?

Jack E. Jordan (October 26, 2006)

A. It was based on performance.
Q. Okay. So the better your performance the better your stock options?
A. Yes.
Q. So your performance would, obviously, be related to the marketing and sales of Zyprexa in the United States?

Jack E. Jordan (October 26, 2006)

A. Yes.
Q. How did that go between 1998 and 2003?

THE WITNESS: How did -- well, I don't understand the question.

MR. ALLEN: Well, you said your stock option grants were based upon your performance. And you testified your performance was based upon the sales of Zyprexa in the United States between '98 and 2003.

QUESTIONS BY MR. ALLEN:
Q. How did your stock options go during that time period, did they increase?
A. Well, it was both performance of Zyprexa as well as my leadership in the organization, also, so it was quantitative and qualitative. But it was appropriate with

my performance.
Q. Right. How was the performance of Zyprexa sales in the United States between 1998 and 2003?

Jack E. Jordan (October 26, 2006)

157: A. They were fine.
Q. Didn't they go up every year while you were a Marketing Manager and Brand Leader until the time you left in the summer of 2003, when it began to fall?
A. Yeah. I was never a marketing manager but --
Q. Marketing Director. I apologize, sir.
A. But it was -- it did go up every year, yes.
Q. I mean sales, as I recall it, were, approximately, over $2 billion, for example, in the year 2000, right?

Jack E. Jordan (October 26, 2006)

158: A. I think that's correct.
Q. And then sales increased above that level in 2001, did they not?
A. They did, yes.
Q. And what was the approximate of the dollar value in sales in the United States in 2001 of Zyprexa?
A. Boy, that's been a while ago. 2.2, 2.3, I don't recall the exact number.
Q. 2.2 or 2.3 what?
A. Billion.
Q. What, sir?
A. Billion.
Q. Billion. And then in 2002, the sales of Zyprexa even, in the United States went higher than that, did they not?
A. Yes, they did.
Q. What were they in that year, approximately, as you recall?

Jack E. Jordan (October 26, 2006)

158: A. Well, it went up another couple hundred million, as I recall.
Q. Almost $3 billion in 2002; is
159: that correct?

Jack E. Jordan (October 26, 2006)

159: A. We monitored net sales. So net sales were, the highest they ever got

while I was there was, I believe, 2.4 or 2.6 billion, I just can't remember.
Q. That's net sales not gross sales, correct?
A. Yeah. I never tracked gross sales.
Q. Okay. Net sales is less than gross sales.
A. It is, yes.
Q. Okay. And then in 2000, 2001, 2002, it went up. In 2003, you got off to a rocky start, didn't you?

Jack E. Jordan (October 26, 2006)

159:20 Q. In regard to sales.
A. I don't remember what happened beginning 2003.
Q. Didn't the engine begin to stall?

Jack E. Jordan (October 26, 2006)

160: 3 A. No. I never remember that term being used around our sales.
Q. Wasn't Zyprexa the engine of the company during the time you were Brand Leader and Marketing Director?

Jack E. Jordan (October 26, 2006)

160:10 Q. Marketing Director, yes, sir. Wasn't it the engine of the company?
A. I never heard that term used for Zyprexa sales.
Q. Wasn't it the flagship of the company?

Jack E. Jordan (October 26, 2006)

160:18 A. It was an important product, yes.

Jack E. Jordan (October 26, 2006)

163: 9 Q. Sir, can you testify whether or not, in your opinion as the Marketing Director and Brand Leader for Zyprexa, as to whether or not Zyprexa was the single most important product for Eli Lilly from at least the fall of 2000 until the time you left in 2003?
A. Our CO had highlighted, I

believe, it was four or five products that were going to be the priority during those years.

Q. Did any product take a priority over Zyprexa?

A. Not that I know of.

Q. What product, what drug product for Eli Lilly, during the time of at least the fall of 2000 until the time you left in the summer of 2003, what drug product for Eli Lilly created Eli Lilly's greatest profit?

Jack E. Jordan (October 26, 2006)

A. Zyprexa was the, was the answer to that. Zyprexa.

Q. Zyprexa was the biggest profit maker for Eli Lilly from at least the fall of 2000 until the time you left; is that correct?

A. Yes.

Q. Your -- as Brand Leader and Marketing Director, one of your things that you did in your role was to watch the stock price and to see what Wall Street was thinking, correct?

Jack E. Jordan (October 26, 2006)

A. I did follow the stock price, yes.

Q. Right. Because as Brand Leader and Marketing Manager, you had an interest into how the market, including the stock market, was responding to Zyprexa and Zyprexa sales, correct?

Jack E. Jordan (October 26, 2006)

A. Yes.

Q. And you follow the stock price on a routine basis every single day, did you not?

Jack E. Jordan (October 26, 2006)

A. I did not.

Q. How often did you follow the stock price?

A. Probably, weekly.

Q. And did you, in fact, report that, or did you keep a record of that in your office, or report it to anyone?

Jack E. Jordan (October 26, 2006)

166: 3 A. I did not, no.
4 Q. Did anybody report to you on

Jack E. Jordan (October 26, 2006)

166: 5 that?

Jack E. Jordan (October 26, 2006)

166: 8 A. No.
9 Q. Did you from time to time
10 receive reports on the stock price?

Jack E. Jordan (October 26, 2006)

166:13 A. I mean, I knew what it was
14 from the newspaper, yes.

Jack E. Jordan (October 26, 2006)

171:22 Q. Okay. We know, and I just
23 want to get, I want to get a complete roll
24 call so we can inform the jury of the lawyers
172: 1 you met with in your role with Zyprexa from
2 August of 2003 until today. Are you with me
3 so far?

Jack E. Jordan (October 26, 2006)

172: 7 Q. Are you with me so far? A
8 list. Roll call.
9 A. Well, I just, August of 2003,
10 is that all the Lilly lawyers?
11 Q. Yes, sir. I'm going to go
12 through all the lawyers you have met with
13 concerning Zyprexa between August of 2003
14 until today, okay?
15 A. Hum.
16 Q. Hum. Is that all right with
17 you?
18 A. Yeah. Yeah, that's fine.
19 Q. Okay. We know you met with
20 Mr. Gold. He's here with you at the
21 deposition today, right?
22 A. Um-hum. Yes.
23 Q. We know you met with Mr. Sean
24 Fahey of Pepper Hamilton, he's sitting to
173: 1 Mr. Gold's right and is with you at the
2 deposition today, correct?

A. Yes.
Q. We know you met with Ms. Traci Greenberg of Mr. Gold's office, and she's sitting to Mr. Fahey's right, and she's here in the deposition with you today, right?
A. Yes.
Q. We know you met with Ms. Seabrook of Mr. Fahey's firm of Pepper Hamilton from Philadelphia, we know that, right?
A. Yes.
Q. What other lawyers have you met with involving Zyprexa since you left in August of 2003 until today?

Jack E. Jordan (October 26, 2006)

174: A. So during -- I was transitioning off the Zyprexa job in August and September. So I would have been involved in a number of Zyprexa meetings that included Lilly lawyers. So do you want me to start there?
Q. Sure.
A. This would have been Lilly-related business, Lou Carol West, Angela Wade. And again, this would be Lilly-related business.
Q. Okay. All involving Zyprexa, right?
A. Yes.
Q. Okay, go ahead.
A. Curt McDaniel. And I think those are all the Lilly lawyers in the context of my Zyprexa Brand Leader job.
Q. Those are in-house Lilly lawyers?
A. They are, yes.
Q. Let's assume then you left
175: the company, and you told us you left the company in 2004. What lawyers have you met with concerning Zyprexa between the time you left the company in 2004 until today, besides Mr. Gold, Mr. Fahey, Ms. Greenberg and Ms. Seabrook?
A. Nina Gussack.
Q. And what law firm is she with?
A. She's with Pepper Hamilton.
Q. In Philadelphia?
A. Philadelphia, yes.
Q. Those are Lilly lawyers?
A. I don't know how that arrangement works. I think they represent Lilly, yes.
Q. So when you met with Mr. Fahey, Ms. Seabrook, and Nina Gussack, you didn't know who they represented?
A. I did, yes. Yeah.
Q. Who did they represent?
A. Eli Lilly.

Q. Thank you.
What other lawyers did you
176: meet with besides Mr. Gold, Mr. Fahey, Ms. Greenberg, Ms. Seabrook, and Nina Gussack, until the time you left Eli Lilly until today?
A. George -- I don't know his last name.
Q. Lehner? Mr. Lehner? He was back here earlier and then he left?
A. Yeah.
Q. Sir?
A. Yes.
Q. And he's from Pepper Hamilton and Eli Lilly's lawyers, correct?
A. That's my understanding, yes.
Q. He was here earlier and he's gone now, right?
A. Yes.
Q. What other lawyers?
A. There were a couple others -- I just -- with Pepper Hamilton, but I don't remember their names.
Q. So Pepper Hamilton lawyers we have Mr. Fahey, Ms. Seabrook, Ms. Gussack, Mr. Lehner, and a couple more that you just
177: can't remember the names, right?
A. Yeah. Yeah. I apologize for that.
Q. By my count that's six. Any other lawyers you met with besides those individuals and Mr. Gold and Ms. Greenberg?
A. Not that I remember, no.
Q. Okay. Did you ever hire personal counsel to investigate filing a lawsuit against Eli Lilly?
A. No.
Q. Did you ever threaten to file a lawsuit or file a lawsuit against Eli Lilly?
A. No, I never did.
Q. Have you ever met with any attorneys for the United States Justice Department or any other law enforcement agency?
A. I've not, no.
Q. Are you aware of any investigations surrounding the marketing and/or sales of Zyprexa?
A. Yeah.
178: Q. What investigations are you aware of?
A. I just know about a federal investigation into the sales and marketing practices of Lilly around its products. I think it's Zyprexa and it might be another one, I'm just not sure.
Q. Are you aware of any investigations besides the federal investigation surrounding the marketing and sales of Zyprexa?
A. There were some state action, is my understanding.

Q. What states? Pennsylvania, among others?

Jack E. Jordan (October 26, 2006)

178:18 A. I don't know what states.
19 Q. Okay. Have you ever met with
20 any lawyers besides -- let me put it this
21 way: Have you met with any lawyers to
22 discuss these criminal investigations?
23 A. I have not, no.
24 Q. Have you ever given any
179: 1 statement to any investigator, be it a lawyer
2 or not, concerning these investigations?
3 A. I have not, no.
4 Q. Have you signed any
5 affidavits, or given any sworn testimony, or
6 testimony on the record, involving your roles
7 and responsibilities as Brand Leader or
8 Marketing Manager concerning Zyprexa?
9 A. I have not, no.
10 Q. Have you ever testified in
11 any forum prior to today, October the 26th,
12 2006?
13 A. I have not, no.
14 Q. Today is the first time
15 you've ever testified in your life?
16 A. It is, actually.
17 Q. Okay. Have you ever been
18 interviewed by any law enforcement agency or
19 any investigator for a law enforcement agency
20 looking into Zyprexa?
21 A. I have not, no.
22 Q. Has anybody ever requested
23 such an interview?
24 A. No, they never have.
180: 1 Q. Has anybody, to your
2 knowledge, tried to reach you to investigate
3 the marketing and sales practices surrounding
4 Zyprexa but been unable to reach you?
5 A. No.

Jack E. Jordan (October 26, 2006)

180:12 Q. Does Eli Lilly have an
13 inspector general or a Compliance department
14 or something along those lines?
15 A. We have a Compliance
16 department.
17 Q. What's the role of the
18 Compliance department?
19 A. When I was on the Zyprexa
20 team, it was to ensure that everything that
21 we did on the Sales and Marketing side was
22 consistent with Good Promotional Practices
23 and the rules and regulations of the FDA.
24 Q. You said their role was to
181: 1 make sure that everything we did in marketing
2 was consistent with Good Promotion Practices

and the FDA. How did the Compliance department assure that that took place?

Jack E. Jordan (October 26, 2006)

A. They had regular training sessions with the marketing and sales people. They did audits around the sales and marketing activities. They had a hotline to report any issues, a confidential hotline to report any potential issues. And I'm sure they did a number of other things that I can't remember right now.

Q. Okay. But the things you remember that the Compliance department did was training, hotlines, and audits of your department?

Jack E. Jordan (October 26, 2006)

A. Of a number of departments. In other words, Marketing, Sales, Business-to-Business. Organizationally, they ensured compliance.

Q. Right. To ensure that you were meeting governmental regulations and Good Promotion Practices?

A. Yes.

Q. Were you ever informed by the Compliance department or any other source at Eli Lilly that the promotion and sales or marketing of Zyprexa was not consistent with Good Promotion Practices or with FDA regulations?

Jack E. Jordan (October 26, 2006)

Q. Did you ever receive any written document or a phone call or e-mail advising you that any of the marketing or sales or promotion practices of Zyprexa were improper and out of compliance?

Jack E. Jordan (October 26, 2006)

A. The only time was when an individual sales rep would have been out of compliance and terminated from the company. They wouldn't give me the sales rep's name, because that would be inappropriate, but they'd let me know that something had been spotted. But at the marketing level, no.

Q. Okay. And you told me that

you could only recall two sales reps that were terminated due to their promotion of Zyprexa, you testified to that earlier.
A. There might have been more than that but that's all I --
Q. You said you were aware of two, that's what you testified.
A. Yes.

Jack E. Jordan (October 26, 2006)

184:24 Q. What were you aware that
185: 1 these sales representatives did that caused
2 them to be terminated?
3 A. I wasn't told the specifics.
4 Q. Were you told anything?
5 A. That they were involved in
6 inappropriate activity.
7 Q. Yes, sir. And it seems like
8 if you were involved -- you were in contact
9 with the Sales department, were you not? You
10 had to coordinate and align your marketing
11 strategy and your marketing mix and your
12 positioning with the Sales department, did
13 you not?

Jack E. Jordan (October 26, 2006)

185:16 A. I did interact regularly with
17 the Sales department, yes.
18 Q. Right. So you'd have to
19 know, you'd have to be informed in order to
20 learn to correct problems, what the sales
21 representatives did that got fired. You'd
22 have to learn that or know that, wouldn't
23 you, sir?

Jack E. Jordan (October 26, 2006)

186: 2 Q. In order to correct the
3 problem and make sure it didn't happen in the
4 future and also to make sure your marketing
5 was aligned across the company, right?

Jack E. Jordan (October 26, 2006)

186: 8 A. In general terms, we would
9 consistently learn from the Compliance Group
10 where there were potential or issues of
11 concern or things we needed to make sure
12 didn't become issues of concern.
13 Q. And what were the two sales
14 reps terminated for that you are aware of?

Jack E. Jordan (October 26, 2006)

186:17 A. I wasn't told the specifics.
18 Q. And you never wanted to in
19 your role determine what this, quote,
20 inappropriate conduct was?
21 A. Again, the Compliance
22 department took the responsibility to make
23 sure. In general terms, that was --
24 Q. Okay. Sir, since you were
187: 1 not aware of any, other than the two sales
2 reps -- let me ask you this question: In
3 your role, sir, and in your opinion as Brand
4 Leader and Director of Marketing for Zyprexa,
5 were the marketing activities surrounding
6 Zyprexa within commonly and normally accepted
7 pharmaceutical practice for the marketing of
8 drugs in the United States?

Jack E. Jordan (October 26, 2006)

187:13 A. Yes, they were consistent
14 with Good Promotional Practices.
15 Q. And they were consistent with
16 industry practices?

Jack E. Jordan (October 26, 2006)

187:19 A. We focused more on Good
20 Promotional Practices and compliance with FDA
21 rules and regulations.
22 Q. Was your promotion, sales,
23 and marketing of Zyprexa, can we tell the
24 jury, at least in your opinion as Brand
188: 1 Leader and Marketing Director, that it is --
2 was exemplary conduct, in your opinion?
3 A. We were consistent with Good
4 Promotional Practices and FDA rules and
5 regulations, yes.
6 Q. Is there anything you're
7 embarrassed about or would like to tell this
8 jury that you would want the jury to be aware
9 of as we sit here today when they listen to
10 your testimony, you'd like to tell this jury,
11 "I'd have to tell you right now there's a
12 couple of things that we did in the marketing
13 department surrounding Zyprexa that we wish
14 we hadn't done." Is there anything like
15 that?
16 A. No.

Jack E. Jordan (October 26, 2006)

188:18 Q. So you can tell the jury that
19 you have no reservations about any of the
20 conduct of which you're aware surrounding the

marketing of Zyprexa during the time you were Brand Leader or Marketing Director?
A. No.
Q. Is that correct? Nothing at all you regret or are embarrassed?
A. No.

Jack E. Jordan (October 26, 2006)

Q. Can you represent to the jury that your conduct, and those with whom you worked in the marketing and sales of Zyprexa, is the best type of marketing conduct that one has to offer?
A. Yes.
Q. Can you market a product -- can you promote a product off-label?
A. No.
Q. Why can't you promote a product off-label?
A. The regulatory environment in the U.S. is that you need to do studies, and get them approved by the FDA, and then your promotion needs to be consistent with the label that's granted by the FDA.
Q. And when you say "consistent with the label," your promotional activities cannot exceed the indications on the label, can it?
A. There's nonpromotional activity and promotional activity. And promotional activity need to be consistent with the label.
Q. I know, sir. And I heard that. But when you say "it needs to be consistent with the label," can you promote for anything other than the specific indications in the label in the indications section?
A. No.
Q. Okay. So all promotional activities have to be only for those specific written indications in the indications section of the label, correct?
A. In the label for the U.S.
Q. Right. Is that correct?
A. It is.
Q. During the time you were Marketing Director, let's take 2000, let's take the fall of 2000, do you recall what the indications in the label were for Zyprexa?
A. The fall of 2000, would have been a schizophrenia indication and a bipolar mania indication.

Jack E. Jordan (October 26, 2006)

Q. Mr. Jordan, the two indications in the label as of the fall of

2000 were bipolar mania, correct?
A. Yes.
Q. And schizophrenia?
A. Yes.
Q. Did you have any other indications for Zyprexa besides bipolar mania and schizophrenia?
A. There was an indication for combination therapy using Zyprexa with lithium or Depakote for bipolar disorder. I can't remember the exact words there.
Q. For bipolar what?
A. I think it was bipolar mania. And then there was an indication for bipolar maintenance after I left the job.
Q. After you left the job?
A. Yes.
Q. So during the entire time you were on the job as Brand Leader and Marketing Director, there was only, according to your testimony, three labeled indications for Zyprexa?
A. Yes.
Q. Those were schizophrenia, No. 1, correct?
A. Yes.
Q. Bipolar mania, No. 2?
A. Yes.
Q. The third indication, which was later added, that you were Zyprexa Brand Leader Marketing Director of, was this combination therapy, right?
A. Yes.
Q. And when did that combination indication come on the label?
A. I don't remember.
Q. Do you remember the year?
A. I do not, no.

Jack E. Jordan (October 26, 2006)

Q. We're back on the record. Let me establish a couple of things with you. I think we have throughout the day, I want to make sure you understand. You understand you are under oath?
A. I do, yes.
Q. If you don't understand a question ask me to rephrase it or repeat it. Okay?
A. Okay.
Q. You've done that thus far, have you not?
A. I have, yes.

Jack E. Jordan (October 26, 2006)

Q. I am going to get into the

issue of marketing and promotion of Zyprexa but I have to backtrack and ask you a couple of things.

You had testified previously on marketing and promotion that you could not market or promote Zyprexa for anything other than the indications listed in the label; is that correct?

A. As far as the -- yeah, as far as the indication part, yes.

Q. And when we say "the indication," we're talking about the indication as written in the label or the package insert on the product, right?

A. Yes. You can't promote for indications outside of what's in the label, yes.

Q. Can you market Zyprexa --

A. Well, I just want to be clear. There's promotional activity, which is on-label promotion, and then there's nonpromotional activity, such as a physician asking our medical department a question. That would be nonpromotional activity.

Q. Okay. Can you actively market or actively promote Zyprexa for anything other than the labeled indications?

Jack E. Jordan (October 26, 2006)

A. All promotional activity needs to be consistent with the label, yes.

Q. How about marketing activity?

A. If you're talking about -- again, marketing in the pharmaceutical industry is divided by promotional and nonpromotional. So nonpromotional activity is a different area as defined by the FDA and Good Promotional Practices.

Q. So you're telling this jury you cannot promote Zyprexa or engage in promotional activities for indications outside of the label, correct?

Jack E. Jordan (October 26, 2006)

A. I'm sorry. You can only promote consistent with the label, promotional activity.

Q. Can you engage in nonpromotional activity for nonindicated uses?

A. Nonpromotional activities.

THE WITNESS: Can you repeat that? It's an awkward phrase.

MR. ALLEN: Yes.

Q. You said marketing had two components -- promotional activities and nonpromotional activities.

A. Yes.
Q. Okay. You told us you cannot engage in promotional activities for any indications outside of the label, correct?
A. Yes.
Q. Okay. Can you engage in nonpromotional activities for indications outside of the label?
A. Nonpromotional activities can be outside of the label, yes.
Q. Did Eli Lilly engage in nonpromotional activities for Zyprexa for indications not in the label?
A. There were communications, a number of communications from our Medical Group and other venues that were nonpromotional, yes.
Q. Outside the indications in the label?
A. Yes, but consistent with guidelines established by the FDA.
Q. So Eli Lilly engaged in nonpromotional communications surrounding Zyprexa for nonindicated uses of Zyprexa?

Jack E. Jordan (October 26, 2006)

A. Yes. Consistent with the guidelines as established by the FDA and the courts, yes.

Jack E. Jordan (October 26, 2006)

Q. What nonpromotional communications outside the indications in the label did Lilly engage in for Zyprexa?
A. A number of times doctors would contact our medical department with questions and when our Clinical Group responded to those questions sometimes they would be non, they would be nonpromotional responses and hence outside of the label. That would be one example.
Q. Any other -- and I want them all, all of the nonpromotional communications outside the label that you are aware of that Eli Lilly engaged in for Zyprexa?

Jack E. Jordan (October 26, 2006)

A. I'm not sure I can give all of them but I'll give you the ones that I recall.
So, Medical Department customer request is a nonpromotional activity.
Q. You mumbled there, sir.

A. I'm sorry.
Q. **The medical department what?**
A. I was just, in my own mind, the medical department communication with customers is often nonpromotional.
Q. **If the doctor asked the question?**
A. Yeah.
Q. **The medical department can't affirmatively discuss with the doctor nonapproved indications, can they?**
A. No. It's got to be a request from the customer.
Q. **Okay. Give me the other nonpromotional communications or activities you are aware of that Eli Lilly engaged in for uses outside the indications in the label?**
A. Another example of a nonpromotional activity is many times medical education providers would come to us with a particular subject that our customers were interested in and we would fund certified medical education, fund those. And they might be on an indication that we have, or it might be a topic that doctors are interested in learning about. So we give grants to, CME, to talk about nonpromotional items.
Q. **Just for the jury, CME, Continuing Medical Education?**
A. Yes.
Q. **So Eli Lilly would engage in nonpromotional activities, including the funding of continuing medical education courses, which might discuss nonlabeled uses of Zyprexa?**
A. It is. But our engagement -- I want to be clear -- our engagement is only on the funding side. It's not on the content side or on the speaker side. But that is an example of nonpromotional activity.
Q. **What other activities did Eli Lilly engage in of a, which you defined as a nonpromotional nature, discussing nonlabeled uses of Zyprexa besides answering doctors questions and CME funding?**

Jack E. Jordan (October 26, 2006)

A. Another way is in the nineteen-ninety, 2000/2001 time frame there was a ruling by the courts, at least as we referred to it, as the Washington Legal Foundation, where the pharmaceutical industry was given First Amendment rights to disseminate information, off-label information to customers.
You couldn't sell from this information but you could disseminate, through your sales reps and through other venues, information that was from valid

studies published in a premier journal and simply disseminated to a physician. So we did that.

Q. So Eli Lilly sales representatives, you are aware of, disseminated medical articles discussing nonapproved uses of Zyprexa that were not in the label?

Jack E. Jordan (October 26, 2006)

A. Yes. Within the guidelines established by the courts and -- mostly by the courts, yeah.

Jack E. Jordan (October 26, 2006)

Q. Anything other than answering doctor's questions, funding of CME courses, and disseminating medical articles for the use of Zyprexa that were not in the indications in the label, that Eli Lilly engaged in?

Jack E. Jordan (October 26, 2006)

A. Yes.

Q. What else?

A. Under FDA guidelines, if a physician asks a question of a sales representative that has to do with potential off-label items, a sales representative can answer a specific question.

Q. Any other activities, besides the medical department responding to doctor's questions, sales representatives responding to doctor's questions, funding of CME, and dissemination of articles, that Eli Lilly engaged in concerning nonapproved or indicated uses of Zyprexa?

Jack E. Jordan (October 26, 2006)

A. This is somewhat consistent with the previous answer but it is different. There's, in the pharmaceutical industry there are medical letters. Again, when customers have specific questions. The earlier one was verbal communication. This one is if a doctor has a specific question they have access to medical letters that sometimes are on-label and sometimes they're off-label but it is part of that nonpromotional group of activity as identified by the FDA.

Q. Any other nonpromotional,

using your term, nonpromotional activities for Zyprexa outside the label besides responding to doctor's verbal questions, funding of CME, dissemination of articles to physicians through the sales representatives, the sales representatives answering questions, and medical letters, that you know Eli Lilly engaged in regarding Zyprexa?

Jack E. Jordan (October 26, 2006)

A. And when a speaker speaks on behalf of Eli Lilly in a promotional program, if there's a question asked by the audience about nonapproved indications, the speaker can answer those questions, and that would be outside the label. That would be nonpromotional but consistent with FDA guidelines.

Q. Anything else besides the activities you've mentioned today that were nonpromotional concerning Zyprexa?

A. You know, Mr. Allen, I'm sure there is, I just don't remember any.

Q. You have done your best job for this jury, who's going to listen to the testimony, of telling us the nonpromotional activities or answering the doctor's questions. And the doctor has to ask the questions, right?

A. Yes.

Jack E. Jordan (October 26, 2006)

Q. Concerning nonpromotional activities, can sales representatives and/or the medical department, or anybody employed by Eli Lilly go to a doctor's office or call a doctor's office and affirmatively discuss uses of Zyprexa that are not indicated in the label?

Jack E. Jordan (October 26, 2006)

A. I can't think of a situation outside of answering a particular clinician's question.

Q. So it would be wrong for a sales representative, for example, to affirmatively go to a doctor's office and affirmatively discuss off-label uses of Zyprexa. That would be wrong?

Jack E. Jordan (October 26, 2006)

A. I mean affirmatively? I just want to be clear --
Q. Yes, sir.
A. They can't promote off-label indications in a doctor's office, "they" being a sales rep, medical department, et cetera, yes.
Q. Right. And Eli Lilly cannot fund CME courses with the intent that those individuals who will speak at the CME will discuss off-label uses, can they?
A. No. We can fund CMEs that, that discuss -- we don't impact content, so they can discuss whatever it wants to discuss.
Q. Did Eli Lilly fund CME courses knowing that those CME courses which they funded would have as part of their content off-label uses of Zyprexa?
A. There was no real way to know that there were going to be off-label. We didn't know what the content was.
Q. So, therefore, Eli Lilly, in your testimony, to your knowledge, never funded CME courses knowing that off-label uses would be discussed?

Jack E. Jordan (October 26, 2006)

A. I didn't interact with the vendor, so I wouldn't be the right person to ask on the specifics you're getting into.
Q. All right. You talked about speakers may speak. You remember you said Eli Lilly speakers may speak to an audience?
A. Yes.
Q. Eli Lilly had a speakers bureau?
A. We did, yes.
Q. And had thought leaders?
A. Yes.
Q. That they paid a fee to or paid money to these doctors, these speakers and thought leaders, to talk to audiences about Zyprexa?
A. We compensated them for their time, yes.
Q. That means you paid them, correct?
A. Yes.
Q. You not only paid these speakers and thought leaders for speaking to these audiences, you also provided them slides and PowerPoint presentations, did you not?
A. Part of the process of promotional programs is to have approved promotional slides, yes.
Q. So you provided them, these speakers and thought leaders, material that they would disseminate and discuss at their

presentation?

Jack E. Jordan (October 26, 2006)

214:12 A. Yeah. That the process was
13 that their promotional slides were reviewed
14 and approved by our medical, regulatory, and
15 legal folks, and then we provided the slides
16 to them, yes.
17 Q. So whatever slides were
18 provided to these speakers or thought leaders
19 when they would go out and speak to
20 physicians, for example, those slide show
21 presentations were reviewed by your ELMR
22 group; is that right?

Jack E. Jordan (October 26, 2006)

215: 3 A. Yeah. Any promotional
4 activity needed to go through the process of
5 approval by medical, regulatory, legal, the
6 editor, they get approved by those folks, and
7 then went out in the various venues.
8 Q. And these speakers and
9 thought leaders to whom you paid money,
10 and/or supplied slide presentation or
11 PowerPoints were considered promotional
12 activities?

Jack E. Jordan (October 26, 2006)

215:17 A. They were promotional
18 programs, yes.
19 Q. And so, therefore, since
20 they're promotional programs, it would be
21 illegal and improper for the speakers to
22 speak on uses of Zyprexa that were not
23 indicated in the label, correct?

Jack E. Jordan (October 26, 2006)

216: 2 A. If it's a promotional program
3 that they were trained on, which was required
4 before they spoke, they needed to have their
5 presentation be consistent with, they need to
6 use the slides and be on-label, yes.
7 Q. Be on-label.
8 A. Yes.
9 Q. Not beyond label but just --
10 A. Thank you. Be consistent
11 with the label, yes.
12 Q. So the speakers in your
13 speakers bureau that you pay had to speak
14 about labeled indications?

Jack E. Jordan (October 26, 2006)

216:17 A. In the -- yeah, their
18 proactive, their proactive presentation
19 needed to be on-label. But again, if they
20 were asked questions, they could answer any
21 question, basically.
22 Q. Yes. But their prepared
23 text, prepared speech, had to be on-label.
24 A. In a promotional program,
217: 1 yes.
2 Q. Are there nonpromotional
3 programs by your speakers and thought leaders
4 that Eli Lilly paid for?
5 A. Sometimes -- you know, I'm
6 trying to think of an example and I can't
7 think of an example, no.
8 Q. Okay. Now you said in
9 promotional activities you always, you at Eli
10 Lilly, either you, or your employees, or your
11 surrogates, who you hired for all of the
12 promotional activities had to be within the
13 indication on the label?

Jack E. Jordan (October 26, 2006)

218:10 A. I mean, I didn't hire all the
11 people. I mean --
12 Q. I didn't think you hired
13 them, I thought Eli Lilly would hire people.
14 A. Okay.
15 Q. I thought Eli Lilly paid
16 people. I'm correct about that, aren't I?
17 A. Yeah.

Jack E. Jordan (October 26, 2006)

219: 2 A. All promotional activities,
3 it needed to go through the approval process
4 before it went out, so yes.
5 Q. So for all promotional
6 activities that Eli Lilly funded or engaged
7 in had to be on label; is that correct?
8 A. Yes, by definition.
9 Q. Tell the jury what
10 promotional activities are. Tell us the
11 examples of promotional activities. Sales
12 reps visiting doctor's offices is
13 promotional; is that correct?
14 A. The message that sales reps
15 would actively deliver to doctors was a
16 promotional message, yes.
17 Q. Yes. Brochures or
18 leave-behinds were promotional materials,
19 were they not?
20 A. Anything that a rep left
21 behind in an office had to go through the
22 ELMR process, be approved, and consistent

with label, yes.
Q. **Sales aids were promotional materials, are they not?**
A. The sales aids used for promotional activity were, by definition, promotional, yes.
Q. **And had to be on-label?**
A. They did, yes.
Q. **I can't think of the word. What's a -- did you have to train your sales representatives to discuss only on-label indications?**
A. There was extensive training with new hires. There was extensive training on the industry, on the requirements of the industry, on Lilly's expectations. So yes, there was there.
And then we had quarterly training from our Good Promotional Practices and Compliance Group on, on what, what we expected from sales representatives.
Q. **Were the resource guides, are those promotional materials?**
A. Those are training materials.
Q. **Did they have to be on-label?**
A. They were, as part of the, as part of the promotional message, they certainly did need to be on-label, yes.
Q. **Core folders, tell the jury what core folders are.**
A. At least how I heard and used the term "core folder" is that's, kind of the basic material that a sales representative would use for his or her detail, on-label detail.
Q. **I'm sorry. That had to be on label, correct?**
A. It did, yes.
Q. **Are there any written materials that Eli Lilly could prepare themselves in order to facilitate off-label usage?**

A. Written materials. Well, by definition, WLF was written materials that we put a cover sheet on to explain that it was, that we didn't have an indication for it. To explain the article a little bit. And, yeah, so I guess in that sense it was prepared by Lilly, the cover sheet, and then the article would come from a journal.
Q. **Anything else? Any other written materials Eli Lilly could prepare for its customers discussing off-label uses of Zyprexa?**
A. The medical letters were written materials that, obviously, went out.
Q. **Now those medical letters could only be sent out in response to a**

doctor's query, correct?
A. Yes. That is correct.
Q. Eli Lilly could not prepare medical letters to send out affirmatively to an audience or a group of doctors unless those medical letters were on-label, correct?

Jack E. Jordan (October 26, 2006)

A. Yeah. Yeah. Correct.
Q. Okay. Besides the cover sheet to a medical article, is there anything, any other -- and the medical letters in response to doctors's inquiries, are there any other written documents that Eli Lilly can prepare and disseminate to its customers concerning off-label uses?

Jack E. Jordan (October 26, 2006)

A. Right off the top of my head I can't think of any others.
Q. Thank you, sir.
I've lost it. I apologize. Here it is.
I'm going to ask you a series of questions, sir, it's going to be the same question about various --
Let me, before I do that, let me ask this: The on-label indication of schizophrenia is a diagnosis, is it not? Schizophrenia is a diagnosis?
A. It is, yes.
Q. It is a defined disease; is it not?
A. I'm not a medical doctor but I've always interpreted it that way, yes.
Q. Okay. Bipolar mania is a diagnosis, is it not?
A. Yes, it is, yes.
Q. And those two diagnoses, schizophrenia and bipolar mania, were the two labeled indication diagnoses for Zyprexa that were indicated in the label; is that correct?

Jack E. Jordan (October 26, 2006)

A. During the time frame after the -- yeah, from March of 2000 on, yes.
Q. Okay. From March of 2000 on, the diagnoses, and the only indications in the label for Zyprexa, were the diagnosis of schizophrenia and the diagnose of bipolar mania, correct?
A. There was the combination indication as part of bipolar mania. So that was, I mean, if you look in the label, it's

the third indication.
Q. Bipolar mania.
A. Yes. Combination use, yes.
Q. My question to you here, sir, is Eli Lilly during the time -- all these questions until I tell you otherwise are during the time you were either Marketing Director or Brand Leader. Okay? Do you
225: 1 follow me?
A. Yes.
Q. During that time period, did Eli Lilly ever promote Zyprexa for anxiety?
A. That would have been a symptom of bipolar mania and schizophrenia so, but for an indication of anxiety, no.
Q. During the time you were a Brand Leader, did Eli Lilly promote Zyprexa for irritability?
A. That would be a symptom of its approved indications but for an indication variability no.
Q. Are you a doctor?
A. I am not, no.
Q. Do you know the symptoms of schizophrenia?
A. Not all of them but some of them.

Jack E. Jordan (October 26, 2006)

226: 7 Q. I'm asking are you trying to indicate to a jury, sir, that if a patient walks into a doctor's office and says "I'm irritable" that Zyprexa would be indicated?
A. No, I'm not. No.
Q. Okay. Back to my questions. Did Eli Lilly ever promote Zyprexa for patients with anxiety unrelated to the indicated uses in the label?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for irritability unrelated to the indications in the label?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for disrupted sleep unrelated to the indications in the label?
227: 1 A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for depression unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for symptoms of depression unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for patients with Alzheimer's?
A. If they had schizophrenia or bipolar mania, yes, but not for Alzheimer's, no.

Q. Did Eli Lilly ever promote Zyprexa for patients with confusion unrelated to schizophrenia or bipolar mania?
A. No.
Q. Did Eli Lilly ever promote Zyprexa for patients with dementia?
A. If they had schizophrenia and bipolar mania, yes, but not for the indication of dementia.
Q. Who's Martha?
A. As I recall, she was a schizophrenia patient profile.
Q. Did Eli Lilly ever market or promote Zyprexa for patients with behavioral disorders unrelated to schizophrenia or bipolar mania?
A. No, we did not.
Q. Did Eli Lilly ever market or promote Zyprexa for patients with complicated mood symptoms unrelated to schizophrenia or bipolar mania?
A. No, we did not.
Q. Did Eli Lilly ever market or promote Zyprexa for patients with attention deficit disorders unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. Did Eli Lilly ever market or promote Zyprexa for children?
A. No, we did not, no.
Q. Did Eli Lilly ever market or promote Zyprexa for patients with hyperactivity unrelated to schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

A. Well, part of marketing, as we talked about earlier, is promotional and nonpromotional activities. So there were nonpromotional things that might or might not have touched what you talked about. But as far as promotionally, no. So I just want to be clear, for all those questions, I was interpreting them as promotional activity.
Q. Thank you, sir.
Did Eli Lilly ever promote Zyprexa for patients in pediatrics unrelated to schizophrenia or bipolar mania?
A. We did not, no.
Q. Did Eli Lilly ever promote Zyprexa for patients for long-term care in geriatrics unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for patients with cognitive thought disorders secondary to aging?
A. Not being a doctor I'm not sure how DSM -- if they had schizophrenia or bipolar mania yes, but independent of that,

no.
Q. Did Eli Lilly ever promote Zyprexa for patients with depression unrelated to schizophrenia or bipolar mania?
MR. FAHEY: Objection. Asked and answered. You can answer again.
A. No, we did not, no.
Q. Who's Donna?
A. She was a patient profile that, as I recall, had bipolar mania.
Q. Did Eli Lilly ever promote Zyprexa for patients with cognitive thought disorder secondary to dementia?
A. Again, I'm not the expert on DSM but if it was outside of schizophrenia or bipolar mania, no.
Q. Did Eli Lilly ever promote Zyprexa as a nursing home drug for patients without schizophrenia or bipolar mania?
A. No, we did not.
Q. Did Eli Lilly ever promote Zyprexa for nausea unrelated to schizophrenia or bipolar mania?
A. We did not, no.
Q. Did Eli Lilly ever promote Zyprexa for irritability or anger management or symptoms of irritability or anger management unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. Did Eli Lilly ever promote Zyprexa for thought disorders unrelated to schizophrenia or bipolar mania?
A. No, we did not, no.
Q. You told us previously you understood, as the Brand Leader and Marketing Director, that schizophrenia and bipolar mania are specific diagnoses, correct?
A. Based on a cluster of symptoms, yes.
Q. Yes, sir. And, of course, you're not a doctor, but the answer to my question is -- see if you and I are communicating -- you would agree that the indications in the label of schizophrenia and bipolar mania are specific diagnoses?

Jack E. Jordan (October 26, 2006)

A. It's a cluster of symptoms is how you get to the diagnosis, so, yes.
Q. Did you want -- Did you at Eli Lilly promote Zyprexa for any symptoms that were not caused by either schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

A. Yeah, the term, I'm sorry,

the term doesn't -- I don't know what that means "caused by."
Q. You don't know what "caused by" means?
A. Well, in the context of your question.
Q. Let me give you an example, see if it helps you.
A. Okay.
Q. I have a headache right now, okay?
A. I'm sorry to hear that.
Q. That's all right. It's caused by the stress of the deposition and the preparation, you understand? Just assume I do. I could have a headache later this afternoon if I went and tripped and hit my head on the pavement. That could also cause a headache. Do you understand that, sir?
A. Yes.
Q. So I could have the symptom of a headache, one could be caused by stress. You've had a stress headache before, have you not?
A. I have, yes.
Q. And I bet you've hit your head before and also had a headache, correct?
A. I have, yes.
Q. So you could have a symptom of a headache but the cause could be different, correct?
A. Yes.
Q. Okay. So my question is: Did Eli Lilly ever promote Zyprexa for symptoms not caused by schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

234:16 A. No. How you communicate diagnoses in mental health is a cluster of symptoms that you get the diagnosis from, so, no.
Q. So no. Is your testimony -- is your testimony that Eli Lilly did not promote Zyprexa for symptoms that were not caused by the patient's schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

235: A. The answer's yes.
Q. What's a mood stabilizing drug, sir?
A. There are different classes of drugs in the treatment of severe mental health and antipsychotics are for psychotic-related disorders, which, ultimately, the FDA reclassified for

schizophrenia specifically.
Mood stabilizers are a general term used for mood disorders, of which there are several classes, some are for depression, some are for bipolar disorder, et cetera. So it's just a general term.
Q. Eli Lilly's Zyprexa was never indicated for bipolar disorder, was it, sir?
A. No. No. Over time --

Jack E. Jordan (October 26, 2006)

A. Over time it was for different phases of bipolar disorder. But mood stabilizer, again, is just a general term that can cover a number of classes.
Q. Yes, sir. Just so the record is clear, Zyprexa was never indicated for bipolar disorder, was it, sir?
A. No, it wasn't. No.
Q. It was only indicated for bipolar mania only, correct, sir?

Jack E. Jordan (October 26, 2006)

A. During the time I was there, yes.
Q. Okay. Now, back to my question. Let me see if we can approach it a different way if I need to. Was Zyprexa approved by the FDA for anything other than bipolar mania and schizophrenia?

Jack E. Jordan (October 26, 2006)

THE WITNESS: During my time?
MR. ALLEN: Yes, sir.
A. Okay. So we're still on my time.
Besides the combination therapy, no, it wasn't.
Q. Okay. So the only two FDA-approved indications during your entire time were bipolar mania and schizophrenia, right?

Jack E. Jordan (October 26, 2006)

A. Well, there was maintenance of schizophrenia, too, yes. So --
Q. Either maintenance or acute bipolar mania or schizophrenia are the only two FDA-approved indications during your time?

237:17 A. Yes.

Jack E. Jordan (October 26, 2006)

237:24 Now, did the FDA ever approve
238: 1 Zyprexa as a mood stabilizer?
2 A. Did they ever approve it as a
3 mood stabilizer? No.
4 Q. Did Lilly ever promote
5 Zyprexa as a mood stabilizer?
6 A. Yes.
7 Q. So Eli Lilly promoted Zyprexa
8 as a mood stabilizer even though the FDA did
9 not approve Zyprexa as a mood stabilizer,
10 correct?
11 A. No. I mean, mood stabilizer
12 is just a general term, a class of products
13 of which bipolar mania drugs are a part of
14 the class of mood stabilizers. So it's a
15 class thing, it's not an indication thing,
16 using your language from earlier.

Jack E. Jordan (October 26, 2006)

238:22 Q. Is it your testimony that the
23 FDA classified Zyprexa as a mood stabilizer?
24 A. They don't name classes of
239: 1 drugs. They're involved in the indication
2 business.
3 Q. Okay. So the FDA never
4 approved Zyprexa as a mood stabilizer, did
5 it?
6 A. The question doesn't make any
7 sense because the FDA doesn't name classes of
8 drugs. I mean, that's -- the field of
9 psychiatry does.
10 Q. Okay. So let me ask this:
11 Did you ever, you at Eli Lilly ever -- what's
12 Depakote?
13 A. It's a mood stabilizer
14 approved for bipolar mania.
15 Q. Is it approved for anything
16 else?
17 A. I don't know what other
18 indications it's got, I mean -- I think,
19 epilepsy.
20 Q. What about lithium, what kind
21 of drug is that?
22 A. It's a mood stabilizer used
23 in bipolar disorder and I don't know what all
24 the indications are.

Jack E. Jordan (October 26, 2006)

240: 7 Q. Did Eli Lilly ever promote
8 Zyprexa for the treatment of symptoms
9 unrelated to schizophrenia or bipolar mania?
10 A. No. It was in the context of
11 those disease states.
12 Q. Did Eli Lilly ever instruct
13 its sales force when they went to doctor's
14 offices to focus on symptoms and not
15 diagnoses?

Jack E. Jordan (October 26, 2006)

240:18 A. We focused on symptoms to
19 discuss the diagnoses.

Jack E. Jordan (October 26, 2006)

243: 8 Q. Oh, symptoms. Did Eli Lilly
9 ever instruct its sales representatives,
10 either in writing or orally, to go to the
11 doctor's office and discuss symptoms and not
12 the diagnosis of schizophrenia or bipolar
13 mania?

Jack E. Jordan (October 26, 2006)

243:16 A. The -- I know when we did our
17 primary care research the primary care docs,
18 we learned that you talk about symptoms first
19 and then get into indications when you share
20 the studies. And so as part of the sales
21 process, we would instruct them to talk about
22 symptoms to engage the physician in the
23 indication of bipolar mania.
24 Q. So you did instruct your
244: 1 sales representatives to go to the doctors
2 and discuss symptoms and not diagnoses first;
3 is that correct?
4 A. Within the context of the
5 sales process, describing the patient up
6 front, we would talk about symptoms and then
7 get into indications when we shared the data
8 of the studies, yes.
9 Q. In fact, you told your sales
10 representatives to focus on symptoms and not
11 diagnoses, did you not?

Jack E. Jordan (October 26, 2006)

244:14 A. As part of the sales process,
15 what we learned from market research is that
16 primary care physicians thought symptoms
17 first, and so we would talk to them about
18 symptoms first but always move on to the
19 indications as you'll see in the studies.

I'm sure you have those documents.

Jack E. Jordan (October 26, 2006)

Q. Hey, Mr. Jordan, you, in fact, at Eli Lilly, prior to the time you launched the primary care physician market knew there was not a specific indication for Lilly representatives to promote in the primary care market, didn't you, sir?

A. As I recall, the early research was they weren't recognizing the disease of bipolar mania in their offices. It was there, but it was unrecognized.

Jack E. Jordan (October 26, 2006)

Q. My question is: You at Eli Lilly knew there was not a specific indication in the primary care physician market to promote to primary care physicians. You knew that, did you not?

Jack E. Jordan (October 26, 2006)

A. No. The patients were in the primary care physician's office, it was they were not diagnosing those patients.

Q. So Eli Lilly when it, according to you, when it marketed Zyprexa to primary care physicians was trying just to help the doctors do a better job of diagnosing their patients?

A. The research that we had, it was taking them, seven, eight, nine years to diagnose their patients in the primary care office so, yes, we did go there to help them with the diagnosis.

Jack E. Jordan (October 26, 2006)

Q. Sir, is it your testimony that in the marketing of Zyprexa you were sending sales representatives into the office to discuss symptoms because the doctors were not making the proper diagnoses?

A. Our research showed that it was taking, six, seven, eight years to diagnose somebody with bipolar disorder in the primary care setting. So, yes, we did go in and identify the symptoms that were part of DSM, the bipolar mania indication, and discussing bipolar mania based on those symptoms, yes.

Q. So you said your market

research, is that what you called it, market research?
A. Yes.
Q. Said that doctors were not making the diagnosis of bipolar mania for six or seven years; is that right?
A. That was what the research was indicating, yes.
Q. And you -- so, therefore, you decided to take your sales representatives -- are they generally physicians?
A. No. They aren't generally physicians, no.
Q. Okay. You decided that you would have your sales representatives go to the office and talk about symptoms and, hopefully, correct the doctors so that they would make the proper diagnosis of bipolar mania according to you?

Jack E. Jordan (October 26, 2006)

A. We did use our sales organization to talk about the symptoms associated with bipolar mania to help physicians identify that patient population, yes.
MR. ALLEN: By the way, sir, here's Exhibit No. 1. A copy for your counsel.
(Whereupon, Deposition Exhibit(s) 1 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. Sir, do you recall the discussions earlier today and your testimony about meeting with lawyers?
A. I do, yes.
Q. Okay. And you told us the lawyers that you met with to discuss the issue of Zyprexa; do you recall that?
A. I do, yes.

Jack E. Jordan (October 26, 2006)

Q. Sir, you began meeting with outside counsel concerning your role in Zyprexa marketing as early as the fall of 2003; isn't that correct?
A. Yes.
Q. And what lawyers did you meet with besides the individuals you've already identified? Do you recall?
A. It would have been, Nina, I

11 guess, Nina Gussack and --

Jack E. Jordan (October 26, 2006)

253:15 A. Boy, I just remember Nina. I
16 don't know, there might have been somebody
17 else I don't know.

Jack E. Jordan (October 26, 2006)

255: 7 Q. Have you reviewed Exhibit
8 No. 1, sir?
9 A. I have, yeah.
10 Q. It's an e-mail from Lisa
11 Zoellner to you, Jack Jordan, that was
12 produced in this case.
13 Do you see the Bates stamp
14 number at the bottom?
15 A. I don't know what the Bates
16 stamp number means.
17 Q. Here, I'll show you. We're
18 going to be talking about Bates numbers all
19 day long.

Jack E. Jordan (October 26, 2006)

256: 3 Q. The Bates numbers down at the
4 bottom I highlighted for you, sir.
5 A. All right, thank you.
6 Q. This was produced to us in
7 this case. This is an e-mail to you, Jack
8 Jordan, correct?
9 A. It is, yes.
10 Q. From Lisa Zoellner. Who's
11 Lisa Zoellner?
12 A. I don't know who she is.
13 Q. It says, "Jack, I support
14 Curt Oltman's and Luanna McFarland in the law
15 division. I was trying to schedule some time
16 with you to meet with Curt, Luanna, and our
17 outside counsel for a Zyprexa interview and
18 understand you're now in Philadelphia." Did
19 I read that correctly?
20 A. You did, yes.
21 Q. It says, "Both Curt and
22 Luanna will be in Philadelphia in October 2,
23 2003, and wanted to try to meet with you that
24 day if you are available." And it goes on to
257: 1 give the flight arrangements. Do you see
2 that?
3 A. Yes.
4 Q. Then Diana Streevey responds.
5 Who's Diana Streevey?
6 A. She was my administrative
7 assistant in the Zyprexa job.
8 Q. Thank you, sir. She's says
9 you're traveling in the east between October

the 16 and then it's redacted; is that right?
A. It is.
Q. And then she says she'll let you see the note requesting the meeting; is that right?
A. Yes.
Q. So you were, in fact, requested to meet with outside counsel regarding your Zyprexa activities in the fall of 2003; were you not, sir?

Jack E. Jordan (October 26, 2006)

258:
Q. You were requested to meet with outside counsel in the fall of 2003, correct?

Jack E. Jordan (October 26, 2006)

260:
Q. Other than Nina Gussack, who else did you meet with, outside counsel-wise, in the fall of 2003?
A. I don't -- I don't remember.
Q. But you do remember a meeting in the law offices of Pepper Hamilton with Nina Gussack in the fall of 2003?
MR. GOLD: Objection as to form.
Q. Is that correct?
A. No, I don't, actually.
Q. Where did the meeting take
261:
place?
A. It was in the Lilly, Lilly Conshohocken office.
Q. Were there other lawyers from Pepper Hamilton there besides Nina Gussack?
A. Actually, I'm not sure if Nina was there but, no, I don't --
Q. Now, sir --
A. -- don't think there was anybody else from --
Q. You testified --
A. -- from Pepper Hamilton.
Q. All right. Sorry, sir. You testified previously, almost right off the bat today, that one of the goals of marketing strategy is to get your customers to think what you want them to think. Do you recall that testimony?
A. Part of the goal of marketing is to do that, yes.
Q. And your customers for Zyprexa were whom, sir? When I say "your customers" I mean Eli Lilly's customers for Zyprexa were whom?
262:
A. Our primary customer was physicians.
Q. Who were your other customers for Zyprexa besides doctors? Third-party

payers would be one, wouldn't they?
A. They would be, yes.
Q. Medicaid would be another customer, correct?
A. Yes.
Q. Community mental health facilities would be another customer, correct?
A. Yes.
Q. Insurance companies would be another customer, correct?
A. A customer of our B-to-B group, yes, Business-to-Business Group, yes, they called on those folks.
Q. Okay. You named doctors, I named some other customers, now I want to ask you besides the customer doctor that you named and the other groups I named, who are the other customers for Zyprexa, if you know?
A. In some states nurse practitioners had prescribing privileges, so we would call on nurses.
Q. Who are the other customers for Zyprexa besides the individuals or groups we had mentioned?
A. Hospitals could be a customer.
Q. Any other customers besides doctors, third-party payers, mental health facilities, hospitals, insurance companies, Medicaid? Any other customers?
A. I mean, there are a whole variety of settings but formulary decision makers are called on by various parts of Lilly's organizations.
Q. That's HMO and PPOs and managed care organizations?

Jack E. Jordan (October 26, 2006)

A. Yes. PBMs. There's just a whole --
Q. PBMs would be, I think it's benefit manager, prescription benefit manager. Sir, let me finish my question.
A. Okay.
Q. PBMs would be customers, that's prescription benefit managers, correct?
A. Yes. Part of our B-to-B organization calls on them, yes.
Q. What other customers besides the ones we've now mentioned, any other customers for Zyprexa?
A. I mean, I'm sure there are more, I'm just not thinking about them right now.
Q. All right. You're forgetting one very important customer, aren't you, sir?
A. We defined, at least I defined, customers as decision makers in the

treatment so, or the formulary status so.
Q. So tell the jury, please, the one important customer you've forgotten off this list?
A. I don't know. I mean --
Q. The patient?
A. At least how I viewed it the patient was the consumer. It was the doctor and others that were decision makers, so we focused on decision makers.
Q. On that point, sir. Let me ask you this question first: Integrated marketing communications, you, at Eli Lilly, engaged in integrated marketing communications, did you not, sir?

Jack E. Jordan (October 26, 2006)

A. At least how I use the term is there was consistency across the marketing mix, so, yes, we did.
Q. Yes, sir. And let's see if this helps and you tell the jury if I'm just totally off the base, but this is the definition of integrated marketing communications that I have. And if it doesn't help or you think I'm wrong you let me know. Is that fair?
A. That's fair.
Q. Integrated marketing communications means you encourage the purchase of your product from all angles of influence. You build branches of communicating with all key players who influence the purchase of your product through multiple communication channels.
Is that a fair definition of integrated marketing communications?
THE WITNESS: Can I hear that again?
MR. ALLEN: Yes, sir.
QUESTIONS BY MR. ALLEN:
Q. Integrated marketing communications means you encourage the purchase of your product from all angles of influence and build brands by communicating with all key players who influence the purchase of your product through multiple communication channels.

Jack E. Jordan (October 26, 2006)

A. Without wordsmithing it at a 30,000-foot level it sounds about right.
Q. Right. That's a fair definition for us to discuss to the jury without wordsmithing it at 30,000 feet, right?
A. At 30,000 feet it sounds

about right, yes.
Q. Yes, sir. Now when you say in marketing communications that you build brands by communicating with all key players who influence the purchase of your product through multiple communication channels, what are multiple communication channels?

Jack E. Jordan (October 26, 2006)

Q. Tell this jury what Eli Lilly means when it communicates through multiple communication channels?
A. Just making it very specific, if a doctor is on the north side of Indianapolis she would have a sales rep call upon her, she might have mailings that go to her office, promotional mailings that go to her office, she might be sent a promotional video that arrives at her office. It's just, it's integrated, they'd have the same consistent message for that given indication.
Q. Well, you also, as we discussed, marketing also includes things beyond promotional activities. You already told us that, right?
A. I have said there's a nonpromotional side --

Jack E. Jordan (October 26, 2006)

A. And nonpromotional marketing is a part of this industry, yes.
Q. So, for example, doctors would get their information from peers and educators?
A. That is part of how most physicians get part of their information, yes.
Q. And Eli Lilly would help sponsor CME courses and pay peers and educators, such as thought leaders and speakers, correct?
A. No. We would -- you're mixing a couple things up. As far as CMEs, we would give a grant to the CME company. We would not pay the thought leader, whatever. The CME company pays who they will.
Q. So, also, Eli Lilly -- doctors get their information through marketing materials, correct?
A. Yeah. Some doctors do get their information through materials, both promotional and nonpromotional, yes.
Q. And Eli Lilly would prepare such materials regarding Zyprexa?
A. The promotional materials, yes, they were prepared by us, yes.
Q. I mean, doctors get their

information from the sales force or the detail people, correct?
A. Part of the information they get is from sales people, yes.
Q. And, clearly, Eli Lilly's involved in that process, true?
A. Yes.
Q. Doctors, as you said, would get information from publications; is that right?
A. They would, yes.
Q. And, clearly, as you've indicated, Eli Lilly would, at times, provide doctors with publications; is that correct?
A. Yes, we would.
Q. Doctors would get information from the package insert or the label; is that correct?
A. Yes.
Q. And Eli Lilly clearly was involved in the package insert; is that correct?
A. Yes. We partnered -- my understanding is, partnered with the FDA to decide what the label language is, yes.
Q. You partnered -- as a matter of fact, you were on labeling discussion calls with the FDA over the years, were you not?
A. I was never on a label discussion call with the FDA.
Q. You were not.
A. I was not.
Q. And if the documents in the case reflect that you were, the document would be inaccurate and your testimony would be accurate; is that your testimony?

Jack E. Jordan (October 26, 2006)

A. Yeah, I was not on calls with the FDA.
Q. Ever?
A. No. Not that I recall.
Q. All right, sir.
Back to how doctors get their information. Doctors get their information through other doctors, right?
A. They do, yes.
Q. And you already told us that Eli Lilly had a speakers bureau, correct?
A. We did, yes.
Q. And those speakers would be other doctors, right?
A. Doctors, and there were some nurses that were speakers.
Q. And Eli Lilly would prepare, as you said, slide presentations and also written documents that were approved by Eli Lilly to be presented to these doctors at these speakers presentations, correct?

A. Yes.
Q. And, of course, Eli Lilly hired the speakers and/or thought leaders. They tried to find other physicians or medical personnel that doctors would respect; isn't that true?

Jack E. Jordan (October 26, 2006)

A. Part of the criteria was that they would be respected individuals, yes.
Q. Right. And Eli Lilly was involved in that process of having a speakers bureau, preparing materials, and approving the materials presented, correct?

Jack E. Jordan (October 26, 2006)

A. Yes.
Q. Eli Lilly also was involved -- And doctors also get their information from medical organizations; is that correct?
A. Yes, they do.
Q. And Eli Lilly also had contacts at medical organizations and was involved in funding or providing money to medical organizations that would pass information on to doctors, correct?

Jack E. Jordan (October 26, 2006)

A. As I recall, there were medical organizations that asked for grants that we would fund, yes.
Q. Okay. And medical organizations that you would fund are, obviously, those type of organizations are a place where doctors get information, right?
A. Yes.
MR. ALLEN: Sir, I'm going to hand you what I've marked as Jordan Exhibit No. 2.

(Whereupon, Deposition Exhibit(s) 2 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

MR. ALLEN: Okay. Sir, can I have Exhibit No. 2? Your lawyer's

Jack E. Jordan (October 26, 2006)

276: 7 MR. ALLEN: Let me get it on
8 the record.
9 (Document displayed to
10 the jury)
11 MR. ALLEN: Tell me when you
12 get a good picture of it and I want
13 it on there at least ten seconds.
14 You got it?
15 QUESTIONS BY MR. ALLEN:
16 Q. Sir, the jury's now seen
17 Jordan Exhibit No. 2. Do you see the various
18 sources of information that you just told me
19 where doctors get it: From the package
20 insert, from medical organizations, from
21 medical education courses, from marketing
22 materials, from the sales force, and from
23 publications, and from peers and educators?
24 Do you see that?
277: 1 A. Yes, I do.

Jack E. Jordan (October 26, 2006)

277:16 Q. Sir, do you see the doctor
17 represented and the various arrows pointing
18 to the doctor?
19 A. I do, yes.
20 Q. And all of those areas
21 pointing to the doctor come from sources
22 where doctor gets information; is that
23 correct?
24 A. As represented here.
278: 1 Q. Well, do you agree with it?
2 A. No, I don't.
3 Q. So tell the jury what source
4 of information do you not agree with where
5 the doctor gets information?
6 A. There is a whole world of
7 four, five, six, seven, competitors from whom
8 he or she gets information.
9 There's the Internet where he
10 or she gets information.
11 There's friends, when they go
12 out golfing they get information.
13 So, no, this is too
14 simplistic. I mean, there's --
15 Q. Sir, so you're saying there's
16 additional sources of information other than
17 reflected on Exhibit 2?
18 A. Yeah. There's competitors --

Jack E. Jordan (October 26, 2006)

278:22 A. -- that provide significant
23 amount of information.
24 Q. All right. But the sources
279: 1 of information as reflected: The package
2 insert, the medical organizations, the
3 medical education CMEs, the marketing

materials, the sales force, the publications, and peers and educators, you agree are all sources where doctors get information?
A. They are, but the indication that Lilly does all this without recognizing that there's five, six, seven, companies disseminating information would be a bit simplistic in my mind.
Q. Okay, sir. My only question to you was -- and we're going to get to Lilly in a second -- my only question is the sources of information, that's some of the sources as reflected on Exhibit 2 where doctors get their information; is that true?

Jack E. Jordan (October 26, 2006)

279:22 A. Yeah, it is true, but this also doesn't highlight promotional versus nonpromotional --
280: 1 Q. I understand.
A. -- information. I just want to make sure that's clear, too.
Q. And you agree that Lilly was involved in all of these sources as reflected on Exhibit 2. Lilly was involved in the package insert, it was involved in funding medical organizations, it was involved in grants to CME courses, it was involved in preparing marketing materials, it was obviously involved in sending its sales force out with materials, it was involved in handing our publications as you discussed earlier today, and it was involved in speakers bureaus who are peers and educators of the doctors. You agree with that?
A. How this is represented to me on this document is that medical education CMEs goes through Lilly before it gets to the doctor. So there's a couple misrepresented. I think it misrepresents on here, I mean, medical education doesn't go through Lilly. The CME provider decides on the content and it goes from them to the physician.

Jack E. Jordan (October 26, 2006)

281: 6 A. So I just want to make sure its clear that it could be misinterpreted that Lilly, quote/unquote influences the content and does these things and that is not the case.
Q. It funds them.
A. Yes.
Q. Okay. So Lilly funds CME, Lilly pays speakers, Lilly gives money to medical organizations, Lilly pays and sends out its sales force, Lilly provides publications to doctors, right?

A. Yes.
Q. Also, Lilly interjects itself before an article is published. It often talks to authors and redrafts or makes proposals to author's publications in the medical literature, does it not?

Jack E. Jordan (October 26, 2006)

Q. Does Lilly review drafts of medical articles prior to the time they appear in the literature and make suggestions concerning the article as it should appear in the literature?
A. That would be part of our medical organization that dealt with publications, so I couldn't answer that question.
Q. Okay. Isn't it true that you are, personally, aware of the fact that Eli Lilly went to medical organizations and asked them to draft certain guidelines that would support the prescription of Zyprexa?
A. We did provide grants to organizations that drafted guidelines, yes.
Q. That would support the administration or prescription of Zyprexa?

Jack E. Jordan (October 26, 2006)

Q. Correct?
A. Well, we really didn't know if they were going to support them or not.

Jack E. Jordan (October 26, 2006)

table before we get a break: Are you familiar with the Lilly Glossary of Marketing Terms?
A. I am, yes.

Jack E. Jordan (October 26, 2006)

Q. Sir, when you used the marketing terms in your memoranda and marketing documents, did you use those terms consistent with Lilly's Glossary of Marketing Terms?
A. I don't know if I did or didn't. I don't know.

Jack E. Jordan (October 26, 2006)

286:23 (At this time, the
24 parties went off the record,
287: 1 after which the following
2 proceedings were had:)
3 THE VIDEOGRAPHER: We're back
4 on the record. This is the
5 beginning of tape No. 4 of the
6 deposition of Jack Jordan.
7 QUESTIONS BY MR. ALLEN:
8 Q. Mr. Jordan, Scott Allen,
9 we're back on the record. We took a break at
10 your request, correct?
11 A. Yes.
12 Q. When you got up on the break
13 you pointed to Exhibit No. 2, did you not?
14 A. Yes, I did. Yes.
15 Q. You made a comment to me, did
16 you not?
17 A. I did.
18 Q. And the comment was
19 "Mr. Allen, you ought to be a marketing
20 professor. That's good." Isn't that what
21 you said?
22 A. I like the conceptual model,
23 with the caveats I pointed out on it being a
24 little simplistic and not accurate as far as
288: 1 some of the things on it, yes.

Jack E. Jordan (October 26, 2006)

288: 7 Q. When you got up what you said
8 to me is pointing at Exhibit 2 is:
9 "Mr. Allen, you ought to be a marketing
10 professor. That's good." Isn't that what
11 you said?

Jack E. Jordan (October 26, 2006)

288:18 A. With the caveats I pointed
19 out under my previous testimony.

Jack E. Jordan (October 26, 2006)

288:23 Q. I didn't ask what your
24 explanation is. Didn't you point at
289: 1 Exhibit 2 and say, "Mr. Allen, that's good.
2 You ought to be a marketing professor?"
3 A. As far as conceptual, yes.
4 It's good.
5 Q. And isn't that what you said?
6 A. I believe I did, yeah.
7 Q. Thank you, sir.
8 (Whereupon, Deposition
9 Exhibit(s) 3 duly received,
10 marked and made a part of the
11 record.)
12

MR. ALLEN: Sir, Jordan Exhibit No. 3 --

Jack E. Jordan (October 26, 2006)

289:21 Q. I just want you to identify
22 it. That is a document entitled Glossary of
23 Marketing Terms, is it not, sir, the title?
24 A. It is, yes.
290: 1 Q. Thank you, sir. You can put
2 it aside. That's all I have on that.
3 Sir, you've previously told
4 us, Mr. Jordan, that you cannot promote for
5 nonindicated uses, right?
6 A. Yes. You cannot promote for
7 nonindicated uses, yes.
8 Q. But didn't, in fact, Eli
9 Lilly drive the depression story with Zyprexa
10 in your direct-to-physician campaigns?

Jack E. Jordan (October 26, 2006)

290:13 A. I mean, I have to see what
14 you're referring to.

Jack E. Jordan (October 26, 2006)

291: 1 Q. I'm asking you, sir, a
2 question. Isn't it true that Eli Lilly drove
3 the depression story in your
4 direct-to-physician campaigns?

Jack E. Jordan (October 26, 2006)

291: 5 A. As I recall, in the context
6 of schizophrenia and depressive symptoms
7 associated with schizophrenia, we did, yes.
8 MR. ALLEN: Okay, sir, I'm
9 going to hand you what's been marked
10 as Jordan Exhibit No. 4.
11 (Whereupon, Deposition
12 Exhibit(s) 4 duly received,
13 marked and made a part of the
14 record.)

Jack E. Jordan (October 26, 2006)

291:17 Q. This is an e-mail dated
18 February the 14th, 2000, addressed to you, is
19 it not?
20 A. It was February 2000.
21 Q. I'm sorry. This is an e-mail
22 dated February 14, 2000; is it not?

A. Yes.
Q. Addressed to you, correct?
A. It is.
Q. From Eric Prouty or Prouty?
A. Prouty.
Q. I'm sorry. That's who it's is carbon copied to.
It's from John Richards, right?

A. Yes, it's from John Richards.
Q. It's in regard to what, sir?
A. It's in regard to an attachment.
Q. What's the subject matter of this e-mail?
A. Depressive DTP slides.
Q. The subject is depressive, DTP stands for direct-to-physician, does it not?
A. Yes.
Q. And the attachment is the JACK file dot doc. What is the JACK file dot doc?
A. I do not know.
Q. Anyhow, who is Mr. Richards?
A. He was a manager at Lilly.
Q. A manager of what?
A. He had various titles. He's a manager on the Zyprexa team.
Q. Yes, sir. And this e-mail from Mr. Richards in February of 2000 says Jack -- and that's you, right, Jack?
A. It is.
Q. "Jack, attached as we discussed. As you can see we have been driving the depression story with Zyprexa in our DTP" -- that's direct-to-physician -- "programs since the quarter three of 1998."
Did I read that correctly?
A. You did, yes.
Q. And is it true that you, at Eli Lilly, had driven the depression story with Zyprexa in your direct-to-physician campaign since the third quarter of 1998?
A. The depressive symptoms, i.e., the subject matter, part of our core strategy during that time was to differentiate on our coverage of depressive symptoms in schizophrenia. So, yes, that is true.
Q. Sir, does this e-mail refer to depressive symptoms related to schizophrenia or bipolar mania or does it say "the depressive story?"
A. Depressive is an adjective and so it was always depressive symptoms in schizophrenia. And I'm sure if I had the attachment I could point that out.

Q. Sir, let's see if you and I, see if we can read this together. Second sentence to you, "Jack, as you can see we have been driving the depression story with Zyprexa." Did I read that correctly?
A. Yeah. But you didn't read the next sentence that said "the importance of this attribute," an attribute associated with schizophrenia. That was our core strategy during that time.
Q. Does it say anything in this e-mail about schizophrenia or bipolar mania?
A. An attribute is not a disease, it's a part of another disease. Depressive is an adjective that we used in association with schizophrenia. If you showed me the attachment I'm sure I could show you that.
Q. I don't have the attachment, sir, it's your attachment. But let me see if you concede this.
296: 1 It would be wrong to
2 encourage a physician to prescribe Zyprexa
3 for depression unrelated to schizophrenia or
4 bipolar mania, would it not?

Jack E. Jordan (October 26, 2006)

296:17 Q. My question is -- My question
18 is, sir, it would be wrong to encourage
19 doctors and to drive a depression story on
20 Zyprexa unrelated to schizophrenia or bipolar
21 mania, correct?
22 A. If it's a promotional
23 activity you can't promote for a depressive
24 symptom outside of the core indications.

Jack E. Jordan (October 26, 2006)

297:13 Q. My question to you is, sir,
14 isn't it true that Eli Lilly tried to get
15 doctors to prescribe Zyprexa for depression
16 without a diagnosis?
17 A. No, that's not.
18 MR. ALLEN: Sir, I'm going to
19 hand you what's been marked as
20 Exhibit No. 5.
21
22 (Whereupon, Deposition
23 Exhibit(s) 5 duly received,
24 marked and made a part of the
record.)

Jack E. Jordan (October 26, 2006)

300:10 Q. Mr. Jordan, at Eli Lilly did
11 you all have product knowledge conference
12 calls?

A. Yeah. There were calls about various issues. That would be one of them, yes.
Q. **Yes, sir. And one of the conference calls you all would have, you all called it the product knowledge conference call, did you not?**
A. I'm not that familiar with that term. I guess we did have it, yes.
Q. **Who's Jill Lake?**
A. I do not know.
Q. **Michael Bandick, at this time** 301: **in December of 2000 worked for you in issues management, did he not, or Marketplace Management?**
A. No. At that point he was, I believe he was the primary care manager.
Q. **Okay, sir.**
A. Working for me.
Q. **Sir?**
A. Working for me.
Q. **Yes, Mr. Bandick was working for you.**

Jack E. Jordan (October 26, 2006)

301:Q. Mr. Bandick and others on this e-mail were in the marketing department that worked for you; is that correct?
A. Yes.
Q. Thank you, sir.
This e-mail concerned a conference call of December the 9th, 2000, did it not? "Hi Crew, wanted to give you a summary of the Zyprexa conference call that 302: was held today." Right?
A. Yes.
Q. If you go to the second page there's a series of questions that were asked concerning Zyprexa, and I'm going to focus on question No. 5.
You see question No. 5, after question No. 4?
A. I do not, no.
Q. Where is it?
A. It said it's been redacted.

Jack E. Jordan (October 26, 2006)

304:Q. Question and answer No. 5 are not present, are they, sir.

Jack E. Jordan (October 26, 2006)

304:A. It is not, no.
Q. Question No. 7 is. What is question seven?

305: 1 A. "Is Zyprexa indicated for
2 depression?"
3 Q. And the answer is what, sir?
4 A. It says, "Zyprexa is not
5 indicated for depression. We know Zyprexa
6 improves depressive symptoms in schizophrenic
7 patients" but need to think of it, "but need
8 to think of as a mood stabilizer."
9 Q. We need to think of it as a
10 mood stabilizer, is that correct? "It" is
11 not there but we need to think of it as a
12 mood stabilizer; is that correct?
13 A. Yes.
14 Q. It says, "Zyprexa is not
15 indicated for depression;" is that correct?
16 A. That's correct. It's not
17 indicated for depression.
18 Q. And that's accurate, is it
19 not?
20 A. That is accurate.
21 Q. Now schizophrenia is a
22 diagnosis. You've already told us that
23 earlier today, right?
24 A. It is, yes.
306: 1 Q. Now in this question and
2 answer document it says "What if the doctor
3 says," this is question No. 8 following
4 question seven, "what if the doctor says I
5 don't see those types of patients?" Do you
6 see that question?
7 A. I do.

Jack E. Jordan (October 26, 2006)

307: 4 Q. Sir, can you read out loud
5 the answer to the question reflected in
6 Exhibit No. 5, "what if the doctor says I
7 don't see those types of patients?" What is
8 the answer written on the piece of paper,
9 Exhibit No. 5?

Jack E. Jordan (October 26, 2006)

307:15 A. Okay. "The doctor's thinking
16 that he does not see a schizophrenic or
17 bipolar patient."
18 Q. Let's stop there. The
19 doctor is thinking that he does not see
20 schizophrenic or bipolar patients; is that
21 right?

Jack E. Jordan (October 26, 2006)

308: 4 Q. Is that correct?
5 A. That is.
6 Q. Okay. Continue reading
7 slowly and distinctly so the jury can hear,

please.

Jack E. Jordan (October 26, 2006)

Q. Okay, go ahead. The document says: "The doctor's thinking that he does not see schizophrenic or bipolar patients."

Continue with reading the document, please, sir.

A. "But he probably does see patients with symptoms of behavior, mood, and thought disturbances."

Q. Or thought disorders -- disturbances, right?

A. Yes.

Q. Is there a difference between schizophrenic and bipolar patients and patients with behavior, mood, or thought disturbances?

A. There might or there might not be.

Q. Okay. Continue reading the answer to the question "what if the doctor says I don't see those types of patients?"

A. "Need to focus on symptoms and patient types of Martha, David, and Christine. Even if the doctor does not have diagnosis, he should treat anyway. He needs to treat the symptoms until a patient can see a psychiatrist. Ask him if he uses drugs like Haldol or risperidal, and Zyprexa has less side effects than either of them."

Q. Question 7 was: "Is Zyprexa indicated for depression?" And the answer to that question indicated in part that "Zyprexa is not indicated for depression. We know Zyprexa improves depressive symptoms in schizophrenic patients, but need to think of as a mood stabilizer." Correct?

Jack E. Jordan (October 26, 2006)

A. That's what the document says.

Q. Then it says, "What if the doctor says I don't see those types of patients?" The answer to that question includes this statement: "Even if the doctor does not have a diagnosis, he should treat anyway." Is that consistent with good marketing practices for Zyprexa?

A. This is -- Martha, David, and Christine are on-label patients. Very clearly spelled out in the detail pieces. And so the studies that go along with them are on-label studies. And so it's hard for me to speculate what they mean by that. But I know the detail piece, I know these patients, and I know the training was

schizophrenia and bipolar mania. And so I don't know exactly what they meant by these words.

Jack E. Jordan (October 26, 2006)

311:11 Q. Should a doctor treat a patient with Zyprexa without the diagnosis of schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

312: 4 A. The detail piece that we had during that time period with these patient types were approved bipolar and schizophrenia patients. And as they share from the detail piece and share the data from bipolar mania studies and schizophrenia studies, we asked them to use the product for these patient types that are on-label patient types.

Jack E. Jordan (October 26, 2006)

312:14 Q. My question to you was: Was it your position in marketing, and when you were Brand Leader and Director of Marketing, that the sales representatives should tell doctors to prescribe Zyprexa even without a diagnosis of schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

313: 2 A. It wasn't my position, no.
Q. And it would be wrong to encourage sales representatives to instruct doctors or to inform doctors that they should go ahead and prescribe Zyprexa without a diagnosis; that would be wrong, wouldn't it?
A. Well, the sales piece and the training never asked them to do that, so.

Jack E. Jordan (October 26, 2006)

313:12 Q. My question wasn't what you say a sales piece says. We're going to get to them later. My question: Would it be wrong from a marketing perspective for the sales force to tell doctors to go ahead and prescribe Zyprexa without a diagnosis of schizophrenia or bipolar mania?
A. In a promotional setting you should ask doctors to prescribe on-label.
Q. And, therefore, would it be

wrong to ask doctors to prescribe Zyprexa without a diagnosis of schizophrenia or bipolar mania?
A. The reps were never trained to do that, so, yes, it would be --
Q. Wrong.
A. -- outside their training.
Q. And, therefore, it would be wrong.

Jack E. Jordan (October 26, 2006)

Q. Would it be wrong?
A. To ask a doctor -- yeah. But I'm not sure that's what they're saying here.
Q. I didn't ask -- sir, you can put that document aside. I'm not going to ask you anything about that document again.
A. Okay.
Q. Would it be wrong to instruct the sales force to tell the doctor they can prescribe Zyprexa without a diagnosis of schizophrenia or bipolar mania?
A. Again, that's why we didn't do it.
Q. Because it was wrong?

Jack E. Jordan (October 26, 2006)

Q. If it was done would it be wrong?
A. If we instructed -- yeah. That's why the training not to do it. To use the detail piece in the way it was.

Jack E. Jordan (October 26, 2006)

Q. You would not, you, at Eli Lilly, would not train sales representatives to inform doctors to prescribe Zyprexa without a diagnosis. You would not do that, would you?

Jack E. Jordan (October 26, 2006)

Q. My only question, there's only one question on this table, Mr. Jordan: It would be wrong of Eli Lilly to train its sales representatives to tell doctors to go ahead and prescribe Zyprexa without a diagnosis of schizophrenia or bipolar mania. That would be wrong?
A. Anything that would be outside the label would be inappropriate.
Q. And would that be outside the

319: 1 label?

Jack E. Jordan (October 26, 2006)

319: 4 A. You'd have to show me. I
5 think it would be but I need to see what
6 you're referring to.
7 Q. Okay, sir. Now, in fact,
8 though, Eli Lilly did instruct its sales
9 force to encourage doctors to prescribe
10 without a diagnosis, didn't they?
11 A. No.
12 Q. What is an implementation
13 guide?
14 A. The one that I'm familiar
15 with is when you have a detail piece there is
16 a training program that goes along with it.
17 And it's reading materials for the sales
18 representative to go through and understand
19 what we're trying to accomplish, and what the
20 promotional message is.
21 Q. So it would give the sales
22 representatives the promotional message in
23 how to handle a doctor as they confront them
24 or talk to them in their office setting or
320: 1 other location?
2 A. It is, yeah, that's a good
3 characterization.
4 Q. Right. And if a doctor told
5 a sales representative that he or she did not
6 treat schizophrenia or bipolar disorder that
7 did not stop you from training your sales
8 representatives to go ahead and get back to
9 selling the doctor on Zyprexa?

Jack E. Jordan (October 26, 2006)

320:12 A. The context of these
13 questions, I'm assuming, is in the context of
14 primary care. And the market research showed
15 us that many primary care physicians said
16 they didn't treat schizophrenia and bipolar
17 mania, and yet the research showed that up to
18 a third of the patients in any given primary
19 care's office, who is treated on an
20 antidepressant, actually, had a bipolar
21 disorder.
22 Q. If a doctor told a sales
23 representative "I do not treat schizophrenia
24 or bipolar disorder," the doctors told that
321: 1 to your sales representative, shouldn't your
2 sales representative tell the doctor then you
3 don't need Zyprexa because it's only
4 indicated for schizophrenia and bipolar
5 disorder?

Jack E. Jordan (October 26, 2006)

321: 8 A. As we did our market research
9 around this very issue, what primary care
10 doctors told us is that once we described the
11 patient based on DSM, based on the given
12 symptoms, that many times they would,
13 actually, come back and say they actually do
14 have those patients and would want to
15 potentially prescribe Zyprexa for that
16 bipolar mania.
17 Q. In fact, you told your sales
18 representatives "if a doctor told you that I
19 do not treat schizophrenia or bipolar
20 disorder, you should still try to sell the
21 doctor on Zyprexa," right?

Jack E. Jordan (October 26, 2006)

321:24 Q. By the way, I misstated
322: 1 something, by the way. Zyprexa is not
2 indicated for bipolar disorder, is it?
3 A. No. It's bipolar mania.
4 Q. Right. So if a sales
5 representative told a doctor "I do not treat
6 bipolar mania and I do not treat
7 schizophrenia," that didn't stop Eli Lilly
8 from training its sales representatives to
9 still sell the doctor on Zyprexa, isn't that
10 right?
11 A. Our market research showed
12 that up to a third of the patients they were
13 treating with an antidepressant were,
14 actually, struggling from bipolar disorder.

Jack E. Jordan (October 26, 2006)

322:17 (Whereupon, Deposition
18 Exhibit(s) 7 duly received,
19 marked and made a part of the
20 record.)

Jack E. Jordan (October 26, 2006)

325:22 Q. Sir, Mr. Robinson, Bill
23 Robinson, Vice-president of Sales and
24 Marketing, was one of your direct
326: 1 supervisors, was he not?
2 A. At one point he was, yes.
3 Q. Yes, sir. And isn't it a
4 fact that he was excited because the sales
5 force had made Zyprexa No. 1 in the field of
6 depression?

Jack E. Jordan (October 26, 2006)

326:10 A. I don't remember that.

Q. Do you recall in the marketing department, and in your role as Zyprexa Brand Leader, that there was excitement expressed because Eli Lilly had made Zyprexa No. 1 in the field of depression?

Jack E. Jordan (October 26, 2006)

A. I don't remember that, no.
MR. ALLEN: Okay, sir, I will hand you what's been marked as Exhibit No. 6.
(Whereupon, Deposition Exhibit(s) 6 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. Sir, do you have exhibit No. 6 in front of you?

Jack E. Jordan (October 26, 2006)

A. I do, yes.
Q. And is this not a document with the front, on the front says "Bill Robinson, Vice-president U.S. Sales and Marketing?"
A. It does say that, yeah.
Q. Okay, sir. Would you mind holding up the second page for the camera so the jury can see it?

Jack E. Jordan (October 26, 2006)

MR. ALLEN: I'll do it.
(Document displayed to the jury)
QUESTIONS BY MR. ALLEN:
Q. Sir, does Mr. Robinson say here "You make us No. 1," exclamation point, exclamation point, exclamation point?
A. I have no idea.
Q. Well, doesn't it say that right there at the top, sir?

Jack E. Jordan (October 26, 2006)

Q. Doesn't the second page of Exhibit No. 6 behind the name "Bill Robinson, Vice-President U.S. Sales and Marketing," say

"You make us No. 1," exclamation point, exclamation point, exclamation point?
A. I don't know where this document came from. I've never seen it before. So it does say that but I don't know --
Q. That's all my question. So you agree it says that, does it not?
A. In a document I don't know where it came from or I've never seen it before.
Q. Right. It says, "You, the Neuroscience division of Lilly."
The Neuroscience division is what, sir -- where Zyprexa is located and what you were in charge of?
A. The Neuroscience division was
330: responsible for neuroscience drugs.
Q. Which would be Zyprexa, right?
A. Was part of it, yes.
Q. Why don't you read after, "You, the Neuroscience division of Lilly," why don't you read the first bullet point after that?
A. It says, "Make us" -- "Make us No. 1 in the past with Prozac depression."
Q. No, sir. It says "Made up No. 1 in the past with Prozac and depression," correct?
A. Yes.
MR. GOLD: Not and depression slash depression.
Q. After that what does it say, sir?
A. And "now making us No. 1 with Zyprexa, redacted, schizophrenia, bipolar mania, depression."
Q. Right. It says you "are now," and that's all caps and bolded letters, correct?
331: A. It is, yep.
Q. It says you "are now making us No. 1 with Zyprexa," comma, right?
A. Yep.
Q. Then we have some redacted information, right?
A. Yes.
Q. It says dash "schizophrenia" comma, right?
A. Yes.
Q. Sir?
A. Yes.
Q. Schizophrenia is an indicated on-label use for Zyprexa, correct?
A. Yes.
Q. After the comma schizophrenia it says "bipolar mania." That's a diagnosis and an indicated on-label use for Zyprexa, correct?
A. Yes.
Q. And it says comma "depression." Depression is not an indicated

on-label use for Zyprexa, is it?
A. Unfortunately, there's another product redacted, which I'm assuming is Prozac Weekly, which was indicated for depression.

Jack E. Jordan (October 26, 2006)

Q. We don't know when we have a redaction in a document.
Does this "And now making us No. 1 with Zyprexa," and it says "depression." And my question to you was isn't it true that depression is not an indication for Zyprexa?
A. Yeah. That's why we didn't promote it there. And there's a redacted product that I'm assuming is Prozac Weekly, which is part of the Neuroscience division, which was indicated for depression.
Q. You also told us previously, however, that you did not promote Zyprexa for the elderly unrelated to schizophrenia or bipolar mania. Didn't you tell us that previously?
A. That is true.
Q. What is product positioning? You've used that term several times today, positioning of a product.
A. Positioning is a general term in marketing. It refers to how a customer perceives yours and other products.
Q. How a customer perceives. Do you want -- do you try to position, Zyprexa in this case, in a particular position so your customer perceives Zyprexa accurately?
A. Positioning is a term that, that is used for, again, how the customer, how you want your customer to perceive your product relative to your competition, yeah.
Q. Right. You said how you want. So you, at Eli Lilly, try to position Zyprexa, correct?
A. Yes. You have a goal on how you want your customers to think appropriately about your product, yes.
Q. Right. That goes back to the very first 20 minutes of the deposition. Positioning is trying to get your customers to think a certain way about your product, in this case Zyprexa, right?
A. Yes.
Q. And did you ever at Eli Lilly try to position Zyprexa for off-label uses?
A. Positioning refers to the long-term view of your product. And so positioning would include indications that came in 2006, 2007, 2008, so it's a longer-term concept.

337:22 Q. Did Eli Lilly, to your
23 knowledge, position Zyprexa for irritable
24 bowel?
338: 1 A. Not that I know of, no.
2 Q. Would it have been wrong for
3 them to do so?
4 A. No, it would not have been.
5 Q. Did Eli Lilly position
6 Zyprexa for behavioral disturbances?
7 A. Again, I don't know who "Eli
8 Lilly" is but not that I know.
9 Q. Did Eli Lilly position, to
10 your knowledge, Zyprexa for anxiety
11 disorders?
12 A. The reason why I'm struggling
13 is we had a lot of planning documents that
14 talked about positioning for a product that
15 doesn't go off until 2011. So it's really
16 hard to say what all plans went into which
17 indications.
18 Q. Was Zyprexa indicated for
19 thought, mood, and behavioral disorders ever?
20 A. No. Those are, actually,
21 general terms to talk about the various
22 indications we planned on having.
23 Q. Okay. So the term thought,
24 mood, and behavioral disorders were various
339: 1 terms for indications you had planned on
2 having; is that correct?
3 A. It was an umbrella for
4 current indications as well as future
5 indications, yes.
6 Q. Wasn't thought, mood -- and
7 my question, back to my original question,
8 was Zyprexa ever indicated for thought, mood,
9 or behavioral disorders?
10 A. Those aren't indications, so,
11 obviously, not.
12 Q. And, therefore, it would be
13 wrong for Eli Lilly to promote Zyprexa for
14 thought, mood, or behavioral disorders, since
15 they are not indications?
16 A. Well, that's a different
17 question. It's not -- those are just general
18 terms that you can talk about with customers.
19 And then when you talk about the indication,
20 schizophrenia is a subset of thought
21 disorder. It's just a categorization. It's
22 not promoting for an indication.
23 Q. Wasn't -- why did you all
24 choose that term "thought, mood, and
340: 1 behavioral disorders," was there a particular
2 reason you chose that term?
3 A. I don't recall any particular
4 reason, no.
5 Q. Wasn't the reason you chose
6 that term because you knew it was broad and
7 vague and it provided latitude for your sales
8 representatives to frame the discussion
9 around symptoms and behavior rather than
10 specific indications in the label?

Jack E. Jordan (October 26, 2006)

340:13 A. I don't recall that being the
14 case.
15 (Whereupon, Deposition
16 Exhibit(s) 8 duly received,
17 marked and made a part of the
18 record.)
19 MR. ALLEN: Okay, sir. I'm
20 going to hand you what's been marked
21 as Jordan Exhibit No. 8, a document
22 I'll provide to counsel. I'll hold
23 it up --

Jack E. Jordan (October 26, 2006)

341: 4 MR. ALLEN: Okay.
5 (Document displayed to
6 the jury)

Jack E. Jordan (October 26, 2006)

342: 8 Q. Sir, do you recognize Exhibit
9 No. 8 as coming from your files?

Jack E. Jordan (October 26, 2006)

342:11 A. I don't know if it did or
12 didn't. My handwriting's there, so.
13 Q. Yes, sir. That is your
14 handwriting at the bottom, correct?
15 A. It is.
16 Q. Okay. You said in this -- is
17 this a positioning document or a marketing
18 document?
19 A. I'm not sure exactly what it
20 is. I don't remember it.
21 Q. Well, if it's in your files
22 it has to be marketing material, is it not?
23 A. It could be from the product
24 team, long-term planning document. I'm just
343: 1 not sure.
2 Q. Okay. It says: "Zyprexa is
3 an agent of choice to help patients with
4 debilitating thought, mood, and behavioral
5 disorders achieve the highest level of
6 long-term functioning." Did I read that
7 correctly?
8 A. You did.
9 Q. Under "Behaviors," do you see
10 "elderly?"
11 A. I see it.
12 Q. Was Zyprexa ever indicated
13 for the treatment of Alzheimer's, dementia,
14 or long-term care in the elderly unrelated to

schizophrenia or bipolar mania?
A. As I communicated with you earlier, a positioning is a long-term objective over the life of the molecule. And I don't see what the time frame is on this, but we had an extensive research program for indications for the elderly: Agitation, we had a cognition studies underway. So in the long-term, yes, we did have research going on for the elderly.

Jack E. Jordan (October 26, 2006)

Q. Was Zyprexa, when you were Brand Leader and Marketing Director, ever approved for the indication for the treatment of the elderly, either in the long-term for dementia or Alzheimer's unrelated to schizophrenia or bipolar mania?

Jack E. Jordan (October 26, 2006)

A. It was not. But we had extensive studies for longer term indications.
Q. Sir, do you remember the primary care physician launch in October of 2000?
A. I do.
Q. Were you intimately involved in that launch?
A. The person that reported to me, Mike Bandick, was responsible for the launch, yes.
Q. And so he had to report to you, so you had to approve his work, right?
A. Yeah. I had a good feel on what was going on, yes.
Q. You did not only have a good feel, you appeared at the launch, itself, and spoke to the audience in Orlando, Florida, correct?
A. I did.

Jack E. Jordan (October 26, 2006)

Q. Wasn't it the biggest thing you did with Zyprexa as of that time, as of October of 2000, was the primary care physician launch?

Jack E. Jordan (October 26, 2006)

A. No, actually it was not.
Q. Okay. Do you recall that you

all did some videos and things of that nature for the launch?
A. I don't remember the specifics but we normally had videos for sessions like that.
Q. Yes, sir. And this was a big deal in your company, this primary care physician launch, wasn't it?
A. We were going to spend about 10 percent of Zyprexa's budget on it. So, I don't know if that's a big deal or small deal but --
Q. You wouldn't describe it as a big deal?
A. It's something that we saw an opportunity to help people with bipolar mania, so that's always important.
Q. So this thing was just an opportunity to help people and not help the company?
A. It was an opportunity to help the company, yes.
Q. In fact, you were trying to help the company because Year X was upon you, wasn't it?
A. No, actually. I mean, no, we had planned it before Year X.
Q. Was Year X -- at the time of

Jack E. Jordan (October 26, 2006)

the primary care physician launch was Year X present?
A. It was. But we started planning for it in June of 2000 which was before we ever had any idea Prozac was going off patent.
Q. This was -- by the time of the launch of Zyprexa Year X was upon you, correct, by that time?
A. It was, yes.
Q. You had lost your patent protection on Prozac, right?
A. We had, yes.
Q. You were anticipating generic competition, correct?
A. We were.
Q. You knew you would have decreased revenues in Prozac, right?
A. We did.
Q. Prozac was your No. 1 selling multibillion dollar blockbuster as of that time, right?
A. It was.
Q. And you wanted Zyprexa to come in and take the place of Prozac at the time of the primary care physician launch and that was your company's intent, was it not?
A. No. We could never take the place of Prozac. But we did want to make sure that, with all of our products, we made

sure we took advantage of the opportunities.
Q. And you were trying to take advantage of the opportunity with Zyprexa primary care physician launch in the fall of 2000, because you wanted to get dollars to the bottom line and increase your company's stock price; isn't that true?

Jack E. Jordan (October 26, 2006)

348:20 A. We certainly are in the business of, of making money by helping people, yes.
Q. Right. So you were, your company was tremendously excited about the
349: 1 primary care physician launch. And, in fact, it was your intent by the primary care physician launch to grow Zyprexa and to grow the company; isn't that true?
A. If you're insinuating that we could make up for all of Prozac, no. But we did want to increase revenues by helping those folks in that marketplace, yes.
Q. You wanted to grow the company?

Jack E. Jordan (October 26, 2006)

349:13 Q. With Zyprexa?

Jack E. Jordan (October 26, 2006)

349:16 Q. Is that true or not true?
A. That's how you make money in this industry is by helping people you make money, yes.
Q. And you did not want -- wouldn't a product for schizophrenia and bipolar mania be a niche product?
A. I mean, most products in the pharmaceutical industry are niche products
350: 1 because they only have one or two indications.
Q. My question to you simply is was Zyprexa, which was indicated for schizophrenia and bipolar mania, a niche product?
A. It was approved for two indications, and so, yes, two niches, I guess, yeah.
Q. So did you consider Zyprexa a niche product?
A. Insofar as any pharmaceutical product is niched for its indication, yeah, I consider all of them niche products, actually.
Q. Yeah. But in the primary

care physician launch you wanted to expand Zyprexa sales and take it out of the niche product category, didn't you?
A. No. We were always going to stay with the niches of schizophrenia and bipolar mania and any other indications we were going to get.
Q. Didn't you, in fact, intend by the primary care physician launch to grow Zyprexa, and it was not a niche strategy at all, was it, sir?
A. I mean, I've heard "niche" used in a variety of ways. I guess I'd have to understand what you meant by that. I mean --
Q. Well, as you've already said, that most products, according to you, in the pharmaceutical industry are niche products. You intended for Zyprexa not to be a niche product after the primary care physician launch but a growth product, did you not?
A. You're trying to make two terms mutually exclusive, which I don't. We were going to grow in the niche that we had the indications for.
I don't see -- you're trying to make it an either/or and I don't view it that way.
Q. What indications did you have for Zyprexa at the time of the primary physician launch?
A. Schizophrenia and bipolar mania.
Q. So your only intent was to grow it -- with the primary care physician launch, in your testimony to this jury, the only intent was to grow it in schizophrenia and bipolar mania only; is that right?
A. In the short term, yes.
Q. Okay, sir. And this was -- you were ecstatic at Eli Lilly for the chance to make Zyprexa a multibillion dollar blockbuster, were you not?
A. I was excited about a lot of opportunities, yeah. To help undiagnosed patients, I was excited about that, yes.
Q. Was the primary goal in the primary care physician launch altruistic, that you were trying to help patients? That was your primary goal according to your testimony?
A. No, I had two primary goals. One goal was to help doctors help their patients, and the second was to increase revenue, yes.
MR. ALLEN: Why don't we -- we're going to mark the tape in a minute. We're going to put this on the conference table so the jury can see it. If you'd like to look at it, I'd ask you to look at it. Go around by your lawyer and watch this video.

Jack E. Jordan (October 26, 2006)

(At this time, the parties went off the record, after which the following proceedings were had:)

Jack E. Jordan (October 26, 2006)

(Video played.)

Jack E. Jordan (October 26, 2006)

Q. Sir, did you get the chance to watch that?
A. I did, yes.
Q. We have to show you one more video.
My question to you was: Was Viva Zyprexa launch a big deal?
A. Um -- the reason why I hesitate is it was only 10 percent of our OPEX that year.

Jack E. Jordan (October 26, 2006)

A. I mean, relative to the core business it wasn't a big deal. I mean, it was only 10 percent of our OPEX and about, potentially, 10 percent of our sales, ultimately so -- but it was exciting to help a group of undiagnosed patients. I don't want to minimize that.
Q. Isn't it true your entire company was geared up around the Viva Zyprexa primary care physician launch? Isn't it true, sir?
A. It was an opportunity that we certainly were excited about helping that patient group and increase revenues, yes.
Q. Okay, sir. I will mark and place in the record Exhibit 9, the video that we produced that was produced to us.
(Whereupon, Deposition Exhibit(s) 9 duly received, marked and made a part of the record.)
(Whereupon, Deposition Exhibit(s) 10 duly received, marked and made a part of the record.)
MR. ALLEN: We now have Exhibit 10, this next video, sir, concerning the Viva Zyprexa launch and see if you recall this.

Jack E. Jordan (October 26, 2006)

356:24 (Video played.)

Jack E. Jordan (October 26, 2006)

357: 5 Q. Sir, were you all very
6 excited? Was that you on that video, weren't
7 you?
8 A. I was, yes.
9 Q. Were you all excited there
10 because you were getting the opportunity to
11 help patients?
12 A. Yes.
13 Q. Okay. Weren't you all
14 excited because Viva Zyprexa primary care
15 physician launch was intended to help your
16 company increase its revenue and increase the
17 stock price?
18 A. As I stated before, that's
19 the nice thing about this industry is you
20 make money by helping people, so, yeah, both
21 those, yes.
22 Q. Sir, the fact of that matter
23 was the primary care physician launch in the
24 fall of 2000 -- it was October of 2000, was
358: 1 it not?
2 A. It was, yes.
3 Q. It was an off-label launch,
4 wasn't it?
5 A. It was not, no.
6 Q. Well, you knew at the time of
7 the launch that the people you were fixing to
8 sell the product to, your customers, were
9 going to use the product in an off-label
10 fashion. You knew that, didn't you?
11 A. We were going to promote it
12 on-label, obviously. But with any market and
13 almost all products customers prescribe it
14 however they want.
15 Q. Sir, my question to you was,
16 you knew at the time of the primary care
17 physician launch, Viva Zyprexa, that you were
18 going to be promoting it to doctors who would
19 be prescribing the product in an off-label
20 fashion?

Jack E. Jordan (October 26, 2006)

358:23 Q. Isn't that true?
24 A. My response is we always, it
359: 1 was our company policy, to always promote
2 on-label. And with all products in all
3 markets, doctors promote or can prescribe
4 however they want.
5 And so it wasn't any
6 different in this market that they would,

probably, prescribe it sometimes off-label, yes.

Q. You wanted the doctors to prescribe it off-label.

Jack E. Jordan (October 26, 2006)

A. The reality is, again, with any product in all markets doctors prescribe off-label; they're allowed to do that.

Jack E. Jordan (October 26, 2006)

Q. You, when you engaged in the primary care physician launch, wanted the doctors to prescribe the product off-label.

Jack E. Jordan (October 26, 2006)

A. I never thought about it. It's just the reality of the market. You promote within FDA guidelines and they use it off-label. So I don't know where to go with the question.

Jack E. Jordan (October 26, 2006)

Q. You, at Eli Lilly, and the company knew at the time of the primary care physician launch it was your intent that the doctors prescribe the product and use it off-label.

A. That's a different question. No, it was not our intention.

(Whereupon, Deposition Exhibit(s) 11 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

THE VIDEOGRAPHER: Off the record.

(At this time, there was a brief recess taken, after which the following proceedings were had:)

Jack E. Jordan (October 26, 2006)

You have read Exhibit No. 11,

is that true?
A. I have, yes.
Q. It's a document that was represented came from your files. It's
363: 1 entitled Zyprexa Primary Care Strategy and Implementation Overview; is that correct?
A. It is, yes.

Jack E. Jordan (October 26, 2006)

363:16 Q. I apologize. Maybe you could help the jury, just help the jury and tell the jury what a strategy and implementation overview is?
A. In the context of this document, it was a document that as I read it Mike Bandick put it together, must have been in the job for a month, maybe a little longer, just kind of his thoughts about where
364: 1 things were going to go.
Q. Mike Bandick, in fact, is the Brand Manager for Zyprexa in August of 2000, was he not?
A. For primary care, yes, he was.
Q. And Zyprexa was being launched into primary care, right?
A. It was, yes.
Q. That's -- the Viva Zyprexa launch is synonymous with the primary care physician launch; one in the same, right?
A. Yeah. That was the theme at the primary care launch was Viva Zyprexa, yes.
Q. And it had a song surrounding it, right?
A. It did, yes.
Q. Okay. And Mr. Bandick is the Brand Manager for Zyprexa in primary care.
A. He was, yes.
Q. At the time that he wrote this document.
A. Yeah. He'd just started the
365: 1 job not too long ago, yeah.
Q. The Strategy and Implementation Overview has paragraphs on the Background, on the Current situation, on the Opportunities, Challenges, Positioning, the Strategy, and Implementation, does it not?
A. It does have those things in here, yes.
Q. Yes, sir. I want to focus first on the Opportunities section of the Zyprexa Primary Care Strategy and Implementation Overview. Are you up there at the Opportunities section?
A. Yes, sir.
Q. "Opportunities: We believe there to be significant unmet medical need among office-based primary care physicians, PCPs. This customer group is huge. Greater

than 250,000 prescribers, 59,000 are key targets, and its potential in this arena is virtually untapped. By targeting the top deciles, we can maximize return while building a strong clinical foundation. Zyprexa's profile is ideal for primary care: Safe, simple, well-tolerated, effective, and versatile. Zyprexa would enjoy first mover advantage in this segment, preempting Janssen, which is Risperdal, Abbott, which is Depakote, and Pfizer, which is Zeldox. Historically, Zyprexa has closed market share gaps in every segment in which we've actively competed."

Did I read that correctly?

A. You did.

Q. The opportunity in the primary care market as reflected here is to sell Zyprexa to a greater number of physicians, that being the primary care physicians which far outnumber psychiatrists, right?

A. There are more primary care physicians than psychiatrists, yes.

Q. Right. And Eli Lilly viewed the potential market for Zyprexa in the primary care market as a huge market, right?

A. No. It says this customer group is huge.

Q. Yes, sir. And then it says you would have first mover advantage. What is first mover advantage?

A. No other product that was approved for schizophrenia or bipolar mania had launched into that market with a sales force.

Q. Yes, sir. Was Depakote an antipsychotic medication?

A. No. It was a mood stabilizer.

Q. Right. And you said Zyprexa would enjoy first mover advantage in this segment preempting, among others, Abbott and Depakote; is that correct?

A. Yes. Well, I didn't say that. That's what Mike wrote in this document.

Q. Right. And Mike was the Brand Manager in the primary care section.

Now we see Challenges. There's some particular challenges that Eli Lilly faced in launching into the primary care market, weren't there?

A. These are Mike's thoughts early in the job that identified these challenges, yes.

Q. Right. Was one of the challenges listed for launching in the

primary care physician market is it listed as follows: "Zyprexa's primary indications, schizophrenia and bipolar, are not viewed as PCP-treated conditions. So there's not a specific indication for Lilly representatives to promote in the PCP market."
Did I read that correctly?
A. You read that correctly.
Q. And the specific indications, sir, for the record, at the time of the PCP launch were bipolar mania and schizophrenia; is that correct?
A. Yes.
Q. And Mr. Bandick, who is then the primary care physician brand manager. Who is in charge and responsible, as you said, for the launch of Zyprexa into the primary care market, right?
A. Yes, he was. Yeah.
Q. He said, quote/unquote, there's not a specific indication for Lilly representatives to promote in the PCP segment, didn't he, sir?
A. He was relatively new on the job. And consistent with what I said earlier is the patients, our research showed that the patients were in the primary care physician's office, they just weren't being identified and treated.
Q. My question to you was, sir, did Mr. Bandick, who was the Brand Manager in the primary care market, responsible for the Viva Zyprexa launch, state, quote, There's not a specific indication for Lilly reps to promote in the PCP segment." Did he say that or not?
A. A few weeks in the job he was brainstorming, is how I read this document, and identified that the docs didn't think they had those patients and yet our research showed that those patients were in their offices.
Q. My question to you is, sir, did Mike Bandick, in the Strategy and Implementation Overview for Zyprexa in the Viva campaign launch state, quote, There's not a specific indication for Lilly reps to promote in the PCP segment, close quotes?
A. It's in this document but --
Q. Thank you, sir. Now, sir, the position --
A. -- having --

Jack E. Jordan (October 26, 2006)

A. But again, I want to make sure, this is a document, he had been weeks into the job. And when we launched it in October it was clear the patients were there and clear that we promoted on-label.

Jack E. Jordan (October 26, 2006)

371: 7 Q. Sir, now, my question to you
8 is we know this came from your files, this
9 has been produced from your files. Did you
10 ever respond to this document in any form
11 that you know of and say "I disagree with
12 you, Mr. Bandick?"

Jack E. Jordan (October 26, 2006)

371:18 A. Specifically to this document
19 I don't remember what action I took but I
20 know --

Jack E. Jordan (October 26, 2006)

372: 1 A. -- in consistent
2 conversations, the market research was very
3 clear that up to a third of the patients on
4 antidepressants had bipolar disorder that
5 weren't being diagnosed by primary care
6 physicians. So we knew we had an opportunity
7 there on-label.
8 Q. My question to you was, sir,
9 did you ever write a response to this
10 document, Exhibit No. 11, and tell
11 Mr. Bandick you disagreed with him?

Jack E. Jordan (October 26, 2006)

372:14 A. No, because we were in
15 alignment at the launch on what we were going
16 to do and how we were going to do it.
17 Q. Now, Mr. Bandick also has a
18 position for Zyprexa, does he not?
19 A. He does write down a position
20 here, yes.
21 Q. And is the position that
22 ended up being the actual position for
23 Zyprexa at the Viva Zyprexa launch, isn't it?
24 A. I'm not sure.
373: 1 Q. "The safe, proven solution in
2 mood, thought, and behavioral disorders," is
3 that what it says in this document?
4 A. It says that in this
5 document, yes.
6 Q. Do you remember the
7 three-by-three strategy for the Viva Zyprexa
8 primary care physician launch?
9 A. I do remember it, yes.
10 Q. And the three-by-three
11 strategy is this: One of the threes is mood,
12 thought, and behavioral disorders. That's
13 three on one side. And the other three sides
14 was broad spectrum efficacy, No. 1; No. 2,

safety; and No. 3, ease of use; isn't that true?
A. I don't recall.
Q. Okay. I thought you told us you recalled the three-by-three strategy?
A. I recall that phrase, I don't recall the specifics.
Q. Okay, sir. Anyhow, the position, tell the jury again if you haven't already, can you explain to the jury what a position is with regard to a medical product such as Zyprexa? What a position is?
A. A position is, ultimately, how you want your customers to think about your product.
Q. Right. And the position listed in this document is "the safe, proven, solution for mood, thought, and behavioral disorders;" is that correct?
A. That's how Mike wrote it in this document, yes.
Q. The very next sentence says, begins, "We will emphasize safety to address the barriers to adoption." Did I read that correctly?
A. You did.
Q. And when you say "will emphasize safety," that means we, in positioning the product for our customers, including the doctors, will emphasize to them that this product is safe, right?
A. As written in this document, yes.
Q. Then going down under position it says, "quote, mental disorders, close quotes, is intentionally broad and vague providing latitude to frame the discussion around symptoms and behaviors rather than specific indications."
Did I read that correctly?
A. You did.
Q. And Mr. Bandick, the brand manager who was responsible for the primary care launch, stated that the position of mood, thought, and behavioral disorders was intentionally broad and vague, right?
A. In August of 2000, a few weeks on the job, he wrote this; however, in October of 2000, I was at the launch meeting, I saw the message, it was on-label, made it through our medical group, regulatory group.
Again, I want to make sure we position this as a brainstorming document early in his, early in his tenure in this responsibility.

Q. My point here is, sir, you said "I want to make sure I position this document as a brainstorm." Is there anywhere

in this document that says it's a brainstorm or does it, specifically, say it's a Strategy and Implementation Overview?

A. It, actually does. If you read the first sentence of the implementation it says "market research, message development, medical support, and the creation of a training calendar is in progress."

So you're talking about a document where market research, message development, medical support, and the calendar hadn't even been put in place. So it's clearly a brainstorming document.

Q. And aren't mental disorders, excuse me, weren't mood, thought, and behavioral disorders the specific launch statement that was given for Viva Zyprexa -- mood, thought, and behavioral disorders?

A. Again, I don't recall the specifics.

Q. Okay. We'll look at that in a minute. But in this document Mr. Bandick specifically says, though, "mental disorders is intentionally broad and vague to frame the latitude around symptoms and behavior rather than the specific indications." Is that correct?

A. But this is a point where market research, message development, medical support, and the creation of training isn't even done yet so I don't know what to do with that phrase. I don't know what he meant by it. We still have a lot of work to do before the launch meeting.

Jack E. Jordan (October 26, 2006)

MR. ALLEN: Exhibit No. 12.

(Whereupon, Deposition Exhibit(s) 12 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. My question is: Do you recall seeing Zyprexa Launch Meeting Viva Zyprexa document, which I have marked as Jordan Exhibit No. 12?

A. I don't remember seeing this specific document, no.

Jack E. Jordan (October 26, 2006)

Q. Mr. Jordan, turn to Page 79.

Jack E. Jordan (October 26, 2006)

382:18 Q. What is the key elements
19 listed under Zyprexa Primary Care?
20 A. Broad efficacy, safety, and
21 ease of use.
22 Q. Doesn't it say, "Zyprexa
23 primary care, quote, three-by-three broad
24 efficacy, safety, ease of use, on one side
383: 1 and mood disturbances, thought disturbances,
2 and behavior disturbances on the other side?
3 A. It does, yes.
4 Q. Did the key message elements
5 in this document, Exhibit No. 12, mirror the
6 key message elements contained in Exhibit
7 No. 11, that is, the broad and vague term
8 mood, thought, and behavior disorders?

Jack E. Jordan (October 26, 2006)

383:11 A. Those terms are used, yes.
12 Q. Right. And those terms, at
13 least according to Mr. Bandick in Exhibit
14 No. 11, were intentionally vague so that the
15 sales representatives could frame the
16 discussion around symptoms and behavior and
17 not specific indications, isn't that true?

Jack E. Jordan (October 26, 2006)

383:20 A. No.
21 Q. Now broad efficacy on the
22 left, exhibit number -- never mind. Broad
23 efficacy -- we list some people, Martha,
24 David, and Christine; is that right?
384: 1 A. Yes.
2 Q. And those are patient
3 profiles -- Martha, David, and Christine,
4 aren't they?
5 A. They are, yes.
6 Q. They're listed in marketing
7 documents that were used not only to train
8 the sales force to market to primary care
9 physicians but were listed as patient
10 profiles in documents actually given to
11 doctors before they prescribe to patients,
12 correct?

Jack E. Jordan (October 26, 2006)

384:15 A. How it worked was the medical
16 department would work with patient profiles
17 using their knowledge in bipolar mania and
18 schizophrenia and, basically, help the
19 marketing department come up with patients
20 that were identified as schizophrenia bipolar

mania.

Jack E. Jordan (October 26, 2006)

Q. Sir, my question to you was, Martha, David, and Christine, are patient profiles listed in marketing materials that were given to train the sales force before they went out and detailed primary care physicians. And were also patient profiles listed in documents actually given to doctors who were being detailed by your sales force.

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A. I don't remember what --
Q. Thank you, sir. If you don't remember --
A. -- the materials were.
Q. You don't remember?
A. I don't remember.
Q. Under ease of use one of the things it says is "no blood monitoring," correct?
A. It does, yes.
Q. How do you diagnose

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hyperglycemia?
A. I'm not a doctor so I don't know.
Q. Did you ever know at any time you were a Zyprexa Marketing Manager and/or Brand Leader for Zyprexa?

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doesn't know. Did he ever know how you diagnose hyperglycemia?
A. Well, that's a different question. Hyperglycemia is simply higher blood sugars. I thought you said diabetes. Hyperglycemia, is just, I think you take tests to see if your blood sugars are higher.
Q. And those are blood monitoring tests, correct?
A. Yeah, I believe, yeah.
Q. Right. And under the Zyprexa Primary Care Key message elements under Ease of use for the primary care physicians it says "no blood monitoring," correct?
A. If you look at the broader detail piece, that's referring to blood monitoring for lithium levels that are

required in many bipolar patients.

Jack E. Jordan (October 26, 2006)

Q. But anyhow, on Page 79, under ease of use for the primary care launch, does it say "no blood monitoring?"
A. It's in the context of several bipolar mania drugs and schizophrenia drugs that require blood monitoring for specific issues.
Q. So the answer is, "Yes, Mr. Allen, it says no blood monitoring?"
A. It does for --

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A. -- for specific blood monitoring that needs to take place for psychotropic drugs.
Q. Now after the launch of Zyprexa into the primary care market, you, in the marketing as the brand leader didn't just leave things to chance, you wanted to see if the proper message was getting out to the doctors, didn't you?
A. We did do message recall, yes.
Q. And you wanted to see whether or not your campaign had been successful and doctors were responding to your message; isn't that true?
A. With all our segments we did do message recall, yes.
Q. Who is Zohar Porat?
A. She was a market research associate.
Q. For Eli Lilly?
A. For Lilly, yes.
(Whereupon, Deposition Exhibit(s) 13 duly received, marked and made a part of the record.)
MR. ALLEN: Sir, I'll hand you what's been marked as Jordan Exhibit No. 13.
MR. GOLD: Thank you, sir.
QUESTIONS BY MR. ALLEN:
Q. This is entitled Qualitative Telephone Focus Groups, Sales Rep and DM -- DM stands for district managers, doesn't it, sir?
A. It does, yes.
Q. Sales Rep and District Manager Topline Reaction to PCP Launch, December 2000, Zohar Porat, Lilly, Answers That Matter; is that correct?
A. Yes.
Q. Under the executive summary

on the second page of this document it has as a third bullet point --
A. I'm sorry, I'd like to read this because --
Q. Do you need to read the whole document to answer what the third bullet point says?
A. I do, because an executive summary has background on it, so.
THE WITNESS: Good. Thank you.
MR. ALLEN: You're welcome, sir.
QUESTIONS BY MR. ALLEN:
Q. This is Exhibit 13, is that right, sir? Jordan Exhibit 13?
A. It is.
Q. In Exhibit 13, this is, as you told us earlier is a marketing kind of survey to determine what the response is to the messages that you've given the sales force in the field and see how the marketing plan's going?

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A. I think it is. I don't know what the sample size was on this but I think it was.
Q. Okay. I'm not asking about the sample size. The sales rep and DM topline reaction to PCP launch you said is a document that came from the marketing department from Zohar Porat, right?

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Q. Right?
A. It is, but it has -- you start with Page 4, Page 7. I mean, it just --
MR. ALLEN: Right. I don't need to ask you about every page because you have to read every page and your lawyers can go back and ask you anything they want about any page, I can promise you, anything.
QUESTIONS BY MR. ALLEN:
Q. But let's get on the record what Exhibit 13 is. Exhibit 13 is where your company's surveying your sales representatives and your district managers to see how doctors are responding to messages on the PCP launch, right?
A. Yeah, part of it, yeah.
Q. Okay. Now let's go to the second page of this document under executive summary, third bullet point says, "SRs," that's sales representatives, right? Isn't

that what it stands for?
A. I believe so, yes.
Q. "SRs are having the most success when their message centers on identifying patient types and treating symptoms instead of focusing on patient diagnosis." Did I read that correctly?
A. Well, the thing I'm struggling with is -- you're reading it correctly -- but I don't know what pages one through three say.
Q. Yes, sir. And your lawyers will have ample opportunity to ask you anything they want. And I will tell you if you're suggesting to the jury, or anybody else, that I'm being unfair, we'll let the lawyers point it out. I'll introduce, myself, pages one through three and any other at trial in this case.

I'm talking about this question that was presented to the sales representatives in the executive summary. Do you see that?

What's a summary?
A. It's an interpretation by one person on what the first three pages of data said. So I don't --
Q. Now doesn't Mr. Porat --
A. It's a female.
Q. Excuse me. I very much apologize.

Doesn't Ms. Porat in Exhibit 13 in Bullet Point No. 3 of the Executive Summary state, "Sales representatives having most success when their message centers on identifying patient types and treating symptoms instead of focusing on patient diagnosis?"
A. That's what it says --
Q. Thank you, sir.
A. -- but here's the issue I have with it is that Bullet Point No. 3, this could be an executive summary of the first page of the detail piece. The first page of the detail piece connects with doctors on symptoms and then goes into bipolar disorder. So I don't know what this is an executive summary of.
Q. Yes, sir. The record will reflect at the time of trial what this is an executive summary of.

My question to you was only: Does the Executive Summary, Exhibit 13, third bullet point state: "Sales representatives having most success when their message centers on identifying patient types and treating symptoms instead of focusing on patient diagnosis?"
A. And our strategy on the message was up front to identify patient symptoms, ask the doctors if they had that cluster of symptoms at the patient level, and then share the data around the diagnosis.

So this could be, as much as I know, a summary of that first page of the detail piece.
Q. Did I read the third bullet point correctly or not?
A. You did.

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Q. Okay, sir, are you on the last page of Exhibit 13 which is also Page 13?
A. I am.
Q. Of the Sales Rep and District Manager Topline Reaction to the Primary Care Physician Launch. Can you read for the jury out loud the first bullet point under Recommendations?
A. Now, I'm going to assume this is a summary, given, you haven't given it to me, of the first part of the detail piece where they talk about symptoms and then go on to diagnosis as part of the message which is what I saw trained. So in that context: "Continue focusing on patient symptomology and having PCPs identify specific patients rather than on patient diagnosis."
Q. Let's see if I can read this a little slower for the jury. The first bullet point under Recommendations on the last page of Exhibit 13 reads as follows: "Continue focusing on patient symptomatology and having primary care physicians identify specific patients rather than on patient diagnoses." Did I read that correctly?
A. You're reading's correct but I don't know, I don't know that it's represented correctly without seeing everything.

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Q. Okay. Sir, do you recall after the launch and periodically over the years, even before the PCP launch, you, at Eli Lilly, would have district and territorial sales meetings concerning the products that you sold?
A. We did have district meetings, yes.
Q. And you've already told us that Mr. Mike Bandick, who worked for you, was the primary care physician brand manager in charge of the Viva Zyprexa launch, right?
A. He was not a physician, no.
Q. Did I say physician?
A. You did.
MR. ALLEN: Well, I don't think I did but if I did I apologize

and let me rephrase it. I do not believe that I did but I could have. I make mistakes. I admit them when I do.

QUESTIONS BY MR. ALLEN:

Q. You have previously testified that Mr. Mike Bandick was the Brand Manager in charge of the primary care physician launch for Zyprexa, Viva Zyprexa launch in October of 2000?

A. Yes.

Q. Okay. That's when I said physician. And I'm going to hand you -- and did you know or not know that Mr. Bandick -- and I think you attended -- let me ask this, did you ever attend district or national sales meetings with the sales force?

A. I did at various times, yes.

Q. Did you, in fact, attend the national sales meeting of March the 13th, 2001, following the Zyprexa PCP launch?

A. I don't know if I did or not.

Q. Okay. But you know that Mr. Bandick certainly when he attends such a national sales meeting, what he says is accurate and truthful, and he is giving the sales representatives good and truthful information, is he not?

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A. That would be my assumption, yes.

Q. Yes, sir.

(Whereupon, Deposition Exhibit(s) 14 duly received, marked and made a part of the record.)

MR. ALLEN: Sir, I'll hand you what's been marked as Exhibit 14, which is portions of a transcript concerning Mr. Bandick's presentation at the Eli Lilly national sales meeting on March the 13th, 2001.

MR. GOLD: Thank you.

QUESTIONS BY MR. ALLEN:

Q. Do you recall being at this meeting or reading this transcript previously?

A. I do not, no.

Q. Sir, I ask you to turn simply to the second page of this transcript. I'm going to talk to you about Mr. Bandick's comments about money, okay? Just the second page.

Do you see where Mr. Bandick tells the sales representatives in March of 2001, "Just imagine the added impact that better sales messages, competitive differentiation and peer-to-peer activity

will have on our future sales line. Don't get me wrong, unit share growth is good, and what we have accomplished in that area has not gone unnoticed. But dollars pay the bills and boost the stock price, so let's look at dollar growth."
Did I read that correctly?
A. You did.
Q. And then we, if you would turn to the next page, which is page four, Mr. Bandick discusses Year X, does he not?
A. Looks like he -- I see it in there.
Q. Yes. And he's talking to the sales representatives that are, actually, going out to sell the product, right?
A. I don't know where this came from.
Q. Sir, the document reflects it came from the national sales meeting. Who comes to the national sales meeting, sales representatives?
Assume with me it's at the national sales meeting. Who goes to the national sales meeting?
A. Most of them are sales people.
Q. Right. Let's see what Mr. Bandick says about Year X to the sales representatives. "This is Year X for Eli Lilly, and the conventional wisdom is that the companies just don't, quote, bounce back, close quotes, from losing patent protection from their biggest product." And then there's a section redacted by Lilly's lawyers, right?
A. I don't know who redacted it.
Q. We'll assume it's Eli Lilly's lawyers.

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Q. Mr. Bandick says, "And the conventional wisdom is that company's just don't bounce back from losing patent protection from their biggest product. We need to own this target, because the affiliate needs our help."
Did I read that correctly?
A. You did.
Q. When we refer to the affiliate we're talking about Eli Lilly U.S.A., are we not?
A. We are, yes.
Q. So Eli Lilly U.S.A. needed help from the Zyprexa primary care sales force to replace the lost sales that they were going to suffer and had suffered from Prozac, correct?
A. No. The forecast never was to make up for the lost sales of Prozac.

Q. Did Mr. Bandick tell the Zyprexa sales force that the affiliate needs our help, yes or no?
A. He did, yes.

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Q. You talked about Martha in this deposition, have you not, sir? Martha?
A. You've mentioned her and I've acknowledged her but I haven't talked about her, no.
Q. Okay. I'm sorry. I mentioned her and you acknowledged her.
Martha, in fact, was the patient profile that Eli Lilly used to try to get doctors to prescribe Zyprexa to the older folks who had dementia or Alzheimer's or had long-term care needs; isn't that right? Isn't that who Martha is?
A. No.
Q. Okay. That's not who Martha is? Let's see what Mr. Bandick says on Page 13 which is the next page, it's the fourth page of Exhibit 14. I'll read what Mr. Bandick tells the sales force. "Let me call a time out and make one quick comment on Martha. What's the first thing you notice about Martha --
THE WITNESS: I'm sorry, I've lost which page you're on, I'm sorry.
MR. ALLEN: Yes, sir.
Page 13.
THE WITNESS: Okay, thank you.
QUESTIONS BY MR. ALLEN:
Q. Mr. Bandick tells the sales force, "Let me call a time out and make one quick comment on Martha. What's the first thing you notice about Martha? She's old exclamation point. That does two things. First, it reinforces Zyprexa as a nursing home drug. Our mission is to build a primary care franchise, and let our long-term care team drive the nursing home business. Second, it limits the perception of behavioral disturbance -- agitation, tension, anger, hostility all show up in primary care in a variety of packages. Young, old, male and female. When you describe Martha, make her symptoms more prominent than her age."
Did I read that correctly?
A. You did.
Q. That's off-label marketing, is it not, sir?
A. No, it's not.
Q. Thank you, sir.
So under your definition that you use at Eli Lilly those comments by Mr. Bandick are purely on-label promotion of

Zyprexa?
A. Well, the process we used around the Martha profile was to have our medical department identify and help us describe an elder schizophrenia patient which is Martha. And so, you know, our physicians were competent in that endeavor, and did what we asked them to do.
Q. Did you see any description in Mr. Bandick's comments that he described Martha as being a schizophrenic?
Did he there in that transcript that I gave you in the national sales meeting describe Martha as a schizophrenic?
A. Well, we jumped so many pages I don't know if he does or doesn't because then -- we're missing so many pages he might have. I don't know. But all I know is it had to go through our medical department to help us identify a schizophrenia on-label patient.
Q. Let's see what Mr. Bandick said. Let me read it. He says it right here, "What's the first thing you notice about Martha? She's old." Doesn't it say that?
A. It does.
Q. Then it says "that does two things. And then he says "it reinforces Zyprexa as a nursing home drug." Does that sound like it's reinforcing Zyprexa as a drug for bipolar mania and schizophrenia to you?
A. I don't know what it says to you but --
Q. Thank you, sir.
A. -- all I know is it had to go through our medical department to identified that Martha had schizophrenia.

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A. Well, I mean, that's just the reality.
Q. So the reality is the medical department had to approve whatever the marketing department did to make sure it's medically proper and in accordance with the label?
A. The Martha profile had to go through the ELMR process which included medical, legal, our regulatory folks to make sure it's aligned with our label.
Q. Thank you, sir, that's a very good point. So the Martha profile, and, I guess, the Donna profile, and all the patients profiles, were not just a function of marketing but also of legal, the lawyers for Eli Lilly, the marketers for Eli Lilly, the regulatory people for Eli Lilly, and the medical team; is that right?

A. Yes.
Q. So Eli Lilly, when it markets to Martha, this is a company-wide agreement, right?

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A. We never marketed to Martha. We marketed to physicians.
Q. For Martha.
A. With a patient profile of Martha.

Jack E. Jordan (October 26, 2006)

What's the next exhibit, sir?
(Whereupon, Deposition Exhibit(s) 16 duly received, marked and made a part of the record.)
MR. ALLEN: I'll hand you Exhibit No. 16. This is an advertisement that has been produced to us.
Exhibit 16, sir. We're moving off of 15. Let me have 15, please.
That was 14. We skipped one right now we'll come back to.
Exhibit 16, this is an advertisement. I'll hold it up.
(Document displayed to the jury)
Do you recall this advertisement, Antipsychotic Power for Routine Use?
A. I do not, no.
Q. Was Zyprexa an everyday routine drug?

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A. Yeah. It was used in over 4 million patients at that point, yes.
Q. Was Zyprexa intended as a routine drug? It says Antipsychotic Power For Routine Use. Was antipsychotic power in Zyprexa intended for routine use?
A. In schizophrenia, later in bipolar mania, it was used routinely, yes.

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Q. Doesn't the second page of this exhibit, the advertisement Antipsychotic

Power For Routine Use, have a nice picture of an elderly woman?
A. Yes, it does.
Q. Is that Martha?
A. I don't know who she is.
Q. Isn't this attempt to market to Martha an Antipsychotic Power For Routine Use promotion of Zyprexa off-label?

Jack E. Jordan (October 26, 2006)

A. No.
Q. Donna. You remember Donna, do you not, sir?
A. I do, yes.

Jack E. Jordan (October 26, 2006)

(Whereupon, Deposition Exhibit(s) 15 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Would you look at Exhibit 15, sir.

Jack E. Jordan (October 26, 2006)

Q. Sir, do you recognize Exhibit No. 15?
A. No, I don't, because the copy is -- I mean, there's words in there that I can't read.
Q. Yes, sir. That's just the best I can do. This is a color document that you're familiar with that has a purple Z with a doctor reaching across to help his patients.
You're familiar with this marketing piece that was given to doctors, aren't you?
A. I'm going to have to read it because I can't tell by the picture.

Jack E. Jordan (October 26, 2006)

Q. Sir, you certainly recognize the cover of this document, don't you, sir?
A. I do not, no.
Q. Okay. This document is, in fact, a detail piece that is provided to physicians, isn't it, sir?
A. I don't know yet.

Q. This is a Primary Care Resource Guide, isn't it, sir?
A. No. I think it's a --
Q. Excuse me, go ahead. You're correcting me properly. There's a primary care resource guide that trains the sales force how to utilize Exhibit No. 15, isn't there?
A. Yeah. I think -- it looks like a detail piece, yes.
Q. Yes, sir. It's a detail piece that is taken by the sales representatives to the doctors in their offices?
A. I believe this is, yes.
Q. Yes. It's also taken, this detail piece can be taken to the other customers of Eli Lilly; isn't that right?
A. Well, the only --
Q. Sir, my question is pending.
A. I'm struggling with it because there's always a number at the bottom of these for final approval and I don't see the LY number.
Q. Sir, this was just produced to us by the defense.
A. Okay.
Q. And my question was not anything dealing with an LY number. But let's go on with Exhibit 15.
By the way, these detail pieces that are given to doctors are not, the sales reps are trained how to talk to the doctors about the detail piece, are they not?
A. They are, yes.
Q. Yes. And, in fact, the sales representatives are given things like the primary care resource guide training to tell them how to present detail pieces such as Exhibit 15 to the doctors, right?
A. There are resource guides and additional training that goes on, yes.
Q. Yes. And, sir, that wasn't my question. That was part of my question. The resource guides that you're talking about that is part of the sales rep's training teaches the sales reps how to present things like Exhibit 15 to the doctors.
A. They do, yes.
Q. Yes, sir, that's my point.
All right, sir. Does this detail piece identify Donna?
A. Yes, it does, on the fourth page.

Jack E. Jordan (October 26, 2006)

Q. Now, sir, let's go to Exhibit 15. Are you there with Donna?

A. On Page 4, yes.
Q. Yes, sir. We have a circle next to Donna that says "anxiety, irritability, mood swings, and disrupted sleep," right?
A. Yes. Those are what's identified.
Q. Okay. I don't see schizophrenia and bipolar mania anywhere in the description of Donna, do you?
A. Well, this is Page 4. Page 2 says Zyprexa is approved for short-term treatment of bipolar mania and short-term treatment and maintenance of schizophrenia.
Q. Yes.
A. So Page 2 has the indications, Page 4 has Donna, yes.
Q. There was no doubt that before the sales rep, or before this whole sales piece was prepared, that Zyprexa was approved for schizophrenia and bipolar mania, right?
A. Yeah. It was on Page 2, which I'm assuming is Page 1 of the piece.
Q. My question to you was, there was no doubt that the only approved indications for which Zyprexa could be promoted was schizophrenia and bipolar mania, right?
MR. GOLD: Asked and answered.
A. Yeah. And it's right here in the first page, yes.
Q. And now we go to the page on Donna. It says, "Donna. Single mom in her mid-30s, presents in drab clothing and seems ill at ease. Quote, I feel so anxious and irritable lately, close quotes. Her history is: Reports she has been sleeping more than usual, has trouble concentrating at work and at home. Several appointments earlier she was talkative, elated, and reported little need for sleep."
Next bullet point: "You have treated her with various medications including antidepressants."
Did I read that correctly?
A. You did.

Jack E. Jordan (October 26, 2006)

Q. My only question to you is, sir, do you see a diagnosis of schizophrenia or bipolar mania in the Donna profile?
A. Now you're asking a question that -- the words, no, but the symptoms, the cluster of symptoms, actually, might be. I mean, that's part of the reason to have that discussion and have the MDQ so they can screen for bipolar mania.
Q. You said MDQ?

A. MDQ, yes.
Q. Yeah. The MDQ is the mood disorder questionnaire that was only released, I believe, in 2003, and the sales representatives were instructed to only use it with their high prescribers; isn't that right?
A. I don't know if that's the case or not.
Q. And you're not suggesting that in order to prescribe Zyprexa that the physicians needed to get an MDQ filed out, are you?
A. No. But we provided various tools to help them diagnose bipolar mania.
Q. Yes, sir. What do you do when you cash your chips?
A. That's a term that the sales organization used at one point. And it's, actually, not a term I'm that familiar with.
Q. What do you do when --
Didn't you instruct all your sales representatives, weren't they instructed that during the sales call they were to collect chips, collect agreements, and at the close of the call to cash the chips and to create action?
A. I heard verbiage like you just used. Again, that was more of a sales organization, sales process, than kind of a marketing language, so.
Q. Sir, as I told you previously I always admit when I make mistakes. I forgot to ask you a question about the Viva Zyprexa document, and I'd like to you to return to the Viva Zyprexa document, if you don't mind?

Jack E. Jordan (October 26, 2006)

Q. Sir, remember earlier in the day I asked you whether or not you, specifically, knew that the primary care physician launch was, in fact, an off-label launch? Do you recall that?

Jack E. Jordan (October 26, 2006)

Q. Do you recall that?
A. That you -- that you said it was?
Q. Yes, sir. That I asked you, and it's my position, do you understand it's my position that the Viva Zyprexa launch is an off-label launch?

Jack E. Jordan (October 26, 2006)

427: 6 A. I remember you insinuating
7 that, yes.
8 Q. Yes, sir. And if you will go
9 to Exhibit 12, the Zyprexa launch meeting
10 Viva Zyprexa document, look at the page 69,
11 which is the fourth page of this exhibit,
12 okay? Do you see Zyprexa --
13 MR. ALLEN: I'll hold it up
14 for the jury.
15 (Document displayed to
16 the jury)
17 QUESTIONS BY MR. ALLEN:
18 Q. Do you see Zyprexa
19 utilization by disease state, sir?
20 A. I do.
21 Q. On the left-hand side they
22 have "Zyprexa utilization by disease state
23 all specialties." Did I read that correctly?
24 A. You do, yes.
428: 1 Q. And what we have is, what we
2 all learned, I think, maybe it's fifth or
3 sixth grade, I can't remember, we had the pie
4 charts. You remember the pie charts? We
5 have a pie chart, right?
6 A. There are pie charts, yes.
7 Q. Yes, sir. And "all
8 specialties," and then it gives the disease
9 states for which Zyprexa was prescribed,
10 correct?
11 A. It does, yes.
12 Q. It says, and this is all
13 specialties, "schizophrenia, 36 percent,"
14 right?
15 A. Yes.
16 Q. "Bipolar" -- now, it doesn't
17 say bipolar mania, does it?
18 A. It does not, no.
19 Q. Okay. And we know there's
20 different types of bipolar illness, do we
21 not? There's bipolar disorder?
22 A. I'm not the expert in it
23 but --
24 Q. You know there's more than
429: 1 one type of bipolar disease, don't you?
2 A. There's bipolar one and
3 bipolar two.
4 Q. Right. And you know Zyprexa
5 was not indicated for all forms of bipolar
6 disease, was it?
7 A. It was not, no.
8 Q. Okay. So we have to assume
9 under "bipolar" it contains some nonindicated
10 uses of Zyprexa, since there's more than one
11 type of bipolar disease, right?

429:14 A. Yeah. Doctors have the
15 ability to prescribe drugs however they have
16 want to prescribe them.
17 Q. Yes, sir. And, of course,

doctors, as you said, customers will think -- you want customers to think what we want them to think, right?

Jack E. Jordan (October 26, 2006)

429:24 Q. Didn't Eli Lilly want doctors
430: 1 to think what Eli Lilly wanted them to think
2 about Zyprexa? That was one of your main
3 goals?
4 A. We had positioning goals for
5 our customers, yes.
6 Q. Okay. At the time of the
7 primary care launch, the utilization of
8 Zyprexa by disease state was 36 percent
9 schizophrenia, 16 percent bipolar. If I add
10 those two numbers up that comes to
11 52 percent, right?
12 A. Yes.
13 Q. So -- and assuming that some
14 of the bipolar -- would you at least agree
15 with me it would be a reasonable assumption
16 to assume some of the bipolar prescriptions
17 are not bipolar mania?
18 A. That is a safe assumption.

Jack E. Jordan (October 26, 2006)

431:14 doesn't this pie chart clearly demonstrate,
15 and don't you agree, that over 50 percent of
16 Zyprexa prescriptions by all specialties at
17 the time of the PCP launch were off-label?
18 A. Yes. Doctors had made the
19 choice to prescribe the product off-label,
20 yes.
21 Q. Right. And we know, and we
22 saw in Exhibit 2, where doctors got their
23 information, right? Remember they got it
24 from CMEs and things of that nature, right?
432: 1 A. There's a whole variety of
2 ways they get their information.
3 Q. Right. And Eli Lilly did not
4 leave -- made sure or tried to interject
5 itself into all channels of communication
6 that would go to doctors, didn't they?

Jack E. Jordan (October 26, 2006)

432:14 A. We used a number of channels
15 to communicate with physicians, yes.
16 Q. Thank you, sir.
17 Now, my question, which I
18 haven't heard you answer yet and I want to
19 see if your answer is correct, isn't it true
20 that at the time of the PCP launch you would
21 agree over 50 percent of Zyprexa
22 prescriptions by all specialties, not just

PCPs, was off-label?

Jack E. Jordan (October 26, 2006)

433: A. Yes. Physicians chose to prescribe the product in a number of patients.
Q. Right. Now, the primary care physicians, if you look back on the prior page, 68 -- look on Page 68, the prior page -- at the time of the PCP launch, only accounted for 18 percent of antipsychotic market; is that right?
A. Yes.
Q. And it was Lilly's intention to make the PCP, or the primary care physicians, account for more than 18 percent of the market, correct?

Jack E. Jordan (October 26, 2006)

433: A. We did want to grow sales, yes.
Q. Thank you, sir.
Now go to the next page, 69,
434: and look at "Zyprexa utilization by disease state of primary care physicians as of the time of the PCP launch." Are you with me?
A. I am, yes.
Q. And we have a box there. It says, pointing to the graph, it says "schizophrenia, 30 percent," right?
A. Yes.
Q. And "bipolar 7 percent," correct?
A. Yes.
Q. And again, you'd have to agree with me that part of that bipolar prescription would be not bipolar mania, right?
A. Yes.
Q. Okay. But even taking the 30 and the seven, you add it together it's 37 percent, correct? Thirty and seven added together is 37?
A. Yes.

Jack E. Jordan (October 26, 2006)

435: Q. My only question to you was, sir, didn't Eli Lilly know, even prior to the time of the launch of the Viva Zyprexa campaign, that 63 percent of the primary care physician's prescriptions were off-label?
A. Yes. Without promotion they were prescribing off-label and we were focusing on the bipolar mania market.

Q. Sir, I know you're not going to give me any different answer. Can you turn to Page 71 of this about your vision and strategy for primary care at the time of the launch.

Jack E. Jordan (October 26, 2006)

Q. Are you at the page Zyprexa Primary Care Vision and Strategy?
A. I am. 71?
Q. Yes. And the vision for the PCP launch was "expand Zyprexa's market by redefining how primary care physicians treat mood, thought, and behavioral disturbances." Did I read that correctly?
A. You did.
Q. Does it say expand Zyprexa's market by having primary care physicians treat schizophrenia and bipolar mania?
A. Again, a vision is what you want in the long-term. And mood is a part of bipolar mania. Thought is what schizophrenia and behavior disturbances are.

We had an active program in the psychosis associated with Alzheimer's.
Q. Wasn't it your strategic intent at the time of the primary care launch to make Zyprexa an everyday agent in primary care?

Jack E. Jordan (October 26, 2006)

A. Given that our data showed that up to 30 percent of patients who were treated with antidepressants were potentially bipolar patients, that would make it an everyday agent in the bipolar -- I mean in the primary care physician's office.
Q. And, in fact, Zyprexa, Page 72, Strategic Intent says: "Zyprexa can and will become an everyday agent in primary care," correct?
A. Given that antidepressants are one of the most frequently used products by primary care physicians, and if you think about potentially up to a third actually have bipolar disorder, there was the opportunity that doctors would write it every day. Primary care physicians would write it every day, yes.
Q. Sir, at the time of the primary care physician launch you were informed that your colleagues, Chris Bomba, Suni Keeling, Robert Baker, Patrizia Cavazzoni, and Charles Beasley had gone to an endocrinology advisory board meeting for independent endocrinologists that advised Lilly in the diabetes section. Did you know

about that?

Jack E. Jordan (October 26, 2006)

Q. That meeting that Ms. Bomba and Mr. Keeling went to?
A. I don't remember that specific meeting but if you have something to refresh my memory.
Q. Were you informed that when Dr. Baker, Dr. Beasley, Chris Bomba, Suni Keeling, and Pat Cavazzoni went to this meeting of the endocrinology advisory board, the advisory board informed them that they were very concerned about diabetes and that it was time for Eli Lilly to come clean on the diabetes issue?
A. I don't remember that specific interchange, no.
Q. Do you recall that at the time Dr. Baker, Dr. Beasley, Chris Bomba, and Suni Keeling, and Pat Cavazzoni went to the endocrinology board meeting in October of 2000, the endocrinologists told Eli Lilly that they were skeptical that weight gain seen in the spontaneous event reports was not associated with higher hyperglycemia rates?

Jack E. Jordan (October 26, 2006)

Q. Do you recall that?
A. Given I don't remember the meeting, I don't recall that, no.
Q. Did you recall that the endocrinology board, you were advised in October of 2000, at or near the time of the PCP launch, wanted all the hyperglycemia data turned over to them?

Jack E. Jordan (October 26, 2006)

A. Again, given I don't remember the meeting, I don't recall that being a desire.
Q. And were you advised when Dr. Baker, and Dr. Beasley, and Chris Bomba, and Suni Keeling, and Pat Cavazzoni returned from the endocrine advisory board meeting, they advised Eli Lilly don't get too aggressive and blame the diabetes you are seeing on the schizophrenia. Do you recall that?

Jack E. Jordan (October 26, 2006)

440:19 A. I just don't remember that
20 specific meeting.
21 Q. Do you recall being informed
22 in May of 2002 about Dr. Newcomer's clamp
23 study?

Jack E. Jordan (October 26, 2006)

441: 2 A. I, vaguely -- I recall that
3 Dr. Newcomer had done a clamp study.
4 Q. Do you recall as the brand
5 manager, excuse me, the Brand Leader and the
6 Marketing Director for Zyprexa, being
7 informed in May of 2002, that Dr. Newcomer's
8 clamp study demonstrated increased adiposity.
9 You know what adiposity is, don't you?
10 A. It's weight gain.
11 Q. Yes.
12 A. In fact, I'm sorry, it's fat,
13 basically.
14 Q. You recall knowing in May of
15 2002, that Dr. Newcomer's clamp study
16 demonstrated that increased adiposity is
17 strongly associated with decreased insulin
18 action in treated patients with
19 schizophrenia. Treatment-induced increases
20 in adiposity, along with additional disease
21 or treatment effects, may contribute to
22 elevated rates of diabetes mellitus in this
23 population."

Jack E. Jordan (October 26, 2006)

442: 2 Q. Do you recall being informed
3 of that?
4 A. Do I recall -- I mean, that
5 whole paragraph, I don't know that I was
6 informed of that whole paragraph, no.
7 Q. Were you informed generally
8 by May of 2002, that Dr. Newcomer's clamp
9 study demonstrated that increased adiposity
10 related or secondary to medication would
11 elevate, would potentially elevate the rates
12 of diabetes mellitus? Do you recall that?

Jack E. Jordan (October 26, 2006)

442:15 A. I remember a discussion with
16 Dr. Baker about Dr. Newcomer's work. And as
17 Dr. Baker and others incorporated into the
18 overall knowledge, it didn't change our
19 belief on our messages around the issue.
20 Q. Were you informed in June of
21 2002, Dr. Newcomer's opinion that "if you
22 have a drug with larger adverse effects on
23 weight, then you're going to see larger
24 effects on glucose and lipid metabolism.

443: 1 Three decades of research indicates the
2 predictive relationship between adiposity, or
3 fat, and abnormalities in glucose and lipid
4 metabolism."

Jack E. Jordan (October 26, 2006)

443: 7 A. I don't remember any
8 discussion about, with Dr. Newcomer, about
9 all those remaining details.

Jack E. Jordan (October 26, 2006)

444: 7 (At this time, there
8 was a brief recess taken,
9 after which the following
10 proceedings were had:)

Jack E. Jordan (October 26, 2006)

444:15 Q. Sir, we're on the topic of
16 diabetes. Let me just ask you generally, by
17 the fall of 2002, if not before, were you
18 aware as Brand Leader and Marketing Director
19 for Eli Lilly that Zyprexa had a problem in
20 the marketplace concerning diabetes?

Jack E. Jordan (October 26, 2006)

444:23 A. There were -- we were getting
24 feedback that there was confusion in the
445: 1 marketplace around the whole diabetes issue
2 in general.
3 Q. And didn't you in the
4 marketing department take on a campaign or
5 several campaigns to get your message out on
6 what you wanted doctors to think about
7 diabetes?

Jack E. Jordan (October 26, 2006)

445:10 A. Again, there was a lot of
11 confusion in the marketplace around this
12 issue. And so, yes, we did want to
13 disseminate information to help customers
14 understand what the data said.
15
16 (Whereupon, Deposition
17 Exhibit(s) 18 duly received,
18 marked and made a part of the
19 record.)
QUESTIONS BY MR. ALLEN:
20 Q. Sir, I'm going to had you
21 what I've marked as Exhibit 18. We'll get

another exhibit sticker later and we'll mark a clean one as opposed to my copy.
Exhibit 18 says "What do we want our customers to believe?" Do you see that?
What do we want our customers to believe. Do you see that, sir?
A. I do, yes.
Q. And doesn't Exhibit 18 reflect that you wanted your customers to believe that the risk of diabetes is pervasive among the severely mentally ill and there is no safe haven among atypicals?
A. I don't remember --
MR. ALLEN: Here's 18, sir.
THE WITNESS: Okay.
A. I don't remember this document.
Q. Isn't this your handwriting on the back on this note?
A. No, it's not.
Q. Okay. Whose -- we were told -- whose handwriting is that?
A. I don't know.
Q. Nevertheless, Exhibit 18, which we were told came from, I believe, your files, but the files of Eli Lilly, states that we want our customers to believe that the, "Risk of diabetes is pervasive among the severely mentally ill and there's no safe haven among atypicals.
Did I read that correctly?
A. You read that correctly but that's not consistent with what our positioning was.
Q. Okay. You did position your product in regard to diabetes, though, did you not?
A. We did have messages for our customers based on the best data available, yes.
(Whereupon, Deposition Exhibit(s) 17 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. And as reflected in Exhibit 18, the Marketplace Management document, partnership agreement meetings February of 2002. Do you recall that, sir?
THE WITNESS: I'm sorry, are we done with this one, now?
MR. ALLEN: Yes, sir.
QUESTIONS BY MR. ALLEN:
Q. Are you on Exhibit 17, Marketplace Management 2002?
A. I'm sorry. I'm not familiar with this document but --
Q. And for the jury's benefit Marketplace Management is people like Cassandra Mehlman, Ms. Armington, and others, who handled the issues that were presented with the product?

A. At different times we had different people that worked in that --
Q. Right. The message as reflected on Exhibit 17 is under "Issues, Diabetes and Hyperglycemia: It occurs with all agents at comparable rates. Depend on Lilly for diabetes care leadership." Did I read that correctly?
A. I'm sorry, I don't know what page you're on.
Q. Yes, sir.
A. Oh, 2002 Priorities.
Q. 2002 Priorities. Diabetes and Hyperglycemia: Occurs with all agents at comparable rates. Depend on Lilly for diabetes care leadership." Did I read that correctly?
A. You did, yes.
Q. And that is exactly what your positioning statement was for diabetes in relation to Zyprexa, that it occurred with all agents at comparable rates and you could depend on Lilly for diabetes care leadership, correct?
A. The consistent message was that diabetes occurred two to four times the rate in people that struggle with schizophrenia and bipolar disorder and that diabetes occurred at comparable rates among the atypical antipsychotics.
Q. Okay. The consistent message that Eli Lilly gave in regard to Zyprexa and diabetes was that diabetes occurred two to four times more frequently in schizophrenics and diabetes occurred at comparable rates with Zyprexa as it does with other antipsychotics; is that correct?
MR. GOLD: Objection as to form.
A. It was comparable rates with, comparable rates with other atypical antipsychotics, yes.
Q. And wasn't it also comparable rates with other atypical antipsychotics and mood stabilizers? Isn't that what your message was?
A. I don't recall in mood stabilizers. I just remember atypical antipsychotics.
Q. Okay. And that's fine, what you recall right now. I'll show you documents in a minute on comparable rates with antipsychotics and mood stabilizers.
A. Okay.
Q. But if the jury is going to be looking at your testimony and depending upon the Brand Leader and Marketing Manager -- is it manager, Marketing Manager -- director, Director of Marketing to be able to tell them what the consistent message was on Zyprexa and diabetes.
So can you state for this jury, into the camera so they can know what,

in your words, the consistent message was on diabetes and its relationship to Zyprexa?

Jack E. Jordan (October 26, 2006)

A. The -- as the medical group and our clinical folks reviewed all the data, they consistently communicated to me and our group that diabetes occurred in two to four times the rate in people who struggle with schizophrenia and bipolar disorder.

And the second thing was that, was that diabetes occurred at comparable rates among atypical antipsychotics.

Q. Is that the message you remember?

A. Those are the general message points. We did share data, we shared what was in our label with folks, obviously, and we shared that compared to placebo that there was a slight increase in glucose that was statistically significant but not necessarily clinically significant.

Q. Do you recall that in the fall of 2000, Eli Lilly made a Changes Being Effected label, and they sent it in to the FDA and they compared the increase in hyperglycemia with Zyprexa to a placebo; do you recall that?

If you don't that's fine.

A. I don't recall it being in the fall of 2000.

(Whereupon, Deposition Exhibit(s) 20 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. And my question is, as reflected in Exhibit 20, it is the marketing department and Zyprexa Brand Team's desire to get the comparable rates message out across the marketing mix?

A. That was not the totality of the message we were trying to get out.

Q. Does this document reflect that you -- Kathy Armington in Marketplace Management's responsibilities included getting the diabetes comparable rates message out across the marketing mix?

A. The document reflects that; however, if you notice these are bullet point form, so it certainly wasn't the complete, completely what we communicated to customers.

Q. Right. What you communicated, what you did in regard to diabetes, as you did in regard to weight

gain, was attempt to minimize, eliminate, and neutralize diabetes as an issue regarding your product, correct?

Jack E. Jordan (October 26, 2006)

A. No. Our goal was to eliminate confusion in the marketplace around the issue.

Jack E. Jordan (October 26, 2006)

Q. Sir, my question to you was as the marketing, Director of Marketing, as Brand Leader, were you responsible for developing and approving the 2001 marketing plan?

A. My team would have been responsible to put it together and I, ultimately, would have been responsible for it, yes.

(Whereupon, Deposition Exhibit(s) 23 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. And I've marked as Exhibit 23 portions of that marketing plan, including your letter on the marketing plan. You signed this letter, did you not?

Jack E. Jordan (October 26, 2006)

Q. You're familiar with the 2001 marketing plan, aren't you?

A. I am, yes.

Q. Okay. You signed the letter attached to the 2001 marketing plan, did you not?

A. I did, yes.

Q. I will read your letter, portions into the record. Turn to your letter.

"Dear Zyprexa Teammates, Last year, you often heard me say "2000 is the critical year." Now that 2000 is complete, we can be proud that we delivered outstanding results in the critical year -- all caps the, exclamation points. We had many successes, not the least of which was that we fulfilled our promise by selling $1.7 billion of Zyprexa. We launched into new markets, launched a new indication, launched new

formulations, forged new relationships with a broader range of customers, improved our internal alignment, and re-established the Zyprexa Team as truly incredible. Thanks for the outstanding performance in 2000. Exclamation point.

The "blank" patent expiration" -- that would be the Prozac expiration, wouldn't it?

A. I'm assuming.

Q. "The Prozac patent expiration presents Lilly with even greater challenges than anticipated and provides new opportunities for the Zyprexa team. Oddly enough, 2000 may be, all caps, the critical year. But 2001 is different -- it's not just critical -- it's a chance to do the extraordinary. Yes, we face challenges. We have to deliver over $400 million of incremental net sales in the same year that Zeldox is launching, and our current competitors will continue to challenge us."

Did I read that correctly?

458: A. You did, yes.

Q. The title of the or the theme of the 2001 marketing plan was Limitless, isn't that true? Limitless?

A. It was, yes.

Q. That's how you positioned your marketing plan for the year 2001?

A. It was the position for what I would hope that people would have a year of top level performance, yeah.

Q. This is Exhibit 23 we're on, is that right, sir?

MR. GOLD: Yes, sir.

THE WITNESS: Twenty-three.

QUESTIONS BY MR. ALLEN:

Q. If you turn to the last page of this exhibit it contains -- The last page of the exhibit contains a page that says "Brand, the first step. The brand identity defines key meanings we want to have associated with this brand, including the positioning, essence, and product function." Did I read that correctly?

A. You did, yes.

459: Q. And then you have the positions for the various issues. And one of them is weight gain and one of them is diabetes; is that correct?

A. Yes.

Q. So this is the position that Eli Lilly wanted to have associated with its brand on diabetes; is that correct?

MR. FAHEY: Objection to the form.

A. It would have been what the product team and U.S. organization agreed would be the high level position, yes.

Q. Yes. And the high level position of the position on diabetes is at follows, I'm reading: Quote, "Diabetes may

occur in patients taking antipsychotics and/or mood stabilizers. Zyprexa and other agents have a comparable rate of diabetes." Did I read that correctly?

A. You did, yes.

Q. And that's, as you call, the high level position on diabetes in the 2001 marketing plan, right?

460: 1 A. Yes.

2 Q. Now, the reason that you
3 established this position, this high level
4 position of diabetes may occur in patients
5 taking antipsychotics and/or mood
6 stabilizers, Zyprexa and other agents have a
7 comparable rate of diabetes, is because you
8 wanted to reduce the perception that diabetes
9 is linked to Zyprexa and help eliminate this
10 risk from the risk/benefit equation; isn't
11 that true, sir?

Jack E. Jordan (October 26, 2006)

460:14 A. No. The reason was it's
15 because our scientists and medical groups
16 analyzed all the data that we had and that
17 was in the marketplace and communicated to us
18 and to me that the data supported the high
19 level of diabetes in this patient population,
20 as well as that diabetes occurred at
21 comparable rates among these patients.
22 Q. Yes. Wasn't diabetes an
23 issue with your company and Zyprexa?
24 A. There was a lot of confusion
461: 1 in the marketplace, yes.
2 Q. And didn't you have an Issues
3 Management team dealing with the diabetes
4 issue?
5 A. They were responsible for the
6 competition and any issues in the
7 marketplace.
8 (Whereupon, Deposition
9 Exhibit(s) 22 duly received,
10 marked and made a part of the
11 record.)
12 Q. Right. I've handed you
13 Exhibit 22. It's Issues Management Planning
14 Diabetes.
15 You've seen this document
16 before, have you not, sir?
17 A. I don't know.
18 Q. Do you see on the second page
19 "Diabetes. Our Position?" The second page,
20 "Diabetes. Our Position?"
21 A. Yes.
22 Q. And doesn't it say just like
23 the 2001 marketing plan, "our position is
24 stated as "Diabetes slash hyperglycemia may
462: 1 occur in patients taking antipsychotics
2 and/or mood stabilizers, including Zyprexa,
3 at comparable rates with the possible
4 exception of Clozapine." Doesn't it say

that?
A. It does.
Q. And isn't that consistent with the stated position on diabetes as contained in the 2001 marketing plan?
A. Yes.
Q. And what is the reason given for the position to state that diabetes occurs at comparable rates with other antipsychotics or mood stabilizers?

Jack E. Jordan (October 26, 2006)

Q. What is the reason stated in the --

Jack E. Jordan (October 26, 2006)

A. Our medical group, our clinical scientists, took a look at all the data, and consistently looked at all the data, and consistently did additional studies, and told us that it continued to reinforce the reality that diabetes -- and did literature searches, and continued to reinforce that there was a higher level of diabetes in this patient population.

Jack E. Jordan (October 26, 2006)

Q. Sir, do you see the section entitled Rationale For Our Position?
A. I do.
Q. Okay. And your position was previously stated on that same page one bullet point up, two bullet points up, Our Position.
A. Yes.
Q. And your position was "Diabetes may occur in patients taking antipsychotics and/or mood stabilizers including Zyprexa at comparable rates with the possible exception of Clozapine," right?
A. It does say that, yes.
Q. And the rationale for the position as stated in Exhibit 22 is "showing that diabetes is a common occurrence for all antipsychotics and not just Zyprexa will help reduce the perception that diabetes is linked, specifically, to Zyprexa, and in turn, will help to eliminate this risk from the risk/benefit equation." Isn't that what it says?
A. It does say that, yes.
Q. Yes. And so wasn't Eli Lilly trying to reduce the perception that diabetes is, specifically, linked to Zyprexa?

Jack E. Jordan (October 26, 2006)

A. Again, as our medical folks did extensive analysis, we saw diabetes as an issue in this patient population because of its incidence. And as they reviewed the data it was comparable across products.

The concern was if the confusion in the marketplace made choosing a product just on one specific attribute and not see the entire, all the data for all the molecules, we were concerned that physicians might make an inappropriate choice for that specific patient.

Jack E. Jordan (October 26, 2006)

Q. Sir, under Rationale For Your Position on diabetes, right, it's the rationale?

A. Yes.

Q. Doesn't your own document state that "the rationale is to help reduce the perception that diabetes is linked, specifically, to diabetes?"

Jack E. Jordan (October 26, 2006)

A. I've tried to be consistent in my answer and be open with my answer is the rationale was that the data showed that it was comparable rates among all products. And there was confusion in the marketplace around that there wasn't, it wasn't comparable rates. So that was our rationale.

Q. Yes, sir. I'm asking what this document states. Doesn't this document state, Exhibit 22, under Rationale, that your position on diabetes was taken, in part, to help reduce the perception that diabetes is linked, specifically, to Zyprexa?

Jack E. Jordan (October 26, 2006)

Q. Yes or no?

A. The issue is I don't remember seeing this document. I don't know who wrote it. I don't know. I just don't know. This document says some things. I'm trying to communicate what the rationale was.

Q. Yes, sir, but I'm entitled to ask my question.

A. Okay.

Q. And my question to you is doesn't the document state that your

rationale for your company's position on diabetes and Zyprexa was, in part, to reduce the perception that diabetes is linked, specifically, to Zyprexa? Doesn't the document state that?

Jack E. Jordan (October 26, 2006)

469:17 A. It does, but I don't agree with the document.
Q. Okay. And doesn't this document also state that your company's position on diabetes was taken in order to help eliminate this risk from the risk/benefit equation?
A. We tried to eliminate the 470: 1 confusion in the marketplace. I would never support, and you'll see in our detailing pieces, they never support eliminating it from the risk/benefit discussion.

Jack E. Jordan (October 26, 2006)

470:11 Q. Yes, sir. Now, Exhibit 18, which you had previously identified, we talked about, says, "We want our customers to believe that the risk of diabetes is pervasive among the severely mentally ill and there's no safe haven among atypicals," correct?

Jack E. Jordan (October 26, 2006)

470:24 A. Again, I'm not familiar with 471: 1 that phrase "no safe haven among atypicals."
Q. As the Brand Leader and the Marketing Director for Zyprexa was there any available atypical antipsychotic option available to a doctor to prescribe to a patient that had a lower risk of diabetes than Zyprexa?
A. As our medical folks and scientists communicated to me, they communicated consistently, even as more data came in, that there were comparable rates among products.
Q. So my question to you is as the Brand Leader and Marketing Director for Zyprexa in the years that you identified, was it your position that doctors could or could not prescribe a different mood stabilizer and/or atypical antipsychotic with a lower risk of diabetes?

Jack E. Jordan (October 26, 2006)

471:22 A. It was our physicians' and
23 scientists' conviction, based on all the data
24 and all the studies they did, that there were
472: 1 comparable rates among these products.
2 Q. **Did Eli Lilly's Zyprexa have**
3 **a higher rate or incidence of diabetes than**
4 **the other products in the atypical**
5 **antipsychotic market?**
6 A. The most frequently used
7 ones. I don't recall what they said on
8 clozapine. I just -- that was so
9 infrequently used I just don't know.

Jack E. Jordan (October 26, 2006)

472:13 Was there a safer atypical
14 antipsychotic in regard to the issue of
15 diabetes than Zyprexa?

Jack E. Jordan (October 26, 2006)

472:18 A. As our medical group and
19 scientists communicated to me, there were
20 comparable rates among these products. So
21 for any individual patient I wouldn't have
22 the expertise to know. I mean, just --
23 Q. **So did you instruct your**
24 **sales force to go in to doctor's offices and**
473: 1 **if they were asked questions about diabetes**
2 **to tell the doctors that the association with**
3 **Zyprexa and diabetes was comparable to all**
4 **other antipsychotics?**

Jack E. Jordan (October 26, 2006)

473: 7 A. No, that was not the message.
8 Q. **What was the message?**
9 A. The message that I remember
10 was this is an issue in this patient
11 population. Diabetes, given its prevalence,
12 is higher than the general population. And
13 that the studies show that there were
14 comparable rates among these products.
15 Q. **Did you ever learn that the**
16 **largest clinical trial done by Eli Lilly**
17 **submitted with the NDA on Zyprexa showed**
18 **statistically significant elevations in blood**
19 **serum glucose?**
20 A. Yes, and I referred to that
21 earlier.
22 (Whereupon, Deposition
23 Exhibit(s) 19 duly received,
24 marked and made a part of the
474: 1 record.)

Jack E. Jordan (October 26, 2006)

474:13 Q. You've seen this before,
14 haven't you, sir?
15 A. I don't remember it, no.
16 Q. Do you know what type of
17 document this is: Partnering with Customers
18 to Address Diabetes Concerns. Background and
19 Key Message Elements. Approaches to Handling
20 Various Customer Concerns.

Jack E. Jordan (October 26, 2006)

475: 1 THE WITNESS: I actually
2 don't know what it is. I've never
3 seen this format.

Jack E. Jordan (October 26, 2006)

475:12 Q. So Exhibit No. 19 does not
13 appear to you to be a training aid that Eli
14 Lilly provided to its sales force to teach
15 them how to address the diabetes issue? Do
16 you know that or not?

Jack E. Jordan (October 26, 2006)

476: 1 A. I don't know. This is not a
2 format --
3 Q. So you have no knowledge, and
4 if this document was in your file you're
5 telling the jury you have no knowledge of
6 Exhibit 19?

Jack E. Jordan (October 26, 2006)

476:13 A. It just -- I don't remember
14 this format at all.
15 Q. Okay. So you couldn't -- in
16 order -- if you were to answer questions on
17 Exhibit 19 it would be based, at least on
18 your recollection, of the first review you've
19 ever had of this document?
20 A. It would be, yes.
21 Q. Thank you. We won't ask you
22 questions then.
23 (Whereupon, Deposition
24 Exhibit(s) 24 duly received,
477: 1 marked and made a part of the
2 record.)
3 QUESTIONS BY MR. ALLEN:
4 Q. Now Exhibit No. 24, do you
5 recall -- let me first ask you before I hand
6 you 24. Do you remember the Japanese label
7 change?
8 A. I do, yes.

Q. And they put a black box warning on Zyprexa in Japan contraindicating Zyprexa for patients with diabetes?

Jack E. Jordan (October 26, 2006)

A. They did, yes.
Q. Yes. And they also, they being the Japanese regulatory authorities, in the spring of 2002 wasn't it -- April?
A. I don't remember the exact date. I think it was 2002.
Q. Right. The evidence will reflect when it was. But they also, they being the Japanese regulatory authorities, required blood monitoring for Zyprexa patients in order to detect elevations in blood serum glucose; isn't that correct?
A. I don't remember the specific requirements of that black box warning.
Q. Nevertheless, Jack Jordan, as the Brand Leader for Zyprexa in the United States of America positioned Zyprexa to still be indicated for patients who had diabetes, isn't that true?
A. The Japanese label changes, this was done by a different regulatory body, and was certainly communicated that to the U.S. regulatory agency, and to our sales organization and customers.
Q. Yes, sir. My only question to you was not what all those people did, I asked about Jack Jordan. Didn't Jack Jordan, Brand Leader and Marketing Director for Zyprexa, even after the Japanese label change, take the position in the United States that the presence or absence of diabetes should not exclude antipsychotic medications?
A. If I would have said something like that it would have been, I would have looked to our medical group to certainly lead me on any clinical representation, so I just don't remember saying that.

Jack E. Jordan (October 26, 2006)

Q. Questions from Jack Jordan Meeting. That's your meeting, right?
A. I would assume so. I don't --

Jack E. Jordan (October 26, 2006)

Q. Sir, now Exhibit 24, Questions from the Jack Jordan Meeting. The

third page of this exhibit, Patients With Diabetes slash Psychosis. Do you see that?
A. I do.

Jack E. Jordan (October 26, 2006)

Q. My question was: Was Zyprexa indicated for psychosis?
A. That was in the label at launch, and in various countries it was indicated for psychosis.
Q. Okay. And this document Exhibit number --
In the United States was Zyprexa indicated for psychosis?
A. The label at launch was psychosis associated with schizophrenia and then they changed all the products to schizophrenia at one point.
Q. Right. By the year 2000, at least, and we can go back and look, by the year 2000 at least, Zyprexa in the United States was not indicated for psychosis, was it, sir?
A. I don't remember when the change was. I just don't remember the date, so.
Q. Okay. All right, sir.
Nevertheless, Jack Jordan meeting. The documents I have to use are the ones given to me. It says, "Questions From Jack Jordan Meeting." The third page of this exhibit says "Patients with Diabetes slash Psychosis. Positioning Statement." Do you see that, sir?
A. I do.
Q. Yes. And you have told us you were responsible for the, aligning the position of Zyprexa across all the departments within, and aligning the message within Eli Lilly, right?

Jack E. Jordan (October 26, 2006)

A. No. Actually -- well, in the U.S., yes.
Q. Okay, in the U.S., yes. And it says in this Jack Jordan meeting document, Patients with Diabetes slash Psychosis Positioning Statement, "The presence or absence of diabetes should not exclude antipsychotic medication." Is that correct?
A. It's written there, but, again, I've never seen this document and it seems to be a global meeting, and it has a lot of clinical information. I'm assuming there were a number of physicians in there because this is mostly clinical language and not language that would reflect my knowledge

of medicine.
Q. Yes, sir. You, in the marketing department, had to get your information, as you've clearly told us, from your medical department and then align that information out across the channels of communication, right?

Jack E. Jordan (October 26, 2006)

A. In the U.S. Affiliate.
Q. That's correct.
A. We did align our messages, yes.

Jack E. Jordan (October 26, 2006)

Q. My question to you is, sir, in the United States of America when you were the Zyprexa Brand Leader and Director of Marketing, did the presence of diabetes exclude Zyprexa administration?

Jack E. Jordan (October 26, 2006)

A. I don't remember ever having a position on that. That would be a clinician -- that would be a clinician question and not a question that I should be answering.
Q. At least in this document, sir, if it is accurate, Exhibit 24, Jack Jordan Meeting, the document reflects that the presence or absence of diabetes should not exclude AP medication.

Jack E. Jordan (October 26, 2006)

Q. Questions from Jack Jordan Meeting, and it has bullet points, and it has positioning statement.
Who took the marketing positions in the company, the marketing department?
A. The -- it's mostly a word used in marketing, yes.
Q. And the positioning statement used in marketing in Exhibit 24 states, see if I'm reading correctly, "the presence or absence of diabetes should not exclude AP medication."

Jack E. Jordan (October 26, 2006)

487:10 Q. Did I read that correctly,
11 sir?

Jack E. Jordan (October 26, 2006)

487:15 A. I don't remember this
16 meeting. I don't remember that positioning.
17 I don't remember implementing anything
18 through any channel that would be around that
19 positioning. So it's --
20 Q. Sir, I didn't ask you
21 anything about that. I didn't ask you what
22 you remembered, what you didn't remember,
23 what you want to remember, what your lawyer
24 would like to tell you and coach you about, I
488: 1 asked you about this document --

Jack E. Jordan (October 26, 2006)

488: 4 Q. -- Exhibit 24.

Jack E. Jordan (October 26, 2006)

488:18 Q. Exhibit 24, third page,
19 Patients with Diabetes and Psychosis. You
20 see that? Doesn't it say "patients with
21 diabetes slash psychosis?"
22 A. It does, yes.
23 Q. Yes, sir. And does that have
24 a position statement underneath that, yes or
489: 1 no?
2 A. It's a positioning that I've
3 never seen, but yes, it does have one.
4 Q. Yes, sir. It does have a
5 position statement, right?
6 A. It does.
7 Q. Okay. Thank you very much,
8 sir, we'll let the jury review what it says.
9 Do you remember verbatims,
10 sir? Verbatims that you gave your sales
11 force on diabetes?
12 (Whereupon, Deposition
13 Exhibit(s) 21 duly received,
14 marked and made a part of the
15 record.)

Jack E. Jordan (October 26, 2006)

489:21 A. We did have verbatims on a
22 number of issues, yes.
23 Q. Right. Is Exhibit 21 --
24 Verbatims are what, sir?
490: 1 Tell the jury what they are.
2 A. They are when a physician has

a specific question they're the approved reply to those questions.
Q. So Exhibit 21 would be the approved reply to the questions if physicians have them; is that correct?

Jack E. Jordan (October 26, 2006)

490: 9 A. I don't know, I've never -- I don't remember ever seeing that document.

Jack E. Jordan (October 26, 2006)

490:14 Q. Let me put it this way, sir, you don't even need to review it, I'm not going to ask you about it.
You can testify under oath to this jury verbatims are approved responses, right?
A. If they go through the ELMR process they are approved, yes.
Q. What is Project BAD? Do you remember Project BAD?
A. I do, yes.
491: 1 Q. Wasn't the goal of Project BAD to reduce the negative impact of the diabetes issue on the Zyprexa business?
A. The D, as I recall, did stand for diabetes --
Q. Yes, sir.
A. -- and to eliminate confusion around that issue in the marketplace.
Q. What did Project BAD, B-A-D stand for in its entirety - BAD?

Jack E. Jordan (October 26, 2006)

491:18 Q. My question is what did BAD stand for, sir?
A. As I recall, the B was for bipolar, one of the As was for appropriate dose, and there was another A, I don't recall, and then D was diabetes.
Q. Wasn't your company's, Eli
492: 1 Lilly's, goal during Project BAD in August of 2000, that they would define success if they reduced the negative impact of diabetes issue on the Zyprexa business?

Jack E. Jordan (October 26, 2006)

492: 9 A. Again, it was, there was a lot of confusion in the marketplace around diabetes and we wanted to make sure that we cleared up that confusion.

(Whereupon, Deposition Exhibit(s) 25 duly received, marked and made a part of the record.)

QUESTIONS BY MR. ALLEN:

Q. Okay, sir. Exhibit 25 is Project BAD, August the 2nd, 2002. Defining Success. Do you see that, sir, Defining Success, the second category?

A. Yes, I do.

Q. The third bullet point under Defining Success of Project BAD, can you read that out loud to the jury, please?

A. It says, "Reduce negative impact of diabetes issue on the Zyprexa business."

Q. Yes, sir. Now, did you or did you not, in marketing, try to reduce the negative impact the issue of diabetes was having on the Zyprexa business?

A. Insofar as customers were -- there was a lot of confusion in the marketplace and we felt like if we could clear up that confusion through good data, we thought it would have a positive impact on the business, yes.

Q. What was the confusion?

A. A lot of -- I shouldn't say -- we were hearing from the marketplace through market research that they were hearing that Zyprexa was causing diabetes. Even went so far as some customers saying they heard that Zyprexa was going to be pulled from the market because of a diabetes issue.

Q. And did you want to clear up the confusion and tell the doctors in the marketplace that Zyprexa did not cause diabetes?

A. At the risk of being redundant, it was around diabetes is an issue in this patient population because of the increased prevalence, and it was comparable rates among the products.

Q. Sir, when -- what is the Zyprexa business for Eli Lilly? It's selling the product, right?

A. Yeah, part of it, yeah, is sales.

Q. So when it says: Defining Success: "Reduce the negative impact of diabetes issue on the Zyprexa business" in regard to Project BAD, what you were trying to do was to increase the sales of Zyprexa, correct?

MR. GOLD: Objection as to form.

A. The first step was to make

sure that the perception was consistent with the data that our medical folks told us reflected the truth. And, yeah, we felt like if we could get that data into the marketplace and help our customers that it would positively impact Zyprexa's business.

Q. So your goal in Project BAD, as reflected in this exhibit, was to reduce the negative impact on Zyprexa sales by indicating to the marketplace that Zyprexa was as safe as other antipsychotics, that it did not cause diabetes, correct?

Jack E. Jordan (October 26, 2006)

A. Success -- you've made success sound like one issue. There are three issues that were focused on here.

Q. Yes, sir. I'm only asking about the third bullet point.

Jack E. Jordan (October 26, 2006)

A. And, no, the words you used were not consistent with what we're communicating with customers in the marketplace.

Jack E. Jordan (October 26, 2006)

(Whereupon, Deposition Exhibit(s) 26 duly received, marked and made a part of the record.)

Jack E. Jordan (October 26, 2006)

Q. How long did Project BAD last?

A. I don't know.

Q. You were involved in Project BAD, aren't you?

A. It looks like the timeline was it began on August 9th.

Q. 2002.

A. Through December. So it was four months, yes.

Q. Right. You were involved in Project BAD, weren't you, sir?

A. I was, yes.

Jack E. Jordan (October 26, 2006)

498: 4 So I'm going to hand you
5 Exhibit No. 26. You recall placing
6 advertisings in medical journals on Zyprexa?

Jack E. Jordan (October 26, 2006)

498:14 Q. Do you recognize Exhibit 26,
15 sir?
16 A. I do.

Jack E. Jordan (October 26, 2006)

500: 1 Q. Sir, is Exhibit 26 an
2 advertisement paid for by Eli Lilly?

Jack E. Jordan (October 26, 2006)

500: 5 A. I don't know if it was an
6 advertisement, or a sell sheet, or if it was
7 a mailing. I don't know how it was used.
8 Q. Okay. I apologize and thank
9 you for the clarification.
10 We do know that Exhibit 26 is
11 an Eli Lilly document.
12 A. Okay.
13 Q. Isn't it, sir? It says Eli
14 Lilly Answers That Matter?
15 A. It does, yes.

Jack E. Jordan (October 26, 2006)

501:10 Q. Exhibit 26, Lilly Answers
11 That Matter. There is a chart, Comparative
12 incidence and odds ratios of developing
13 diabetes, is there not, sir?
14 A. There is, yes.

Jack E. Jordan (October 26, 2006)

503:15 (At this time, the
16 parties went off the record,
17 after which the following
18 proceedings were had:).
19 THE VIDEOGRAPHER: We are
20 back on the record.

Jack E. Jordan (October 26, 2006)

503:24 I'm referring to Page 4, "Comparative
504: 1 incidence and odds ratios of developing
2 diabetes." Do you see that page?

A. Yeah, I do, yeah.
Q. Okay. On this chart it gives an odds ratio from a Lilly Advanced PCS Database, correct?
A. That is one of four, yes.
Q. Yes, sir. From the Lilly database in Exhibit 26 it gives an odds ratio of developing diabetes on Zyprexa of 1.4 percent, correct?
A. Well, it's, actually, not the Lilly database, it's the PCS database, but yeah.
Q. It says Lilly Advanced PCS Database, right?
A. Yes. It's the PCS database, yes.
Q. It's under Lilly, right?
A. It is, but I'm not sure what that means.
Q. Okay. Under that category Lilly Advanced PCS Database, it gives an odds ratio of developing diabetes of 1.4 percent, right?
A. Yeah, I'm sorry, I don't know if it's an odds ratio or comparative incidence, that's just what's unclear, odds ratio.
Q. Do you see 1.4 percent, sir?
A. I do. I don't know if that's an incidence rate or an odds ratio.

Q. Doesn't it say under Lilly Advanced PCS Database, olanzapine 1.4 percent, yes or no?
A. It does.
Q. And under for risperidone, which is Risperdal, it says 1.9 percent, a greater number, correct?
A. It does, yes.
Q. And for quetiapine, which is Seroquel, it says 1 percent; is that right?
A. It does, yes.
Q. And for typical antipsychotics it says 1.6 percent, which is still a greater number than Zyprexa's 1.4 percent, doesn't it?
A. It does, yes.
Q. And this is a Lilly document. It says Lilly Answers That Matter?
A. Yes, it does, yeah.
Q. And then it also says that this information was printed in the U.S.A. by Eli Lilly and Company in 2002. Do you see that?
A. No, I don't actually.
Q. Here, if you hand it to me I'll highlight it for you to make it real easy.
A. Okay. Thank you.

Q. Printed in the United States of America for Eli Lilly in 2002?
A. Yes.
Q. And I take it that this is a Lilly document. It is sending accurate information to the prescribers and the customers of Eli Lilly.
A. Given it has a OL number it would have had to have gone through the review process with medical, regulatory, legal, et cetera, yeah. So it would have had to have been approved by that process.
Q. Yes, sir.
Now, sir, would you agree with me that --
Well, let's look at another document.
Yes or no, when you were at Eli Lilly when somebody asked does Zyprexa cause diabetes, what was the answer?

Jack E. Jordan (October 26, 2006)

508: A. Without being redundant on -- well, it is being redundant with the answer, it was that diabetes is an issue in this patient population, very complex issue. That it was comparable among products. And as I asked our medical team, the data never proved that Zyprexa caused diabetes.
Q. And wasn't the answer then when people asked does Zyprexa cause diabetes, wasn't the answer no?
A. Actually, it was -- this is a very complex issue, there's no data that proves we cause diabetes, Zyprexa causes diabetes, and we'd share the prevalence, the prevalence and the comparable rates.
Q. That's exactly what the sales reps would say?

Jack E. Jordan (October 26, 2006)

509: A. That's my recollection that was, that was --
Q. The message?
A. The message, yes.
Q. Thank you, sir.
(Whereupon, Deposition Exhibit(s) 27 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Exhibit 27 is an e-mail with an attached letter. The e-mail's dated June 30, 2003, from Michael Bandick. What was Mr. Bandick doing in June of 2003 on Zyprexa?
A. He would have been on the

Global Product Team as a director, marketing director.

Jack E. Jordan (October 26, 2006)

510:11 Q. If Ms. Cassandra Mehlman testified --

Jack E. Jordan (October 26, 2006)

510:15 Q. -- Mr. Bandick, one of his roles was issues management, would that be correct?
A. I believe his title was Marketing Director and he was responsible, part of his responsibility was issues management.
Q. And one of the issues that Zyprexa faced was diabetes.
A. There was confusion in the
511: 1 marketplace, yes.

Jack E. Jordan (October 26, 2006)

511: 8 Q. Was one of the issues that Zyprexa faced the diabetes issue?
A. Yeah. The confusion in the marketplace was making it an issue, yes.
Q. Yes. And you've told us now, you said confusion in the marketplace, and your goal is, what you're telling this jury, was to clear up the confusion and tell the doctors that Zyprexa had comparable rates; is that correct?
A. No, it's not.
Q. Okay. Sir, well, let me see, Exhibit 27, it's an e-mail that you were carbon copied on, from Mike Bandick of June the 30, 2003, attaching a corporate response document final. Do you see that?

Jack E. Jordan (October 26, 2006)

512: 8 Q. Sir, I was asking about the first page of Exhibit 27 is an e-mail attaching a final corporate response document, correct?
A. That is what the e-mail says, yes.
Q. Yes, sir. It's from Mike Bandick. And you received this e-mail, right?
A. I was cc'd on the e-mail, yes.
Q. And you, obviously, then

would have received the attachment, right?
A. Yes, I would have received the attachment.
Q. Is this one of these letters that you were talking about earlier that would go out to the doctors if they asked a question and would give the corporate position of Eli Lilly on an issue?

Jack E. Jordan (October 26, 2006)

A. As I recall the concept of this document, it was we were going to send it to, I think -- the final, at least the final decision I remember is sending it to our customers in general.
Q. Yes, sir. Now, if you look on the attachment, the first page, there's a question: "Does Zyprexa cause diabetes" question mark. Do you see that?
A. I do.
Q. And the answer that was given in this corporate document in the summer of 2003, is "The available data do not establish a causal link between diabetes and Zyprexa or any other antipsychotic for that matter." Did I read that correctly?

Jack E. Jordan (October 26, 2006)

A. You did. The only thing I'm struggling with is this is an unsigned document so I'm not sure this is a final draft. And I don't recall this being sent out while I was on the Zyprexa Brand Team.

Jack E. Jordan (October 26, 2006)

Q. Sir, let me tell you -- do you have a -- some people write a private diary. Do you take a dairy or have a journal?
A. At various times I do, yes.
Q. Yes. And you may not send that journal out but that contains your thoughts, your feelings, your emotions, your intent, does it not?
A. Sometimes, yeah. Sometimes it --
Q. Yes. So the fact that something's not sent out, according to you, does not --
Let me put it this way, does this document, Exhibit 27, at least say Corporate Response Document Final?
A. It does. But it wasn't --
Q. Thank you, sir.

A. I don't know if it was sent out. It just wasn't under the timeline.
Q. We know at least the e-mail calls it a final corporate response document, right?
A. The e-mail does.
Q. Yes, sir. And it came from Mr. Bandick. The last page of this letter: "What are the clinical implications of the diabetes, quote, debate, close quotes, question mark." Did I read that question correctly?
A. It does, yes.
Q. And Eli Lilly's answer, and I need to, I think this is some language that may be difficult for laymen to understand and I'd like you to explain this answer, it says: "Risk for diabetes should be considered among patients with serious mental illness regardless of medication choice. A negative outcome would be the perception that choosing a particular psychotropic will determine diabetes risk."
Did I read that correctly?
A. You did.

Jack E. Jordan (October 26, 2006)

519:19 Q. Sir, what does it mean when it says "a negative outcome would be the perception that choosing a particular psychotropic will determine diabetes risk?" A negative outcome?
520: 1 A. I'm not sure what -- I mean that's clinical language. I'm not sure --
Q. Okay. So you're not sure.
A. -- what that means.
Q. But weren't you responsible, as you say, for aligning the corporate message and isn't that why you got documents such as this?

Jack E. Jordan (October 26, 2006)

520:13 A. It would be aligning the U.S. strategy.
Q. Yes. And you've already told this jury some hours ago that letters were included as part of the marketing mix and marketing messages, right? And you had to approve those, right, to make sure the messages were aligned?

Jack E. Jordan (October 26, 2006)

521: 1 Q. Wasn't that your responsibility?

A. As long as it was -- we were to align with the global positioning. And Dr. Breier was in charge of global so he, obviously, was above me and --

Q. Sir, what is the exhibit number on that exhibit?

A. Twenty-seven.

Q. Sir, as we've, as you've testified earlier, sales of Zyprexa in the United States while you were the Marketing Director and Brand Leader from 1998 through 2002, continually increased; is that correct?

A. They grew every year, yes.

Q. It became a multibillion dollar blockbuster for Eli Lilly?

Jack E. Jordan (October 26, 2006)

522:

Q. Right?

A. It was successful, yes.

Q. Sir, you know the term blockbuster, you used it in your business every single day, didn't you? Blockbuster.

A. Not every single day, no.

Q. Tell the jury what a blockbuster drug is?

A. There are various definitions. Most of the time, as I understand it now, it's any product whose sales is above a billion dollars.

Q. Yes. And my question to you is was Zyprexa a multibillion dollar blockbuster for Eli Lilly?

A. Its sales were above $1 billion, yes.

Jack E. Jordan (October 26, 2006)

523:

Q. Was it a multibillion dollar blockbuster?

Jack E. Jordan (October 26, 2006)

523:

Q. What's the answer, sir?

A. Yes. Worldwide it was.

Q. In the United States it was a multibillion dollar blockbuster, wasn't it?

A. It was successful, yes.

Q. My question to you is: In the United States Zyprexa was a multibillion dollar blockbuster, wasn't it?

Jack E. Jordan (October 26, 2006)

523:15

A. It was successful, yeah.

Q. So was it a multibillion dollar blockbuster in the United States?

Jack E. Jordan (October 26, 2006)

523:20 A. Yes, it was successful.
Q. Okay, sir. Now, your message alignment and your activities as Brand Leader suddenly came to a halt in 2003 and things suddenly weren't going so well, was it?
524: 1 A. No.
Q. That's not true?
A. No.
Q. Isn't it true that your boss, Glyn Parkin, informed you and the other individuals on the Zyprexa Brand Team that our business with Zyprexa, the heart and the soul of this corporation, the engine room, the best mental health product on this planet is faltering, slowing, and the slowdown has been a sudden one?

Jack E. Jordan (October 26, 2006)

524:18 A. I don't recall that, no.
Q. Right. Let me ask you this, though. I asked you that question almost off the top this morning as the evidence will reflect. Isn't it true that Zyprexa was the heart and soul of the corporation and Lilly's engine room?
525: 1 A. I never heard it.
(Whereupon, Deposition Exhibit(s) 28 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Sir, I'll hand you what's been marked Exhibit 28. You know Mr. Glyn Parkin, he was your superior and you've already identified him as such, right?
A. Yes. At various times. I don't know --
Q. In 2003, he was your superior, was he not?
A. For part of the year, yes.
Q. What part of the year?
A. The first five or six months of the year.
Q. Right. Glyn Parkin, your superior first five or six months of 2003 --
By the way this says: "Filed, JEJ Presentations," does it not?
A. It does, yes.
Q. That's you, isn't it?
526: 1 A. Yes.
Q. This was contained within your files, wasn't it?
A. It might have been.

Q. Might have been. Whose handwriting is that?
A. That's my writing so I'm assuming it was.
Q. All right, sir. Do you see where Glyn Parkin says "Neuro Sales Operation" -- these are PowerPoints, are they not?
A. They are.
Q. Isn't this a presentation you gave at the request of Mr. Parkin?
A. I don't know what it -- I don't know.
Q. Well, doesn't your handwriting reflect in the top right-hand corner "File JEJ Presentation?"

Jack E. Jordan (October 26, 2006)

A. I never gave this as a presentation, no.
Q. Well, does that, your handwriting reflect "File," colon, "JEJ Presentation?"
A. It does.
Q. Okay. Glyn Parkin -- Are these PowerPoint presentations?
A. I don't know if it was ever presented but it's a PowerPoint -- yeah, the format's PowerPoint, yes.
Q. Yes. And it says "Glyn Parkin: The Challenge. I need your leadership, the corporation needs your leadership, at this time your leadership is needed in a massive way and in a way that" -- will look back -- "that you will look back on as a defining moment in your leadership careers. All of you." Doesn't it say that?
A. It does, yes.
Q. And doesn't he say, "Glyn Parkin: The Challenge. Our business with Zyprexa, the heart and soul of this corporation, the engine room, the best mental health product on this planet, is faltering, slowing, and the slowdown has been a sudden one."
Bullet point: "Zyprexa details have decreased."
Bullet point: "Zyprexa contacts as perceived by our customers have decreased."
Bullet point: "Zyprexa is losing a disproportionate amount of business to Abilify."
Bullet point: "Zyprexa is capturing new business more slowly."
Bullet point: "Zyprexa's share of the market is decreasing in both private practice and CMHC settings."

Doesn't it say that?
A. It does, yes.
Q. Wasn't a red alert sent out by the company concerning what happened to Zyprexa in 2003?

Jack E. Jordan (October 26, 2006)

530: A. I don't recall a red alert.
Q. You certainly recall a red alert, don't you, sir, you got the red alert?

Jack E. Jordan (October 26, 2006)

530: Q. Didn't you?
A. No, I don't recall.
(Whereupon, Deposition Exhibit(s) 20 duly received, marked and made a part of the record.)
QUESTIONS BY MR. ALLEN:
Q. Sure. Well, here's Exhibit 29.

Exhibit 8
Bruce Kinon, M.D.

Bruce Kinon, M. D. (July 10, 2006)

27:18 Q. Sir, would you please state
19 your full name for the record.
20 A. Bruce Jerome Kinon.

Bruce Kinon, M. D. (July 10, 2006)

27:23 Q. And what's your occupation?
24 A. Physician.
28: 1 Q. And you're a physician
2 employed by Eli Lilly; is that correct?
3 A. That's correct.
4 Q. And what's your job title?
5 A. Medical Fellow II.

Bruce Kinon, M. D. (July 10, 2006)

31:11 Q. You've been with Eli Lilly
12 ever since 1996; is that correct?
13 A. Yes, that's correct.

Bruce Kinon, M. D. (July 10, 2006)

32:24 Q. Okay. Can you describe the
33: 1 positions that you've held at Lilly since
2 joining the company in 1996?
3 A. Since joining Eli Lilly and
4 Company in 1996, I've been a clinical
5 research physician, and I've received several
6 technical promotions over the ensuing years.
7 Q. And what do you mean by
8 "technical promotions?"
9 A. There's a track where
10 physicians receive increased title over a
11 period of time.
12 Q. And does your job title now
13 of Medical Fellow II represent a technical
14 promotion that you referred to?
15 A. Yes, that's correct.
16 Q. And are you still functioning
17 as a clinical research physician?
18 A. Yes.

Bruce Kinon, M. D. (July 10, 2006)

34: 6 Q. Is it fair to say that your
7 job function has stayed pretty much the same
8 at Eli Lilly since 1996?
9 A. Although I'm a clinical
10 research physician generically, as one
11 becomes, receives promotions and title on its
12 technical track that indicates you have more
13 and more positions of seniority, of
14 supervision, of leadership.

Q. Okay. And what is the job description of the clinical research physician?
A. A clinical research physician is the medical component of the medical team. The clinical research physician is one who's involved with the medical management of Lilly clinical trials, the interpretation of data from a medical point of view, and interacting with the medical community.

Bruce Kinon, M. D. (July 10, 2006)

Q. How much of your time has been spent dealing with Zyprexa-related matters since 1996?
A. The majority of my time is involved with Zyprexa.
Q. More than 90 percent?
A. Approximately, 90 percent.
Q. Okay. And can you, please, describe the responsibilities you had regarding Zyprexa since joining the company?
A. Since joining the company, I've been involved as a clinical research physician in the component of Eli Lilly known as the U.S. Affiliate. The U.S. Affiliate is, basically, the U.S. area of the company that is involved with the sales, marketing, and medical management of sites within the United States.

Bruce Kinon, M. D. (July 10, 2006)

Q. During your time at the company can you describe the activities that you engage in in connection with marketing of Zyprexa?
A. I served in the capacity of being a medical consultant to marketing.
Q. And what did that entail?
A. It was the responsibility of medical to present data to marketing, help them with the understanding of the medical data, as well as review the various medical data that was used in promotional pieces, as well as other activities.
Q. And did you draft portions of the marketing pieces with respect to the medical content?
A. At times I would. But generally, that was not my responsibility.

Bruce Kinon, M. D. (July 10, 2006)

Q. If you didn't draft the marketing pieces themselves, was it your

function to review what was drafted and provide comments back to the marketing people?

A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Q. Did you give presentations to various outside audiences about the risks and benefits of Zyprexa?

A. Yes, I did.

Q. And what types of outside audiences would you give presentations to?

A. I would give presentations at scientific congresses, to advisory boards. That was, generally, what I would do.

Q. A scientific congress, what is that?

A. There are many different scientific congresses that meet on a regular basis, such as the American College of Neuropsychopharmacology or the American Psychiatric Association. I would present my data, data that we thought was new, relevant, at those various congresses.

Q. And you also mentioned that you gave presentations to advisory boards. What are those?

A. Advisory boards would be groups of physicians that Eli Lilly would contract as consultants to help us with better understanding of our products.

Q. And did Eli Lilly have advisory boards that they used in connection with Zyprexa?

A. Yes, they did.

Q. And did any of these advisory boards deal with the issue of diabetes or hyperglycemia?

A. At various times that topic certainly did come up.

Bruce Kinon, M. D. (July 10, 2006)

Q. Do you recall that you were a member of what was referred to as the core team on what was referred to as the hyperglycemia/diabetes project?

A. I don't recall that, specifically.

MR. SUGGS: Okay. Let me show you what has been previously marked as Exhibit 4517.

Bruce Kinon, M. D. (July 10, 2006)

Q. For the record, this

Exhibit 4517 is a six-page document. The first page has the heading Hyperglycemia/Diabetes Project. Do you see that?
A. Yes.
Q. And it also makes reference to a core team. Do you see that reference?
A. I'll need a minute to review this document, please.
Q. Okay. Sir, I'm only going to be asking you questions about the first page. So that should shorten things up.
For the record, I'll represent that the database that was provided to us by Lilly in connection with the production of documents indicates this document is dated August 31, 2000, rather than the 9/1/2004 date that's in the lower left-hand corner.
Do you recall being a member of this core team of the hyperglycemia/diabetes project back in 2000?

Bruce Kinon, M. D. (July 10, 2006)

A. When this team was initially developed, I was a member of the medical component of this team.
Q. So you do remember there being a project referred to as the hyperglycemia/diabetes project?
A. I wasn't aware that this was the name of that particular project, but I see that from the title of this document.
Q. And you do recall, though, being a member of the core team on that project?
A. I was a member of the core team initially, and then, basically, I delegated that responsibility to the other medical components.
Q. Okay. The goal of this project, apparently, was to stop hyperglycemia/diabetes from becoming a top ten attribute, do you see that?
A. Although I see on the first sheet, I was unaware that that was the goal of this particular meeting, of this particular group. It's my recollection that

Bruce Kinon, M. D. (July 10, 2006)

Q. Dr. Kinon, the first page of Exhibit 4517 states that -- a list of project goals, does it not?
A. Yes, it does.
Q. And the number one goal there was to stop hyperglycemia and diabetes from becoming a top ten attribute. Isn't that

what's listed there?

Bruce Kinon, M. D. (July 10, 2006)

THE WITNESS: Repeat the question, please.
QUESTIONS BY MR. SUGGS:
Q. The very first goal that's listed for this group was to stop hyperglycemia/diabetes from becoming a top ten attribute; isn't that correct?
A. As far as I understand that was not the goal of this group. I didn't write this document. This document was apparently written by Suni Keeling, whose name is on the bottom of it.

Bruce Kinon, M. D. (July 10, 2006)

Q. Suni Keeling was in the marketing department, correct?
A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Q. And at least, according to this document, the number one goal of this project was to stop hyperglycemia and diabetes from becoming a top ten attribute; isn't that correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I'm not able to answer that. I did not write this document.
Q. You can look at the document and that's what's listed there as the first goal, isn't it?
A. If I'm to read the document in front of me the title is hyperglycemia/diabetes project. The second line says: On the forefront of managing the issue. The third line says: Project goals. And the fourth line says: Stop H/D from becoming a top ten attribute.

Bruce Kinon, M. D. (July 10, 2006)

Q. Sir, would you agree with me that this goal of the hyperglycemia/diabetes project of stopping hyperglycemia and diabetes from becoming a top ten attribute had nothing, whatsoever, to do with the

manipulation or change the physical properties of the drug itself but rather, had to do with what the company wanted doctors to think about the drug?

Bruce Kinon, M. D. (July 10, 2006)

A. It's my understanding that the point of this group was to better understand the hyperglycemia issue from a medical point of view and to provide the answers that doctors needed through the marketing channel if need be.

Q. Sir, isn't it just a plain fact that the company didn't want doctors to think that hyperglycemia and diabetes were linked with the use of Zyprexa?

A. No, not at all.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: Let me hand you what's been previously marked as Exhibit 8905.

Bruce Kinon, M. D. (July 10, 2006)

Q. For the record, this is a two-page e-mail from Paula Trzepacz -- am I pronouncing her name correctly?

A. Trzepacz.

Q. Trzepacz. To a number of individuals.

Bruce Kinon, M. D. (July 10, 2006)

Q. Including Dr. Kinon; is that correct?

A. I'll have to review the document.

Q. You've reviewed the document, haven't you, sir?

A. Yes, I have.

Q. And this e-mail from Dr. Paula Trzepacz went to both people in the medical department and in the marketing department, correct?

A. That's correct.

Q. And Dr. Trzepacz was who you reported to, correct?

A. That's correct.

Q. And what was her job title again?

A. Medical director.

Q. Medical director. And in

this e-mail she's talk about redistributing the medical workload that, in her words, involve important issues that affect more than one Zyprexa silo. Do you see that language?

A. Yes.

Q. And what's a Zyprexa silo?

A. What she's referring to is, for example, the schizophrenia group would be one silo, the bipolar group would be another silo.

Bruce Kinon, M. D. (July 10, 2006)

Q. Okay. In any event, in her second paragraph in about the middle of it Dr. Trzepacz says, quote, "The primary person responsible will be held accountable to drive the medical marketing strategy from the medical side." Do you see that?

A. Yes, I do.

Q. Okay. And then her plan was to have you be the number one guy on the issue of weight gain with Dr. Baker and Dr. Hay being the No. 2s and No. 3s, correct?

A. Yes.

Q. And her plan also entailed you, pardon me, Dr. Baker being the No. 1 guy on glucose issues, with you being the number two man, and Dr. Kennedy being the number three man; is that correct?

A. That's correct.

Q. And was that plan, in fact, carried out?

A. Yes, it was.

Q. So you were the number one guy dealing about the issue of weight gain, correct?

A. I was the number one physician in the U.S. Affiliate Zyprexa team.

Q. And you were the number two guy dealing with issues of glucose, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Q. Okay. Is it fair to say, though, that you were very actively involved in both the weight gain and the glucose issues with respect to Zyprexa?

Bruce Kinon, M. D. (July 10, 2006)

66:14 A. My pre inant effort was in
15 the weight gain area.
16 Q. Okay. But were you also
17 involved in the glucose area?
18 A. To some degree.

Bruce Kinon, M. D. (July 10, 2006)

67:22 Q. When you got this e-mail from
23 Dr. Trzepacz, what did you understand her to
24 mean when she told you that you were going to
68: 1 be held accountable to drive the medical
2 marketing strategy from the medical side with
3 respect to weight gain?
4 A. I was led to believe, or my
5 understanding of this was, that as part of
6 our evaluation in terms of what are the
7 deliverables, what type of things that we
8 would accomplish in terms of our clinical
9 plan, that we need to clearly define a
10 target, and then try to develop that target.
11 So, for instance, if a
12 particular type of weight gain analysis was
13 our target, we should complete those results
14 and distribute them amongst the team.
15 Q. Well, and your work product
16 consisted not just of statistical or data
17 analysis, but also write-ups, descriptions of
18 the company's position with respect to weight
19 gain; is that correct?
20 A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

69:16 Q. Do you recall that one of
17 your key messages about weight gain was no
18 significant weight gain over the long-term?

Bruce Kinon, M. D. (July 10, 2006)

69:21 A. No, I have no recollection of
22 that message at all.
23 Q. Do you recall that another of
24 your key messages was "no association between
70: 1 weight gain with olanzapine and hyperglycemia
2 and diabetes?"
3 A. I don't, specifically, recall
4 that at all.
5 MR. SUGGS: Let me show you
6 what's been previously marked as
7 Exhibit 1213.

Bruce Kinon, M. D. (July 10, 2006)

70:13 Q. Sir, I'm going to represent

that the database that was produced to us by Lilly in conjunction with the production of documents states that this particular document was produced from your files. Do you have any basis to dispute that?

Bruce Kinon, M. D. (July 10, 2006)

THE WITNESS: I have to review the document, please.
Q. Do you recall my question?
A. No, I don't.

Bruce Kinon, M. D. (July 10, 2006)

Q. Okay. As I mentioned before, the database that was provided to us by Lilly states that this document was produced to us from your files. Do you have any basis to dispute that?
A. I've never seen this document before.
Q. Okay. So are you denying that this document came from your files as represented to us by Eli Lilly?

Bruce Kinon, M. D. (July 10, 2006)

A. I have no basis to deny or not. I just have never seen this document before.
Q. Okay. The title of the document is: Olanzapine Issues Surrounding Weight Gain, Diabetes and Hyperglycemia. Key Messages. Is that correct?
A. That's correct.
Q. And then about midway through the page there's a heading that says: No Significant Weight Gain Over Long-term. Do you see that language?
A. I see that on this document before me.
Q. And that was, in fact, one of the key messages that you wanted doctors to believe about Zyprexa, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. That is certainly incorrect.

Bruce Kinon, M. D. (July 10, 2006)

Q. So you're denying that one of

your key messages for l sicians was that there was no significant weight gain over the long-term?

Bruce Kinon, M. D. (July 10, 2006)

73: Q. Is that correct?
A. I deny that that was a statement.
Q. Okay. And then the one right below that says, quote, "No association between weight gain with olanzapine and hyperglycemia and diabetes." Do you see that language?
A. I do see that.
Q. And that was another key message that the company wanted doctors to believe; isn't that correct?
A. I have no idea whether these were key messages or not. As far as I could

Bruce Kinon, M. D. (July 10, 2006)

74: Q. Directing your attention to the following page. There's a bolded heading about a third of the way down that says: Explain the Data Results and Reemphasize Its Importance. Do you see that?
A. Yes, I do.
Q. And then it says, "In this study, 70 percent of patients treated with olanzapine either lost weight, remained stable, or gained less than or equal to 22 pounds over the long-term." Do you see that language?
A. Yes.
Q. And do you know what study that's referring to?
A. I don't know, specifically. This may be, this may be referring to one of my studies. But I certainly did not write these conclusions.
Q. Did you do a study in which you found that 70 percent of patients treated with olanzapine either lost weight, remained stable, or gained less than or equal to 22 pounds over the long-term?
75: A. We published on long-term weight gain with Zyprexa. We never presented the data this way at all in the article.

Bruce Kinon, M. D. (July 10, 2006)

75: Q. Well, did your study find that 70 percent of the patients treated with Zyprexa either lost weight, remained stable or gained less than or equal to 22 pounds

over the long-term?
A. I'm not aware of that calculation. How that was arrived at.
Q. So is that language describing the results from the study false?
A. In my opinion that would be false.

Bruce Kinon, M. D. (July 10, 2006)

Q. Did the data that the company had show that 30 percent of the Zyprexa users gained more than 22 pounds over the long-term?
A. The data would be consistent with that.
Q. Okay. And if, in fact, 70 percent of -- and by the way, there were reports of people gaining like 80, 90 pounds of weight while they were using the drug; is that correct?
A. There were some reports, yes.
Q. Okay. And about 30 percent of them gained more than 22 pounds, correct, over the long-term?
A. It might have been that.
Q. And 22 pounds of weight gain is a lot of weight gain, isn't it?
MR. WASSON: Objection to the form.
A. That would be considered a significant amount of weight.
Q. Clinically significant, correct?
A. Depends upon the amount of time.
Q. Well, it also depends on the weight of the individual, right?
A. That's correct.
Q. Because don't doctors, typically think if you have weight gain more than 7 percent of your body weight that is clinically significant?
A. That's correct.
Q. So if you had people gaining more than 22 pounds on the drug, for anybody who weighed less than 300 pounds that would be clinically significant, correct?
A. Seven percent or greater increase in body weight would be clinically significant.

Bruce Kinon, M. D. (July 10, 2006)

Q. Okay. When it says here that 70 percent of patients treated with olanzapine either lost weight, remained stable, or gained less than or equal to 22 pounds, do you recall from your studies

how many people gained, say, 15 to 20 pounds of weight while on the drug?
A. The long-term weight gain on olanzapine that we published on over a period of one to three years, the mean weight gain is, approximately, 15 pounds or 6 to 7 kilograms.
Q. So that means if you look at all the people who take the drug, the average weight gain for everybody is, when you consider all of those folks, is 15 pounds, right?

Bruce Kinon, M. D. (July 10, 2006)

80: Q. So what you're saying is that the studies that were done by you showed that if you looked at all the people who took the Zyprexa in your study that the average weight gain for the entire group was 15 pounds, correct?
A. The average weight gain over a long period of time, one to three years, would be about 15 pounds, that's correct.

Bruce Kinon, M. D. (July 10, 2006)

81:22 Q. Okay. So bottom line what your studies were showing is that on average people were going to have clinically
82: 1 significant weight gain with Zyprexa, correct?
A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

82:19 Q. Now if you could direct your attention back to Exhibit 1213, the last bolded item there says Summarize and Disassociate Olanzapine and Weight Gain From Diabetes and Hyperglycemia. Do you see that on there, sir?
83: 1 A. Yes, I do.
Q. Now, that was a tough goal to accomplish, wasn't it, sir?

Bruce Kinon, M. D. (July 10, 2006)

83: 9 Q. The goal of disassociating olanzapine and weight gain from diabetes and hyperglycemia was a tough goal to accomplish, wasn't it, sir?
A. I don't know, specifically, what is meant by this statement in this particular document. I did not write it and

I'm not aware of it.
Q. Sir, weight gain, trying to say that weight gain is not linked with diabetes is flying in the face of accepted medical principles, is it not, sir?
MR. WASSON: Objection to the form.
A. If one were, tried to remove or distance weight gain from diabetes as a risk factor, yes, that would be.
Q. Because it's generally accepted that if you gain weight you're more likely to develop diabetes, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. Weight gain is known to be a risk factor for the development of diabetes.
Q. And, in fact, in 1995, before Zyprexa even went on the market, a group of outside consultants warned Lilly that clinically significant weight gain is a risk factor for developing other medical conditions including type two diabetes. Were you aware of that, sir?

Bruce Kinon, M. D. (July 10, 2006)

A. I was not aware of that.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: Okay. Let me show you what's been previously marked as Exhibit 1586.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record this is a document entitled Executive Summary, The Third United States Schizophrenia Advisory Panel Meeting dated December 10, 1995.
Apparently, the meeting was held in San Juan, Puerto Rico.

Bruce Kinon, M. D. (July 10, 2006)

Q. Dr. Kinon, can I direct your attention, please, sir, to Page 2. In the second paragraph it starts off by saying, "the meeting began with first-time presentation of efficacy and safety results

from HGAJ, the pivotal ase 3 trial by Charles Beasley Jr." Do you see that language, sir?
A. Yes, I do.
Q. And are you familiar with a study that was known within Lilly as HGAJ?
A. Yes.
Q. And what was that?
A. Study HGAJ was a randomized double-blind clinical trial comparing Zyprexa, olanzapine, versus haloperidol.
Q. And haloperidol is another antipsychotic drug; is that correct?
A. That's correct.
Q. Okay. And haloperidol was, I believe, what was often referred to as a first generation antipsychotic; is that correct?
A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Q. Thank you. Now if I could direct your attention to Page 8. At the end of the first full paragraph on that page it states that, "Patients who remained on olanzapine for 12 months gained an average of 24 pounds at the end of the 24-month" -- pardon me -- "at the end of the 12 months." Did I read that correctly?
A. Yes.

Bruce Kinon, M. D. (July 10, 2006)

Q. Okay. Were you -- do you recall being informed that the studies that had been done before Zyprexa went on the market found that the average weight gain for people who were on the drug for at least a year was about 24 pounds on average?
A. No. We clearly state in our

Bruce Kinon, M. D. (July 10, 2006)

Q. So is it your testimony as you sit here today that up until now you were not aware of this statement that patients who remained on olanzapine for 12 months gained an average of 24 pounds at the end of 12 months?
A. It's something that I'm not familiar with now, no.

Bruce Kinon, M. D. (July 10, 2006)

98: 3 Q. Dr. Kin[illegible], would you agree
4 with me that the Zyprexa package labeling did
5 not state to doctors that if they had their
6 patients on Zyprexa for 12 months that on
7 average they could expect their patients to
8 gain 24 pounds of weight?
9 A. That specific language is not
10 in the label.
11 Q. Thank you.
12 If I could direct your
13 attention back to Page 8 of Exhibit 1586. In
14 the middle of the page there is some
15 italicized language. It states, quote,
16 Several advisors commented on the association
17 of olanzapine with weight gain and encouraged
18 Lilly to subject the data to a full analysis.
19 Clinically significant weight gain is a risk
20 factor for other conditions such as increased
21 blood pressure, increased cholesterol and
22 type two diabetes. The advisors also noted
23 that Lilly has an opportunity to develop
24 strategies to help manage the weight gain."
99: 1 Do you see that language?
2 A. Yes, I do.

Bruce Kinon, M. D. (July 10, 2006)

99:19 company -- well, let's take it this way. At
20 least by 1996 were you, through the virtue of
21 your training and experience or your reading
22 in the field or whatever, were you aware that
23 clinically significant weight gain is a risk
24 factor for other conditions, such as
100: 1 increased blood pressure, increased
2 cholesterol, and type two diabetes?
3 A. Yes, I was aware of that.

Bruce Kinon, M. D. (July 10, 2006)

101:23 simple. Did anyone tell you back in 1995
24 analysis was done which showed a
102: 1 statistically significant increased incidence
2 of high glucose in Lilly's own clinical
3 trials? Yes or no?
4 A. I'm not aware that anyone,
5 specifically, told me of that analysis that
6 you're referring to.
7 MR. SUGGS: Okay. I'm going
8 to show you what's been previously
9 marked as Exhibit 1605.

Bruce Kinon, M. D. (July 10, 2006)

102:14 MR. SUGGS: For the record
15 this is a computer printout dated
16 June 19, 1995 and it's entitled
17 Treatment Emergent Abnormal High or

Low Laborato[illegible] Values at Any Time
FID-MC-HGAJ Acute Phase.
Sir, do you recall that the HGAJ study that we were referring to before, I believe you said that was the largest clinical study that was done with respect to Zyprexa?
A. Yes, I am.
Q. And do you recall that it had an acute phase?
A. Yes.
Q. And do you recall, I think you testified before that study involved a comparison between the use of olanzapine or Zyprexa and haloperidol; is that correct?
A. That's correct.
Q. Okay. If I could direct your attention to Page 11. At about the middle of the page are the results of nonfasting glucose, do you see that?
A. Yes, I do.
Q. And can you explain to the jury what nonfasting glucose testing is?
A. Nonfasting glucose is what we call random glucose testing. The patient has not fasted for eight hours prior to obtaining a blood sample for the determination of glucose or sugar.
Q. Okay. And in this particular computer analysis the two categories there are low and high, correct?
A. That's correct.
Q. And for the high it shows that there was a statically significant increased incidence of high glucose in the olanzapine or Zyprexa users, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. It would appear from this analysis that there was a higher incidence of the high glucose values versus the haloperidol group.
Q. And that it was statistically significant, correct?

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A. That's correct.
Q. Okay. And what it found was that the incidence of high glucose in Zyprexa users was more than twice that in the haloperidol group, correct?
A. Based upon this particular analysis, which is looking at a random blood value at any time over the course of many, many, days. This is one value.

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110:22 sir. All the -- is it fair to say, sir, that
23 all the clinical trials that your company did
24 with respect to Zyprexa to get it approved to
111: 1 market here in the United States, to the
2 extent it looked at glucose levels at all, it
3 did so in terms of random glucose testing?
4 A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

115:20 Q. Sir, do you recall that when
21 Lilly brought Zyprexa to market in 1996 it
22 made false and misleading statements about
23 weight gain?

Bruce Kinon, M. D. (July 10, 2006)

116: 2 A. I'm not aware that Eli Lilly
3 ever made any false misleading statements
4 about weight gain.
5 MR. SUGGS: Let me show you
6 what's been previously marked as
7 Plaintiff's Exhibit No. 1169.

Bruce Kinon, M. D. (July 10, 2006)

116:12 MR. SUGGS: For the record,
13 this is a letter from the FDA to
14 Charles R. Perry at Eli Lilly dated
15 November 14, 1996. And I'll
16 represent on the record that the
17 database that was provided to us by
18 Lilly with respect to this document
19 says that it was produced from the
20 files of Dr. Kinon.

Bruce Kinon, M. D. (July 10, 2006)

121: 1 Q. Dr. Kinon, I'd like to direct
2 your attention to Exhibit 1169. The first
3 paragraph states quote, "This concerns a
4 number of labeling pieces for Zyprexa
5 identified as a multi-page detail aid,
6 OL-0026 Stat-Grams identified as OL-0077 and
7 OL-0078; a letter to the California
8 Department of Health Sciences assumed to be
9 an example of other letters to other states
10 with an attached backgrounder; and a John Q
11 Public letter, all submitted as required with
12 a form FDA 2253 and also found during normal
13 surveillance activities. This also concerns
14 other promotional activities such as, an
15 interactive teleconference held on or about

October 2, 1996. The Division of Drug Marketing, Advertising and Communications, DDMAC, considers these promotional labeling pieces, and promotional activities to be false or misleading, and in violation of the Federal Food, Drug, and Cosmetic Act." Do you see that language, sir?

A. Yes.

Bruce Kinon, M. D. (July 10, 2006)

Q. Now if I could direct your attention to Page 4 at the top, there's reference made to an interactive teleconference held on or about October 2, 1996, by Gary D. Tollefson, Vice-President of Lilly Research Laboratories. Do you see that?

A. Yes, I do.

Q. And who is Dr. Gary D. Tollefson? Did you report to him in any way back in October 1996?

A. No, I did not.

Q. Was he a senior person there in the company at that time?

A. Yes. He was a vice-president for Lilly Research Laboratories.

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Q. His position in the company, how high up in the company was he?

A. He would be considered senior management.

Q. If I could direct your attention to the following page it states quote, "When asked a question about weight gain, Dr. Tollefson's response misleadingly turned an adverse event into a therapeutic benefit. He states, so we went back and analyzed the data and saw that the vast majority of weight gain reported initially as an adverse event, in fact, was weight gain occurring in patients who had baseline, before starting treatment, had been below their ideal body weight."

And the following language is bolded, it says, "So we really look at this, with the majority of patients, as being part of a therapeutic recovery rather than an adverse event. And that data, I think is fairly compelling, because it was included in our label."

Did I read that correctly? Doctor?

A. I'm reading it.

Q. My question was: Did I read that correctly?

A. Yes, you did.

Q. Okay. And then the FDA goes on to state quote, "The information on weight gain was indeed included in the approved labeling, but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading.

Now, sir, does that refresh your recollection that when Lilly brought Zyprexa to market in 1996 it made false and misleading statements about weight gain?

Bruce Kinon, M. D. (July 10, 2006)

125:24 A. I was not aware that Lilly
126: 1 ever made any false and misleading statements
2 about weight gain.

Bruce Kinon, M. D. (July 10, 2006)

127: 4 Q. Sir, do you deny that,
5 thereafter, Lilly continued to make
6 statements that weight gain was beneficial in
7 some patients?
8 A. No. We had made those
9 statements.
10 Q. Okay. And according to the
11 FDA, to make statements like that with
12 reference to weight gain, that it was a
13 benefit, or a part of the therapeutic
14 recovery, was false and misleading according
15 to the FDA, correct?
16 A. According to the FDA in this
17 document, yes.

Bruce Kinon, M. D. (July 10, 2006)

129:18 MR. SUGGS: Let me show you
19 what's been previously marked as
20 Exhibit 6890.

Bruce Kinon, M. D. (July 10, 2006)

130: 2 MR. SUGGS: For the record,
3 this is a document dated December 9,
4 1998, and refers to a Zyprexa
5 Medical Marketing Meeting Agenda for
6 a meeting on December 9, 1998.

Bruce Kinon, M. D. (July 10, 2006)

131:21 Q. Okay. And in about the
22 middle of the page of this particular agenda
23 from December of 1998 it says: Weight gain
24 and link to diabetes question mark. What
132: 1 does the data say and what is our action
2 plan, question mark.
3 Do you see that?
4 A. Yes, I see that.
5 Q. And was your team, your
6 medical marketing team also engaged in this
7 issue of whether or not there was a link
8 between weight gain and diabetes with
9 Zyprexa?
10 A. Yes, we were.
11 Q. Okay. And you see that there
12 are handwritten notes on this document?
13 A. Yes, I do.
14 Q. Do you recognize the
15 handwriting?
16 A. No, I don't.
17 Q. The very bottom handwritten
18 note says: "Weight gain plus genetic
19 vulnerability lead to hyperglycemia." Do you
20 see that language?
21 A. Yes, I do.
22 Q. And that formula, if you
23 will, is a generally-accepted scientific view

Bruce Kinon, M. D. (July 10, 2006)

132:24 then; is that correct?

Bruce Kinon, M. D. (July 10, 2006)

133: 3 A. As far as I understand it
4 weight gain is believed to be a risk factor
5 for hyperglycemia in patients with a genetic
6 predisposition.
7 Q. So you would agree with that
8 statement "weight gain plus genetic
9 vulnerability lead to hyperglycemia,"
10 correct?

Bruce Kinon, M. D. (July 10, 2006)

133:13 A. I would agree to it in terms
14 of general medical knowledge. I have no idea
15 what this person is referring to,
16 specifically.
17 Q. Would you say, sir, I realize
18 this is calling for an opinion on your part,
19 but based on the discussions you had with
20 people back in Lilly at or around this time
21 back in December of 1998, would it be your
22 belief and understanding that it was well
23 understood by the people that you dealt with

in the medical marketing area, that weight gain and genetic vulnerability lead to hyperglycemia?

Bruce Kinon, M. D. (July 10, 2006)

A. I don't know what other people believed. It's common medical knowledge that weight gain or excessive weight gain is a risk factor for diabetes. This could be a vulnerability based upon patient's family history and also many other factors.

Q. But, sir, you wanted to, you personally wanted to avoid linking weight gain and diabetes or hyperglycemia; isn't that correct?

Bruce Kinon, M. D. (July 10, 2006)

A. That's definitely not the case at all.

MR. SUGGS: I'm going to show you what's been previously marked as Exhibit 1215.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record Exhibit 1215 is an e-mail chain starting off with an e-mail from Peter Clark on November 30, 1998, at 9:26 a.m. and ending up with an e-mail from Robert Schmid on December 1, 1998.

QUESTIONS BY MR. SUGGS:

Q. You've reviewed the document?

A. Yes, I have.

Q. Okay. Let's start off talking about the first e-mail, at least chronologically, which was Peter Clark's e-mail to Jack Jordan, yourself, John R. Richard, with copies to Jeffrey Ramsey, Robert Schmid regarding the Wishing/Goldstein articles.

A. Yes.

Q. Am I correct that Peter Clark was in the marketing department?

A. He was a marketing associate, I believe, on the product team.

Q. And Jack Jordan was also in marketing?

A. Yes, he was.

Q. And was John Richards in marketing?

A. Yes.

Q. And Jeffrey Ramsey, was he in

marketing?
A. I believe he was in with statistics.
Q. And Robert Schmid, who is he with?
A. Marketing on the product team.
Q. Okay. So you're the only medical guy, apparently, who's being copied on this e-mail?
A. Apparently.
Q. Okay. And there are references to articles by Wishing and Goldstein. Do you see that reference, sir?
A. Yes.
Q. And apparently, there had been an article published by Wishing in the Society of Biological Psychiatry that linked hyperglycemia with Zyprexa use, correct?

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THE WITNESS: Specifically, what are you asking?
Q. Well, just read on to the e-mail it states, quote, "Rob has asked me to summarize the points we would raise in response to the recent reports of hyperglycemia linked with Zyprexa use raised in the Wishing, published in the Society of Biological Psychiatry, and Goldstein, soon to be published in Psychosomatics Journal, articles." Do you see that language, sir?
A. I see that language, yes.
Q. So the marketing department was aware that there were these articles this that were either published or about to be published that were linking hyperglycemia with the use of Zyprexa, correct? Isn't that what it indicates?
A. That's what -- these articles do not link Zyprexa with diabetes. They're based on case reports of a very small number of patients. This is the opinion of Peter Clark.
Q. Okay. Anyway, in any event, the marketing department was concerned about these reports that were being published and wanted to know what the response was going to be, correct?
A. As reflected by Peter Clark's e-mail I would say yes.
Q. Okay. And then in the rest of the text of the e-mail contains what they were planning on saying at that point in time, correct?
A. That's correct.
Q. Okay. And he's got that set out in various bullet points there, correct?
A. That's correct.
Q. And if you drop down to the

bullet points, the second and third bullet points say: Use of antipsychotics may result in weight gain. And then the bullet point below that says: Patients who gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes. Correct?

A. That's what the bullet points say, that's correct.

Q. And that chain of weight gain, developing insulin resistance which may lead to hyperglycemia, and which may then go on to diabetes, that chain that's being talked about there was the type of medical chain, if you will, that was generally accepted in the field?

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Q. Correct? That if you gain weight that can lead to, ultimately, diabetes, correct?

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A. I don't know, specifically, what Peter Clark was referring to but in general medical knowledge weight gain can lead, in some patients, into insulin resistance, which in some patients may eventually go on to be diabetes.

Q. Okay. After you got this e-mail back from those guys you said, you wrote back to Peter Clark and copied the others and you said, quote, "Thank you for advising me of the response to the hyperglycemia issue. I do have concerns regarding making any connections between olanzapine-induced weight gain and hyperglycemia. Therefore, in my opinion, I would not include your following statement, quote, Patients who gain weight may develop insulin resistance which may lead to hyperglycemia and diabetes, end quote, correct?

A. That's correct.

Q. Okay. And so then they wrote back, pardon me, not they, Robert Schmid wrote back and said to you: The statement that Peter outlined is the result of a discussion with Charles Beasley and the first attempt to establish what the scientific information is concerning diabetes/hyperglycemia.

Did I read that correctly?

A. Yes.

Q. And did you have any interaction with Charles Beasley about whether or not that language that you suggested should be dropped out should, in

fact, be dropped out?
A. I don't recall, specifically, whether I did or not.

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Let me ask you this, were you ever informed, do you recall being informed in early 2000 there was a recommendation that the Zyprexa level be changed because yet another analysis of the company's clinical trials showed that the incidence of treatment emergent hyperglycemia was about three and-a-half times higher in the Zyprexa group as compared to the group that did not receive Zyprexa?

Bruce Kinon, M. D. (July 10, 2006)

A. I'm not, specifically, aware of that analysis.
MR. SUGGS: Let me know show you what's been previously marked as Plaintiff's Exhibit 990.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record this is a seven-page document. The first page bears the legend Confidential. And it says: Do not forward. To be distributed only by global operations labeling department. Attachment E. If I could direct your attention to the second page.
There is a title on this second page which states: Olanzapine Labeling Change On Hyperglycemia for 2/21/2000 GPLC Meeting.
Do you see that reference, sir?
A. Yes.
Q. **And what was the GPLC?**
A. The Global Operations Labeling Committee. I think, the Global Product Labeling Committee.
Q. **Okay. And were you a member of that committee?**
A. No.
Q. **Do you know who was?**
A. I don't know, specifically, at that time. Dr. Tim Fransen may have been and Dr. Alan Weinstein might have been. I don't know, specifically, who the members were.

Q. Do you know the departments who were part of that group?
A. I believe that it is a committee that's comprised of representatives from regulatory, legal, and medical.
Q. Okay. If you could drop your attention down to the top of that first box
153: 1 that's on the page that says: Proposal of
2 the product team and PHV, do you see that?
3 A. Yes.
4 Q. Is it your understanding that
5 PHV refers to pharmacovigilance?
6 A. Yes.
7 Q. And what was the product
8 team?
9 A. The product team is the
10 global Zyprexa team.
11 Q. Okay. As apart from the U.S.
12 Affiliate team?
13 A. That's correct.
14 Q. So this would have been, the
15 product team would have been the team which
16 included Dr. Beasley that we talked about
17 before, correct?
18 A. I would think so.
19 Q. And in fact, if you looked at
20 the last page, this is, this document was,
21 apparently, reviewed by Charles Beasley, a
22 global product physician, and also by, from
23 pharmacovigilance Dr. Kenneth Kwong, do you
24 see that, sir?
154: 1 A. I see that.
2 Q. Did you have any dealings
3 with Dr. Kenneth Kwong?
4 A. Yes, I did.
5 Q. Regarding Zyprexa?
6 A. Yes.
7 Q. Okay. If I could direct your
8 attention back again to Page 2. In the first
9 box at the top there it states, quote,
10 Spontaneous reporting rate for hyperglycemia
11 less than .01 percent is currently in the
12 core data sheet as a core adverse event in
13 the adverse drug table. The proposal is to
14 add the following information regarding
15 hyperglycemia to the core data sheet in C.8.
16 Then it has the new
17 statement: Random glucose, 160 milligrams
18 per deciliter in patients with baseline
19 random glucose, 140 deciliter, has been
20 occasionally seen in clinical trials. Do you
21 see that language, sir?
22 A. Yes.
23 Q. And then they talked about
24 making a revision of the frequency of
155: 1 hyperglycemia in the adverse reaction chart,
2 correct?
3 A. Yes.
4 Q. Okay. And then below that
5 there's a box that says: How has this
6 proposal arisen? Do you see where I'm at?
7 A. Yes.
8 Q. And the language in that box

states, quote, Recent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment-emergent hyperglycemia in olanzapine group 3.6 percent was higher than in the placebo group 1.05 percent. For common events, incidences from clinical trials provide more meaningful information." Do you see that language?

A. Yes.

Q. At least according to the data that is presented in that little box there, what that's saying, let me back up for a second. What does the phrase "treatment emergent hyperglycemia" mean to you apart from this document? Just, generally, what does that phrase mean to you?

A. Treatment emergent hyperglycemia would refer to patients who enter a clinical trial with a normal blood glucose level, and then at any time in the trial at least one level is found to be above the normal level of glucose.

Q. Okay. And the reason why it's referred to as treatment emergent is because this situation was discovered while they were under treatment in the study, correct?

A. That's correct.

Q. And what the data in this particular little box says is that the incidence of that treatment-emergent hyperglycemia in the Zyprexa treated group was about three and-a-half times higher than in the placebo group, correct?

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A. That's correct.

Q. Okay. And I believe you said that you were not a regular member of the global product labeling committee; is that correct?

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A. I was not a member of that committee.

Q. Were you involved in the labeling change that was being discussed here?

A. As far as I could recollect I was not.

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Q. Would you agree with me, sir,

that Lilly could have changed its labeling to just say, as was said in that little box there: Recent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment emergent diabetes in the olanzapine group, 3.6 percent, was higher than that in the placebo group, 1.05 percent?

Bruce Kinon, M. D. (July 10, 2006)

158:17 Q. You're not aware of anything
18 that would have prevented Lilly from putting
19 that language in the labeling, correct?
20 A. I, specifically, don't know
21 what this list is referring to. It clearly
22 does not state whether this is a
23 statistically significant difference nor does
24 it give any recommendations at all that these
159: 1 levels are indicative of diabetes. They're,
2 basically, saying there seems to be a
3 difference in rates for the development of
4 hyperglycemia. The significance of it, the
5 consequences of that are not stated, at least
6 not in this document.

Bruce Kinon, M. D. (July 10, 2006)

159: 9 Q. Sir, there would have been
10 nothing that prevented Lilly from putting
11 that language in. They could have done a
12 changes being effected supplement to the
13 label and sent that off to the FDA and said
14 this is the language we're going to put in
15 our label. They could have done that, right?
16 A. The label clearly indicates,
17 back then as well as when we launched the
18 product in 1996, that the adverse event, the
19 adverse reactions of Zyprexa did, in fact,
20 include hyperglycemia. That was already in
21 the label.
22 MR. SUGGS: Sir, that's not
23 my. --
24 MR. ALLEN: Objection,
160: 1 nonresponsive. It must be hard to

Bruce Kinon, M. D. (July 10, 2006)

160: 6 Q. Sir, my question had to do
7 with this particular language. There was
8 nothing that prevented the company from
9 sending this off to the FDA and a changes
10 being effected supplement and proposing that
11 this be in the label, correct?

Bruce Kinon, M. D. (July 10, 2006)

160:14 A. I'm not aware whether this
15 was or was not sent to the FDA. I'm not in
16 possession of that information.
17 Q. You do know for a fact that
18 that language that we've just been talking
19 about never made it in your label, correct?
20 We know that for a fact?
21 A. I don't know whether that's a
22 fact or not.
23 Q. You don't know whether that's
24 a fact?
161: 1 A. There was a label change that
2 did, in fact, state the incidence of
3 hyperglycemia, olanzapine versus placebo.

Bruce Kinon, M. D. (July 10, 2006)

161: 4 Q. Indeed, we're going to talk
5 about that in some detail.

Bruce Kinon, M. D. (July 10, 2006)

172:14 Sir, do you recall that in
15 May of 2000 the company did submit a special
16 supplement changes being effected label
17 change with respect to Zyprexa and the
18 incidence of hyperglycemia?
19 A. I was aware that some
20 submission was made. I do not, though, know
21 the details of that.
22 Q. In fact, you worked on that
23 labeling change, didn't you?
24 A. I don't have any recollection
173: 1 that I worked, specifically, on that labeling
2 change.
3 MR. SUGGS: Well, let me show
4 you what's been previously marked as
5 Plaintiff's Exhibit 7012.

Bruce Kinon, M. D. (July 10, 2006)

173:10 MR. SUGGS: For the record
11 this is a March 27, 2000, e-mail
12 from Michele Sharp to Robert Baker,
13 Charles Beasley, Alan Breier, Barry
14 Jones, Bruce Kinon, Kenneth Kwong,
15 Paula Trzepacz with a copy to John
16 Roth, the subject being Proposed
17 Zyprexa USPI Revision --
18 Hyperglycemia.
19 QUESTIONS BY MR. SUGGS:
20 Q. Do you see that language,
21 sir?
22 A. Yes, I do.
23 Q. And do you recall at the time
24 getting this memo on or about, pardon me, do

you recall getting th[illegible]e-mail on or about that date?
A. I will have to read the e-mail, please.
Q. Okay. Now that you've read it do you recall getting this e-mail on or about March 27, 2000?
A. I don't recall specifically, no.
Q. The e-mail states -- by the way Michele Sharp is with the regulatory affairs department, correct?
A. That's correct.
Q. And the other people there, Robert Baker, Charles Beasley, Alan Breier, and yourself, and Kenneth Kwong and Paula Trzepacz are all medical people, correct?
A. Yes.
Q. Was Barry Jones also medical?
A. Yes.
Q. And you'll recall from the prior exhibit that we looked at that this label change that was proposed in February, a month before this, was signed off on by Dr. Beasley and Kenneth Kwong, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. No, I'm not clear whether this was a signed document or what. All I see is two names in the back of a document that I have not had the opportunity to read. I don't know who signed off on it or whether this is just, basically, a draft.
Q. Well, we can see in the last page of Exhibit 990 it says, there's a box there consultation process reviewed by, and it has the names of Dr. Beasley and Kenneth Kwong. And then it has a date that it was reviewed, correct? And it's dated, correct?
THE WITNESS: Could you please repeat that?
MR. SUGGS: Sure.
Q. If you look at the last page of Exhibit 990 it shows that, the document says it was reviewed by Dr. Beasley and Kenneth Kwong on February 15, correct, 2000?
A. It says that, yes.
Q. Okay. And then the document that we're now looking at, Exhibit 7012, is dated about a month after that, correct?
A. That's correct.
Q. Okay. And it says: Following a meeting on Friday, March 24 with Charles, referring to Charles Beasley, Barry, referring to Barry Jones, Bruce, referring to you, and Paula, referring to Paula Trzepacz, a new proposal for the Zyprexa USPI change with regards to hyperglycemia was developed. Do you see that language, sir?

A. Yes.
Q. Now, USPI stands for United States Package Insert, correct?
A. Yes.
Q. Okay. And this is referring to a change, a new proposal for the package insert change with regards to hyperglycemia, correct?
A. That's correct.
Q. And, sir, doesn't that indicate that you and those other folks there were working on a change in the language in the label about hyperglycemia?

Bruce Kinon, M. D. (July 10, 2006)

A. Again, I don't, specifically, recollect this but that seems what this e-mail is referring to.
Q. And is it still your testimony that you never saw what had originally been proposed a month earlier as reflected in Exhibit 990?

Bruce Kinon, M. D. (July 10, 2006)

A. I don't, specifically, remember seeing Exhibit 990.

Bruce Kinon, M. D. (July 10, 2006)

QUESTIONS BY MR. SUGGS:
Q. Dr. Kinon, you'll recall that in Exhibit 990 the reason for the proposed label change by Dr. Beasley and Dr. Kwong was that their review of the random glucose levels of patients in the olanzapine clinical trials revealed that incidence of treatment-emergent hyperglycemia that was three and-a-half times higher in the Zyprexa group as compared to the placebo group, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I would like to be very accurate in how I answer your question. If I don't have an opportunity to read this document I'm basically just reading a paragraph that you've directed me into a four-page document.

Bruce Kinon, M. D. (July 10, 2006)

179: 7 In Exhibit 990, which is the
8 proposal for the label change in February of
9 2000, there is a section on Page 2 that says:
10 How has this proposal arisen, correct?
11 A. Yes.
12 Q. And in that, in the text of
13 that box there it indicates that a review of
14 the random glucose levels of patients that
15 were treated with Zyprexa revealed that the
16 incidence of treatment-emergent hyperglycemia
17 that was about three and-a-half times higher
18 than that in the placebo group, correct?
19 Isn't that what's indicated there?
20 A. That's what the language
21 says, sir. I have no idea what hyperglycemia
22 is referring to in these patients. We just
23 spoke about what the cutoff volumes are.
24 MR. SUGGS: Let's continue
180: 1 on, sir.

Bruce Kinon, M. D. (July 10, 2006)

180: 4 MR. SUGGS: And then, sir,
5 several months later we'll have,
6 I'll show you the 4858 exhibit.

Bruce Kinon, M. D. (July 10, 2006)

180:12 MR. SUGGS: Which is a letter
13 dated May 9, 2000, to the FDA
14 consisting of a special supplement
15 changes being affected change to the
16 Zyprexa label.
17 QUESTIONS BY MR. SUGGS:
18 Q. Have you seen this document
19 before, sir?
20 A. No, I'm not aware that I
21 have.
22 Q. Well, you do recall in May of
23 2000 there was a label change, correct?
24 A. I believe there was.
181: 1 Q. And let me ask you this,
2 could you read, well, let me back up for a
3 second. The letter has three sections to it
4 noting that there were three changes that
5 were made. I'm concerned with the ones
6 relating to diabetes or hyperglycemia type
7 issues, which were changes two and three.
8 Let's talk about change three
9 first. It notes that at that time in the
10 adverse reaction sections -- strike that.
11 The third change was in the
12 adverse reactions, postintroduction reports
13 section, inclusion of diabetic coma was made,
14 correct?
15 A. Yes, that's correct.
16 Q. And then on the previous page
17 under item two it points out that in the

adverse reactions, additional findings observed in clinical trials, laboratory changes section, there was inclusion of data from the olanzapine clinical trial database with respect to random plasma glucose levels; is that correct?

A. Yes.

Q. And those are the same, it's the same type of data that was referred to in Exhibit 990 in that How Has This Proposal Arisen section; is that correct?

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A. I have to read this because this is a significantly different statement than what you showed me before.

Q. I would certainly agree with you there, sir. It's far different. And that's what we're going to be talking about. But right now let's just take this a step at a time.

And I would ask you, sir, whether it is true or not that in Exhibit 990 in that How Has This Proposal Arisen section, when they're referring to random glucose levels there, is that the same as random plasma glucose levels that's referred to over in Exhibit 4858?

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MR. SUGGS: Are you referring to the letter to the FDA?

THE WITNESS: Yes.

MR. SUGGS: I'm going to have to read that section, please.

Q. Well, let me just ask you, sir, when you talk about random glucose levels, if I use that phrase, is that the same as the phrase random plasma glucose levels or is there some difference there I'm not aware of?

A. There should not be a difference.

Q. That's all I was concerned with at this point.

Sir, what I would like you to do if you could is read aloud for us that paragraph below there, which is the language that was, in fact, changed and put in the label. Can you read it aloud for us, sir?

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A. And I quote, "This section now reads, quote, 'In the olanzapine clinical

trial database as of September 30, 1999, 4577 olanzapine-treated patients representing, approximately, 2255 patient-years exposure and 445 placebo-treated patients who had no history of diabetes melitis and whose baseline random plasma glucose levels were 140 milligrams per deciliter or lower were identified. Persistent random glucose levels greater than 200 milligrams per deciliter, suggestive of possible diabetes, were observed in 0.8 percent of olanzapine-treated patients as compared to placebo of 0.7 percent. Transient, i.e., resolved while the patients remained on treatment, random glucose levels greater than 200 milligrams per deciliter were found in 0.2 percent of olanzapine-treated patients as compared to placebo of 0.2 percent. Persistent random glucose levels greater than or equal to 160 milligrams per deciliter but less than 200 milligrams per deciliter, possibly hyperglycemia, not necessarily diabetes, were observed in 1 percent of olanzapine-treated patients compared to placebo of 1.1 percent. Transient random glucose levels greater than or equal to 160 milligrams per deciliter but less than 200 milligrams per deciliter were found in 1 percent of olanzapine treated patients as compared to placebo 0.4 percent.

Q. And sir, was that the language that you were working on that was reflected in that e-mail of Michele Sharp's that we looked at before that was Exhibit 7012?

A. I believe so. I don't know. There was an attachment to Michele Sharp's e-mail which you did not provide me.

Q. I would if I had it but I don't have it.

A. I would assume that it's similar.

Q. Okay. So it would be fair to say that the, at least based on your recollection, that the language that we see here reflected in this May 9, 2000, changes being effected label change grew out of the discussion that occurred between you and Charles Beasley, Barry Jones, and Paula Trzepacz with Michele Sharp back in that March 27, 2000, meeting?

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Q. Is that fair to say?

A. At least based upon the people who were contacted on the e-mail. I'm sure there were certainly other people involved.

Q. Okay.

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186:13 Q. Now that the sirens have
14 passed we'll continue on with our
15 questioning. Would you agree, sir, that this
16 label change that we just, that you just read
17 for us would have been found to be reassuring
18 by physicians?

Bruce Kinon, M. D. (July 10, 2006)

186:21 A. I don't know whether it would
22 be reassuring or not. I think that this was
23 information that at the time we thought was
24 valuable to share with clinicians.
187: 1 Q. In fact, what it showed was
2 essentially, no, at least if it was taken to
3 be true, it would show that there really
4 wasn't much of a difference in terms of
5 glycemic levels between people who use
6 Zyprexa and placebo, patients who didn't,
7 correct?

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187:10 A. Although it showed that, it
11 also gave very specific information about the
12 incidence of diabetes of patients with
13 schizophrenia who were treated with
14 antipsychotic agents.

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187:17 Q. Sir, what it showed was, for
18 example, if we looked at the persistent
19 random glucose levels in excess of 200
20 milligrams per deciliter, the difference was,
21 the rates were .8 percent in Zyprexa patients
22 versus .7 in placebo patients, at least as
23 described here in the label, correct?
24 A. That's correct.

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188: 1 Q. And there's really not much
2 difference between .7 and .8, right?

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188: 5 A. That's correct.
6 Q. And in the transient level,
7 which was greater than 200 milligrams, it was
8 only .3 percent for Zyprexa and .2 percent

for placebo, correct?
A. That's correct.
Q. Again, not much difference, there, right?

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188:15 A. There -- it doesn't matter whether there's much difference or not, this represents thousands of patients. This is a difference. Whether it's real or not these are the facts as stated.
Q. I know. But, well, those are the facts as stated in this paragraph. I can guarantee you we're going to disagree about whether those are really the facts. But any person, any doctor reading this label change would look at this and say, gosh, there's not really much of an effect on hyperglycemia here with people who take patients (sic) at least according to this data.

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189: 7 Q. Because there's not much difference between the Zyprexa patients and the placebo patients, right?

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189:12 A. I have no idea what some doctor might take as their opinion. This is, basically, provided for clinicians so they understand what is the incidence of diabetes in patients on placebo versus Zyprexa.
Q. Okay. Who was it that made the decision that the label would use this language?
A. This would be a, as far as I am aware because I did not finalize the language, this would be a decision by the product global, the global product labeling committee.

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190: 5 Q. Okay. And can you explain to us how the label went from the three and-a-half times higher finding of hyperglycemia as reflected in Exhibit 990 to, essentially, no difference in what actually was submitted to FDA in May of 2000?

Bruce Kinon, M. D. (July 10, 2006)

190:14 A. Yes. There's a very clear
15 explanation, the prior document, Exhibit 990
16 uses a cutoff value of 160 milligrams,
17 therefore, it is a different cutoff than the
18 one that's used here of 200. So more
19 patients are coming in over the cutoff of
20 160.
21 I want to bring to your
22 attention that the difference between 3.6
23 versus 1.5 is not necessarily statistically
24 significant. There is no greater accuracy in
191: 1 this number as compared to the number that
2 was finally submitted.

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191: 5 Am I correct, sir, that this
6 information that was contained in the label
7 change here was incorporated in a sell sheet
8 to be used by the sales force?
9 A. I'm not aware of that at all.
10 Q. Do you recall that Lilly was
11 representing to physicians that there was,
12 essentially, no difference between Zyprexa
13 and placebo in terms of hyperglycemia?

Bruce Kinon, M. D. (July 10, 2006)

191:16 A. I don't recall that at all.
17 Q. Who was it that made the
18 decision that there would be a cutoff of 200
19 as opposed to a cutoff of 160?

Bruce Kinon, M. D. (July 10, 2006)

191:22 A. For random blood glucose the
23 American --
24 Q. My question, sir --
192: 1 THE WITNESS: I wasn't
2 finished, sir.
3 MR. SUGGS: I think you may
4 not have understood my question.
5 THE WITNESS: Could you
6 repeat the question, then?
7 Q. My question was: Who in the
8 company made the decision as to what cutoffs
9 would be used in this label change that was
10 made?
11 A. I don't know, specifically.

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192:20 Q. Sir, do you recall that the
21 FDA made the company take this labeling out

in October of 2000?

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A. I wasn't aware of those discussions but I know the language has been removed from the label.

MR. SUGGS: Let me show you what's been previously marked as Exhibit 195.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record this is an October 11, 2000, letter from the FDA to Gregory T. Brophy at Lilly.

QUESTIONS BY MR. SUGGS:

Q. Have you seen that document before, sir?

A. No, I have not.

Q. Directing your attention to the first page, the FDA notes at the bottom of the page, by the way, this -- strike that.

This document was dated October 11, 2000, which would have been almost exactly five months after you went ahead and changed the labeling on your own initiative through a changes being effected supplement, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I was not directly involved in that submission but I assume if those are the dates those are the dates. I'm not aware of them.

Q. The date on the letter we looked at before was May 9, 2000, that was, the change in labeling was sent in to FDA.

Correct?

A. That's correct.

Q. And the date of Exhibit 195 is almost exactly five months later, right?

A. That's correct.

Q. Okay. And in the FDA response five months later they said that Lilly would have to take out that language talking about the comparison in random glucose levels between olanzapine patients and placebo, correct?

A. That's correct.

Q. And the reason why they said you should take it out was because -- it's reflected on the second page of the document, correct?

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195: 7 THE WITNESS: And you're
8 referring to what section?
9 Q. The second paragraph. There
10 it states, quote, "The descriptive data that
11 is provided expresses a certain level of
12 implied safety with respect to treatment
13 emergent hyperglycemia. This reassuring
14 language is not appropriate for submission
15 under 21 CFR 314.70 as a special supplement
16 changes being effected." Do you see that?
17 A. Yes, I see that.
18 Q. So the FDA wouldn't permit
19 that label change and you had to take it out,
20 right?
21 A. Yes.

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197: 7 Q. What's your understanding of
8 the term continuous analysis of data?
9 A. Several things come to mind.
10 Continuous analysis of data, a type of
11 statistical analysis where data is looked at
12 as a continuum rather than as a categorical
13 analysis.
14 Q. In that situation if you had
15 whatever variable you're looking at and you
16 had data going from values of, say, zero to
17 500 and scattered all throughout there, with
18 continuous analysis of data you would like at
19 means and conduct statistics with respect to
20 all of those points of data, correct?

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197:23 A. That's my understanding as
24 one possible answer for continuous analysis.
198: 1 Q. And as compared to what's
2 sometimes referred to as categorical
3 analysis. What's your understanding of that
4 phrase?
5 A. A categorical analysis is
6 where you group data into categories and you
7 do your analysis based upon the differences
8 in categories rather than a continuous
9 variable.
10 Q. So for example, if we had the
11 same type of testing I was talking about
12 where you had data with values ranging from
13 zero to 500, if you were going to be doing a
14 categorical analysis you might look at, well,
15 how many people are in the zero to 100 group,
16 versus the 100 to 200, versus the greater
17 than 400-type analysis. That's the type of
18 categorical analysis that you were talking
19 about?

A. Yes.
Q. Okay. And am I correct that the analysis that we looked at in terms of the label change that was made in May of 2000 regarding hyperglycemia values was a type of categorical analysis?
A. Specifically, which document are you referring to?
Q. The Exhibit 4858.
A. Yes, that's a categorical analysis.

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Q. In Exhibit 990, which was the proposal for the label change -- oh, here it is, I got it -- which was made in February of 2000, that was also a categorical analysis, correct?
A. That's my understanding. There seems to be some type of symbols missing but that would be my interpretation of it.
Q. And the symbols that are, probably, missing there, would you agree with me that the way that that section under new statement would make sense would be if it said random glucose greater than 160 milligrams per deciliter in patients with baseline random glucose less than 140 milligrams deciliters has been occasionally seen in clinical trials?

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A. Perhaps, either less than or equal to or greater than or equal to, I don't know.
Q. Okay. So what the proposed label change was saying if you did that type of categorical analysis, what you were seeing was an increase in, you were seeing an increase in random glucose above 160 in people who previously, before they started on the drug, had been at 140 or below; is that correct?

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A. That's my understanding of that analysis.
Q. Okay. And we know that according to the ADA if you have a random glucose in excess of 140 that that's a measure of something to be concerned and monitored, correct?

Bruce Kinon, M. D. (July 10, 2006)

201:18 A. I don't know, specifically,
19 what you're referring to.
20 Q. Well, I thought we saw a
21 document before, but perhaps I'm mistaken,
22 that the ADA had taken the position that if
23 he had a random glucose in excess of 140 that
24 that was something to, that warranted
202: 1 monitoring and caution about; is that
2 correct? Is that your understanding?

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202: 5 A. I know the ADA has changed
6 its criteria. It may represent impaired but
7 not diabetes.
8 Q. Okay. That's fine. And you
9 know also from Exhibit 990 that, apparently,
10 they were seeing a three-fold increased
11 incidence in treatment-emergent hyperglycemia
12 in at least the way they were doing the
13 analysis as reflected in Exhibit 990,
14 correct?

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202:17 A. For levels that went above
18 160, yes.
19 Q. Okay. And when you guys made
20 the label change in May of 2000, you did a
21 categorical analysis that, as we discussed
22 previously, essentially, showed that there
23 was little, if any, difference between the
24 levels of hyperglycemia in Zyprexa users
203: 1 versus placebo uses, correct?

Bruce Kinon, M. D. (July 10, 2006)

203: 4 A. The numbers were provided for
5 comparison. There was no statement that
6 there was a small or large difference.
7 Q. Okay. But, clearly, the FDA
8 thought that doctors would, in their words,
9 be reassured by that, correct?

Bruce Kinon, M. D. (July 10, 2006)

203:12 A. According to the memo from
13 the FDA that was their term.
14 Q. They thought, and the FDA
15 thought that it expressed a certain level of
16 implied safety with respect to

treatment-emergent hyperglycemia, correct?
A. Based upon what the FDA said, yes.
Q. And the FDA made you take that out, the label change, right?
A. That's correct.
Q. Okay.
And in fact, your company knew that if you did a continuous analysis of the data that it showed statistically significant mean increases in random glucose relative to placebo and haloperidol; isn't that correct?

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A. Some of our data sets have shown a mean increase, yes. We have published upon that.
MR. SUGGS: Okay. Let me show you what's been previously marked as Exhibit 5565.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record, this is an e-mail from, actually, it's an e-mail chain consisting of several e-mails. But the one I would like to focus you on in particular is an e-mail from Charles Beasley to Ralph Dittmann on February 22nd, 2001, which is on the very first page of this exhibit.
QUESTIONS BY MR. SUGGS:
Q. And you see how --
A. I don't see that.
Q. Okay, on the very first page of Exhibit 5565 there is an e-mail starting about a third of the way down the page from Charles Beasley --
A. Oh, yes.
Q. -- to Ralph Dittmann with copies to Alan Breier, Patrizia Cavazzoni, Mark Millikan, Anna Thornton and Jerry Tollefson, correct?
A. Yes.
Q. And of those people that are listed there, which ones would you say were in senior management at Lilly?
A. Dr. Breier and Dr. Tollefson.
Q. Okay. And do you recall what Dr. Breier's title would have been back at that point in time in February of 2001?
A. I don't recall, specifically, but, perhaps, he was the product team leader at that time.
Q. Okay. And how about Dr. Tollefson, was he still a vice-president?

A. I believe so.
Q. Okay. So, clearly, this e-mail went to some pretty high ranking people within the corporation, correct?

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206:10 A. Yes.
Q. And if I could direct your attention to the third sentence in Mr. Beasley's or Dr. Beasley's e-mail, he says, our continuous analyses show that olanzapine does result in statistically significant mean increases in random glucoses relative to placebo and haloperidol. Did I read that correctly?
A. Yes.
Q. And were you informed of that at that time?
A. I was aware of that, yes.
Q. And for how long had you been aware of that?
207: 1 A. That analysis was one that was presented. I believe I remember it being presented.
Q. Presented where?
A. In the scientific congress.
Q. Okay. And was it also presented -- were you aware of that before you made the label change in May of 2000.
A. I wouldn't know that.
Q. Who would know that?
A. I guess, Dr. Beasley would know that.
Q. Okay. The memo goes on to say -- by the way, that statement there, that continuous analyses showed that olanzapine does result in statistically significant mean increases in random glucose relative to placebo and haloperidol was not included in your label at that time; is that correct?
A. That's correct. Because that

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211: 3 Q. Do you recall being informed that an early October 2000, that various representatives of Lilly met with outside consultants who were experts in diabetes to present them with the company's analysis of the glucose data the company had?

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211: 9 A. I don't know what meeting you're, specifically, referring to.

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211:11 MR. SUGGS: Okay. Let me see
12 if I can help you there. Let me
13 show you two e-mails, the first one
14 is Exhibit 6998 dated October 9,
15 2000, and the second is
16 Exhibit 6999, dated October 10,
17 2000.

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211:24 Q. Sir, let's first talk about
212: 1 Exhibit 6998. That is an e-mail from Robert
2 Baker to Dr. Beasley, Christopher Bomba, Alan
3 Breier, Thomas Brodie, Patrizia Cavazzoni,
4 James B. Gregory, John Holcombe, Jack Jordan,
5 Suni Keeling, Bruce Kinon, Michael Murray,
6 John Richards, Eugene Thiem, Mauricio Tohen
7 and Paula Trzepacz; is that correct?
8 A. Yes.
9 Q. And those people were all
10 either in the medical department or in the
11 marketing department, am I correct?
12 A. Some of the names I'm not
13 familiar with but the ones I am familiar with
14 that would be correct.
15 Q. And this included at least
16 several people who were in senior management
17 at the company, were they not?
18 A. Yes.
19 Q. And beside Alan Breier, who
20 else would have been regarded as senior
21 management at the company?
22 A. That's the only one that I
23 would see that I would state that.
24 Q. Okay. And it's pointed out
213: 1 here that the Lilly's diabetes endocrine
2 group held an academic advisory board meeting
3 this weekend in Atlanta. They kindly
4 allotted two hours for discussion of
5 olanzapine's potential hyperglycemia risks
6 and Charles Beasley, Chris Bomba, Patrizia
7 Cavazzoni, Suni Keeling attended. Did I read
8 that correctly?
9 A. Yes.
10 Q. And the Lilly company sells a
11 number of antidiabetic drugs, correct?
12 A. That's correct.
13 Q. That's a large part of your
14 business?

Bruce Kinon, M. D. (July 10, 2006)

213:17 A. It's a significant portion,
18 as far as I understand.
19 Q. And Dr. Baker goes on to
20 state, "Unfortunately, this consultation

reinforced my impressi[illegible] that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic."
Do you see that language, sir?
A. Yes, I do.

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Q. Sir, the threat that existed for Lilly was the threat that concern about diabetes and hyperglycemia was going to impact sales, correct?

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A. This memo was written by Robert Baker not myself. I have no idea in what way he was using the term threat.

Bruce Kinon, M. D. (July 10, 2006)

Q. Sir, if doctors became concerned about hyperglycemia and diabetes with Zyprexa they wouldn't use it as much as they would other drugs, correct?

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A. It's my understanding that if clinicians are concerned about diabetes they would want to know more information about diabetes, the risk of antipsychotic drugs, the inherent increased risk of diabetes with schizophrenia, as well as the profile of Zyprexa. That's the type of information they would want.
Q. Sir, there were many other competitive drugs out there that doctors could have used, correct, instead of Zyprexa?
A. If they felt that was appropriate for the patients they could make other choices.
Q. And the other drug companies were pointing out the risks of hyperglycemia and diabetes with the use of Zyprexa, were they not?
A. Some of them were.

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Q. Sir, Lilly's response to the

competitive attacks on others was to say that the rates of hyperglycemia and diabetes were comparable between the various antipsychotic drugs, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. That's wrong. Lilly's response was to get more data and better understand what effect was the side effect profile of Zyprexa in terms of hyperglycemia, weight gain and diabetes.

Q. Sir, do you deny that the company had what was referred to as a comparable incident story?

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A. I'm not aware of that.

MR. SUGGS: Well, let me show you what's been previously marked as Plaintiff's Exhibit 9722.

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MR. SUGGS: For the record, Exhibit 9722 is a July, pardon me, June 27, 2003, e-mail from Walter Deberdt to a number of individuals at Lilly, including Dr. Kinon.

QUESTIONS BY MR. SUGGS:

Q. And, sir, do you recall receiving this e-mail on or about June 27, 2003?

A. I'm going to have to read it.

Q. Do you recall receiving this e-mail on or about June 27, 2003?

A. No, I do not.

Q. Do you have any basis to dispute that you, in fact, did receive this e-mail that was addressed to?

A. No, I do not.

Q. The text of the introductory paragraph states in part: "I come to the conclusion that we have a balanced, complete, and clear message as summarized in the famous bullet-point slide that we discussed at length and in detail, except from the fact that we fail to situate the role of weight gain in the comparable incidence of diabetes while under antipsychotic treatment. Since in the minds of doctors weight gain is directly linked to increased risk for diabetes, they don't buy the comparable incidence story."

Did I read that language correct?

A. Yes.
Q. And does that refresh your recollection that Lilly had a comparable incidence story it was trying to sell doctors?

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220: A. No, it does not.
Q. It doesn't refresh your recollection at all?
MR. WASSON: Objection.
Asked and answered.
A. I don't, specifically, recall what comparable incidence story means.
MR. SUGGS: Okay. Well, let me show you another document. Let me show you Exhibit 7668.

Bruce Kinon, M. D. (July 10, 2006)

220:17 MR. SUGGS: For the record, Exhibit 7668 are the meeting minutes of the U.S. Zyprexa Medical Marketing Strategic Alignment Committee meeting on July 28, 2003.
QUESTIONS BY MR. SUGGS:
Q. Do you recall receiving this document, sir?
221: A. I'm going to have to review the document.
Q. Do you recall receiving this document on or about July 28, 2003, sir?
A. I don't, specifically, recall this document.
Q. According to the document these meeting minutes were submitted by you and Vince Truax as co-chairs of that meeting; is that correct?
A. I just don't recall them.
Q. Well, the document indicates there was a presentation by Mike Magdycz, regarding Lilly's new strategy for weight gain and diabetes; is that correct?
A. Yes, that's correct.
Q. And one of the, and what it has there is a section "from," and it lists a bunch of bullet points, and then a section called "to" with another bunch of bullet points, right?
A. Yes.
Q. And what the "from", the things that were under "from" is the things
222: that Lilly had been doing in the past, and the things that under the "to" category are the things that you were going to switch to, right?

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222: 6 A. I don't, specifically, recall
7 what that presentation was about.
8 Q. You don't recall. Well,
9 under the "from" category what Lilly had been
10 doing before is listed diabetes risk as a
11 class effect with comparable rates across all
12 products, correct?
13 A. Yes.
14 Q. And, in fact, for years Lilly
15 had been saying that there were comparable
16 rates of diabetes across all products,
17 correct?

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222:20 A. There are comparable rates
21 amongst all the antipsychotic drugs.
22 Q. That is what you were
23 claiming?

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223: 2 Q. Now getting back to
3 Exhibit 6998, which is the e-mail that you
4 got back in October of 2000.
5 A. Okay. Yep.
6 Q. In the second paragraph
7 Dr. Baker is discussing the comments that
8 have been made by the outside experts.
9 By the way, this, let me nail
10 that down. This academic advisory board
11 meeting that was held in Atlanta at that time
12 was a deal where they brought in a bunch of
13 outside experts, outside the company, who
14 were experts in the field of diabetes,
15 correct?
16 A. That's my understanding.
17 Q. And what happened there was
18 Lilly told these experts what they thought,
19 what Lilly thought, the data was showing with
20 respect to weight gain and diabetes, correct?

Bruce Kinon, M. D. (July 10, 2006)

223:23 A. Lilly would share its data
24 with the consultants to get their feedback.
224: 1 Q. Exactly. And what these,
2 what Dr. Baker is doing in this memo is he's
3 reporting on that what feedback was, correct?
4 A. It appears to be the case.
5 Q. And one of his impressions
6 was that hyperglycemia remains quite a threat
7 for olanzapine and may merit increasing even
8 further medical attention and marketing focus
9 on the topic, correct?

A. That's correct.
Q. And in the second paragraph he says in part, "they," referring to the outside consulting folks "were concerned by our spontaneous AE reports and quite impressed by the magnitude of weight gain on olanzapine and implications for glucose." Did I read that correctly?
A. Yes.
Q. Now the reference to spontaneous AE reports, that's to spontaneous adverse event reports, correct?
A. It appears to be that.
Q. And adverse event reports are reports that are made by physicians to the company about problems that their patients have had with use of a drug, correct?
A. That's correct.
Q. So what's being said here by Dr. Baker is that the outside experts were concerned by the spontaneous adverse event reports and they were quite impressed with the magnitude of the weight gain on the drug and the implications that had for glucose, correct?

Bruce Kinon, M. D. (July 10, 2006)

Q. Correct?
A. That's what this particular paragraph states.
Q. And he notes that much of their input for helpful steps came back to addressing weight gain, correct?
A. That's what this document states.
Q. So clearly you took away from this e-mail that, wow, weight gain is really a big factor, at least to these outside experts that our guys met with, right?

Bruce Kinon, M. D. (July 10, 2006)

A. Basically, reading this memo which I don't recollect, that would be my conclusion reading it today.
Q. And then Dr. Baker goes on to say, "Citing methodological questions, at least the vocal members, were not reassured adequately by our analyses, such as the finding that the relative risk was not higher than comparative drugs." Do you see that language?
A. I don't know what -- I see the language, I don't know what analyses he's referring to.
Q. Okay. But at least, apparently, according to this e-mail, it appears that there was some presentation by

Lilly where your guys made the presentation to them that there were comparable rates of diabetes between Zyprexa and other drugs, and the experts came back and said that they were not reassured adequately by those analyses, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I don't know if that's a conclusion. From what I read they're talking about the weight gain analyses.
Q. Okay. Dr. Baker's e-mail goes on to say, "Disconcertingly, one member compared our approach to Warner-Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class." Do you know what that refers to?
A. Just the common knowledge that Rezulin was taken off the market because of hepatic toxicity.
Q. If I could direct your attention to Exhibit 6999, which is the one you got the following day. This is an e-mail from John Holcombe to a number of people, including yourself, correct?
A. Yes, that's correct.
Q. And John Holcombe, I believe, was on the endocrine side of the company. The side of the company that sold diabetes drugs, correct?
A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Q. Was he a medical doctor?
A. Yes, Dr. Holcombe's a physician.
Q. Okay. In the second paragraph of -- well, let me back up for a second.
Would you agree with me that Dr. Holcombe's e-mail is also referring to that endocrine advisory group meeting that occurred?
A. I will have to read the memo first.
Q. Sure, go ahead.
Have you finished reviewing the document?
A. Yes.
Q. And in the second paragraph of -- well, answer that question I had pending. Would you agree with me that Dr. Holcombe's e-mail also concerned the endocrine advisory group that had been held in Atlanta in that early 2000 time period?
A. Yes.
Q. He's responding to other

e-mails that had been ing around about this, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I believe so.
Q. Okay. In the second paragraph of his e-mail Dr. Holcombe says starting about the middle, he says, "At any rate the ADA says that a blood glucose of 140 or greater should be further evaluated. As you know, the consultants wanted to see all glucose values at baseline and over time." Do you see that language, sir?
A. Yes.
Q. But, sir, we know that the continuous analysis of your glucose data showed that there were statistically significant increased levels of hyperglycemia, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. No, that is incorrect. The continuous analysis showed that the mean increase, the mean levels of glucose slightly increase with olanzapine as compared to haloperidol and placebo. It makes no mention, whatsoever, that those values were elevated to the point of being hyperglycemia.
Q. It showed that there were statistically significant increased levels of blood glucose with Zyprexa as compared to haloperidol and placebo, correct?

Bruce Kinon, M. D. (July 10, 2006)

Q. Sir, would you agree with me that it would appear from the language here in this e-mail that that outside advisory group was not even shown the continuous analyses that had been done by the company?

Bruce Kinon, M. D. (July 10, 2006)

A. There is nothing in Dr. Holcombe's memo that even talks about the continuous analysis. He's talking about the categorical analysis. And the analysis he's talking about is exactly the analysis that was proposed to the FDA.
Q. And which is exactly the analysis that the FDA rejected, correct?
A. Whether they rejected it or not, Lilly offered that analysis to the FDA.

Q. And the FDA rejected it, correct?
A. The analysis that Dr. Holcombe is discussing, that uses the cutoffs of 200, 140, 160, et cetera, were offered to the FDA.
Q. And the FDA rejected that label change based on that, correct?
A. Subsequently, yes.
Q. And in fact, the thrust of this e-mail here, the one before and this one as well, Exhibit 6998 and 6999, was that the outside advisory group didn't care for your categorical analysis either and that they wanted to see all of the data, isn't that right?

Bruce Kinon, M. D. (July 10, 2006)

A. No, that's wrong.
Q. Sir, doesn't he say in here that "as you know the consultants wanted to see all glucose values at baseline and over time?"
A. When I read this, what I hear is that the experts are looking for the categorical analysis.
Q. Sir, you need to answer my question.

Bruce Kinon, M. D. (July 10, 2006)

Q. My question was doesn't this e-mail say, "As you know the consultants wanted to see all glucose values at baseline and over time" and, in fact, the word "all" is in all caps; isn't that correct?
A. But that's wrong because the next sentence says "showing a large number of values greater than 140 baseline will underscore the likelihood." It goes on to say that you want to do a categorical analysis.
Q. Lilly sure wanted to do a categorical analysis. But these consultants are come back and saying, no, we want to see all the data. Because they didn't trust the data that they were seeing from Lilly; isn't that correct?

Bruce Kinon, M. D. (July 10, 2006)

A. I have no basis to answer that. I don't know what Dr. Holcombe was saying. I don't know if he's saying what you're saying or he's saying what I'm saying. I have an e-mail here that

says nothing at all about continuous variables, that you've been talking now for the last 15 minutes.

Q. In the middle of that paragraph Dr. Holcombe says, "The point was that Lilly has to be forthcoming with the data to gain and maintain our just credibility. Showing our advisory group a slightly modified analysis with, all, and again the word "all" is in all caps, glucose values would be a vital step forward here." Isn't that what it says?

A. That's what it says. What it means I don't know.

Q. Sir, in fact, you know that the consultants were skeptical of Eli Lilly's presentation of data because of the categorical analyses and they wanted to see all the data and Lilly didn't show it to them; isn't that right?

Bruce Kinon, M. D. (July 10, 2006)

A. I have no knowledge of that. This is the first time I'm ever hearing that the categorical analysis was considered to be a less than more reliable analysis.

Q. Okay. Now, sir, in the e-mails that we've looked at we've seen that the outside consultants were concerned about the weight gain with the drug, correct?

THE WITNESS: Specifically, which what e-mail are you speaking of?

Q. For example, in 6998 in the second paragraph of his e-mail Dr. Baker says "that the outside consultants were quite impressed by the magnitude of weight gain on olanzapine and the implications for glucose," correct?

A. That's correct.

Q. And, sir, in fact, Lilly had been minimizing the weight gain problem in its communications with physicians; isn't that correct?

Bruce Kinon, M. D. (July 10, 2006)

A. Lilly has never minimized the weight gain. We have been very proactive in sharing all of our weight gain data, both prospective as well as retrospective, with all clinicians through scientific presentations, medical letters.

MR. SUGGS: Sir, let me show you what's been previously marked as Exhibit 4532.

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: For the record it's a seven page document, appears to be a PowerPoint presentation with the first page having the title Weight Change Strategy and Tactics.

QUESTIONS BY MR. SUGGS:

Q. Do you recall seeing this document, sir?

A. I'll have to take a look at it and read it, please.

Q. Do you recall seeing this document before, sir?

A. No, I do not.

Q. Let me direct your attention to Page 3. There's a heading on Page 3 Zyprexa Market Research Weight Gain and Other Side Effects June 1999. And below that it says Key Results with several bulleted items; is that correct?

A. Yes, that's correct.

Q. And the second bulleted item is "Lilly perceived as minimizing weight gain problem," do you see that language?

A. Yes, I do.

Q. And were you informed that the market research showed that physicians believed that Lilly was minimizing the weight gain problem?

A. Yes, I've heard about that.

Q. And from whom did you hear that?

A. We've heard that through market research.

Q. And when did you first learn that physicians believed that Lilly was minimizing weight gain?

Bruce Kinon, M. D. (July 10, 2006)

MR. SUGGS: Move to strike as nonresponsive.

Q. Sir, my question was when did you first learn that Lilly was perceived as minimizing weight gain by physicians?

A. I don't know exactly but certainly around the time of 1999, perhaps, 2000.

Q. And did that perception continue?

A. I don't know.

Q. The third bullet point item on that page three is Need For More Data On Weight Gain?

A. That's correct.

Q. Do you see that?

A. I see that.

Q. And you, as we talked about at the beginning of your deposition, were designated by Dr. Trzepacz as the number one

person responsible for driving the medical marketing strategy with respect to weight gain, correct?

A. I was certainly significantly involved in the weight gain analyses.

Q. And you were certainly significantly involved in reviewing and approving the messages that went out to physicians about that issue, correct?

A. In part.

Q. Okay. Let me direct your attention to the following page. There's a reference to marketing materials. And they make reference to a new visual aid adherence section which accomplished three things, and then they have three bullet point items there, correct?

A. Yes.

Q. And the second one states Added Additional Facts. And the word "facts" is in quotes, to show that it is common with psychotropics, most patients gain little if any weight and few discontinue if they do gain and weight change plateaus over time without intervention." Do you see that language, sir?

A. Yes, I see that language.

Q. Did you review and approve that material?

Bruce Kinon, M. D. (July 10, 2006)

A. This material, as far as I understand, never left the company. This never went into any promotional pieces that I've had to review. I've never seen this type of language before.

Q. And is that language that "weight change plateaus over time without intervention," is that factually accurate?

A. No, that's not. The published data that we have is that weight plateaus over time.

Q. And the bottom line bullet point there as to, or it says "bottom line weight change is manageable." Did you review and approve that part of the message?

A. No, I did not.

Q. Sir, isn't it a fact that the company repeatedly told physicians that weight gain was manageable?

A. When you say it's a fact, I don't know what you're referring to.

Q. Didn't the company instruct its sales people that weight gain was manageable?

242: 3 Q. Sir, [redacted] you could direct your
4 attention back to Exhibit 7668. Again, this
5 is the strategic alignment committee meeting
6 minutes from July 28, 2003, that were
7 submitted by you and Vince Truax where there
8 was the presentation about Lilly's new
9 strategy for weight gain and diabetes.
10 A. Yes.
11 Q. And do you see that the first
12 bulleted item under there in the From section
13 is weight gain is manageable?
14 A. Yes.
15 Q. And do you deny that Lilly
16 had a position which it promoted to
17 physicians that weight gain is manageable?

Bruce Kinon, M. D. (July 10, 2006)

242:20 A. There's no denial of that.
21 Q. Well, I thought you just did
22 a few minutes ago, which is why I was asking
23 the question again?
24 A. No. That was not my answer.
243: 1 Q. So you would agree with me,
2 sir, then that Lilly had a position which it
3 expressed to physicians through its sales
4 force and other marketing materials that
5 weight change is manageable?

Bruce Kinon, M. D. (July 10, 2006)

243: 8 A. Weight change -- I can only
9 speak from the medical point of view. We had
10 provided medical data --
11 Q. No, sir, I'm not asking that
12 question. I'm asking what the company --
13 well, let me backup for a second.
14 You were part of the medical
15 marketing arm of the company, correct, where
16 the medical department and the marketing
17 department work together, correct?
18 A. That's correct.
19 Q. You were aware of what
20 messages went out through the marketing
21 force, correct?

Bruce Kinon, M. D. (July 10, 2006)

243:24 A. In part.
244: 1 Q. With respect to weight change
2 you certainly were, correct?
3 A. In part.
4 Q. You were the number one guy
5 in charge of weight change, correct?
6 A. In the U.S. affiliate, that's
7 correct.
8 Q. And in fact, Lilly had a

policy and a practice of promoting to physicians, stating to physicians, that weight gain with Zyprexa was manageable, correct?

A. That's correct, yes.

Q. Great. That's all I was looking for.

And the reason why you had that position was because you wanted to minimize the liability of weight gain, correct?

Bruce Kinon, M. D. (July 10, 2006)

244:22 A. That's not correct.
23 MR. SUGGS: Let me show you
24 what's been previously marked as
245: 1 Exhibit 1110.

Bruce Kinon, M. D. (July 10, 2006)

245: 6 MR. SUGGS: For the record,
7 this is a six-page document.
8 Appears to be a PowerPoint
9 presentation. Has the title page
10 stating Issues Management Planning
11 Weight Gain.
12 QUESTIONS BY MR. SUGGS:
13 Q. Have you seen this document
14 before?
15 A. I'll have to take a look and
16 read it, please.

Bruce Kinon, M. D. (July 10, 2006)

247:10 Q. Dr. Kinon, my question was
11 have you seen this document before?
12 A. No, I have not.
13 Q. If I can direct your
14 attention to the second page. There's a
15 bolded heading entitled Issue, do you see
16 that section?
17 A. Yes.
18 Q. And the first point says
19 "weight gain remains the number one liability
20 of Zyprexa and is leading to many of the new
21 issues surrounding the drugs i.e. diabetes,
22 lipids, et cetera." Correct?
23 A. Yes.
24 Q. And you were aware of that,
248: 1 correct?
2 A. Yes, I was.
3 Q. And then below that it's
4 stated Our Position.
5 Is that right?
6 A. Yes.
7 Q. And the company's position as

reflected in this document is, quote, "Weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers. For most patients, this can be managed allowing them to receive the overwhelming benefits Zyprexa offers." Do you see that language, sir?

A. Yes, I do.

Q. And that was a position that was developed in conjunction between the medical department, your shop, and the marketing department, correct?

Bruce Kinon, M. D. (July 10, 2006)

248:22 A. This is a marketing document. This is, basically, a marketing position that is reflected in this document.

249: 1 Q. And do you deny that this was the message that went out to doctors?

A. I do not know if this was used in sales calls or not. I'm not aware of that information. As far as I see this is an internal document.

Q. If I could direct your attention down to the bottom. It states the rationale for the position, correct?

A. Yes.

Q. And the rationale is quote: "To minimize the liability of weight gain while at the same time increasing focus on Zyprexa's superior efficacy." Do you see that language, sir?

A. I see that language, yes.

Q. And did anyone inform you that the rationale for the position was to minimize the liability of weight gain?

A. Again, I'm not aware of how this language is used, whether this is an internal document. I'm sure this type of language was not used in direct sales calls as far as I know.

Bruce Kinon, M. D. (July 10, 2006)

250: 3 Q. Well, I'm sure they didn't tell the doctors that they were trying to minimize the liability of weight gain.

My question to you, sir, is did anyone tell you that the position of the marketing department with respect to weight gain was to minimize the liability of weight gain?

A. That is consistent with marketing's goals.

Q. And how did you learn of that? Who told you that?

A. Some of the points on this document were strategies that marketing was

trying to determine whether these would be viable strategies or not.
Q. And from whom did you learn that that's what they were doing?
A. I don't know, specifically, whom.
Q. Is this because of meetings you were sitting in with the marketing people?
A. That's correct.
Q. So you were at meetings with the marketing folks where they talked about what their position was or what the rationale was and so forth with respect to weight gain; is that correct?
A. That's correct.

Bruce Kinon, M. D. (July 10, 2006)

Next direct your attention to Page 4, please. There's a section there entitled What We Know. Do you see that section?
A. Yes.
Q. The last four bullet items state quote "Weight gain begins to be linked to the possible cause of hyperglycemia. Weight gain and hyperglycemia are directly linked in MD's minds. Weight gain is now linked or in the process of being linked to hyperglycemia/diabetes, hyperlipidemia, cardiovascular disease and compliance."
Do you see that language, sir?
A. Yes, I do.
Q. Were you informed of all those things in your meetings with the marketing people?
A. I don't recall if I was informed of all of those things but I may have been aware of them, yes.
Q. And then there's another section down there that says What We Don't Know. And the last bullet point states "Knowing that weight loss programs only work approximately 5 percent of the time in normal volunteers, does Lilly want to provide a program where if it doesn't work it may be looked at as another laughable attempt?" Do you see that language, sir?
A. I see that language, yes.
Q. Was that your understanding, also, that weight loss programs only work, approximately, 5 percent of the time in normal volunteers?
A. Definitely not. We've done extensive research on behavioral programs and we've funded those independent investigators, and they clearly show that these type of programs do help patients lose weight or help prevent excessive weight gain on all

psychotropic drugs. I do not agree with this statement at all.

Bruce Kinon, M. D. (July 10, 2006)

Q. Sir, the feedback that you got from physicians finally got to the point in the summer of 2003 that you had to make a substantial change in the approach that you were taking; isn't that correct?
A. I don't know --

Bruce Kinon, M. D. (July 10, 2006)

A. I don't, specifically, know what you're referring to.
Q. If you could refer again to Exhibit 7668. This again is the meeting minutes from July 28, 2003, that were submitted by you and Vince Truax, correct?
A. Yes, we've been over that, that's correct.
Q. And who is Vince Truax?
A. Vince Truax is the Brand Manager for schizophrenia in the U.S. affiliate.
Q. Okay. And we've talked several times about this presentation by Mike Magdycz. Am I pronouncing his name correctly?
A. I believe it's Magdycz.
Q. Magdycz, okay. Was he in the marketing department?
A. Yes.
Q. And he talks about having a new strategy for weight gain and diabetes, correct?
A. That's correct.
Q. And the change was to go from weight gain as manageable. Weight gain is predictable. Weight gain is not the only predictor of diabetes. Diabetes risk is a class effect with comparable rates across all products. Diabetes is mainly a patient population issue. And handling diabetes and weight gain as an objection.
All those things are what the company had been, the approach the company had been taking before, correct?

Bruce Kinon, M. D. (July 10, 2006)

A. This is a summarization of Mike Magdycz's, and this is, basically, a very shorthand notation of what was a very extensively detailed program that we offered physicians.

Q. Basically, what, all the items, the bullet points under the from section, are shorthand descriptions, if you wish, of what had been their strategy up to that time, correct?

Bruce Kinon, M. D. (July 10, 2006)

259:21 A. In part, yes.
22 Q. And then he lays out below
23 there in the "to" section, or this memo later
24 out below there in the "to" section, what you
260: 1 were going to switch to, correct?

Bruce Kinon, M. D. (July 10, 2006)

260: 4 A. It wasn't a matter of
5 switching to it was a matter of changing the
6 emphasis to.
7 Q. However, the to items are
8 then -- Lilly understands the challenges
9 physicians face in treating this population.
10 Lilly acknowledges weight
11 gain challenges and potential consequences.
12 Lilly is providing me with
13 options to address weight gain in some of my
14 patients.
15 I am armed with the facts
16 regarding diabetes.
17 Lilly is providing help
18 regarding how to assess, counsel, and refer
19 patients at risk for diabetes.
20 Is that correct?
21 A. That's correct.
22 Q. And this was regarded as a
23 major change in emphasis, correct?

Bruce Kinon, M. D. (July 10, 2006)

261: 2 A. It's the same message. It's,
3 basically, going from one of being
4 adversarial to one of being an ally for the
5 physician. The third bullet point clearly
6 says that Lilly is providing me, the
7 clinician, with options to address weight
8 gain in some of my patients. That's the same
9 message as weight gain is manageable but now
10 we are partnering with the physician. That
11 was the change in emphasis.
12 Q. Sir, wasn't this program
13 referred to internally as the "sorry we lied"
14 campaign?

Bruce Kinon, M. D. (July 10, 2006)

261:17 A. I've never heard that
18 expression.
19 MR. SUGGS: Let me show you
20 what's been previously marked as
21 Exhibit 5522.

Bruce Kinon, M. D. (July 10, 2006)

262:14 Q. I'll represent to you that
15 the database as provided to us by Lilly
16 states that this exhibit, 5522, is August 1,
17 2003, and that date is several days after
18 Exhibit 7668, correct?
19 A. Correct.
20 Q. Okay. And, sir, do you
21 recall that there was the endocrine advisory
22 board that was called upon to review the
23 change in the approach that you guys were
24 going to be taking?

Bruce Kinon, M. D. (July 10, 2006)

263: 3 A. I don't recall that.
4 Q. Sir, if I could direct your
5 attention in Exhibit 5522 to the second page.
6 Let me back up for a second.
7 On the first page the title
8 at the top says Endocrine Advisory Board
9 Areas For Opportunities. And then below that
10 there are several items listed. One is
11 "weight gain, strawman on the table, right
12 message, tone and guidelines emerging, need
13 to provide something practical for
14 physicians."
15 Do you see that language,
16 sir?
17 A. Yes, I do.
18 Q. And, sir, that would clearly
19 indicate that the endocrine advisory board
20 was commenting on the various messages that
21 Lilly had with respect to weight gain,
22 correct?

Bruce Kinon, M. D. (July 10, 2006)

264: 1 A. I've never seen this document
2 before. This is a spreadsheet. It has no
3 introductory comments on it. I have no idea
4 where these comments -- for all I know this
5 is someone's, basically, notes that they took
6 during some meeting. There's not even an
7 idea of where this meeting took place. I
8 have no idea what this is about.
9 I could read through this
10 and, perhaps, I will be able to piece it
11 together.
12 Q. Actually, I just want to draw

your attention in particular to one item on Page 2.

In the bottom box in the left-hand margin there's a heading Response to Letter and Statements, do you see that?

A. Yes.

Q. And about the fourth, fifth, column down it says, quote, change, end quote, in weight to, quote, potential, end quote, weight gain. And then to the right of that it says "want to keep the, quote, sorry we lied message really clean. Do you see that language?

A. I see that. I've never seen this before. I have no idea what this is about.

Q. You know what the sorry we lied message was?

A. I've never heard sorry we lied, with due respect.

Q. I didn't write this someone in your company did.

Bruce Kinon, M. D. (July 10, 2006)

Q. Isn't that what the new message was about? Your new message in the approach in your marketing was the sorry we lied approach?

Bruce Kinon, M. D. (July 10, 2006)

THE WITNESS: What is the question, please?

Q. This new message, this new approach you guys were taking where you were going from various things, like, weight gain is manageable, weight gain is predictable, weight gain is not the only predictor of diabetes. Where you were moving away from that is your sorry we lied message?

Bruce Kinon, M. D. (July 10, 2006)

A. As I've answered I've never been aware of this term -- sorry we lied.

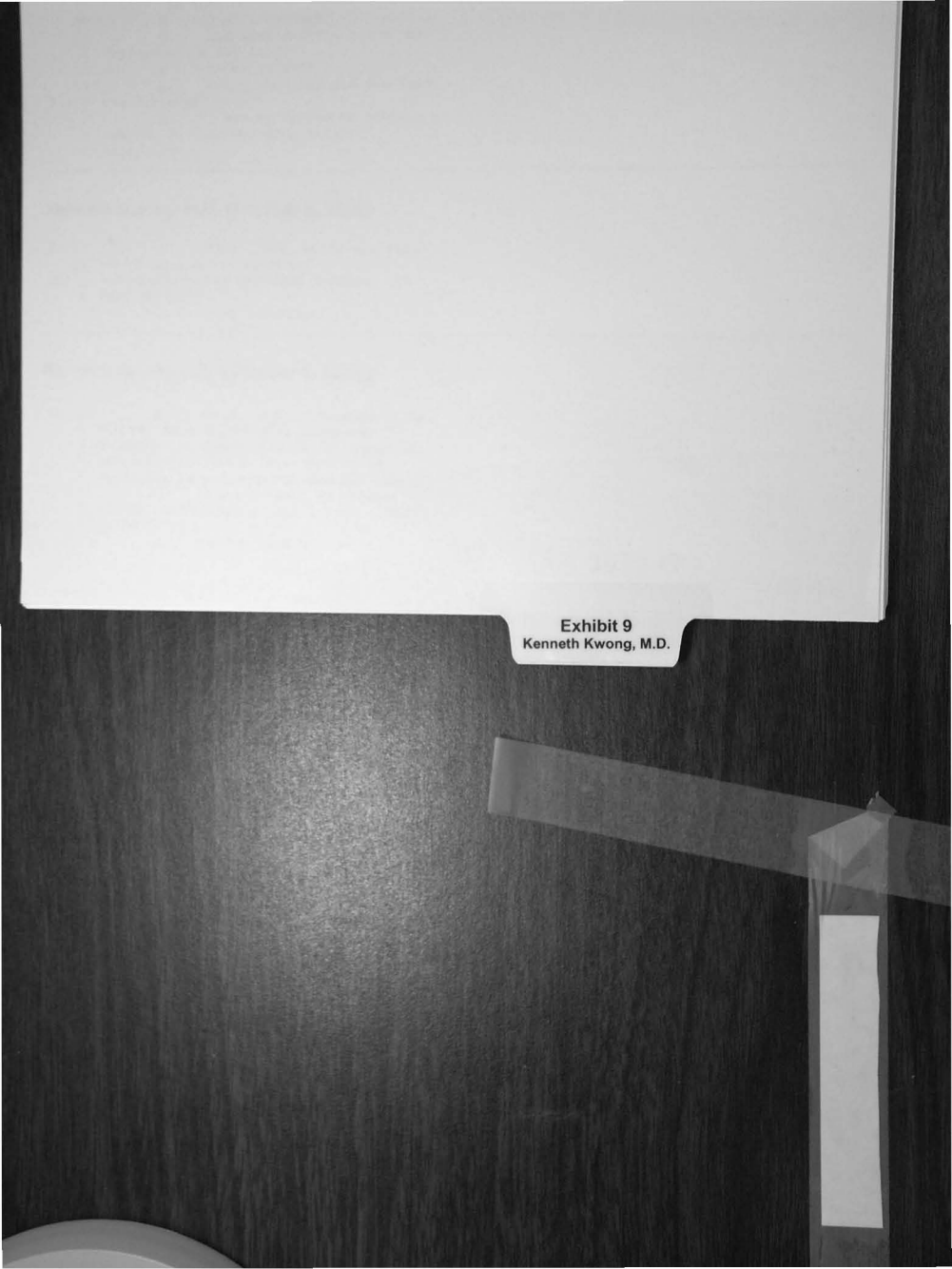
Exhibit 9
Kenneth Kwong, M.D.

Kenneth Kwong, M.D. (Octob 5, 2006)

29:11 Q. Good morning, Dr. Kwong.
12 A. Good morning.
13 Q. Would you state your full
14 name for the record, please?
15 A. Kenneth Cheung Kwong.

Kenneth Kwong, M.D. (October 6, 2006)

30: 2 Q. Okay. And what's your
3 present occupation?
4 A. I am a safety surveillance
5 physician at Johnson & Johnson.
6 Q. I'm sorry, did you say
7 safety surveillance?
8 A. Safety surveillance
9 physician.
10 Q. Okay. At Johnson & Johnson.
11 And what do you do in that position?
12 A. I do safety surveillance.
13 Q. And what do you mean by
14 that?
15 A. To identify safety signal
16 and to evaluate them in conjunction with
17 other physicians.
18 Q. And you used to work for Eli
19 Lilly. Is that correct?
20 A. That's correct.
21 Q. And when did you leave the
22 employment of Eli Lilly?
23 A. November 2001.
24 Q. Okay. And why did you leave
31: 1 the company?
2 A. I was recruited by Johnson &
3 Johnson to head the drug safety
4 department.

Kenneth Kwong, M.D. (October 6, 2006)

37:23 Q. Okay. Now, while you were
24 at Lilly, some of your job
38: 1 responsibilities involved Zyprexa. Is
2 that correct?
3 A. That's correct.

Kenneth Kwong, M.D. (October 6, 2006)

42: 2 Q. Okay. Before joining Lilly,
3 did you have any special training,
4 expertise or experience in the field of
5 endocrinology other than what would
6 typically be presented in medical school?
7 A. I was trained in medical
8 school, in residency also to see diabetic
9 patients.
10 Q. So you were trained in --

A. Medical school and also in residency. And we have rotations on endocrinology, diabetic clinics.
Q. Okay. And that would be a typical medical school training, correct, and typical residency training?
A. That is correct.
Q. Okay. And are you board certified in any specialties?
A. I'm board certified in internal medicine and also allergy and immunology.
Q. Okay. Did you -- before joining Lilly, did you have any special
43: 1 training, expertise or experience regarding the diagnosis or treatment of diabetes other than would be typically presented in medical school or residency?
A. I received general training.

Kenneth Kwong, M.D. (October 6, 2006)

46: 9 Q. Okay. And I believe you said you left the company in 2000 -- November of 2001. Correct?
A. Correct.
Q. Okay. So for -- you worked on Zyprexa for about two years?
A. Approximately.
Q. Okay. And what was your job title when you were in the pharmacovigilance department?
A. At Eli Lilly it was a senior clinical research physician.

Kenneth Kwong, M.D. (October 6, 2006)

48:12 Q. Okay. What was your understanding of the purpose of the pharmacovigilance department?
A. It is to monitor the safety profile of the product. To identify any safety concern and then to investigate further, to the best that you can, what's the role of drug might be in those signals that might come about.

Kenneth Kwong, M.D. (October 6, 2006)

49: 7 Q. If you detected a safety signal with the drug, did you feel that you had an obligation to do anything after that?

Kenneth Kwong, M.D. (October 6, 2006)

49:13 THE WITNESS: Of course, the
14 responsibility to investigate
15 further. I think we have to
16 understand what a signal means,
17 because it means different things
18 to different people. A signal
19 depends on -- there's really three
20 to four definitions available.
21 And the gist of it is really
22 increase reporting on something
23 unusual about certain type of
24 event that stand out, that's
50: 1 unexpected.

Kenneth Kwong, M.D. (October 6, 2006)

54:13 Q. Would you agree, sir, that
14 if Lilly did not warn doctors of
15 potential safety problems with the use of
16 Zyprexa, that would be wrong?

Kenneth Kwong, M.D. (October 6, 2006)

54:19 THE WITNESS: This is
20 hypothesis that you just phrased.
21 If -- I do not agree with that, so
22 I can't answer that.

Kenneth Kwong, M.D. (October 6, 2006)

57:18 Q. Okay. Now, when you joined
19 the pharmacovigilance department in '99
20 and started working on Zyprexa, how long
21 after you started working in that
22 department did you begin dealing with the
23 issue of hyperglycemia?
24 A. Hyperglycemia is an event
58: 1 that is identified by my predecessor. At
2 least people that worked with the product
3 before. So it's not something new.
4 Q. Okay. So at the time you
5 came to the pharmacovigilance department,
6 are you telling me that Dr. Man Fung had
7 already identified hyperglycemia as a
8 potential safety issue with respect to
9 the use of Zyprexa?

Kenneth Kwong, M.D. (October 6, 2006)

58:12 THE WITNESS: I don't know
13 who identified, but it was during
14 the time that he served as the
15 physician there. As I mentioned
16 earlier, there were multiple
17 people that work with a product.

He is one of th... So it could be him or it could be someone else.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. I'm going to show you what's been previously marked as MDL Plaintiffs' Exhibit Number 1605. For the record, this is a computer printout dated June 19, 1995 showing "Treatment-Emergent Abnormal, High, or Low Laboratory Values at Any Time" in the HGAJ study in the acute phase of the study.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Let me show you what's been previously marked as Plaintiffs' Exhibit 4176. For the record, this is a multi-page document with the title "Hyperglycemia, Weight Gain and Olanzapine." It's dated November 17, 1999. And I'll represent to you, sir, that when the documents are produced to us by Lilly, they sometimes in a database say from whose files they were produced. And the database in this instance said that this document was produced from your files. Just sort of looking at the document, generally, do you recognize it as something that you were involved in?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: I was the person who prepared this document.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Dr. Kwong, when was the last time you saw this document?
A. When I was at Eli Lilly.
Q. Okay. So you have not seen it in the last week or two?
A. That's correct.
Q. Okay.
A. I need time to refresh myself.
Q. Well, sir, it's a rather lengthy document. Can I suggest this, rather than taking the time to read through it word by word, page by page, I would request that you let me ask a question and if you feel you need to read more than what I've directed you to, to

answer the question, then by all means, you can take the time. But I think we can expedite this if you listen to the question, and if you feel comfortable answering the question, fine. If not, you need more time, we can take the time. But first let me direct your attention to the handwritten word on the first page, it says "Draft." Is that your handwriting?

A. That's correct.

Q. And also, too, on the second page, sir, in the right-hand margin,

112: there is some handwriting that appears to say "Need verification with later data," and then the initials KK. Is that your handwriting as well?

A. Yes.

Q. Okay. Were you -- were you asked to prepare this document?

A. My recollection is that's something I did on my own.

Q. Okay. And do you know, sir, was there a final version of this?

A. I cannot remember.

Q. Okay. Do you recall whether you -- this is a document that you would have sent around to others within the company?

A. I do not remember. I don't remember. I really don't.

Q. On the first page of the document, on the cover page --

A. Right. Uh-huh.

Q. No, sir, you need to turn back to the very front --

A. A cover page?

113: Q. The very cover page.

A. The cover page, okay.

Q. Okay. There's a box in the middle, which says inside the box, "This document contains trade secrets, or commercial or financial information, privileged or confidential, delivered in confidence and reliance that such information will not be made available to the public without express written consent of Eli Lilly and Company." Did I read that correctly?

A. Yes.

Q. And you were the one who put that on there. Correct?

A. I believe so.

Q. Okay. Did someone tell you to put that on there?

A. No. I think in general it's a good practice to do that. But often time I just forget.

Q. Okay. If I could direct your attention to the second physical page.

114: A. The second page?

Q. Yes.

A. Okay.
Q. And there is a bold heading at the top there entitled "SUMMARY."
A. Right.
Q. And then there's a section where you're referring to registration trials. Do you see that?
A. Yes.
Q. Now, the registration trials, those would be clinical trials that Eli Lilly did in support of getting approval from various regulatory agencies to market the drugs in different countries. Correct?
A. To my understanding, right.
Q. Okay. And in the first sentence in that section you state, 1.7 percent of 2,500 patients who received olanzapine experienced treatment-emergent hyperglycemia with non-fasting blood glucose greater than 250 milligrams per deciliter. Did I read that correctly?
A. Yes.
Q. And what does the term treatment-emergent hypergly -- strike that.

What does the phrase "treatment-emergent hyperglycemia" mean, or what did it mean to you when you wrote this?
A. It is something that occur after the treatment with olanzapine.
Q. Okay. So these would be 1.7 percent of the patients who received the drug experienced hyperglycemia after they began treatment with the drug. Correct?
A. Yes.
Q. Okay. And this was 1.7 percent who had non-fasting blood glucose greater than 250 milligrams per deciliter. Correct?
A. That's what it says here.
Q. And as we talked about before, the American Diabetes Association cutoff for the blood glucose values diagnostic for diabetes is only 200. Correct?
A. That's correct.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. On page 2, in that same paragraph that we were talking about before, the section regarding registration trials, the second sentence states "Most studies were 6-8 weeks in duration." That's referring to the clinical trials that had been done by Lilly. Do you know offhand what

proportion of studies were only six to eight weeks?
A. I do not know.
Q. Okay. Then you go on to note, "Studies of longer duration are needed to determine the true incidence as the mean time of onset of hyperglycemia was 16 weeks based on spontaneous reports, and weight gain plateau occurred after 38 weeks." Did I read that correctly?
A. Yes.
Q. Okay. And then you have a section called "Retrospective Study" where you make a reference to a Dr. Daniel Casey. Is that correct?
A. Yes.
Q. And you note that he, who
118: 1 was at the Portland Veteran Health
2 Science Center, reviewed the charts of
3 136 patients who had taken olanzapine for
4 four months or more. Sir, do you know
5 whether that study that he did was funded
6 by Lilly?
7 A. I only hear about this study
8 through other people. My recollection,
9 that he came to Eli Lilly to give a
10 presentation, so -- but I was not able to
11 make it, so I gather this from someone
12 else. I don't remember where I get it
13 from.
14 Q. So Dr. Casey apparently came
15 to Lilly to make a presentation about his
16 study, but you weren't able to attend,
17 but somebody told you about it?
18 A. Right.
19 Q. Who was it that told you
20 about it?
21 A. I do not remember.
22 Q. Okay. You note that in the
23 study Dr. Casey did review the charts of
24 patients who had used Zyprexa, the
119: 1 average treatment for those patients was
2 17 months, and 50 percent of 138 patients
3 experienced weight gain of 7 pounds or
4 more after initiating Zyprexa therapy.
5 Correct?
6 A. Yes.
7 Q. And then you note that
8 "Seven of the 39 patients (18%) who had
9 normal blood glucose levels at baseline
10 developed treatment-emergent
11 hyperglycemia." Did I read that
12 correctly?
13 A. Seven -- can you repeat
14 that? Seven --
15 Q. Seven of 39 patients or
16 18 percent who had normal blood glucose
17 levels at baseline developed
18 treatment-emergent hyperglycemia.
19 Correct? Is that what you wrote?
20 A. Yes.
21 Q. Okay. So what you're saying

there is of the group people that Dr. Casey was looking at who had normal blood glucose before they started taking the drug, 18 percent of those people who had been normal before became hyperglycemic after they took the drug. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: I don't have good recollection of this study here, because I've not seen the publication or attend the lecture.
BY MR. SUGGS:
Q. Sir, I was asking about what you wrote. What you wrote here says that seven of the -- pardon me -- that 18 percent of the patients that he looked at who had normal blood glucose levels when they started -- before they started taking the drug, developed treatment-emergent hyperglycemia after they took the drug. That's what that -- what you wrote, that's what that means. Correct?
A. That's what it says. What I don't remember, whether the blood glucose was fasting glucose or not, because fasting or non-fasting does make a difference depending on the compliance of patients on fasting or not.

Kenneth Kwong, M.D. (October 6, 2006)

This -- sir, one question I want to ask you now is, why would you regard the fact that 18 percent of the people developed hyperglycemia as something that should be kept from the public?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: What do you mean from the public? This is someone who do the work. He go to speak to a lot of places. I don't know who commissioned him to do a study. Could it be the government? So why do you say to the public? I'm not clear about that.
BY MR. SUGGS:
Q. Well, this Dr. Casey, he does a study where he finds 18 percent of the people who were normal were later hyperglycemic after using your company's

drug, he comes to the drug company to tell them that, and you write it up, or you mention it, and then you have a label on the first page here that says that this document contains trade secrets, commercial or financial information, privileged or confidential...that such information will not be made available to the public without express written consent of Eli Lilly and Company. Why would you want to keep that secret? Why wouldn't you want to tell doctors, prescribing doctors who are considering using your drug that, hey, you know, we heard from Dr. Casey out here that 18 percent of the people who take this drug develop hyperglycemia? Why wouldn't you want to tell treating doctors that, sir?

Kenneth Kwong, M.D. (October 6, 2006)

Q. Your labeling never ever told treating doctors that Dr. Casey had found that 18 percent of the people who had normal blood glucose before they started using the drug developed hyperglycemia afterwards. Your labeling never said that, did it?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: There are many studies.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Sir, my question was about what Dr. Casey said. What Dr. Casey told your company back in 1999. And is it not a fact, sir, that Lilly never warned about that in the labeling?

Kenneth Kwong, M.D. (October 6, 2006)

Q. Yes or no? Did they warn about that or did they not? Sir, they did not, did they?

A. There was no mention of the study, but not having seen this study myself, I don't know whether it was a quality study.

Q. Sir, the answer to my question is, no, Lilly did not warn treating doctors about that, isn't that

correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: As I mentioned, we did not mention this study.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. If I could direct your attention to the bottom of page 8, sir. There's a sentence -- pardon me, a paragraph at the very bottom of the page, it's in all bold font. Correct?
A. Bottom. Okay.
Q. And you would have been the one who put that in bold font. Correct?
A. I'm reading it. It was in bold font.
Q. Okay. And you were the one that would have put it in bold front. Correct?
A. I prepared the document, so unless someone change it, then it would be me.
Q. Okay. And you put it in bold font because you wanted to emphasize it and you thought it was important information. Correct?
A. Bold font for my purpose is to highlight things so that people can get the -- can get the main points as they read it.
Q. Okay. So you thought that the information in that bold paragraph down there was one of the main points you were trying to make. Correct?
A. Under that section it was the main point, because we were looking at obesity and hyperglycemia.
Q. Okay. And what that paragraph states is "Obesity or weight gain of 30 pounds or more were risk factors for developing hyperglycemia. Obese patients were 2.7 times more likely to report hyperglycemia than those who were not." Correct?
A. Yes.
Q. And clearly there was a link between Zyprexa-induced weight gain or diabetes. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: There's a temporal link.

Kenneth Kwong, M.D. (October 6, 2006)

147:21 Q. If I could direct your
22 attention to page 10. Actually, page 11,
23 sir. On page 11, you have a discussion
24 of weight gain. Correct?
148: 1 A. Yes.
2 Q. And you note that Dr. Bruce
3 Kinon had analyzed data from 70
4 olanzapine clinical trials, and found
5 that the mean weight gain of patients was
6 6.5 kilograms. Correct?
7 A. Yes.
8 Q. Now, 6.5 kilograms would
9 translate out to 14 pounds. Correct?
10 A. Approximately.
11 Q. Okay. And were you aware,
12 sir, that it's generally regarded as
13 clinically significant weight gain if
14 it's more than 7 percent of your body
15 weight?
16 A. Yes.
17 Q. Okay. And so this weight
18 gain, this average weight gain -- by the
19 way, the mean refers to the average.
20 Correct?
21 A. Yes.
22 Q. Okay. So some people are
23 going to gain less or nothing, and some
24 people are going to gain more. Correct?
149: 1 A. That's correct.
2 Q. And some people, in fact,
3 gained a lot more than that. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

149: 6 THE WITNESS: That I don't
7 remember.
8 BY MR. SUGGS:
9 Q. Do you remember Dr. Beasley
10 telling you that there were reports of
11 people gaining 80 or even 90 pounds of
12 weight on Zyprexa?
13 A. I don't remember.
14 Q. Okay. You wouldn't be
15 surprised if we've seen memos and e-mails
16 from him about that, would you?

Kenneth Kwong, M.D. (October 6, 2006)

149:19 THE WITNESS: I don't
20 remember.
21 BY MR. SUGGS:
22 Q. Okay. Well, this 14 -- this
23 average 14-pound of weight gain would be
24 clinically significant for anybody who
150: 1 weighed less than 200 pounds. Isn't that

correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: A 200-pound person would what, become 214? For some people might.
BY MR. SUGGS:
Q. It would be more than --
A. For some people might not.
Q. Okay. And you go on to say about 55 percent of patients had weight gain of over 5 kilograms after 1 year of olanzapine treatment. 16 percent had weight gain of 30 kilograms or more. Correct?
A. That's what it said here.
Q. And 30 kilograms would be 66 pounds. Correct?
A. Yes.
Q. And if I could direct your attention back to page 8, at the bottom, that bolded language that you said was, you know, one of your critical points of information you wanted to get across, the first sentence of which is obesity or weight gain of 30 pounds or more was -- were risk factors for developing hyperglycemia. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: That's what it says here.
BY MR. SUGGS:
Q. So clearly if we look back at page 11, that 16 percent of the people who had weight gain of 30 kilograms, which is 66 pounds, they would clearly have an increased risk of diabetes, according to what you said there. Right?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: Obesity is a risk factor for hyperglycemia and diabetes.
BY MR. SUGGS:
Q. Well, not only obesity. According to you, what you said on page 8, "Obesity or weight gain of 30 pounds or more were risk factors for developing hyperglycemia." You say that on page 8. And on page 11, you point out that according to your own clinical data from Lilly's trials, 16 percent of the people in the studies had weight gain of 30

kilograms or more, and 30 kilograms is 66 pounds. Correct?
A. Yes.
Q. So clearly those people who gained 66 pounds, 16 percent of everybody who took Zyprexa were at an increased risk for developing hyperglycemia. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

152:18 THE WITNESS: As I mentioned, obesity is a risk factor, so it's consistent.
BY MR. SUGGS:
Q. Well, not just obesity, you said weight gain. These aren't just people -- just fat people who took -- or
153: 1 obese people, I shouldn't -- I hope there's no sense of disparagement there, because I think if the camera was trained on me, the camera would probably say I'm obese or fat, but this isn't just a case of people who happen to be overweight taking the drug, they were at risk anyway, these were people that gained a lot of weight on the drug. Isn't that right?

Kenneth Kwong, M.D. (October 6, 2006)

153:14 Q. You have 16 percent of the people who took Zyprexa were gaining over 66 pounds. Correct?
A. That's what I said here.

Kenneth Kwong, M.D. (October 6, 2006)

158: 2 increase of 9 -- strike that. You point out that there was an "Average increase of 9.7% in body mass index." Correct?
A. Let me read this here.
Q. Okay.
A. Yes.

Kenneth Kwong, M.D. (October 6, 2006)

158:19 Q. Okay. So if the average increase was 9.7 percent in body mass index, that means that the average weight gain with Zyprexa was clinically significant. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

159: 2 THE WITNESS: Yes.

Kenneth Kwong, M.D. (October 6, 2006)

159:10 If the average weight gain
11 was more than 9.7 percent of the body
12 mass index, wouldn't that indicate that
13 the average weight gain on Zyprexa was
14 clinically significant?

Kenneth Kwong, M.D. (October 6, 2006)

159:17 THE WITNESS: Yes.

Kenneth Kwong, M.D. (October 6, 2006)

178:17 Q. I'm going to show you what's
18 been previously marked as Plaintiffs'
19 Exhibit 990. For the record, this is a
20 multi-page document, the first page of
21 which says "Attachment E." You've seen
22 this document before, haven't you, sir?
23 A. Yes, I think so.
24 Q. In fact, you helped write
179: 1 it?
2 A. It looks familiar.

Kenneth Kwong, M.D. (October 6, 2006)

179: 8 Q. Okay. If I could direct
9 your attention to the last physical page.
10 A. Okay.
11 Q. It states -- there's a
12 heading there called "Consultation
13 Process," and then it says, "REVIEWED
14 BY." One of the people listed there was
15 Dr. Charles Beasley, who is described as
16 the global products physician. Correct?
17 A. Yes.
18 Q. And the other person was
19 yourself being in the pharmacovigilance
20 group. Correct?
21 A. Yes.

Kenneth Kwong, M.D. (October 6, 2006)

186: 6 Q. Well, this document
7 generally talks about safety information
8 pertaining to Zyprexa and a proposed
9 label change. Correct?

Kenneth Kwong, M.D. (Octob[illegible]6, 2006)

186:23 THE WITNESS: I think
24 there's some proposed language
187: 1 changes, yes.
2 BY MR. SUGGS:
3 Q. And the purpose of the
4 proposed label change was to advise
5 prescribing physicians about information
6 pertaining to hyperglycemia with the use
7 of Zyprexa. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

187:18 THE WITNESS: As I can look
19 at the proposed language, that
20 seems to be that's the case.

Kenneth Kwong, M.D. (October 6, 2006)

190: 5 Q. Did the FDA make you put on
6 the front of this document that we were
7 looking at before, Exhibit 4176, that
8 talked about trade secrets and this
9 information will not be made available to
10 the public, did the FDA make you do that?

Kenneth Kwong, M.D. (October 6, 2006)

190:13 THE WITNESS: No, they did
14 not.
15 BY MR. SUGGS:
16 Q. That was your company that
17 decided what was going to be kept secret
18 and what wasn't, isn't it, sir?

Kenneth Kwong, M.D. (October 6, 2006)

190:21 THE WITNESS: I think in
22 general it's that you don't want
23 to release information until you
24 have quality check to outside
191: 1 folks.
2 BY MR. SUGGS:
3 Q. In general, you didn't want
4 to release information that was going to
5 potentially hurt your sales, that's what
6 was involved here, wasn't it, sir?

Kenneth Kwong, M.D. (October 6, 2006)

191: 9 THE WITNESS: I did not put
10 this language to this document.

The best person to answer this question is the people who prepared the document.
BY MR. SUGGS:
Q. Okay. Let's talk about the second page here. There's a box there in the middle that talks about how the proposal has arisen. Correct?
A. The second page?
Q. Yes.
A. Proposal?
Q. There's a box that has a title in bold print that says, "How Has this Proposal Arisen." Do you see where I'm at?
A. Yes. Uh-huh.
Q. And the text of that says, "Recent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment-emergent hyperglycemia in the olanzapine group (3.6%) was higher than that in the placebo group (1.05%)." Did I read that correctly?
A. Yes.
Q. And so the incidence was about three-and-a-half times higher in the Zyprexa treated group than it was in the placebo group. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

192:23 Q. Sir, what the -- what the document says is that there was about a 193: 1 three-and-a-half times higher incidence in the Zyprexa group as compared to placebo. Correct?
A. Right. Whoever prepared this document came up with this number.
Q. And who was it that did that recent review that showed that three-and-a-half times higher incidence in Zyprexa users?

Kenneth Kwong, M.D. (October 6, 2006)

193:12 THE WITNESS: As I said, this is -- I don't know.
BY MR. SUGGS:
Q. Okay. Sir, if you went out and told doctors in February of 2000 in a labeling change that the incidence of treatment-emergent hyperglycemia was three-and-a-half times higher in patients treated with Zyprexa as compared to placebo, that would have really hurt your sales, wouldn't it?

Kenneth Kwong, M.D. (Octob 6, 2006)

194: 9 THE WITNESS: It's not my
10 responsibility to say to
11 physicians, to say what the
12 language will affect sale.
13 BY MR. SUGGS:
14 Q. Well, sir, how long have you
15 been working in the pharmaceutical
16 industry?
17 A. Been with -- nine years.
18 Q. Nine years?
19 A. Right.
20 Q. In that nine years'
21 experience, you understand, don't you,
22 sir, that if you were to tell treating
23 doctors that your drug has a
24 three-and-a-half times higher incidence
195: 1 of hyperglycemia as compared to placebo,
2 that isn't going to help your sales, it's
3 going to hurt your sales, isn't it?

Kenneth Kwong, M.D. (October 6, 2006)

195: 6 THE WITNESS: This is a
7 question you can best ask the
8 people in marketing or sales and
9 not someone who -- probably
10 concerns the safety of patients.
11 BY MR. SUGGS:
12 Q. And between February
13 of 2000, when this labeling change was
14 proposed and you and Dr. Beasley reviewed
15 it, and May of 2000, several months
16 later, you, along with others, worked
17 with generating the label language that
18 actually was implemented. Correct?
19 A. Yes, to my recollection.
20 Q. Okay. And the people that
21 you worked with were Charles Beasley,
22 Alan Breier, Robert Baker, Barry Jones,
23 Bruce Kinon, Paula Trzepacz, Michele
24 Sharp. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

196: 3 THE WITNESS: I only
4 remember working with Charles
5 Beasley.
6 BY MR. SUGGS:
7 Q. Okay. Let me show you
8 what's been previously marked as --
9 A. And Michele Sharp after the
10 language was draft.
11 Q. Let me show you what's been
12 previously marked as Plaintiffs'
13 Exhibit 7012. For the record, this is a
14 March 27, 2000 e-mail from Michele Sharp
15 to Robert Baker, Charles Beasley, Alan

Breier, Barry Jones, Bruce Kinon, Kenneth Kwong, Paula Trzepacz, with copies to John Roth, Michele Sharp. Subject was "Proposed Zyprexa USPI revision -- hyperglycemia."

A. Yes.

Q. Do you recall receiving this e-mail on or about March 27, 2000?

A. I don't remember.

Q. Okay. By the way, when it says that the subject is "Proposed Zyprexa USPI revision," USPI refers to United States package insert. Correct?

A. Yes.

Q. The text of Michele Sharp's e-mail says, "Following a meeting on Friday, March 24 with Charles, Barry, Bruce and Paula, a new proposal for the Zyprexa USPI change with regards to hyperglycemia was developed. These words are in alignment with the Core Data Sheet wording." Did I read that correctly?

A. Yes.

Q. And then she goes on to say, Attached is the Adverse Reaction section of the label with the new words in large font (under the Laboratory Changes subsection). Please review the words that I crafted based on the conversation from Friday and send me any suggestions for improvement by Thursday, March 30. Also note that I included "diabetic coma" under the Post-Introduction sections sub -- Post-Introduction Reports subsection. We had previously proposed the inclusion of this COSTART term based on spontaneous reports, but we did NOT discuss this on Friday. I am assuming that we will be including this term in the label. Did I read that correctly?

A. Yes.

Q. And then there's a little box there that indicates that she probably attached a document that was entitled "Adverse Reactions and Hyperglycemia." Correct?

A. Right.

Q. Okay. We don't have the attachment that was produced to us, but then the following -- below that there is some more text from Michele Sharp, which says, "Following your review, I am planning to send the proposed text to our marketing colleagues in preparation for next Tuesday's (April 4) meeting (Weight Gain and Hyperglycemia -- Advisory Group). Please let me know if you will NOT be attending the April 4th meeting." Did I read that correctly?

A. Yes.

Q. Now, sir, who were the members of the weight gain and hyperglycemia advisory group?

A. I do not know. I did not participate in that group.
Q. Sir, that would have also included marketing people. Correct?
A. I don't know.
Q. Sir, it's clear from the text of this e-mail that what you had here was a group of people, including yourself, reviewing a proposed label change with respect to hyperglycemia in connection with the Zyprexa label, and that Michele Sharp had marshaled all of those things together, she's asking for your comments, and then it was her intent to send the proposed text to the marketing people in the company. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

200:
THE WITNESS: I do not know what her intent is. I did not participate in that meeting.

Kenneth Kwong, M.D. (October 6, 2006)

203:
Let me direct your attention to what's been previously marked as Plaintiffs' Exhibit 4858. For the record, this is a May 9, 2000 letter from Gregory T. Brophy to the FDA.
Have you seen this before, sir?
A. Me -- let me read this first.
Q. Sure.
A. Yes.

Kenneth Kwong, M.D. (October 6, 2006)

204:
Q. Okay. Do you see in the upper right-hand corner of the first page there's a bolded text which says, Special Supplement Changes Being Effected? Upper right-hand corner.
A. Upper right-hand. Changes being effective. I saw that.
Q. You see that. And you understand, don't you, sir, that the FDA regulations have a provision which permits a drug company to unilaterally change its label without prior FDA approval if the subject of the label change is to enhance the warranties?

Kenneth Kwong, M.D. (October 6, 2006)

204:24 Q. Is that correct?

205: 1 A. I'm not familiar with this
2 precatory language.
3 Q. I'm sorry, you say you were
4 not --
5 A. I'm not familiar with this
6 change being effective.
7 Q. Okay. If I could direct
8 your attention to the second page of the
9 exhibit -- well, let me back up for a
10 second.
11 In Mr. Brophy's letter to
12 the FDA, he says, pursuant to provisions
13 of 21 CFR, and he gives the citation to
14 the regulations, we are submitting a
15 revised package labeling for Zyprexa.
16 Correct?
17 A. Yes.
18 Q. And there are three changes
19 that are noted there. Correct?
20 A. One, two, three.
21 Q. Right. And the first one
22 has to do with a revision to the warning
23 section regarding reports of neuroleptic
24 malignant syndrome. Correct?
206: 1 A. Yes.
2 Q. And that has nothing to do
3 with diabetes, does it?
4 A. That's correct.
5 Q. Okay. And then there are
6 two other revisions in there that do
7 pertain to diabetes. Correct?
8 A. Yes.
9 Q. Okay. Let's talk about the
10 third change there first.
11 A. All right.
12 Q. What was done there was to
13 list in the adverse reactions
14 post-introduction report section of the
15 labeling inclusion of the term "diabetic
16 coma." Correct?
17 A. Yes.
18 Q. And they say this section
19 now reads, adverse events reported since
20 market introduction which were
21 temporally, but not necessarily causally
22 related to Zyprexa therapy include the
23 following: Diabetic coma and priapism?
24 A. Yes.
207: 1 Q. And priapism is uncontrolled
2 and prolonged erection of the male penis.
3 Correct?
4 A. Yes.
5 Q. No relation to diabetes.
6 Right?
7 A. That's right.
8 Q. Okay. And then item 2

data from the clinical trials as well. Correct?

A. Yes.

Q. Okay. For example, in the box "How Has this Proposal Arisen," in addition to noting, as we discussed before, an incidence of treatment-emergent hyperglycemia in the Zyprexa group that was three-and-a-half times higher than in the placebo, it also goes on to say in that box, "For common events, incidences from clinical trials provide more meaningful information." Correct?

A. Yes.

Q. Okay. That's what was proposed back in 2000. That proposal came from clinical trial information. Correct?

A. Yes.

Q. Okay. And then three months later, in May of 2000, after Michele Sharp has gotten involved and you're working with these other people, and marketing apparently gets the language to review, and then on May 9, 2000, what we have is what was actually sent to the FDA as the label change. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

Q. Isn't that paragraph 2?

A. Paragraph 2, this one here?

Q. Yes.

A. Okay.

Q. That's what was actually implemented. Correct?

A. Yes.

Q. And, in fact, this proposal to change the label was, in fact, made, and the label was changed and went out with the product after that point. Correct?

A. That's -- to my recollection, it did.

Q. Okay. And what is -- what came out here in this numbered item 2, essentially says there's not much difference between hyperglycemia in the Zyprexa group versus the placebo group. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: That's my recollection.

Kenneth Kwong, M.D. (October 6, 2006)

212:11 There's nothing in this
12 labeling that actually came out in May
13 of 2000 indicating that the incidence of
14 treatment-emergent hyperglycemia was
15 three-and-a-half times higher in Zyprexa
16 users. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

212:19 THE WITNESS: Yes, but I
20 don't know why -- how they come up
21 with those numbers before.
22 BY MR. SUGGS:
23 Q. It's a mystery, sir.

Kenneth Kwong, M.D. (October 6, 2006)

213: 6 So the labeling was changed
7 in May of 2000, it goes out to doctors.
8 Right?
9 A. Yes.
10 Q. Okay. And you also know
11 that the sales force was instructed about
12 the label change. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

213:15 THE WITNESS: I don't know
16 how -- what the sales force were
17 instructed, so I was not involved
18 in that.
19 BY MR. SUGGS:
20 Q. Well, sir, you know that
21 this label change here was viewed as
22 something very favorable for Lilly, and
23 Lilly wanted to get the word out about
24 this, didn't they?

Kenneth Kwong, M.D. (October 6, 2006)

214: 4 Q. They wanted -- they wanted
5 doctors to think that there wasn't much
6 difference between hyperglycemia in
7 Zyprexa users versus placebo. Is that
8 right?

Kenneth Kwong, M.D. (October 6, 2006)

214:11 THE WITNESS: As far as my
12 understanding, that we be sent the
13 data as we see it.
14 BY MR. SUGGS:
15 Q. Sir, this information was

put into what's referred to as a sell sheet, are you aware of that?
A. I'm not.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. Well, do you recall that you and Dr. Beasley and Paul Berg and Cindy Taylor and Jamie Dananberg and Alan Breier wrote up the data that formed the basis of this label change into a paper that you --
A. Yes.
Q. -- tried to get published?
A. Yes.
Q. Okay. Let me show you what's been previously marked as Plaintiffs' Exhibit 858. I think I gave you the wrong copy. Can I have that one back? I think I may have -- yes, I gave you my highlighted version. Let me give you these unhighlighted versions.
A. Thank you.
Q. For the record, this is a lengthy document entitled "Incidence and Rate of Treatment-emergent Potential Impaired Glucose Tolerance (IGT) and Potential Diabetes with Olanzapine Compared to Other Antipsychotic Agents and Placebo."
A. Yes.
Q. And this was a paper that was prepared by you along with Charles Beasley, Paul Berg, Cindy Taylor, Jamie Dananberg and Alan Breier. Correct?
A. Those are the authors listed.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Sure. Essentially what you did in this paper was a very similar analysis of glucose with -- blood glucose in connection with Zyprexa as what was done and reflected in this May 2000 label change. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: To my recollection, right.

Kenneth Kwong, M.D. (October 6, 2006)

Q. And I'm not going to be

asking you a lot of details about the question, but -- about the study, but if I could direct your attention to the second page, there's the abstract section of the paper. Correct?

A. Yes.

Q. And in the publication or attempted publication of scientific papers, they always start off with an abstract at the beginning that sort of summarizes generally, you know, what the background of the issue is, the method that's being used to perform the study, what the results were and what the conclusions were. Correct?

A. Yes.

Q. That's standard practice to do that. Right?

A. That's correct.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. And what you did in this analysis here and also in the label change that was reflected in Exhibit 4858 was you did an analysis where you broke out the data that you had with respect to glucose into various categories with various cut points of levels of blood glucose, and then you did analyses within those and between those categories. Is that correct, a clear statement?

A. Yes.

Q. Okay. And when you did that, as we noted here before, as reflected in the May 2000 label change, there was essentially no difference that you talked about with respect to the incidence of hyperglycemia between Zyprexa and placebo users. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: This statistically was not something different between the olanzapine arm versus the placebo arm.

BY MR. SUGGS:

Q. Okay. And then in this --

A. -- in 4,000 patients included.

Q. Right. And then the -- what this published paper or this attempted published paper, 858, was, it looked not only at the categorical analysis of hyperglycemia between Zyprexa as compared to placebo, but also did that type of analysis with respect to comparing olanzapine with haloperidol and also

risperidone. Correct?
A. I have to go back to read it.
Q. Okay. Well, let me -- let me help you out here, sir. I think I can save us some time. If I can direct your attention to the second physical page --
A. Second physical page.
Q. -- under the "Results" section in the second sentence you state quote -- or the paper states, "For the time to IGT...," which is impaired glucose tolerance "...or diabetes, olanzapine was not statistically different from placebo, haloperidol, or risperidone." Correct?
A. Yes.
Q. Okay.
A. Yes.
Q. And, in fact, on the third physical page, in the conclusion section, the second sentence states, quote, In these analyses, the estimated rate during treatment of -- with olanzapine was comparable -- well, let me back up for a second. In the first sentence of the conclusion you're talking about the rates of treatment-emergent impaired glucose tolerance and diabetes. Correct?
A. Can you repeat that?
Q. Sure. In the first sentence of the conclusion --
A. Yes.
Q. -- there is some discussion about the rates of treatment-emergent impaired glucose tolerance and diabetes. Correct?
A. Yes.
Q. Okay. And then in the second sentences, you say, "In these analyses, the estimated rate during treatment with olanzapine was comparable to the rates with placebo, haloperidol, and risperidone." Correct?
A. Yes.
Q. So the basic thrust of this paper was rates of diabetes, rates of impaired glucose tolerance, they're comparable between Zyprexa, placebo, haloperidol and Risperdal. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: That's what the data suggests.
BY MR. SUGGS:
Q. Okay. And you attempted to get this paper published in a journal called Biological Psychiatry. Correct?
A. That's correct.
Q. Okay. And it was rejected

for publication, was it not?
A. Yeah, it was rejected, right.
Q. Okay. Now, I'm going to get into the reasons why it was rejected in just a little bit, but it's also fair to say, and it was your understanding that this -- these conclusions of this paper which was rejected for publication were, in fact, used by Lilly repeatedly in marketing Zyprexa. Is that not true?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: I don't know.
BY MR. SUGGS:
Q. Did anybody tell you that the sales force was using this paper?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: I'm not aware of that.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Okay. I'm going to hand you what's been previously marked as Plaintiffs' Exhibit Number 1440. For the record, this is a -- what appears to be a fax from Biological Psychiatry dated November 3, 2000?
A. Yes.
Q. And do you recognize this document?
A. It looks familiar.
Q. Okay. Do you recognize this as the comments by -- let me back up for a second.
Biological Psychiatry was a peer-reviewed journal, was it not?
A. That's my understanding.
Q. Okay. And when we use the term "peer-reviewed journal," what that means is that the journal asks various people who are regarded as knowledgeable in the field, peers of the authors, to review the manuscript and then make comments and recommendations for changes and even recommendations as to whether or not the article should be published or not. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

230:17 THE WITNESS: That is my
18 understanding.
19 BY MR. SUGGS:
20 Q. Okay. And would you agree
21 with me, sir, that this particular
22 document, Exhibit 1440, appears to be the
23 reviewers' comments, the peer reviewers'
24 comments for the article that you wrote
231: 1 along with Charles Beasley and others
2 entitled Incidence and Rate of
3 Treatment-emergent Potential Impaired
4 Glucose Tolerance and Potential Diabetes
5 with Olanzapine Compared with Other
6 Antipsychotic Agents and Placebo?
7 A. That's the name of title.
8 Q. Okay. And that's the same
9 document that we -- pardon me. That
10 title is the -- refers to the paper that
11 we were just looking at before, which was
12 Exhibit 858. Correct?
13 A. Yes.
14 Q. Okay. And you would have
15 seen these reviewers' comments, I'm
16 assuming, back in November of 2000.
17 Would that be correct?
18 A. That was the same paper that
19 we just looked at, to my understanding.
20 Q. Right. And my question,
21 though -- my pending question has to do
22 with Exhibit 1440.
23 A. Okay. 1440.
24 Q. These reviewers' comments,
232: 1 you would have seen these reviewers'
2 comments relating to the article you
3 wrote with Dr. Beasley and others back in
4 November of 2000. Correct?
5 A. I remember reading it.

Kenneth Kwong, M.D. (October 6, 2006)

233: 9 Q. In the second paragraph --
10 A. Second paragraph.
11 Q. -- of referee number 1, he
12 states, "The importance of the study thus
13 rests with its ability to compare the
14 incidence and rate of treatment-emergent
15 IGT or diabetes during treatment with
16 various atypical antipsychotics versus
17 typicals and placebo." Correct?
18 A. That's what he --
19 Q. Is that what he said?
20 A. That's what he said.
21 Q. Okay. But then this
22 reviewer went on to say, quote, My only
23 concern regarding the methods of this
24 study, and thus with interpretation of
234: 1 their results, is whether the data were
2 biased toward short-term studies of
3 insufficient duration to detect the
4 effect the authors were examining. This
5 is especially relevant to the estimates

obtained for patients receiving placebo. It would be very helpful to know how many of the 6,374 patients in the database were actually in treatment beyond 8 weeks. Did I read that correctly?
A. That's what it says.
Q. And, in fact, sir, we know from examination of another document that we went over earlier today, in fact, most of the patients were involved in short-term trials. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

234:19 THE WITNESS: I don't remember the detail.
BY MR. SUGGS:
Q. Do you recall that in your Exhibit 4176, you stated, referring to the clinical trials, "Most studies were
235: 1 6-8 weeks in duration"?
A. You're talking about this paper here?
Q. No, I'm talking about your document that you wrote back in November of 1999.
A. November '99.
Q. I can pull it out for you, if you want.
A. November 1999. Okay.
Q. Let me hand it to you, I think it will go quicker. I'm referring to the second sentence in the first paragraph on that second page there. You note that most of the studies, most of the clinical studies were six to eight weeks in duration. Correct?
A. Yes. Uh-huh.
Q. So, in fact, this reviewer's comment and concern about whether the data were biased toward short-term studies of insufficient duration was, in fact, correct.

Kenneth Kwong, M.D. (October 6, 2006)

236: 3 Q. Is that right?
A. I think the merit of the reviewer's comment -- there is merit.
Q. I'm sorry, there is merit?
A. There's merit on the duration.
Q. Okay. If I could direct your attention to the second page of the document, which is the comments of the second referee, he stated, "The authors present a highly curious dataset. Since their own work has shown that olanzapine is associated with a clinically and

statistically pertine[redacted] increase in weight compared to both haloperidol and placebo, they seem to be suggesting that olanzapine exerts a sizable antidiabetic power."

Do you see that language, sir?

A. Yes.

Q. And then he later goes on to say, it's estimated that by the American Diabetic Association that a one pound increase in adipose tissue is associated with a 4 percent increase in the risk of diabetes. Given that olanzapine induces significant weight changes and the authors believe and report that it does not increase the risk of diabetes, olanzapine appears to be in the enviable position of eliminating the known risk of glucose intolerance associated with weight gain.

Do you see that language sir?

A. I saw that.

Q. So basically you would agree with me that this referee was saying that your article just didn't -- or your conclusions just didn't make sense --

---

Kenneth Kwong, M.D. (October 6, 2006)

Q. -- to say that, yes, there's weight gain, but, no, it doesn't increase the risk of diabetes. That's basically what this reviewer was expressing skepticism about. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

A. There was skepticism.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Directing your attention, sir, to the third page of the exhibit which appear to be the comments of referee number 4. He essentially offered four criticisms, and the first of which was "The authors do not adequately emphasize how crude their method is for finding an effect. Random glucose values represent an insensitive method for assessing glucose tolerance."

Do you see that language, sir?

A. Yes.

Q. And, in fact, it's generally

recommended that if you're going to be assessing the effect of a drug or treatment on blood glucose values, that you use fasting glucose values. Is that not correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: That is -- fasting glucose is preferable to random glucose.

BY MR. SUGGS:

Q. Okay. And in the second criticism of this referee, he said "Most of the values were probably drawn during the first three months of each trial. It would be helpful to know the number of samples in each condition that were collected during the later stages of the trial. For example, the number of specimens that were drawn for each drug condition during months 6-12." And, again, that criticism would go to the length of the studies involved. Correct?

A. That's correct.

Kenneth Kwong, M.D. (October 6, 2006)

Q. And, in fact, as we discussed before, most of the studies upon which you were basing your conclusions were only six to eight-week studies. Correct?

A. Yes.

Q. Okay. His third criticism was, Many of the early studies of olanzapine were biased toward low doses of the drug. Since there is a consensus that most patients require 10 milligrams or more of olanzapine, it would be helpful to know if there's a -- if there is a dosage effect on glucose tolerance. Do you see that language?

A. Yes.

Kenneth Kwong, M.D. (October 6, 2006)

Q. Well, if the -- if the length of the trials is less than would be expected in a normal clinical treatment with a drug, and if the dose is less, then your chances of this study actually describing what was going on in the real world would be a lot less. Right?

Kenneth Kwong, M.D. (October 6, 2006)

243:16 THE WITNESS: That would be
17 the case if there's a dose
18 depending effect.
19 BY MR. SUGGS:
20 Q. Okay. And then his fourth
21 statement was, "This study is important
22 since there is relatively little
23 controlled data in this area. At the
24 same time, it is a study with a good deal
244: 1 of commercial interest, and a study that
2 was designed and the data was analyzed by
3 olanzapine's manufacturer. For this
4 reason, it would be important to have an
5 independent analysis of the findings. If
6 there is a Type II error in these
7 findings, this could lead clinicians to
8 underestimate a serious drug risk."
9 Do you see that language,
10 sir?
11 A. I saw that language.
12 Q. Okay. So -- and let me
13 explore some of that with you. A Type II
14 error is a -- is a reference to -- in
15 science to not detecting a difference
16 when, in fact, there is a difference.
17 Correct?
18 A. Right.
19 Q. So what he was saying there
20 when he was referring to Type II error in
21 these findings, what he was saying was
22 that, if, in fact, these authors have
23 failed to detect a difference because of
24 the length of the trial or the dose that
245: 1 was involved or, you know, for whatever
2 reason, then this could lead clinicians,
3 that would be treating doctors, to
4 underestimate a serious drug risk.
5 Correct?

Kenneth Kwong, M.D. (October 6, 2006)

245: 8 THE WITNESS: This is the
9 reviewer's point of view.
10 BY MR. SUGGS:
11 Q. Okay. Clearly this reviewer
12 regarded hyperglycemia as a serious drug
13 risk. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

245:16 THE WITNESS: That's what
17 his language is.

Kenneth Kwong, M.D. (October 6, 2006)

246: 6 Q. Well, you were aware, were
7 you not, that back at that point in time,
8 in the fall of 2000, that Lilly's
9 competitors were beating up on Zyprexa,
10 if you will, pointing out potential risks
11 of hyperglycemia, and, in fact, the
12 company was having to struggle with that
13 issue in its -- out in the marketplace,
14 was it not?

Kenneth Kwong, M.D. (October 6, 2006)

246:17 THE WITNESS: I don't know
18 the marketplace. I did see
19 commercials on how other companies
20 that market antipsychotic.

Kenneth Kwong, M.D. (October 6, 2006)

249:10 Q. Well, clearly you were aware
11 that in the fall of 1999 you were having
12 the regulatory and pharmacovigilance team
13 and the Zyprexa team beefed up, you were
14 getting broader involvement of more
15 people. And in addition to that, you had
16 this cross-functional action team that
17 was led by Alan Breier. That's putting a
18 lot of resources into this issue, wasn't
19 it?

Kenneth Kwong, M.D. (October 6, 2006)

250: 2 THE WITNESS: That's more
3 than before, that's correct.

Kenneth Kwong, M.D. (October 6, 2006)

250:22 Your conclusions in the
23 paper that there was just comparable
24 rates of hyperglycemia --
251: 1 A. Basing on data that we have.
2 Q. I needed to finish the
3 question. But your conclusion was
4 obviously going to be beneficial for the
5 marketing efforts of Zyprexa. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

251: 8 THE WITNESS: That, I don't
9 know.
10 BY MR. SUGGS:
11 Q. Well, when this -- that's
12 exactly what was being referred to here

by this reviewer number 4 when he said it's a study with a good deal of commercial interest, isn't it?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: That's what the reviewer's point of view.

BY MR. SUGGS:

Q. Okay. Then he suggested that because the study was designed and analyzed by olanzapine's manufacturer, it would be important to have an independent analysis of the findings. Correct?

A. That's what the reviewer said.

Q. Okay. And were you informed by Dr. Beasley or anyone else that, in fact, a month earlier, in October of 2000, Lilly had convened a meeting with a number of outside experts in the field of diabetes to discuss Lilly's analysis of the hyperglycemia data?

A. I was not aware of it.

Q. I'm sorry, you were not aware of it?

A. I was not aware of it.

Q. Okay. I'm not doubting you, sir, but I want to show you a couple of documents just to see if they would perhaps refresh your recollection.

A. Okay.

Q. I'm going to show you what's been previously marked as MDL Plaintiffs' Exhibit Number 6998.

And by the way, before I get to that, can I have you pull out your boss' memo, Mr. -- Dr. Muniz's -- I think that's his -- yes, that's it. Here we go. This is -- I'm referring to Exhibit 8042.

In -- you see how he describe the cross action team led by Dr. Breier, and then there's a reference to the regulatory pharmacovigilance team and the Zyprexa team? There's a lot of names there. Sir, to your knowledge, were any of the people who were listed in that e-mail as being involved in either the cross-functional team led by Alan Breier or the regulatory pharmacovigilance and Zyprexa team, were any of those individuals experts in the field of diabetes?

A. I don't know all the names here, so I couldn't tell.

Q. Okay.

A. I know a few persons like Mike Clayman, Tim Franson, Edmundo, Greg Brophy.

Q. Recognizing, sir, that you

254: 1 don't know all of the people, is there
2 anyone there who you would say was, in
3 fact, an expert in the field of diabetes?
4 A. Half the people that I know
5 in this -- the list here, they are not
6 specialists in diabetes.
7 Q. Okay. No one. Okay. And
8 Lilly was, in fact -- liked to refer to
9 itself as the diabetes care company, did
10 it not?

Kenneth Kwong, M.D. (October 6, 2006)

254:13 THE WITNESS: I note that
14 Lilly market insulin and all
15 hyperglycemic. I don't know
16 whether it's called a diabetes
17 company.
18 BY MR. SUGGS:
19 Q. Okay.
20 A. Because also sell other --
21 many other products.
22 Q. But you understand that
23 Lilly had, in fact, been in the business
24 of marketing drugs for the treatment of
255: 1 diabetes for decades. Right?
2 A. That's correct.
3 Q. They have lots of people in
4 a whole different part of the company,
5 experts, scientists, medical doctors, who
6 dealt with diabetes on a day in/day out
7 basis. Correct?
8 A. They're experts. I don't
9 know where they're located.
10 Q. Not one of them was involved
11 in your group over here in the list
12 referred to by your boss, Dr. Muniz.
13 Correct?

Kenneth Kwong, M.D. (October 6, 2006)

255:16 THE WITNESS: Not the people
17 that I know.
18 BY MR. SUGGS:
19 Q. Okay. Directing your
20 attention back to Exhibit 6898, which I
21 handed you just a moment ago.
22 A. Okay.
23 Q. For the record, it's an
24 e-mail from Robert Baker to Charles
256: 1 Beasley, Christopher Bomba, Alan Breier,
2 Thomas Brodie, Patrizia Cavazzoni, James
3 B. Gregory, John Holcombe, Jack Jordan,
4 Suni Keeling, Bruce Kinon, Michael
5 Murray, John Richards, Eugene Thiem,
6 Mauricio Tohen and Paula Trzepacz,
7 with -- and the subject being "meeting
8 with endocrinologic consultants." And,
9 sir, you are not listed as a recipient of

this e-mail?
A. That is correct.
Q. Okay. In the first paragraph, Dr. Baker states, quote, for your information, The Lilly diabetes/endocrine group held an academic advisory board meeting this weekend in Atlanta. They kindly allotted two hours for discussion of olanzapine's potential hyperglycemia risks, and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling, and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic.
Do you see that language, sir?
A. Yes.
Q. Were you informed of that meeting at any time?
A. Not that I remember.
Q. Okay. In the following paragraph, at about the middle of the paragraph, Dr. Baker states "Citing methodological questions, at least the vocal members were not reassured adequately by our analyses, such as the finding that relative risk was not higher than comparative drugs. Disconcertingly, one member compared our approach to Warner-Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class."
Do you see that language, sir?
A. Yes.
Q. Were you informed that members of an outside advisory board formed of endocrine specialists had been concerned or raised questions about the methodologies of Lilly's analysis of hyperglycemia data?
A. I was not aware of it.
Q. Okay. I'm going to show you another document. This is Plaintiffs' Exhibit 1453. This is a multi-page document. And, sir, I would like to -- we've used this as an exhibit with Dr. Beasley and other folks. I'd like to direct your attention to page 4. This is an October 9, 2000 e-mail from Thomas Brodie to Robert Baker. Did you know who Dr. Robert Baker was?
A. My recollection, that he worked in the medical affair.
Q. And he was involved in the hyperglycemia issue, was he not?

258:24 THE WITNESS: I'm aware of
259: 1 it only through the things that
2 you have shown me so far, because
3 I did not interact with him --
4 BY MR. SUGGS:
5 Q. Okay.
6 A. -- on that particular issue.
7 Q. Okay. The text of the first
8 paragraph of Mr. Brodie's e-mail states,
9 "Robert.....clearly, this group of
10 Endocrinologists (who spoke up and I
11 would rate those who did speak up as the
12 leaders of the pack) are very concerned
13 with the approach Lilly is taking towards
14 the issue that Zyprexa leads to diabetes.
15 I can only hope that you and all of the
16 team who attended the NADAB meeting are
17 gaining the ear of senior leadership and
18 articulating this finding. Although the
19 board's recommendation is probably not
20 the way Lilly typically does business, I
21 do believe that they made a very strong
22 point that unless we come clean on this,
23 it could get much more serious than we
24 might anticipate."
260: 1 Do you see that language,
2 sir?
3 A. Yes.
4 Q. Did anyone inform you that
5 these outside consultants were warning
6 the company that unless Lilly came clean
7 on the issue of hyperglycemia, the issue
8 is going to get a lot more serious?

Kenneth Kwong, M.D. (October 6, 2006)

260:11 THE WITNESS: No. No one
12 did.
13 BY MR. SUGGS:
14 Q. Did anyone inform you that
15 this board of outside consultants had
16 also suggested, like the reviewer that we
17 saw in the prior exhibit, that there be
18 an independent analysis of the data?

Kenneth Kwong, M.D. (October 6, 2006)

260:21 THE WITNESS: As I said, I'm
22 not aware of that.
23 BY MR. SUGGS:
24 Q. Pardon?
261: 1 A. I'm not aware of the
2 recommendation.
3 Q. Were you aware that the
4 outside consultants who were experts in
5 the field of diabetes, recommended that
6 instead of doing the categorical
7 analysis, which you guys did, that

instead you look at t[illegible]data in continuous fashion and do a continuous analysis? Were you informed of that?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: No, I was not.
BY MR. SUGGS:
Q. When in 2001 did you leave the company?
A. November.
Q. November of 2001. So you would have been present back in February, correct, of 2001?
A. Correct.
Q. Let me show you what's been previously marked as Plaintiffs' Exhibit 5565. For the record, this is a February 22, 2001 e-mail from Charles Beasley to Ralf Dittmann, with copies to Alan Breier, Patrizia Cavazzoni, Ralf Dittmann, Mark Millikan, Anna Thornton and Gary Tollefson. You are not listed as a recipient, sir. At this time in February of 2001, were you still working on Zyprexa issues?
A. Yes.
Q. And you were still responsible for doing pharmacovigilance to detect safety signals?
A. Yes.

Kenneth Kwong, M.D. (October 6, 2006)

Q. If, in fact, there was evidence that Zyprexa users had an increased incidence of hyperglycemia, that is something that you, as a member of pharmacovigilance, should have been made aware of. Correct?

Kenneth Kwong, M.D. (October 6, 2006)

THE WITNESS: This is something I would be interested to know.

Exhibit 10
John Lechleiter, Ph.D.

John Lechleiter, PhD (March 28, 2007)

23: 5 Q. State your name for the
6 record, please, sir.
7 A. My name is John Clifford
8 Lechleiter.

John Lechleiter, PhD (March 28, 2007)

24:11 Q. Dr. Lechleiter, can you
12 please tell the jury your position with
13 Eli Lilly?
14 A. I am presently president and
15 chief operating officer of Eli Lilly &
16 Company.
17 Q. And that is the number two
18 position in the entire company, is it
19 not?
20 A. Yes, it is.
21 Q. You're also on the board of
22 directors of Eli Lilly?
23 A. Yes. I'm presently on the
24 board of directors.

John Lechleiter, PhD (March 28, 2007)

25:18 Q. You have been president and
19 chief operating officer of Eli Lilly
20 since approximately October of 2005; is
21 that correct?
22 A. Yes, that's correct.
23 Q. The only person more senior
24 to you in the entire company is Mr.
26: 1 Taurel; is that correct?
2 A. That's correct.
3 Q. And he is the chairman of
4 the board and CEO of Eli Lilly?
5 A. That's correct.
6 Q. And right underneath him is
7 you, Dr. John Lechleiter, president and
8 COO of Eli Lilly?
9 A. Yes. I report to Mr.
10 Taurel.
11 Q. Yes, sir.
12 You've been with Eli Lilly
13 since 1979?
14 A. That's correct.

John Lechleiter, PhD (March 28, 2007)

27: 8 Q. Do you also serve on the
9 policy and strategy committee of Eli
10 Lilly?
11 A. Yes, I do.
12 Q. How long have you been on
13 that committee?
14 A. The policy and strategy

007727

committee was renamed in October 2005. Prior to that, it was called the policy committee, and my membership on the policy committee dates from May 1998.

John Lechleiter, PhD (March 28, 2007)

32: 6 Q. The most recent report I have found is that you have direct ownership of approximately 150,000 shares of Eli Lilly stock?
A. Yes.
Q. And the current price of Eli Lilly Stock is in the neighborhood of $53 a share; is that correct?
A. I believe it's between 53 and $54.
Q. If my math is correct, that would be close to $10 million of Eli Lilly stock that you own?
A. Yes.

John Lechleiter, PhD (March 28, 2007)

33: 5 In 2005, reported cash compensation was close to $4 million, and your stock options in 2005 were a little over $400,000; is that correct?
A. I'm sorry. I'm just looking at this information.
Q. Yes, sir.
It's also on the screen. I've highlighted it for you. Does that sound about right, cash compensation of close to $4 million and stock options of 400,000?
A. Yes.

John Lechleiter, PhD (March 28, 2007)

39:10 Lechleiter. By the way, Dr. Lechleiter, for the record, I'm calling you Dr. Lechleiter because you are a doctor; is that correct?
A. I have a Ph.D. in organic chemistry.
Q. You have a Ph.D.
For the record, you're not a medical doctor, correct?
A. That's correct.
Q. You're not an expert in diabetes, for example; is that correct?
A. I'm not an expert in diabetes.
Q. You're not an expert in
40: 1 epidemiology?
2 A. I'm not an expert in

epidemiology.
Q. You're not an expert in psychiatry?
A. I'm not an expert in psychiatry.
Q. You're not an expert more particularly on schizophrenia or bipolar mania, are you, sir?
A. That's correct. I'm not a medical expert in those areas.

John Lechleiter, PhD (March 28, 2007)

42:17 For the record, from 1996 to 1998, you were vice president for Lilly Research Laboratories; correct?
A. I became vice president for Lilly Research Laboratories actually in 1993, and I served in that position until 1998. I served in a vice president position until 1998. The nature of what
43: 1 I did during that period of time changed.
Q. Yes, sir.
In 1998 you became senior vice president of pharmaceutical products for Eli Lilly; is that correct?
A. That's correct.
Q. In 2001 you became executive vice president of pharmaceutical products and corporate development; correct?
A. That's correct.
Q. In 2004 you became executive vice president for pharmaceutical operations; is that correct?
A. Yes. That's correct.
Q. In 2005, as we've already discussed, you were promoted and you became the number two individual at Eli Lilly as president and COO of Eli Lilly Corporation; is that correct?
A. I was promoted to president and COO in October 2005.

John Lechleiter, PhD (March 28, 2007)

47: 5 Q. You would agree that Zyprexa clearly exceeded all expectations of Eli Lilly on its income after it was placed on the market? You'd agree with that?
MR. LEHNER: Object to the form. Go ahead and answer.
THE WITNESS: In fact, from the time we launched Zyprexa, it did exceed our expectations. It actually has been a product that's been used by more than 20 million people around the world to treat some very, very serious disorders, schizophrenia and bipolar

disorder.
BY MR. ALLEN:
Q. In fact, sir, just for the record, it has never received any indication other than for the treatment of schizophrenia or bipolar mania; is that correct?
A. I believe that's correct. There's an intramuscular form of the product that I think has a slightly different indication, but it's in the same domain. I would also point out that the precise wording of an indication for a particular product, depending on where we market the product in the world, can be slightly different.
Q. Yes.
A. But in general, these are the two indications. Schizophrenia and bipolar mania are the two indications, you're correct.

John Lechleiter, PhD (March 28, 2007)

I also have seen your website, and some of the documents we'll see in this case describes Eli Lilly as the diabetes care company. Have you ever heard the company described in that nature?
A. Diabetes care is an important aspect of our business. It has been for over 80 years. We're not a diabetes care company, but it is an important part of our business.
Q. Yes, sir.
How many products and drug or pharmaceutical products does Eli Lilly market or sell that treat the disease diabetes?
A. We have several products that treat the disease, diabetes.
Q. What is the annual sales, if you know, approximately, of all of your diabetes products, Eli Lilly's diabetes products in 2006? What was your worldwide sales of diabetes products?
A. I don't have that number.
Q. Would it be in excess of a billion dollars?
A. Yes, it would be in excess of a billion dollars, but I don't know beyond that how much that would be.

John Lechleiter, PhD (March 28, 2007)

Q. Did you have any responsibilities regarding Zyprexa since 1996?

A. Well, in 1996, I was responsible for Lilly's global regulatory affairs function. That organization was mainly involved in helping Lilly gain registration approval for products including Zyprexa.

In 1998, I became head of essentially Lilly's drug development effort. That was the time when I became senior vice president for pharmaceutical products. That's a position that I held until January 2004. And during that time, my responsibilities included teams of scientists and physicians who were charged with bringing new drugs to market and also with developing new indications and new scientific data for existing products.

John Lechleiter, PhD (March 28, 2007)

Q. In fact, Dr. Alan Breier reported to you quite often as head of the Zyprexa product team about Zyprexa, did he not?

A. Dr. Breier was head of our Zyprexa product team for a period of time. During that time, he did not report directly to me, but certainly shared information on, I'm sure, a number of occasions in the time that he was in that position.

John Lechleiter, PhD (March 28, 2007)

Did Eli Lilly itself and its employees ever refer to the drug Zyprexa as a Lilly blockbuster?

A. I can't say that I recall Lilly specifically calling Zyprexa a blockbuster. It's been referred to as a blockbuster, I'm sure, by others. Generally, within our industry, any drug that exceeds about $1 billion in sales would be called by outside observers or referred to by outside observers as a blockbuster.

John Lechleiter, PhD (March 28, 2007)

In fact, Zyprexa, during the time period it was on the market, starting in year X, Zyprexa was the most important product for your company, was it not?

MR. LEHNER: Object to the form.

THE WITNESS: Sir, I'd like you to repeat the question. I don't -- your reference to "year X," I don't -- I wasn't quite following that.

BY MR. ALLEN:

Q. You know what "year X" is, though?

A. We've used the term -- we used the term "year X" to describe the point in time when Prozac, another Lilly product, was about to have its U.S. patent expire.

Q. Prozac was another Lilly blockbuster, was it not?

A. Prozac was an important product for Lilly and for millions and millions of patients. And it was also a drug whose sales in the course of its time on the market did exceed a billion dollars.

Q. In fact, Eli Lilly referred to Prozac as a blockbuster, did it not?

A. I don't recall that specifically.

Q. Okay.

Do you recall after the Court ruling, I believe it was in August of 2000, when Lilly's patent for Prozac was not upheld, that 2001 became year X?. You recall that, don't you?

A. I recall being aware of the appeal verdict in August of 2000 and having the knowledge at that time that within that year, we would lose the U.S. patent for Prozac, yes.

Q. That became year X?

A. That became year X. The

John Lechleiter, PhD (March 28, 2007)

MR. ALLEN: I'm going to hand you Exhibit 3, and this is a copy for your attorney.

\- - -

(Whereupon, Deposition Exhibit Lechleiter-3, "Summary of Historical Analysis - Zyprexa" Slide set ZY203323915 - ZY203323921, was marked for identification.)

John Lechleiter, PhD (March 28, 2007)

Exhibit Number 3 is a company confidential memo dated -- "Summary of Historical Analysis - Zyprexa, April 6, 2003." I'd like to go

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75: 3 produced to me. Let me say also
4 for the record, Exhibit Number 3
5 on the database was reflected as
6 coming from Dr. Lechleiter's
7 files.
8 BY MR. ALLEN:
9 Q. You recognize this, don't
10 you, Dr. Lechleiter?
11 A. I do not.
12 Q. Okay.
13 Nevertheless, the database
14 says that this document came from your
15 files. I'd like to read it along, parts
16 of it, and then ask you some questions.
17 It says, "Zyprexa was first launched in
18 late 1996. The estimated R&D" -- that's
19 research and development; is that
20 correct, sir?
21 MR. LEHNER: I'm going to
22 object to the form, but go ahead
23 and answer the question.
24 BY MR. ALLEN:
76: 1 Q. R&D is research and
2 development?
3 A. R&D stands for research and
4 development.
5 Q. "The estimated research and
6 development spend to first launch was
7 $195 million." Is that correct, sir?
8 A. That's what's written here
9 on the paper.
10 Q. Yes, sir.
11 Well, I'm sure your company
12 confidential memo would be accurate,
13 would it not, sir?
14 A. Sir, I'd have to say,
15 although you indicate this was found from
16 my files, not only do I not recall this
17 being in my files, as I sit and look at
18 the two pages you've provided, I have
19 absolutely no idea where this document
20 was produced or why. It's very difficult
21 for me to understand the information in
22 it without that context.
23 Q. Well, nevertheless, it was
24 produced by your attorneys in this case
77: 1 from your files, and we're just going to
2 go on. I'll read the document.
3 "The estimated R&D spend to
4 first launch was $195 million. Since
5 then, Lilly has sent approximately $750
6 million plus on R&D for Zyprexa's
7 multiple indications."
8 The multiple indications
9 we're talking about here, as you
10 previously told me, are schizophrenia and
11 bipolar mania, correct?
12 A. No. That's not correct.
13 Those are the current approved
14 indications. We've invested a huge sum

of money, $750 million, studying Zyprexa for a variety of indications, including dementia psychosis, bipolar depression and other things that may or may not have resulted in an approved FDA indication.

John Lechleiter, PhD (March 28, 2007)

The approved indications are schizophrenia and bipolar mania, correct?

John Lechleiter, PhD (March 28, 2007)

A. Those are the approved indications today for Zyprexa.
Q. Right.
And you said you may have spent money on looking into other indications. I think you talked about dementia. Did you talk about that?
A. Psychosis associated with dementia.
Q. Zyprexa has never been approved for that?
A. No, but we studied that extensively for many years.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-4, E-mails ZY207409274 - ZY207409275, was marked for identification.)

- - -

BY MR. ALLEN:
Q. Yes, sir.
I've handed you what I marked as Exhibit Number 4. It's an e-mail chain, John Lechleiter at the top, November 20, 2001. It was also marked in Ms. Denice Torres's deposition as Exhibit 26. It's an e-mail you wrote to Dr. Alan Breier; Sidney Taurel, the CEO of the company; Gino Santini, senior management; Gary Tollefson, one of your designated experts in this case; Dr. Albertus van den Bergh, who is also senior management, "Update on Zyprexa Dementia Program." Do you see that, sir?
A. Yes. I see that. But I don't think you've characterized the e-mail correctly. The e-mail that I sent went to the Lilly policy committee. That consisted of myself and other members of the senior management of the company. I copied on this message individuals including Dr. Breier and Dr. Tollefson

since Dr. Breier had sent me an earlier message here, and I believe copied some of those same people.

John Lechleiter, PhD (March 28, 2007)

And you are responding to an e-mail that was written to you by Dr. Breier dated November 19, 2001, correct?
A. That's correct.
Q. Dr. Breier said to you, "Update on Zyprexa's Dementia Program." He said "John, Following is an update on our Alzheimer's psychosis program: Zyprexa Product Team conducted 4 clinical trials with mixed results to support an indication for Alzheimer's psychosis." And then he gives you results of those studies, did he not?
A. Yes, he does.

John Lechleiter, PhD (March 28, 2007)

Q. The bottom line which is on Page 2, it says, "We recommend not pursuing a formal indication for Alzheimer's psychosis because of the mixed clinical results, the need to initiate another global trial, the high FDA threshold, concerning safety risks, and strategic focus on high dose segments. The recommended approach is to support this segment with a publication strategy."
Did I read that correctly, sir?
A. That's what's written in Dr. Breier's memo.
Q. Right.
You agreed with Dr. Breier, did you not?
A. I believe I forwarded his message to the policy committee indicating what Dr. Breier was recommending, and I indicated in this message that if anyone had any questions, they could -- we could discuss this further.
Q. You said you accepted Dr. Breier's recommendation not to seek an indication for psychosis related to dementia, correct?
A. My wording in the memo was "I accept their recommendation at this point."

John Lechleiter, PhD (March 28, 2007)

92: 5 Q. The product, pharmaceutical
6 product Zyprexa has been approved by the
7 FDA?
8 A. It's approved by the FDA.
9 Q. That product has never been
10 approved for depression; is that correct?
11 A. That product itself has
12 never been approved for depression.
13 Q. Either depression or bipolar
14 depression?
15 A. That product itself has not
16 been approved for bipolar depression. I

John Lechleiter, PhD (March 28, 2007)

92:22 Q. Zyprexa has never been and
23 is currently not -- or never been
24 approved for dementia, correct?
93: 1 A. Zyprexa has not been
2 approved for dementia.
3 Q. And it's never been?
4 A. Zyprexa has never had an
5 indication for dementia or the treatment
6 of the psychosis associated with dementia
7 nor for dementia.
8 Q. The FDA has never approved
9 Zyprexa for Alzheimer's disease; correct?
10 A. The FDA has not approved
11 Zyprexa for Alzheimer's disease.
12 Q. And it never has?
13 A. That's correct.
14 Q. Zyprexa has never been
15 approved for autism, correct?
16 A. Correct.
17 Q. Is has never been approved
18 for obsessive compulsive disorder or
19 attention deficit disorder, correct?
20 A. Correct.
21 Q. Zyprexa is not indicated for
22 and has never been approved by the FDA
23 for sleep disturbances, correct?
24 A. Correct.
94: 1 Q. Zyprexa is not approved and
2 has never been approved for irritability,
3 correct?
4 A. Correct.
5 Q. Zyprexa is not approved and
6 has never been approved for any pediatric
7 indication, correct?
8 A. Correct.
9 Q. Back to Exhibit Number 3, do
10 you have in front of you, sir?
11 A. Yes.
12 Q. Exhibit Number 3, April 6,
13 2003, "Summary of Historical Analysis"
14 talking about Zyprexa. "On a cumulative
15 IBT basis" -- that's income before taxes;
16 is that correct, sir?
17 A. That's what IBT refers to.
18 Q. -- "Zyprexa will bring in
19 approximately $16.1 billion in IBT

through 2004."
Did I read that correctly?
A. You read that from the document correctly.
Q. Right.
"Sales and IBT have greatly exceeded the initial pre-launch PMC" values.
Can you tell the jury what "PMC valuations" stand for?
A. "PMC" stands for the portfolio management committee. It's our top decision-making body within Lilly Research Laboratories.
Q. Are you on that committee?
A. No, I'm not on that committee.
Q. Have you ever been?
A. Yes, I have been on that committee.

John Lechleiter, PhD (March 28, 2007)

Q. "Have greatly exceeded the pre-launch PMC valuations for Psychosis and Schizophrenia combined. Through 2004, sales and IBT will be approximately $14.3 billion and $9.2 billion, respectively, above the initial PMC valuations."
Did I read that correctly?
A. That's what the document says, sir.
Q. So, the sales of Zyprexa through 2004 exceeded the portfolio management committee's evaluations by $14.3 billion, and the income before taxes of Zyprexa to Eli Lilly from 1996 exceeded the PMC valuations by over $9.2 billion. Is that correct, sir?
A. That's correct.

John Lechleiter, PhD (March 28, 2007)

I've handed you Exhibit 5. It's an e-mail from Marni Lemons, who I take it works in y'all's department dealing with the press, the press department?
A. I believe she works or worked at the time in our corporate communications group.
Q. Right.
She's sending this to the U.S. Zyprexa people on February 25, 2003. Really the only thing I really want to ask you about, she's saying, "The following article appears in today's Wall Street Journal." That's a

well-recognized business newspaper, is it not?
A. Yes, it is.

John Lechleiter, PhD (March 28, 2007)

Anyhow, "The following article appears in today's Wall Street Journal. It is based on a press release issued by IMS (press release is below)." You know who IMS is, do you not?
A. Yes, I know who IMS is.
Q. Tell the jury who IMS is.
A. IMS is a company that deals in information including information about prescription drug trends.
Q. Right.
In fact, Eli Lilly utilizes IMS's services itself, does it not?
A. I believe that nearly every pharmaceutical company relies on IMS for this kind of data.
Q. Yes, sir.
-- "Press release issued today by IMS (press release below) which states that Zyprexa is the number 4 drug in the world in terms of sales, and had the largest growth in sales, worldwide, of any other drug." This, again, was dated February 25, 2003. Did you see that?
A. Yes, it is. I want to make one comment, and that is Ms. Lemons was and may still be in our corporate communications group, but you characterized the address list as the U.S. Zyprexa people, and I don't know that. It's a group list of some kind. So, sir, I can't tell you precisely who that e-mail would have gone to. I just want to make that point.
Q. This data is talking about 2002. Do you agree and recall that Zyprexa was the Number 4 selling drug in terms of sales in the world?
A. I don't -- I would not have recalled that, but I'm taking that from this information you've provided me here.
Q. Okay.
If you go to Page 5 of this document, it says -- it is Table 3. "Leading Products in 2002" in the world. Are you there?
A. Yes, I am.
Q. I actually highlighted it for you so you can see what I was going to talk about, did I not?
A. Yes.
Q. The number one selling drug was Lipitor. That's for high cholesterol, right?

A. Yes, it i
Q. Number 2 was Zocor. That's for high cholesterol, correct?
A. Yes, I believe it is.
Q. Number 3 was Losec or Prilosec. That's for GERD, gastroesophageal reflux disease and ulcers; is that correct?
A. Yes, it is, I believe.
Q. The Number 4 drug in the world was for Zyprexa, which is indicated for schizophrenia and bipolar mania; is that correct?
A. Yes, it is.
Q. Number 5 is Norvasc, which is for high blood pressure; is that correct?
A. Yes, I believe it is. I'm

John Lechleiter, PhD (March 28, 2007)

Q. Dr. Lechleiter, using your common sense and your knowledge, you know that Zyprexa's indications are teeny, tiny compared to the population that suffers from high blood pressure, high cholesterol, joint pain and depression? Don't you know that?
MR. LEHNER: Object to the form.
THE WITNESS: I do not concede that.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-6, Wall Street Journal Web Page (1 page), was marked for identification.)
- - -
BY MR. ALLEN:
Q. Sir, I've handed you what's been marked as Deposition Exhibit Number 6. This is an on line document I got from the Wall Street Journal's web page concerning stock prices. Particularly I was looking at the stock price of Eli Lilly in the year 2000 from August 1st to October 10th. On August the 1st, Eli Lilly's stock price was somewhere near $110 per share. And before the end of August, it had dropped to $75 a share in August of 2000. What happened --
MR. LEHNER: Object to the form.
BY MR. ALLEN:
Q. -- to cause this stock price fall?
A. Stock price is generally

responsive to -- can be responsive to external events. In this case, we were surprised to receive, I believe, in early August, at about the time that you point to this stock price decline, word that was quite unexpected that a three-judge panel had reversed an earlier court's decision about the validity of our Prozac patent.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-8 (Zyprexa MDL Plaintiff's Exhibit No. 05913), Eli Lilly 2000 Annual Report ZY1 00205080 - ZY1 00205131, was marked for identification.)

- - -

BY MR. ALLEN:

Q. I'm going to hand you what I've marked -- it'll be -- it's Exhibit 8. It's Plaintiffs's Exhibit 5913. It's Eli Lilly's 2000 Annual Report. The front cover is a bad copy, but I think it says "Straight talk." But I'm going to turn to Page 6 of this report.

John Lechleiter, PhD (March 28, 2007)

Q. You're obviously familiar with the annual report?

A. Yes, I am.

John Lechleiter, PhD (March 28, 2007)

But anyhow, so, the 2000 annual report would have come out in March of 2001; is that correct?

A. That's right.

John Lechleiter, PhD (March 28, 2007)

we look at the 2000 annual report, it says, "No company would relish losing the patent on its biggest product three years early. We certainly don't." You're talking about Prozac, are you not, what happened with Prozac? Doesn't it say that -- it's right there. Page 6. Right in the middle of the page it says, "What happened with Prozac?"

A. Yes. I'm sorry. I was looking to see if it was a continuation, but it's not. It starts right there.

Q. Yes, sir. I'm trying to be fair.
Now, it says, "What happened with Prozac?"
It says, "No company would relish losing the patent on its biggest product three years early. We certainly don't."
A. That's what it says.
Q. Now, you didn't expect this, to lose this patent. You were surprised to have lost this patent?
A. Sir, we were surprised, but we were prepared.
Q. You were not only surprised, your report says you were "very surprised and disappointed by the judicial ruling." Is that correct?
A. That's correct.
Q. So, this loss of the Prozac patent that caused your company to lose over $36 billion in market cap came as a big surprise to Eli Lilly, did it not?
A. We were surprised at the ruling by the three judge panel.

John Lechleiter, PhD (March 28, 2007)

Q. Going on down, it's on the screen, sir, it says, what did y'all do? "We've significantly increased the size of our global sales force and will continue to do so in order to have the 'firepower' we need to successfully launch and sell the next wave of products from our pipeline."
Did you consider your global sales force fire power, sir?
MR. LEHNER: Object to the form.
THE WITNESS: Sir, our global sales force is the main way in which we engage our customers and help physicians make the right decisions for patients.

John Lechleiter, PhD (March 28, 2007)

Q. Go ahead and skip to Page 9, and we'll talk about this blockbuster term that we discussed earlier which is used by your company regarding Zyprexa.

John Lechleiter, PhD (March 28, 2007)

"So, what now?" Your company says, "Our newer products will

stand as our front line against
inevitable generic competition for
Prozac. Introduced throughout the last
half of the 1990s" -- that would be
Prozac, right? I mean, excuse me,
Zyprexa was introduced in the last half
of the '90s, right?
A. Yes. Zyprexa would be one
of several products introduced through
the last half of the '90s.
Q. -- "they'll be the key to
our ability to produce earnings growth
during that time and resume our strong
performance thereafter."
The number one product you
list, it's number one, and not in the
alphabet, it's number 26 in the alphabet,
is Zyprexa; is that correct?
A. Zyprexa is next in the text
here, yes.

John Lechleiter, PhD (March 28, 2007)

Q. "Zyprexa is a genuine
blockbuster, surpassing the $2 billion
sales mark in 2000 and becoming Lilly's
number-one-selling product in the fourth
quarter. Just as Prozac changed the
treatment of depression, Zyprexa has
redefined the standard of care for
schizophrenia, a devastating disease that
ravages the mind and has been called the
'cancer of mental illness.'" Did I read
that correctly?
A. Yes.
Q. You used the term in one of
your answers earlier, "the cancer of
mental illness"? Correct?
A. Yes.

John Lechleiter, PhD (March 28, 2007)

What you're just saying is,
once Prozac came off patent, you were
going to lose revenue, that's income to
Eli Lilly, and Zyprexa was going to be
one of the products that replaced
Prozac's lost revenue, true?
MR. LEHNER: Object to the
form.
THE WITNESS: As stated here
very clearly, Zyprexa, along with
Evista, insulins, Actos and these
new submissions which are noted
here and which I talked about
earlier, were all going to be
important for the company to
continue its growth trajectory
after the Prozac patent expired.

BY MR. ALLEN:
Q. Okay. The "growth trajectory," what does that mean?
A. Investors -- people invest in companies and expect companies to grow. So, this was about how are we going to resume growth after losing a substantial portion of sales of an important product, Prozac.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-9 (Zyprexa MDL Plaintiffs' Exhibit No. 8584), "Zyprexa Product Team Off-Site July 25, 2001" ZY201548768 - ZY201548789, was marked for identification.)
- - -
BY MR. ALLEN:
Q. I'm going to hand you what we've marked as Exhibit Number 9.

John Lechleiter, PhD (March 28, 2007)

Q. I've marked as Exhibit Number 9 a Zyprexa product team off site meeting, July 25, 2000. My first question to you is just tell the jury what the Zyprexa product team is.
A. First of all, I'd just like to make a correction. It's July 25, 2001.
Q. What did I say?
A. 2000.
Q. I apologize.
A. 2001.
Q. My question is, can you tell the jury what the Zyprexa product team is?
A. The Zyprexa product team is a group of clinicians, clinical scientists and other R&D personnel who are charged with the development of the Zyprexa molecule and the stewardship of the molecule from a scientific/regulatory point of view.

John Lechleiter, PhD (March 28, 2007)

Q. If you go one, two, three, four, the fifth page back in the PowerPoint presentation of Zyprexa product team, we'll see the heading --

John Lechleiter, PhD (March 28, 2007)

133:21 It says, "The company is betting the farm
22 on Zyprexa...the ability of Eli Lilly to
23 remain independent and emerge as the
24 fastest growing pharma company of the
134: 1 decade depends solely on our ability to
2 achieve world class commercialization of
3 Zyprexa."
4 Did I read that correctly?
5 A. You read correctly what's on
6 the slide.

John Lechleiter, PhD (March 28, 2007)

137:19 (Whereupon, Deposition
20 Exhibit Lechleiter-10 (Zyprexa MDL
21 Plaintiffs' Exhibit No. 01079),
22 "Zyprexa Primary Care
23 Presentation" (Bandick) 3-13-01
24 excerpts ZY1 00041630; ZY1
138: 1 00041632 - ZY1 00041633; ZY1
2 00041642 - ZY1 00041643; ZY1
3 00041645; ZY1 00041647; ZY1
4 00041650 - ZY1 00041651, was
5 marked for identification.)
6 - - -
7 BY MR. ALLEN:
8 Q. Okay.
9 Well, sir, I'm going to hand
10 you what I marked as Zyprexa Exhibit
11 Number 10. I have a copy for you and
12 both your counsel, Mr. Oltman and Mr.
13 Lehner.
14 This is a presentation put
15 on by Mike Bandick, "Zyprexa brand
16 manager, Eli Lilly National Sales
17 Meeting," on March 13, 2001. Do you see
18 that, sir?
19 A. I do see that.

John Lechleiter, PhD (March 28, 2007)

139:20 Q. This document reflects at
21 least that Michael Bandick was Zyprexa's
22 brand manager, right?
23 A. That's what this document
24 indicates.

John Lechleiter, PhD (March 28, 2007)

141: 7 Q. Page 4.
8 A. Okay.
9 Q. Mr. Bandick, continuing,
10 "This is year X for Eli Lilly, and the
11 conventional wisdom is that companies"
12 don't just -- "just don't 'bounce back'

from losing patent protection from their biggest product. We need to OWN this target, because the affiliate" -- that's Eli Lilly, isn't that the affiliate, Eli Lilly USA?

A. No. The affiliate refers to one of our businesses. So, when he's talking about "the affiliate" here, it would refer to not the company, but our U.S.-based business.

John Lechleiter, PhD (March 28, 2007)

143:20 Q. Sir, in order for year X to be exceptional and for Zyprexa to succeed, your company had to neutralize, minimize and eliminate the issues of weight gain, hyperglycemia and diabetes, 144: 1 isn't that true?

MR. LEHNER: Objection to the form.

THE WITNESS: That's an inappropriate characterization. I would not say it's true at all.

BY MR. ALLEN:

Q. Isn't it true, sir, that your company attempted to neutralize the issue of hyperglycemia and diabetes as a risk of Zyprexa?

A. I don't recall those --

MR. LEHNER: Objection to form.

THE WITNESS: I don't recall those terms being used. Our goal was to make sure that Zyprexa was used for the patients who could benefit from it.

BY MR. ALLEN:

Q. You, yourself, sir, personally, you, personally, Dr. Lechleiter, considered the disclosure of Zyprexa's side effect profile as a 145: 1 corporate crisis, didn't you?

MR. LEHNER: Object to the form.

THE WITNESS: I don't recall that.

- - -

(Whereupon, Deposition Exhibit Lechleiter-11 (Zyprexa MDL Plaintiffs' Exhibit No. 02368), "Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes" Diabetes Care Vol. 27, No. 2, February 2004 ZY200381764 - ZY200381769, was marked for identification.)

- - -

BY MR. ALLEN:

Q. Sir, I'll hand you what's been marked as Exhibit Number 11. It's

the consensus statement on antipsychotic drugs and obesity and diabetes. I have one for you and one for both of your counsel. I have highlighted your copy, and I will put it on the board.

You're familiar with this, are you not, sir, this consensus statement? You know exactly what this is, don't you?

A. Yes, I've seen this document before.

John Lechleiter, PhD (March 28, 2007)

This consensus statement, by the way, was put out by the American Diabetes Association, the American Psychiatric Association, the American of Clinical Endocrinologists, and the North American Association for the Study of Obesity, correct?

A. That's what I read here, yes.

Q. Yes, sir.

Also you know that they had a panel of experts and Eli Lilly made presentations before this panel before this consensus statement was published, correct?

A. I believe that's correct.

John Lechleiter, PhD (March 28, 2007)

Q. And once this thing was published, the consensus statement, once it was published, you considered it a corporate crisis for Eli Lilly, correct?

A. I considered the conclusions reached in this consensus statement to be dead wrong.

Q. Yes, sir. Of course you're not an expert in diabetes, are you?

A. I'm not an expert in diabetes, but I think if you --

John Lechleiter, PhD (March 28, 2007)

Q. Sir, you understand the American Diabetes Association, the American Psychiatric Association and the American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity is made up of individuals who do not manufacture nor sell antipsychotic medications. You understand that?

A. Sir, I know who these

associations are and what they are.

John Lechleiter, PhD (March 28, 2007)

Q. Well, nevertheless, you're not trying to tell this jury that these organizations, the American Diabetes Association and the American Psychiatric Association and the American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity are somehow not good organizations, are you?

MR. LEHNER: Objection to the form.

THE WITNESS: Sir, these are well known organizations. They're quality organizations. Regardless of that, we still take great issue with the conclusions drawn from this consensus conference. Their status or standing as organizations has nothing to do with the contents of this article you've put in front of me.

John Lechleiter, PhD (March 28, 2007)

Q. At least Table 2 reflects that under weight gain, diabetes and worsening lipid profile, clozapine and olanzapine are greater than Risperdal, Seroquel, Abilify and Geodon, correct?

A. Sir, we object to the fact and we objected to the fact as soon as this was published that these conclusions in Table 2 were drawn. We believe they're erroneous. We believe that a consensus panel could not have arrived at adequate conclusions and appropriate conclusions based on the process they used and the data they cited.

John Lechleiter, PhD (March 28, 2007)

Q. Sir, go to the next page, Page 598, under the issue of diabetes, I've highlighted it for you, it's on the board. It says, "Despite limitations in study design, the data consistently show an increased risk for diabetes in patients treated with clozapine or olanzapine compared with patients not receiving treatment with first generation antipsychotics or with other SGAs." Have I read that correctly?

A. You read that correctly.

Q. Yes, sir.
If you go to the summary, as in any articles or in most articles you'll see a summary, last page, it says, "Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia."
Skipping down, "Aripiprazole," and that's Abilify, "and ziprasidone," that's Geodon, "are associated with little or no significant weight gain, diabetes or dyslipidemia." And it goes on.
Did I read that correctly?
A. You read it correctly. We disagree with that conclusion.
Q. Nevertheless, it's their conclusion, correct?
A. It's their conclusion, but it's not the conclusion of Eli Lilly and company, nor of the U.S. FDA.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-12 (Zyprexa MDL Plaintiffs' Exhibit No. 03109), E-mails ZY200569220 - ZY200569223, was marked for identification.)
- - -
BY MR. ALLEN:
Q. Again, this was produced by your company. This is an e-mail on 1/27/04. We don't have time to read it, but if you look at the back initial e-mail, you'll see Eli Lilly received the consensus statement in advance, and you've already testified you recall getting the consensus statement in advance, correct?
A. I recall -- yes, I do recall that we received a consensus statement in advance.
Q. Okay.
Hunter Heath. Tell the jury who Hunter Heath is.
A. Hunter Heath, in this time period, I believe was the head of our medical function, our medical organization within the Lilly U.S. affiliate or the U.S. business. Hunter Heath is a physician.

John Lechleiter, PhD (March 28, 2007)

Q. Hunter Heath says, "Dear all, If you are not aware at the time you read this, you will soon know that we have been asked by Messrs.," that's you,

"Messrs. Lechleiter and Santini" -- tell the jury who Mr. Santini is.
A. Mr. Santini, at that time, was the president of our Lilly U.S. business.
Q. "We have been asked by Messrs. Lechleiter and Santini to gear up for a major assault on Zyprexa, because of the ADA consensus statement copied below. This is regarded as potentially a corporate-level crisis."
Did I read that correctly?
A. You're reading correctly from Hunter's memo, yes.
Q. And it concludes -- by the way, you're not saying that Dr. Heath is telling the -- he's being accurate here, isn't he?
A. I know only what you show me on this document. I don't recall this particular conversation, if it took place with Dr. Heath.
Q. Well, that's why you put things in writing, because it's hard to remember conversations you had over three years ago, correct?
MR. LEHNER: Object to form.
THE WITNESS: Sometimes it is.

John Lechleiter, PhD (March 28, 2007)

You understood that individuals within Eli Lilly believed that any "fair-minded, scholarly evaluation of the available data" in regard to Zyprexa would "support several conclusions," including that "Zyprexa, like other members of the class, causes weight gain," and 2, "like other causes of weight gain, Zyprexa-induced weight gain probably increases the risk of diabetes." You knew that, did you not?
MR. LEHNER: Object to the form.
THE WITNESS: No, I did not.
- - -
(Whereupon, Deposition Exhibit Lechleiter-13 (Zyprexa MDL Plaintiffs' Exhibit No. 08666), E-mails ZY201584949 - ZY201584951, was marked for identification.)
- - -
BY MR. ALLEN:
Q. Okay, sir.
And I think you've identified Dr. Taylor as a, you believe to be a research scientist. We're just going to put Exhibit 13 on the board. This is an e-mail written by Dr. Taylor on June 27th, 2002 to Hunter Heath and

192: 1 Dr. Tollefson, one of your designated
2 experts in this case, and other
3 individuals. And Dr. Taylor says,
4 "Ultimately, I...expect that a
5 fair-minded, scholarly evaluation of the
6 available data is likely to support
7 several conclusions."
8 I'm going to read 1 and 2.
9 "Zyprexa, like other members of the
10 class, causes weight gain."
11 "Like other causes of weight
12 gain, Zyprexa-induced weight gain
13 probably increases the risk of diabetes."
14 Did I read that correctly?
15 A. You read those two
16 correctly. This is pure hypothesis and
17 surmisal by this Dr. Taylor.
18 Q. Well, we saw where the
19 consensus statement that came out in
20 January of 2004 concluded that Zyprexa
21 had greater weight gain than the other
22 second generation antipsychotics and had
23 a greater risk of diabetes. Did you see
24 that conclusion in the consensus
193: 1 statement?
2 A. That was the conclusion
3 reached in this consensus statement that
4 we disagree with.
5 Q. Right.
6 And, Dr. Taylor, two years
7 before that, in the summer of 2002 at Eli
8 Lilly, said any -- that "a fair-minded,
9 scholarly evaluation of the available
10 data is likely to support" the fact that
11 "Zyprexa-induced weight gain probably
12 increases the risk of diabetes."
13 Doesn't he say that?
14 A. Sir, that's what's written

John Lechleiter, PhD (March 28, 2007)

200:15 My question to you is, you
16 at Eli Lilly knew that after the
17 consensus statement came out, Zyprexa
18 sales would suffer, correct?
19 MR. LEHNER: Same objection.
20 THE WITNESS: We did not
21 know that.

John Lechleiter, PhD (March 28, 2007)

246:19 And, in fact, sir, you at
20 Eli Lilly understood in October of 2000
21 that the weight gain and hyperglycemia
22 were major threats to your successful
23 marketing of Zyprexa, true?
24 MR. LEHNER: Object to the
247: 1 form.
2 THE WITNESS: I cannot

accept that as true. I don't know specifically what you're referring to.

John Lechleiter, PhD (March 28, 2007)

Q. So, nobody ever told you that in October of 2000 an endocrinology advisory board to Eli Lilly that met in Atlanta was concerned about the issues of weight gain and hyperglycemia as it related to Zyprexa?

A. No. I don't recall being told that.

Q. Do you think you should have been told?

A. Sir, what I should have been told represents the judgment of the people who work for me about whether a certain issue, a certain concern, a certain event, a piece of data warrants my consideration.

\- - -

(Whereupon, Deposition Exhibit Lechleiter-18 (Zyprexa MDL Plaintiffs' Exhibit No. 06998), E-mail ZY1 00378053, was marked for identification.)

John Lechleiter, PhD (March 28, 2007)

This is an e-mail by Dr. Robert Baker in October of 2000. Now, this e-mail written in October of 2000, just to put us in context, was shortly after the court decision that said Eli Lilly would lose its patent protection on Prozac in 2001, correct?

A. This is dated in October, and I believe the court decision was in that previous August.

Q. That's right.

So, we're approaching year X, correct?

A. Yes. We would have been in that time period.

John Lechleiter, PhD (March 28, 2007)

"FYI: The Lilly diabetes/endocrine group held an academic advisory board meeting this weekend in Atlanta."

Now, is this coming back to you, you recall this meeting in Atlanta?

A. No, I don't.

Q. "They kindly allotted two

hours for a discussion of olanzapine's potential hyperglycemia risk, and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling, and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic."

Do you recall that?

A. I don't recall seeing this document.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-19 (Zyprexa MDL Plaintiffs' Exhibit No. 01449), E-mails ZY1 00378054 - ZY1 00378056 was marked for identification.)

- - -

BY MR. ALLEN:

Q. I want to hand you Exhibit Number 19, another report on that meeting. I provided this to you last week. This is an e-mail from Tom Brodie.

John Lechleiter, PhD (March 28, 2007)

Q. Let's see what Mr. Brodie -- or is that Dr. Brodie?

A. I believe it would be Mr. Brodie.

Q. Mr. Brodie from the diabetes care side of the company says, "Subject: Re: Meeting with endocrinologic consultants." I'm sorry if I mangled that word.

He says, "Robert," he sent it to Robert Baker. The jury will know who Dr. Baker is. "Robert...clearly this group of Endocrinologists (who spoke up and I would rate those who did speak up as the leaders of the pack) are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes. I can only hope that you and all of the team who attended the North American Diabetes Advisory Board," that's NADAB, is it not?

A. I believe it is, yes.

Q. -- board "meeting are gaining the ear of senior leadership and articulating this finding. Although the board's recommendation is probably not the way Lilly typically does business, I do believe they made a very strong point

that unless we come clean on this, it could get much more serious than we might anticipate."
Did I read that correctly?
A. You read that correctly.

John Lechleiter, PhD (March 28, 2007)

269:13 sir, did anybody come and report on the
14 meeting to you?

John Lechleiter, PhD (March 28, 2007)

269:21 A. No one reported specifically
22 on the outcome of this meeting to me --
23 Q. At any time?
24 A. -- but I believe other
270: 1 members of senior leadership would have
2 been aware of this.

John Lechleiter, PhD (March 28, 2007)

271:21 (Whereupon, Deposition
22 Exhibit Lechleiter-20 (Zyprexa MDL
23 Plaintiffs' Exhibit No. 04051),
24 "Policy Committee Meeting April
272: 1 12, 2002 Zyprexa Safety Overview"
2 ZY1 00583063 - ZY1 00583066, was
3 marked for identification.)

John Lechleiter, PhD (March 28, 2007)

272:10 Of course you were kept
11 informed on matters involving Zyprexa as
12 a member of the policy committee, were
13 you not?
14 A. As a member of the policy
15 committee, I would have been kept
16 informed of important matters pertaining
17 to the product that were deemed to be
18 appropriate for the policy committee to
19 be knowledgeable of.

John Lechleiter, PhD (March 28, 2007)

273: 5 That's an exhibit -- this is
6 Exhibit 20, also MDL Exhibit 4051, policy
7 committee meeting, April the 12th, 2002,
8 "Zyprexa Safety Overview."

John Lechleiter, PhD (March 28, 2007)

committee Zyprexa safety overview. We've established you're on the policy committee, correct?

A. That's correct.

John Lechleiter, PhD (March 28, 2007)

"Clinical Data. Weight gain. Five atypical antipsychotic agents are associated with more weight gain than most traditional neuroleptic agents in the following order (most to least)."

Did I read that correctly?

A. You've read the statement correctly.

Q. Now, I would assume, since this is a policy committee on Zyprexa product safety, the individuals at this committee meeting are going to be reporting accurately and truthfully and being honest and forthright, correct?

A. I would believe that to be the case. I have no knowledge of who presented this information for the record.

John Lechleiter, PhD (March 28, 2007)

The policy committee had this report. It says, "in the following order (most to least)." Clozaril is the most, Zyprexa is next, Zyprexa is more than Seroquel, and Seroquel is more than Risperdal. Do you see that?

A. I see what's written here.

Q. That's in the policy committee meeting. That's very similar to Table 2 of the consensus statement published in January of 2004, is it not, sir?

A. I don't think it's similar to Table 2. Table 2 doesn't have the same order shown here.

Q. We'll let others be the judge of that.

All right. The next bullet point. "Zyprexa weight gain is roughly twice that of Risperdal. (Average 7 kilograms versus 3-and-a-half kilograms)."

Did I read that correctly?

A. You've read what's here correctly.

Q. All right.

And then it says, "Pfizer's Geodon and BMS's aripiprazole" -- now, that's Abilify, is it not?

A. I believe that's the product

name.
Q. You know it's the product name, do you not, sir?
A. Aripiprazole, I think that is Abilify. Is that what you said?
Q. Don't you know it's Abilify?
A. Yes. I'm very sure of that.
Q. Okay.
"Pfizer's Geodon and BMS's" Abilify "appear to have less metabolic issues than other atypicals."
Did I read that correctly?
A. That's what's written there.
Q. So, internally at Eli Lilly in April of 2002, the policy committee was told that Zyprexa has more weight gain than Seroquel and Risperdal, that Zyprexa weight gain is twice that of Risperdal, and that the other products on the market, Abilify and Geodon, have less metabolic issues than the other atypicals, correct?
MR. LEHNER: Object. Mischaracterizes the document.
THE WITNESS: This is a set of statements made in this document. I don't know what the basis was for this. I don't know how they were developed. What I

John Lechleiter, PhD (March 28, 2007)

Q. "A recent Zyprexa clinical trial analysis indicates patients with baseline diabetes risk factors (obesity, family history, non-Caucasian, advanced age) have higher occurrences of diabetes during," what treatment, sir?
A. During treatment with Zyprexa and other antipsychotics drugs.
Q. "Higher occurrences of diabetes during Zyprexa treatment and treatment with other antipsychotic drugs."
You were told that at the policy committee, were you not, sir?
MR. LEHNER: Object to the form.
BY MR. ALLEN:
Q. Or the policy committee was told that, right?
A. I don't recall this discussion in the policy committee, but I do see that that's written in this document.
Q. Next bullet point under diabetes to the policy committee in April of 2002. "Results of two Lilly epidemiological studies."
Did I read that correctly, sir?

A. Yes. We had quite a few studies in this area.
Q. Right.
"Results of two...epidemiological studies (analysis of AdvancePCS" -- what's AdvancePCS stand for, sir?
A. AdvancePCS is a pharmaceutical benefit manager that handles prescription execution for customers.
Q. So, you got their database. "(Analysis of AdvancePCS and GPRD," what's that?
A. I don't know what that refers to.
Q. "(Analysis of AdvancePCS and GPRD databases) indicate that the risk of diabetes is increased in patients treated with antipsychotics including Zyprexa."
Did I read that correctly?
A. That's what that sentence states, and that was information that

John Lechleiter, PhD (March 28, 2007)

question. As of April the 12th, 2002, there was no warning in the Zyprexa product label, as that term is defined by the FDA, concerning hyperglycemia and diabetes, correct?
A. There was nothing of that nature in the section under warnings, but

John Lechleiter, PhD (March 28, 2007)

We'll go back to the policy committee report on Zyprexa safety and see what you said internally. "FDA Freedom of Information Database of reports of diabetes cases: Clozaril: 542, Zyprexa: 434, Risperdal: 244, Seroquel: 57. Possible explanations for differences among these drugs are differences in weight gain, illness severity in target populations, and reporting bias."
Did I read that correctly?
A. That's what's written. There could be other reasons, as well, for the differences.
Q. Right.
So, individuals at Eli Lilly considered as a possible explanation for the increased reporting of diabetes related to Zyprexa was the issue of weight gain, correct?
A. No. I would not concede that. I would say that individuals,

whoever it was that prepared this report, looking at sheer raw numbers, that's what these 542, 434 are, just raw numbers, are speculating about why these numbers may be different. I can cite other reasons, and there are other reasons why they might be different, in addition to the ones cited, which include weight gain, illness severity and reporting bias.

John Lechleiter, PhD (March 28, 2007)

Diabetic ketoacidosis, second bullet point. "FDA Freedom of Information Database cases of DKA (cases" and "total exposures):" Clozaril, 103 cases, total exposure not available; Zyprexa 132 cases, 3.7 million exposures. Did I read that correctly?

A. That's what's written here.

Q. And of the gross number of cases of diabetic ketoacidosis as reported to the Zyprexa policy committee -- I mean, excuse me, Lilly's policy committee, Zyprexa had the most cases; is that correct?

A. Numerically, as it is shown here, Zyprexa had the most cases. It

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-21 (Zyprexa MDL Plaintiffs' Exhibit No. 00320), "Appendix 6: Japanese Dear Doctor Letter" ZY 4051 1633 - ZY 4051 1638, was marked for identification.)

John Lechleiter, PhD (March 28, 2007)

Q. This is the Japanese "Dear Doctor" letter label change. It's produced out of your company's files. It's Plaintiff's Exhibit 320. Is this bringing it back to you that there was a Japanese label change in April of 2002?

A. Yes, I'm aware of that.

John Lechleiter, PhD (March 28, 2007)

Q. And what happened was, Japan modified their label to put a warning about diabetes and hyperglycemia into their label, did they not?

A. Yes. Our label for Zyprexa in Japan was modified at that point.
Q. At the insistence of the Japanese regulatory authorities, correct?
A. That's correct.
Q. And they had a contraindication added that patients with a history of diabetes shouldn't even be given the drug, did they not?
A. They had a contraindication that we were forced to accept. We did not agree with that.
Q. Sir, you sell drugs in a country, you're bound by their regulations, are you not?
A. Yes, sir.
Q. So, you changed this package insert. According to Japanese regulatory authorities, you had to add a warning on hyperglycemia and diabetes, correct?
A. Yes. As I said earlier --

John Lechleiter, PhD (March 28, 2007)

306:21 Q. In April of 2002, you added
22 a warning on hyperglycemia and diabetes,
23 a contraindication for patients with a
24 history of diabetes, and you added
307: 1 precautions, including a precaution
2 concerning blood glucose monitoring of
3 patients on Zyprexa in Japan, correct?
4 A. These were required by the
5 Japanese regulatory authorities and based
6 on an unfortunate series of events where
7 several patients suffered from
8 complications of diabetes, based
9 primarily on poor medical care and not
10 ascribable to Zyprexa, in our opinion.
11 MR. SUGGS: Objection.
12 BY MR. ALLEN:
13 Q. Oh, so, you're blaming what
14 happened on the doctors in Japan?
15 A. There are individual cases,
16 I believe there were half a dozen or so
17 individual cases. I forget exactly what
18 the complications were, but it was very
19 clear to us at the time, in the short
20 time we had to analyze this data once we
21 were made aware of these cases, that
22 several of these patients who suffered
23 these complications had received very
24 poor medical care.

John Lechleiter, PhD (March 28, 2007)

310:24 Q. Doctor, you know, for a
311: 1 person that's not a medical doctor, are
2 you trying to suggest that you can judge
3 medical care of doctors in Japan, whether

it's good or bad, what doctors in Japan think about your product?
A. Sir --
MR. LEHNER: Objection to the form.
Go ahead.
THE WITNESS: -- I would never do that.

John Lechleiter, PhD (March 28, 2007)

Q. I've handed you what's been marked as Exhibit 23. You're familiar with this exhibit, are you not, sir?
A. I recall having seen this document.
Q. Sir, this document is a letter that was written to you or a memo written to you on July the 1st, 2002 by two members of senior management at Eli Lilly, correct?
A. Yes. It was written to me by Mr. Bert van den Bergh and Dr. Alan Breier.
Q. For the jury, who is Mr. van den Bergh?
A. Mr. van den Bergh was -- is a Lilly executive. At the time, I believe he was responsible for a group of neuroscience product teams, including Zyprexa.
Q. And the memo is written to you and Mr. G -- how do you pronounce that?
A. Mayr.
Q. And what's his title?
A. At that time, Mr. Mayr was responsible for global sales and marketing for Lilly.

John Lechleiter, PhD (March 28, 2007)

And it says trip summary to Japan in June of 2002. This would have been after the label change with the addition of the warnings, the contraindications and the precautions we previously discussed, correct?
A. Yes.

John Lechleiter, PhD (March 28, 2007)

Q. Do you recall receiving this memo?
A. I do recall receiving this memo.
Q. And did you pass the

findings of this memo [illegible] up to Mr. Sidney Taurel and the board of directors of Eli Lilly?

A. I don't recall doing that.

John Lechleiter, PhD (March 28, 2007)

316:19 Q. Was Mr. Mayr on the policy committee?
A. Mr. Mayr was on the policy and strategy committee.
Q. Okay.
So, at least two members of the policy and strategy committee in 2002 were provided this memo, correct?
A. That's correct.
Q. Okay.
We can't read it all, we don't have time.
"Japan Trip Summary." "It is clear that the impact of the label change in Japan has been very profound. We concluded we have lost substantial ground and trust in our relationships with the MHLW."
And that's the Japan equivalent of the FDA, correct?
A. Yes, it is.
Q. "Market research shows we have also lost quite a bit of credibility with prescribers and opinion leaders, basically because they felt left in the dark with what they perceived as the late sharing of...information" -- "the late sharing of safety information. As a result, there has been a 75% drop in new patients who are being put on the drug, and a continuing fairly high drop-out rate."
Did I read that correctly?
A. You read that correctly as it's stated. The reason why we lost -- why Dr. Breier might have stated we lost substantial ground and trust in our relationships with the MHLW is because, as I stated earlier, we did not agree with the MHLW's action, and we expressed that to them in discussions prior to the label change.

John Lechleiter, PhD (March 28, 2007)

320:14 Q. So, what you're saying is when you were required to inform the prescribing physicians specifically of the label change, you saw a dropoff in prescribing by 75 percent, correct?
MR. LEHNER: Object to the characterization.

THE WITNESS: What's written in this memo, which was written --

BY MR. ALLEN:

Q. Is that correct, what I said, or not?

A. I'm going to answer your question. This memo was written about four months, I guess, after the label change, and I can only answer what I can read from this memo, and that is that there was a substantial dropoff in new patients being put on the drug following that event.

Q. Right.

And not only on new patients, of patients that were on the drug, there was a fairly high dropout rate, correct?

A. That's what I read here from this memo.

Q. Then it also gives a forecast, Dr. Breier and Mr. van den Bergh expected that to continue. It says, "We need to also revise our forecast for the year to reflect the post label change environment and discuss how to communicate it to the sales force because it is very unlikely the affiliate will make plan."

Did read that correctly?

A. You did. This is a simple statement of fact that because prescriptions had fallen off, it was unlikely, at least according to this memo, that the forecasted sales of Zyprexa would be achieved that year, the plan -- I should say the planned sales of Zyprexa in Japan would be achieved that year.

Q. Yes, sir.

But we know at least for patients, Dr. Van den Bergh and Dr. Breier reported to Lilly that the patients were going to benefit by the label change, correct?

A. No, I don't know what you're referring to. I can't answer that question.

Q. Well, sir, let's look at the last page, where they sign off and make their conclusions. I'll start here. "Moreover, as patients with diabetes are shifted away from Zyprexa to Risperdal and Seroquel, there should be a balancing of the playing field on this issue over time. There appears to be a decrease of hyperglycemic, AEs"-- that's adverse events; is that correct?

A. Yes.

Q. -- "since the label changes. Again, we will make every effort through promotional efforts and physician-to-physician and medical

communications to ensure that we promote the use of the drug within the label, which would by design dramatically reduce the number of events."
Did I read that correctly?
A. You read it correctly. The other two products that are referred there, Risperdal and Seroquel, were not required at that time to adopt this warning language. I believe one of those products subsequently shortly thereafter was required to adopt this warning language. This refers to the fact that if patients who were at risk of diabetes or who had diabetes were contraindicated for use of our drug and they were subsequently treated with Risperdal or Seroquel, we might expect to see additional adverse events occur there. The fact that a decrease of hyperglycemic AEs was reported is, to me, a function of fewer people taking Zyprexa, consistent with what was said earlier in the memo.

John Lechleiter, PhD (March 28, 2007)

Q. At least Dr. Breier and Mr. van den Bergh reported you, "There appears to be a decrease of hyperglycemia adverse events," and they conclude that they're going to promote the product within the label, "which would by design dramatically reduce the number of events." Isn't that what they say at the time, sir?
A. Yes. We report -- we always promote our products within the label. As you pointed out, the label change that occurred in April of 2002 put much greater restrictions on Zyprexa prescribing than on the other products. One would expect, therefore, that if this label was followed in our promotional practices and in prescribing, physicians would likely see less reports of diabetes, because people with diabetes or predisposed in some way to diabetes would not be using our drug, they would be using another one of the products.

John Lechleiter, PhD (March 28, 2007)

(Whereupon, Deposition Exhibit Lechleiter-29, E-mails (4 pages), was marked for identification.)

John Lechleiter, PhD (March 28, 2007)

360: 3 Q. Dr. Lechleiter, you went out
4 to try to promote Zyprexa off label
5 yourself, did you not?
6 A. No, I did not.

John Lechleiter, PhD (March 28, 2007)

361: 6 Eli Lilly -- Exhibit 29 contains an
7 e-mail that you wrote, first of all,
8 right?
9 A. Yes.
10 Q. Okay.
11 Do you recall after you
12 wrote this e-mail that you had any
13 discussions with anybody about this
14 e-mail?
15 A. No, I don't recall. This
16 e-mail is a summary of a day I spent in
17 the field with one of our
18 representatives. I don't recall the note
19 back from -- that you've included here
20 from Mr. Ackerman.

John Lechleiter, PhD (March 28, 2007)

363: 3 Q. Did anybody come to you and
4 say your conduct and your statements in
5 this e-mail are inappropriate? Did
6 anybody come and make that statement to
7 you?
8 A. No, because I don't think my
9 conduct and statements were
10 inappropriate.
11 Q. Well, Denice Torres
12 testified that your conduct and
13 statements in this e-mail were
14 inappropriate from a marketing and
15 promotional perspective. Do you disagree
16 with Ms. Torres?
17 MR. LEHNER: Objection to
18 the form, characterization.
19 THE WITNESS: I don't know
20 what Ms. Torres objected to, but
21 my comments here were not
22 promotional in nature. My
23 comments were information I
24 gathered from being out and
364: 1 talking to doctors who prescribe
2 our products.
3 BY MR. ALLEN:
4 Q. You wrote this e-mail, John
5 Lechleiter, you wrote it. That's Mayr,
6 he's on the policy committee, Bill
7 Robinson, Gino Santini, Mauricio Tohen,
8 Gary Tollefson, Denice Torres, Alburtus
9 van den Bergh, Watanabe and Sydney Taurel
10 is on this. And Sydney Taurel, the CEO
11 of the company is on this e-mail, is he

not?
A. Yes. This would not have been unusual. This is a combination of my peers in both sales and marketing, and also in our research laboratories, including Dr. Tollefson, Dr. Watanabe, Dr. Tohen, et cetera.
Q. And as you said, this is notes from the field, when you went out with actual sales representatives in Cincinnati to assist them in promotion of Zyprexa?
A. I did not go out with sales reps to assist them in promotion. I go out with sales reps to observe them doing their jobs.
Q. Okay.
Here's what you said. "I have highlighted in bold the inputs that I consider to be most significant" --
So, these are your inputs, correct?
A. "Or that came up most often."
Q. -- "or that came up most often, and would appreciate if the global and U.S. teams would follow up as appropriate."
A. Yes. I read that in the document.
Q. And then you bolded, "'With child psychs,'" you put quotes, "'With child psychs, Zyprexa is a distant third across a range of disorders...'"
Did I read that correctly?
A. Yes, I wrote that.
Q. Okay.
And you're quoting from the comments that you heard when you went out in the field, right?
A. Yes, I must have been in this case. A physician must have made that statement.
Q. Then you made an editorial note yourself. This is your note.
A. Yes.
Q. It says, "Editorial note:" This is your view, correct?
A. Yes.
Q. "It appears to me that the fact that we are now talking to child psychologists and pediatricians and others about Strattera means that we must" -- must is a mandatory word, right? Must?
A. No. I would not call that a mandatory word. I start off by saying "It appears to me."
Q. Okay.
"It appears to me that the fact that we are now talking to child psychiatrists and pediatricians and others about Strattera means that we must

seize the opportunity to expand our work with" what drug, sir?

A. With Zyprexa.

Q. In what populations?

A. In the same population that Strattera typically treats.

Q. And that population is the child and adolescent population?

A. That's what's stated here.

Q. At the time this e-mail was written or at any time up until today, March 28th, 2007, did Zyprexa ever have an indication for treatment of adolescents and children?

A. Sir, my comments here were based on inputs I got from physicians directly during my visit, who stated to me that, in fact, they use Zyprexa and apparently other psychotics across a range of disorders. My role at the time in the company was the head of our product teams, our development teams. The questions they were asking me about Zyprexa must have suggested to me that there's more information that we needed to develop about Zyprexa in this population so that we can answer questions that they might have asked. In fact, we were also studying Zyprexa and continue to study Zyprexa in child and adolescent populations and recently were made aware by the FDA that that work has been deemed satisfactory enough for us to receive a pediatric patent extension.

MR. ALLEN: Objection, nonresponsive.

MR. LEHNER: And that will be the end of the deposition.

MR. ALLEN: No, no, no. I'm entitled to wrap up my questioning, and, no, you can't just stop it.

MR. LEHNER: Sure, I can.

MR. ALLEN: I'm asking your indulgence to wrap up my questioning.

MR. LEHNER: No. We finished the deposition.

Exhibit 11
David Noesges

David Thomas Noesges (January 11, 2008)

6:11 Q Would you state your full name for the record,
12 please?
13 A Yes. It's David Thomas Noesges.
14 Q And how do you spell your last name?
15 A Last name is spelled N-o-e-s-g-e-s.

David Thomas Noesges (January 11, 2008)

6:19 What is your occupation, sir?
20 A I am employed by Eli Lilly and Company.
21 Q And what's your job title?
22 A I'm currently the national sales director for our
23 U.S. diabetes unit.
24 Q For the U.S. diabetes unit.
25 Have you previously had responsibility with
7: 1 responsibility to Zyprexa?
2 A Yes, I have.
3 Q And what were your job titles? When did you work
4 on Zyprexa projects?
5 A I first began working for Zyprexa in 1999 as the
6 sales and marketing operations manager.
7 Q Was that based here in Indianapolis?
8 A Yes, it was.
9 Q Did you have any other jobs with respect to Zyprexa
10 after that?
11 A Yes, subsequent to that in 2000 through 2001 I was
12 the sales director for what was in our Midwest
13 area.
14 Q Okay. And did you have any job responsibilities
15 after 2001 with respect to Zyprexa?
16 A Yes. From 2003 -- late 2003, November, I believe
17 of 2003, until October of 2004 I was Zyprexa
18 marketing director.
19 Q And did you have any responsibilities for Zyprexa
20 after 2004?
21 A Yes. Then from 2004 until the end of 2007 I was in
22 a sales leadership role, first as the national sales
23 director for our neuroscience retail organization
24 from 2004 until basically the end of 2005.
25 Q Okay.
8: 1 A And then through -- from 2005 through 2007 I was
2 our executive sales director for the west region
3 of neurosciences.
4 Q Would that include Alaska --
5 A Yes.

David Thomas Noesges (January 11, 2008)

10: 9 First, can you tell me just generally your
10 educational background?
11 A Yes. I have an undergraduate degree from the
12 Unites States Military Academy at West Point.
13 Q Okay. And what year did you graduate?
14 A I graduated in 1984.
15 Q And did you serve in the Army then for some years
16 after that?
17 A Yes, I did.

Q And how long?
A I served for five years in the Army.
Q And did you have any -- when did you join Lilly?
A I joined Lilly first as a summer intern in the summer of 1990.
Q Okay. And when did you join them full-time?
A I joined full-time, then, in July of 1991.
Q Okay. Am I correct that you would have completed your service with the Army in 1989?
A Yes, that's correct.
Q What did you do jobwise between 1989 and 1991?
A I was a full-time student, graduate student, at the Wharton School of Business in Philadelphia.
Q Did you receive a degree there?
A Yes, I did.
Q Was it a Master's in Business Administration?
A Yes.

David Thomas Noesges (January 11, 2008)

Q Would it be fair to say that you did not have any experience in the pharmaceutical industry before joining Eli Lilly in 1991?
A Yes, that's correct.

David Thomas Noesges (January 11, 2008)

It would be fair to say, would it not, that your involvement with Zyprexa primarily had to do with sales?
MR. BOISE: Object to the form.
QUESTIONS BY MR. SUGGS:
Q Is that correct?
A My responsibilities were predominantly sales and marketing.

David Thomas Noesges (January 11, 2008)

You would agree that Zyprexa was one of Lilly's biggest selling products in terms of dollar sales, correct?
MR. BOISE: Time frame?
QUESTIONS BY MR. SUGGS:
Q From the time you began working on Zyprexa until you stopped.
A Yes, that's correct.
Q In fact, during that time period from 1999 throughout 2007 it was the largest selling product in the company, was it not?
A Yes, that's correct.
Q And do you happen to know what the annual sales of Zyprexa were in 2007 approximately to the nearest billion dollars?
MR. BOISE: U.S. sales?
MR. SUGGS: Yes.
THE WITNESS: I believe U.S. sales would have been between 2 and $3 billion.

QUESTIONS BY MR. SUGGS:
Q Was that lower than it had been the previous year?
A Yes.

David Thomas Noesges (January 11, 2008)

Q Would you agree with me that sales of Zyprexa declined after 2004?
MR. BOISE: Object to the form, beyond the scope.
THE WITNESS: Yes.

David Thomas Noesges (January 11, 2008)

Q Do you recall that the company increased the price of Zyprexa after 2004?
MR. BOISE: Object to the form, beyond the scope.
THE WITNESS: Yes.
QUESTIONS BY MR. SUGGS:
Q And did the company do that after sales began to decline?
MR. BOISE: Object to the form, beyond the scope.
THE WITNESS: Yes.

David Thomas Noesges (January 11, 2008)

Q Okay. Where are the sales reps trained?
A Depends on what phase of their training and where that would take place.
Q Tell me about the different phases that there are.
A Every new Lilly representative starts with an entry level sales school that we call ID school. It's initial training school which is conducted in Indianapolis.
Q How long does that last?
A It varies, depending on the products they have in a different time frame, but it's typically anywhere from a four- to six-week initial program.
Q And what programs follow after that?
A After that we currently have a three-month school which is done typically regionally in a decentralized fashion and they now come back for a nine-month school again which is a week-long program conducted again in Indianapolis.
Q When you said a "three-month school," is that how long the schooling lasts or does that take place after they have been a sales rep for three months?
A Takes place after three months as a sales representative.
Q How long is that training session?
A The program is approximately two to three days.
Q Okay. And then the nine-month school, I would presume, also does not last nine months but occurs after they have been a sales rep for nine months, correct?

A Yes, that is correct.
Q And how long does that take place?
A That's currently a week-long program.
Q Does the training process differ by state?
A Every representative goes through the comprehensive program I outlined and then we do a lot of ongoing training for our representatives throughout the country.
Q Is it fair to say that sales reps are expected to say particular things about Zyprexa and not say other things when they are selling the product?
MR. BOISE: Objection, vague.
THE WITNESS: Our sales representatives are required to follow our promotional guidelines and the promotional message that we establish for them.
QUESTIONS BY MR. SUGGS:
Q And that -- those promotional guidelines and the message that you establish are for the product throughout the United States and they are not particular for any given state or region, correct?
A Yes, that's correct. We have one promotional message throughout the United States.

David Thomas Noesges (January 11, 2008)

Q It's not left up to the individual sales reps to decide what the appropriate messages are with respect to Zyprexa, correct?
THE WITNESS: Each of the sales representatives are required to use the messages that we establish for them nationally and then to determine, based on the customer needs, how to appropriately utilize those messages.
QUESTIONS BY MR. SUGGS:
Q In fact, sales reps are prohibited from developing their own promotional materials, correct?
A That's correct. The sales representatives can't develop homemade materials.

David Thomas Noesges (January 11, 2008)

Q What is the knowledge management database?
A Knowledge management is a database available for the sales representatives to receive communications from Indianapolis and information and tools.
Q Okay. And would sales representatives be alerted that there was something on the database that they have to be aware of? Like, would they receive an E-mail or something telling them that something was on the --
A Yes, oftentimes there's something on knowledge management --
MR. BOISE: Let me interpose an objection. Vague.
You can answer the question.
THE WITNESS: Yes, oftentimes they would be notified if there was something new in knowledge management that they needed to access.

David Thomas Noesges (January 11, 2008)

44: 3 Q Let's talk about the content of the sales messages
4 that were used by Lilly sales reps for Zyprexa, in
5 particular, regarding hyperglycemia and diabetes.
6 Were you -- I believe you said you began
7 working on Zyprexa in 1999; is that correct?
8 A Yes, that's correct.
9 Q What month?
10 A I believe it would have been October or November of
11 1999.
12 Q Okay. And at that time you were aware that there
13 had been concerns expressed in the marketplace and
14 in published medical articles that weight gain
15 associated with Zyprexa could cause patients to
16 develop diabetes, correct?
17 A Yes, I'm aware of those concerns.

David Thomas Noesges (January 11, 2008)

45: 4 Q Sir, weight gain and possible hyperglycemia was
5 recognized as a major threat to Zyprexa, which was
6 a critically important product to the company,
7 correct?
8 MR. BOISE: Object to the form of the
9 question, compound.
10 THE WITNESS: I would not regard -- major
11 threat would not be a characterization that I made
12 at that time.
13 QUESTIONS BY MR. SUGGS:
14 Q Let me hand you what's been previously marked as
15 Plaintiffs' Exhibit No. 8262. For the record this
16 is a string of E-mails in November of 1999.
17 I would direct your attention, in particular,
18 sir, to the E-mail at the bottom of the first page,
19 which is a November 9, 1999, E-mail from Alan
20 Breier to a number of individuals, looks like about
21 a dozen or more, including several top executives,
22 such as John Lechleiter and August Watanabe.
23 Do you recognize the names of any of those
24 individuals, sir?
25 A Yes, I do.
46: 1 Q And were you aware that Alan Breier was the head of
2 Zyprexa product team?
3 A Yes, I am.

David Thomas Noesges (January 11, 2008)

47: 2 Q And in the first sentence in this E-mail from
3 November 1999 it states, quote, Olanzapine-
4 associated weight gain and possible hyperglycemia
5 is a major threat to the long-term success of this
6 critically important molecule.
7 Do you see that language?
8 A Yes, I do.

David Thomas Noesges (January 11, 2008)

48: 4 Q No one ever told you that?

David Thomas Noesges (January 11, 2008)

48: 5 MR. BOISE: Objection, foundation, compound
6 question, beyond the scope.
7 THE WITNESS: I don't believe in 1999 that
8 weight gain and possible hyperglycemia were
9 characterized to me as a major threat to a
10 long-term success.
11 QUESTIONS BY MR. SUGGS:
12 Q So apparently people like Alan Breier and John
13 Lechleiter were aware of that, but you were not in
14 your position --
15 MR. BOISE: Object to the form.
16 QUESTIONS BY MR. SUGGS:
17 Q -- correct?
18 MR. BOISE: Foundation, beyond the scope.
19 THE WITNESS: I don't believe they
20 characterized weight gain or hyperglycemia as a
21 major threat to me in November of 1999.

David Thomas Noesges (January 11, 2008)

55: 2 Q In fact, your sales reps have been taught to say
3 that there is no causal relationship between
4 Zyprexa and the onset of diabetes, isn't that true,
5 sir?
6 MR. BOISE: Objection, foundation.
7 THE WITNESS: Our position as
8 communicated to the sales representatives is that
9 based on our analysis of the data we cannot
10 determine a causal relationship between Zyprexa and
11 diabetes.
12 QUESTIONS BY MR. SUGGS:
13 Q I'm going to hand you what's been previously marked
14 as Plaintiffs' Exhibit 1941. For the record this
15 is a document entitled "ZYPREXA 'FREQUENT AREAS OF
16 CONCERN' OR 'FAOC.'" I'll also represent to you,
17 sir, that the database that has been provided to us
18 by Lilly states that this document was generated on
19 June 28, 2002.
20 And I'll also represent to you that Lilly has
21 stated in answers to interrogatory in this case in
22 Alaska that this document was in the knowledge
23 management database and made available to sales
24 representatives.

David Thomas Noesges (January 11, 2008)

58: 5 Q What this document does is identify various
6 concerns that physicians had about Zyprexa and then
7 tells the sales rep how to respond, correct?
8 A Yes. This document is a training document to help
9 provide sales representatives to answers to

frequently asked questions of physicians.
Q One of the questions is Question No. 6 on page 2. The question is: "I am concerned about diabetes." And below that it says "Cushion."
What does cushion mean?
A Cushion quite simply means to -- as it describes here to thank the doctor for the concern and to show empathy for the doctor, that this is a valid concern that we want to address.
Q And then it says "Clarify," and there to clarify it says, "Is this something you have seen or heard about?" Correct?
A Yes.
Q And then there is -- below that it says, "Address AOC." AOC stands for area of concern, correct?
A Yes, that's correct.
59: Q And in this response -- pardon me, and in that section there the sales rep is told what to tell the doctor, correct?
A Yes, that's correct.
Q And in the third sentence of that paragraph it states, quote, In every study examining this subject, no causal relationship has been established between patients being treated with Zyprexa and the onset of diabetes, correct?
A Yes, that's correct.

David Thomas Noesges (January 11, 2008)

60: Q Have sales reps ever to your knowledge been instructed to go out and admit to physicians that Zyprexa can cause diabetes?
A No, that has never been a specific verbatim for our sales representatives.
Q In fact, they go on to say in this document, the following sentence says, "The incidence of diagnosed treatment-emergent diabetes with patients taking Zyprexa was comparable to those patients treated with Risperdal, Haldol and Depakote in every clinical study conducted by Lilly ir by our competitors."
Did I read that correctly?
A Yes, you did.
Q And Risperdal, Haldol and Depakote are other psychiatric drugs, correct?
A Yes, Risperdal and Haldol are antipsychotic medicines and Depakote is a mood stabilizer.

David Thomas Noesges (January 11, 2008)

63: If I could direct your attention to the first page of this document. Let's stay with the page that we were on, at least the question we were on.
This document, after instructing the sales reps to address the area of concern, then says that the sales reps should check for agreement and then get back to selling, correct?

David Thomas Noesges (January 11, 2008)

63:11 Q That's what the sales reps were told, give this
12 message here that was developed out in
13 Indianapolis -- strike that.
14 The sales reps were told that if a doctor said
15 he was concerned about diabetes they should address
16 that area of concern using that language that we've
17 talked about here and after doing that they should
18 then check for agreement and get back to selling,
19 correct?
20 A Yes, that's correct.

David Thomas Noesges (January 11, 2008)

66: 5 Q Sir, I'm going to hand you two exhibits now. One
6 is -- has been previously marked as Plaintiffs'
7 Exhibit 995 and the other one is Plaintiffs'
8 Exhibit 9201.
9 For the record Exhibit 995 is a memo from Alan
10 Breier, Jack Jordan, Dennis Torres, Mike Bandick to
11 the policy committee dated July 7, 2003.

David Thomas Noesges (January 11, 2008)

66:20 You are familiar with what the policy
21 committee is at Lilly, are you not, sir?
22 A Yes, I am.
23 Q It's the principal governing body of the
24 corporation made up of top level executives,
25 correct?
67: 1 A Yes, that my understanding.
2 Q It's chaired by the CEO of the company who at the
3 time this memo was written was Mr. Sidney Taurel,
4 correct?
5 A Yes, that is correct.

David Thomas Noesges (January 11, 2008)

71: 2 Q Okay. Directing your attention to the following
3 paragraph that states, quote, Our goal is to
4 influence key stakeholders (clinicians ... sales
5 representatives, patients, Wall Street, the media,
6 Lilly senior management, caregivers and thought
7 leaders) with the facts about diabetes relative
8 to the seriously mentally ill, Zyprexa, and other
9 atypical agents. Our message: "-- and then they list
10 five different--pardon me, seven points, correct?
11 A Yes, that's correct.
12 Q And point No. 4 was stated as a, quote, Data do
13 NOT -- it's in all caps and bold font.
14 "Data do NOT support a causal link between
15 Zyprexa and diabetes; while the scientific
16 literature is mixed, there does not appear to be
17 consistent differences among atypicals"; is that
18 correct?
19 A Yes, that's what the document reads.

David Thomas Noesges (January 11, 2008)

74: 2 Q Doesn't -- when it says there is no consistent
3 differences, isn't that the same thing as saying
4 that Zyprexa was no worse than anybody else?
5 A No, sir, it's not.
6 Q I would like to direct your attention to the second
7 page of the document. In about the middle of the
8 page there is a heading there for Corporate
9 Response Letter. And it states, "On July 11,
10 customers will begin to receive the Corporate
11 Response Letter (Attachment 1), a letter targeted
12 to clinicians, delivered by their Lilly sales
13 representative. The letter is written on behalf
14 of Lilly and signed by Dr. Alan Breier."
15 Do you see that language, sir?
16 A Yes, I do.
17 Q If I could direct your attention to the
18 following -- the other exhibit I handed you, which
19 is Exhibit 9201, which is sitting on the table in
20 front of you.
21 A Um-hmm.
22 Q That is, in fact, the letter that was being
23 referred to there by Alan Breier, is it not?
24 A I can't say for certain that this is the letter
25 that this document is referring to.
75: 1 Q I'll represent to you, sir, that we have had
2 testimony from Dr. Breier himself that this is
3 indeed a letter that he wrote that was, in fact,
4 distributed.
5 Do you have any basis to dispute that?
6 A No, sir, I do not.

David Thomas Noesges (January 11, 2008)

77:22 Q Directing your attention to Exhibit 9201, there is
23 in the third paragraph a bolded question says: "Does
24 Zyprexa cause diabetes?" Do you see that language, sir?
25 A Yes, sir I do.
78: 1 Q And the answer to that in the first sentence is:
2 "The available data do not establish a causal link
3 between diabetes and Zyprexa -- or any other
4 antipsychotic, for that matter."
5 Do you see that language?
6 A Yes, sir I do.
7 Q And that's essentially saying the same thing that
8 we saw before in Exhibit 1941, when in response to
9 a doctor saying that he was concerned about
10 diabetes, the sales reps were told to say, "In every
11 study examining the subject, no causal relationship
12 has been established between patients being treated
13 with Zyprexa and the onset of diabetes." Those are
14 certainly saying the same thing, isn't it, sir?

David Thomas Noesges (January 11, 2008)

78:22 THE WITNESS: Sir, in the context of what our

reps can say promotionally, the words that we choose are important. If the words are identical I would agree with you it is the same statement. If they are not identical then the different words are important.
QUESTIONS BY MR. SUGGS:
Q So you think there is a significant difference between saying, "The available data do not establish a causal link between diabetes and Zyprexa," in the 2003 letter, and the language in the 2003 Area of Concern document. "In every study examining the subject, no causal relationship has been established?" What's the difference there? I guess I'm just not getting it.

David Thomas Noesges (January 11, 2008)

Q In both instances the company is denying that Zyprexa causes diabetes, correct?

David Thomas Noesges (January 11, 2008)

THE WITNESS: No, sir, that is not correct. What the company is saying, "The available data do not establish a causal link between diabetes and Zyprexa."
QUESTIONS BY MR. SUGGS:
Q And it's your testimony that that does not deny that Zyprexa causes diabetes?
A Yes, sir. What we are saying is that the available data do not establish a causal link between diabetes and Zyprexa.
Q And if you are making that claim then you are denying that there's a causal relationship, correct?

David Thomas Noesges (January 11, 2008)

THE WITNESS: No, sir, we are saying that the available data do not establish a causal link between diabetes and Zyprexa.
QUESTIONS BY MR. SUGGS:
Q Well, does the company admit that Zyprexa can cause diabetes?

David Thomas Noesges (January 11, 2008)

THE WITNESS: No, sir. Our position is that the available data do not establish a causal link between diabetes and Zyprexa at this time.

David Thomas Noesges (January 11, 2008)

81: 5 Q And then in about the middle of the paragraph there
6 is a sentence that states, "The fact is,
7 head-to-head clinical studies and epidemiology
8 studies show no consistent or clinically
9 significant difference in the risk of diabetes
10 among patients treated with different atypical
11 antipsychotics, despite differences in the
12 respective weight gain profiles."
13 Do you see that language, sir?
14 A Yes, sir, I do.
15 Q And that was the message that sales reps were
16 expected to use with physicians, correct?

David Thomas Noesges (January 11, 2008)

81:22 THE WITNESS: No, sir. This -- this document
23 is not an approved document for a sale
24 representative to communicate. It's a document
25 with Alan Breier's statements to physicians.
82: 1 QUESTIONS BY MR. SUGGS:
2 Q Well, sir, the sales reps, according to
3 Exhibit 995, were instructed to deliver this to
4 clinicians, correct?
5 A Yes, sir, that's correct.

David Thomas Noesges (January 11, 2008)

89:10 Q Okay. Sir, to the extent documents found on the
11 knowledge management database did talk about
12 company products like Zyprexa and did talk about
13 the messages of a product like Zyprexa, would it be
14 fair to say that those materials would have been
15 reviewed by management before they were put on
16 there for the sales reps to -- to view?
17 MR. BOISE: Object to the form of the
18 question, foundation.
19 THE WITNESS: For any document that's -- on
20 knowledge management that is designed for the reps
21 to use promotionally with their customers would
22 have gone through our normal medical/legal/
23 regulatory process.
24 There may also be informational documents that
25 are clearly not intended for representatives to use
90: 1 with their -- with clinicians which would not be
2 part of the promotional message.
3 QUESTIONS BY MR. SUGGS:
4 Q Okay. But if there are documents that are on the
5 knowledge management database for sales reps to use
6 to inform them about the product, even if the
7 document was not intended for use in detailing per
8 se, the information in that document would have
9 been reviewed by management before it was put out
10 there for sales reps, wouldn't it?
11 MR. BOISE: Object to the form of the question,
12 foundation.
13 THE WITNESS: Yes, sir, that's correct.
14 QUESTIONS BY MR. SUGGS:
15 Q Thank you. I'm going to hand you what's been previously
16 marked as Plaintiffs' Exhibit 1970. For the record

Exhibit 1970 bears the date of February 2, 2001.
And I'll represent to you, sir, that Lilly has stated in answers to interrogatories in the Alaska case that this document was on the knowledge management database and made available to sales reps.

David Thomas Noesges (January 11, 2008)

92:21 Q If I could direct your attention to page 7 in the upper left-hand corner. There is a box -- actually, there's two boxes; but there is one with text in it.
"Briefly, diabetes may occur in patients
93: 1 taking antipsychotics and/or mood stabilizers including ZYPREXA, at rates that are comparable to each other."
Do you see that language, sir?
A Yes, sir, I do.
Q So at least by February of 2001 the sales reps would have had this information made available to them in the knowledge management database, correct?
A Sir, I can't tell from this document whether this was information made available to the sales representatives. It's not clear where this document came from or least in the portions you have allowed me to read thus far who it was intended for.
And also there is a comment saying that the document has not been proofread -- proofread, which suggests to me that perhaps it's not a final document, maybe in draft form.
Q Well, sir, I'll represent to you that in its answers to interrogatories in this case Lilly has stated on the record to us that this document was on the knowledge management database and made available to sales reps. That's my understanding of what their answers to interrogatories are with respect to this document.
94: 1 You don't have any basis to dispute that, do you?
A No, sir, I don't, other than the sentence on there about the document not having been proofread would be inconsistent with what I would expect to be in knowledge management.

David Thomas Noesges (January 11, 2008)

99: 1 Q When sales reps were provided scripts, they were expected to follow the script, were they not?
A The scripts were part of their training documents, so certainly their message is required to be consistent with the final message script that would support the promotional document; but we didn't expect sales representatives to memorize a script like this and then to communicate it word for word to the doctors.
Q They did not have to do it word for word; but you certainly did not expect or intend for them to give

any presentation that differed in substance from what was provided, correct?
A Yes, that's correct.
Q If I could direct your attention to the left-hand column of page 26. There's a heading about a third of the way down called "High Ground Opener."
A Yes.
Q And there's two paragraphs below that heading, correct?
A Yes.
Q And the second one starts off by saying, quote, There are two main points that I want you to walk away with.
And this is -- would be a sales rep talking to a doctor, correct?
A Yes.
Q So there were two main points that he wanted the doctor to walk away with. And he goes on to say, quote, The first is that in this head-to-head data, incidence of diagnosed treatment-emergent diabetes was comparable between ZYPREXA and risperidone and also between ZYPREXA and haloperidol.
The second point I want you to walk away with is that incidence of increased random blood glucose is also comparable across these 3 treatment groups.
Do you see that language, sir?
A Yes, sir, I do.
Q Okay. Now, you mentioned earlier that you knew a Dr. Charles Beasley, correct?
A Yes.
Q How did you know Dr. Charles Beasley?
A He's worked as part of the Zyprexa molecule as a clinical research physician.
Q Did you have any dealings with him yourself?
A I don't believe I have ever had any direct interactions with Dr. Beasley.
Q Were you ever informed that in February of 2001, the same month this document was apparently dated, that Dr. Beasley wrote an E-mail in which he noted that Zyprexa had a statistically significant mean increase on random glucose as compared to Haldol?

David Thomas Noesges (January 11, 2008)

THE WITNESS: No, sir, I haven't.
QUESTIONS BY MR. SUGGS:
Q Haldol is the same thing as haloperidol that is referred to in this Exhibit 1970, correct?
A Haldol is the branded name for haloperidol which is a generic name.

David Thomas Noesges (January 11, 2008)

the bases here. Is it your testimony that neither Dr. Beasley nor anyone else ever told you in February 2001 that analyses of data done by Lilly showed that Zyprexa had a statistically significant mean increase in random glucose as compared to Haldol? Is that a fair statement? No one ever

told you about any analysis showing that?
MR. BOISE: Object to the form, foundation.
THE WITNESS: I don't recall anyone ever telling me that in February 2001, no.
QUESTIONS BY MR. BOISE:
Q Do you recall anyone ever telling you that at any other, later time?

David Thomas Noesges (January 11, 2008)

THE WITNESS: No, I don't recall anyone ever telling me that.
QUESTIONS BY MR. SUGGS:
Q Okay. Did anyone -- did Dr. Beasley or anyone else ever tell you that the increases in blood glucose with Zyprexa were occurring as early as the first week of Zyprexa treatment?
MR. BOISE: Could you read back the question?
MR. SUGGS: Can you read it back?
(Record read.)
THE WITNESS: No, sir, I don't believe so.
MR. SUGGS: I'm going to hand you next what's been previously marked as Plaintiffs' Exhibit 1901. And I'm also going to hand you what we'll have marked as Exhibit 4.
(Deposition Exhibit 4 marked for identification.)
QUESTIONS BY MR. SUGGS:
Q By the way, when you make copies of Exhibit 4 and Exhibit 5, for the record, I would like those to be color copies. I did not notice you wrote a note. Sorry.
For the record, Exhibit 1901 was dated January 14, 2002, according to the database provided to us by Lilly, and Lilly has represented to us in answers to interrogatories in the Alaska litigation that this document, Exhibit 1901, was also in the knowledge management database.
Do you have any basis to dispute that?
A No.

David Thomas Noesges (January 11, 2008)

Q Would you agree with me, sir, that the longer Zyprexa was on the market the more psychiatrists became concerned about the issue of diabetes with the drug?
MR. BOISE: Object to the form, vague.
THE WITNESS: Yes.
QUESTIONS BY MR. SUGGS:
Q Okay. About the middle of the page there's a paragraph that starts off, "By knowing the facts" -- do you see that?
A Yes.
Q It states, "By knowing the facts, you can more effectively and efficiently handle any objections raised by physicians BEFORE it becomes an issue. Four Key Message points in bold," and then there are some bullet points below that, correct?

5 A Yes.

David Thomas Noesges (January 11, 2008)

107: 3 Q The four key message points in bold were, No. 1,
4 comparable rates. No. 2, there is no direct
5 one-to-one correlation.
6 Diabetes is common in the general adult
7 population and is even more common in psychiatric
8 patients, correct?
9 MR. BOISE: Object to that characterization.
10 QUESTIONS BY MR. SUGGS:
11 Q And the third -- or the fourth bolded key factor
12 was -- or key message was, A number of factors
13 affect a person's risk for diabetes.
14 Those were the bolded key messages being
15 referred to, correct?
16 MR. BOISE: Object to the form, added a few
17 words.
18 THE WITNESS: What you described was close to
19 what's bolded there, not exactly.
20 QUESTIONS BY MR. SUGGS:
21 Q Okay. Sorry if I added an extra word in there.
22 MR. BOISE: It was two.
23 MR. SUGGS: Two extra words.

David Thomas Noesges (January 11, 2008)

108:11 Q Okay. And then towards the bottom of the page it
12 refers to "Explanation of Diabetes Sell Sheet
13 (OL 21620)."
14 Do you see that?
15 A Yes, sir.
16 Q Am I correct that what we marked as Exhibit 4
17 is the diabetes sell sheet that is being referred
18 to there?
19 A Yes, that's correct.

David Thomas Noesges (January 11, 2008)

109:11 Q Okay. On the top of page exhibit -- on the top of
12 the first page of Exhibit 4 is a chart that has the
13 title -- or the heading above the chart, it says,
14 "Comparable rates of diabetes and hyperglycemia
15 among psychotropics," correct?
16 A Yes.

David Thomas Noesges (January 11, 2008)

109:25 Q Okay. And then it notes that -- the second graph
110: 1 on that page has a heading Baseline to endpoint
2 increase in average glucose levels across
3 comparative studies, correct?
4 A Yes.

David Thomas Noesges (January 11, 2008)

110:23 Q Okay. Okay. In all of -- both of these charts
24 relate to Message Point No. 1, which was that there
25 are comparable rates in treatment-emergent
111: 1 diabetes and hyperglycemia, correct?
2 A These data represent evidence from the clinical
3 trials to support comparable rates of diabetes and
4 hyperglycemia among psychotropic agents, and also
5 support that the two other message points of
6 patients treated with Zyprexa had rates of diabetes
7 and hyperglycemia comparable to those in patients
8 treated with risperidone, haloperidol and
9 divalproex sodium in clinical trials, and also that
10 the baseline to endpoint increase in average
11 glucose levels across the comparative studies.

David Thomas Noesges (January 11, 2008)

113:13 of Exhibit -- I'm sorry. You are right, third page
14 of Exhibit 1901.
15 THE WITNESS: Yes.
16 QUESTIONS BY MR. SUGGS:
17 Q The first paragraph in that section states, quote,
18 Many physicians think there is a logical link
19 between weight gain and diabetes. In market
20 research we see that many of them even use these
21 two words interchangeably. We believe it is
22 essential to weaken this link in order to
23 neutralize the diabetes/hyperglycemia issue.
24 Do you see that language, sir?
25 A Yes, sir, I do.

David Thomas Noesges (January 11, 2008)

114: 6 Q If I could direct your attention to the Summary at
7 the bottom of page 3. It states, "Eli Lilly ... has
8 a proud history in innovative diabetes research.
9 The relationship between Zyprexa and diabetes, slash,
10 hyperglycemia is a top priority for the company and
11 has been studied extensively. The facts illustrate
12 no difference in the incidence of
13 treatment-emergent hyperglycemia and diabetes for
14 patients Zyprexa, haloperidol, risperidone,
15 ziprasidone, or divalproex. Neutralizing any
16 concern from our customers will be essential to the
17 future growth of Zyprexa in" the "marketplace."
18 Do you see that language, sir?
19 A Yes, sir, I do.

David Thomas Noesges (January 11, 2008)

118: 8 Q I know that's not what you said, but the fact of the
9 matter is that the sell sheet was designed to
10 neutralize concerns physicians had about Zyprexa
11 having -- causing more diabetes than other drugs;

isn't that correct?
MR. BOISE: Objection, asked and answered.
THE WITNESS: No, sir. The sell sheet was designed to communicate the results from our clinical trials and our analysis of what the risk of diabetes was associated with Zyprexa and other psychotropic agents.

David Thomas Noesges (January 11, 2008)

Q The purpose of a sell sheet is to sell?
MR. BOISE: Object to the form, asked and answered.
QUESTIONS BY MR. SUGGS:
Q Right? That's why they call it a sell sheet, isn't it?
MR. BOISE: Object to the form.
THE WITNESS: Sir, the purpose of the sell sheet is to communicate to clinicians the risk and benefits of our products recognizing they are going to make the ultimate decision.
Certainly, a goal is to increase the sales of the product for what clinicians determine to be the appropriate patients for our product.

David Thomas Noesges (January 11, 2008)

Let me backtrack here and hand you what's been previously marked as Exhibit No. 5.
(Deposition Exhibit 5 marked for identification.)

David Thomas Noesges (January 11, 2008)

Q If I could direct your attention to the last page. By the way, would you agree that this document -- would you characterize this document as a sell sheet or brochure or something different?
A I think both brochure and/or sell sheet would probably be a reasonable characterization of this.
Q If you look at the last page at the very bottom there is number 60, dash, OL26280.
Do you see that?
A Yes.
Q What does that refer to?
A That's a reference number so that we know what the document is.
Q And it indicates that the copyright for this would have been 2003, correct?
A Yes.
Q So it would appear that this sell sheet or brochure would have been later in time than Exhibit 4, correct?
A Which one was Exhibit 4?
Q That was the other color brochure or sell sheet that we were just talking about.
A It appears to be based on the copyright, yes.

25 Q Yep, about two years later, correct?
122: 1 MR. BOISE: Object to form. It speaks for
2 itself.
3 QUESTIONS BY MR. SUGGS:
4 Q One was a 2001 copyright date, the other one has
5 2003 copyright; two years' difference, correct?
6 A Yes, that would be about two years.

David Thomas Noesges (January 11, 2008)

122:24 Q The heading is "How do the medications you use
25 compare?" Right below that it says, "Rates of
123: 1 diabetes were comparable for commonly prescribed
2 psychotropics during longer-term clinical trials,"
3 correct?
4 A Yes.
5 Q And then if I direct your attention to the
6 following page with the red bordered heading at the
7 top, it states, "Incidence and odd ratios of
8 developing diabetes during treatment with
9 antipsychotics"; and right below that it says,
10 "Findings from 5 epidemiological studies show no
11 consistent differences regardless of the agent
12 studied," correct?
13 A That's what it says, yes.
14 Q It was expected that sales reps would use these
15 brochures in their sales representations to
16 physicians, correct?
17 MR. BOISE: Object to the form.
18 THE WITNESS: I would have to refer to the
19 implementation guide to know exactly what the
20 direction was provided to sales representatives;
21 but this clearly was a promotional tool that
22 could have been part of their sales message to
23 customers, yes.

David Thomas Noesges (January 11, 2008)

124: 2 In November of 2003, you came back to the U.S.
3 to head up U.S. marketing to take over from Jack
4 Jordan, correct?
5 A Yes.
6 Q And also in November of 2003, the American Diabetes
7 Association and the American Psychiatric
8 Association, the American Association of Clinical
9 Endocrinologists and also the North American
10 Association For the Study of Obesity convened a
11 consensus conference to address the issue of
12 diabetes in connection with the use of various
13 antipsychotic drugs, correct?
14 A Yes, that's correct.
15 Q Okay. And you were aware that, although that
16 conference was held in November of 2003, in, I
17 believe, it was February of 2004 those four medical
18 associations published their consensus statement,
19 were you not?
20 A Yes, my recollection is that it was in February of
21 2004.
22 Q You would have reviewed that consensus statement

when it came out in 2004, would you, correct?
A Yes.
Q Let me hand you a copy of what's been previously marked as Plaintiffs' Exhibit 2368, which for the record is the consensus statement, an article titled "Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes." It was published in Diabetes Care in February of 2004 and it's been previously marked as Plaintiffs' Exhibit 2368.
Sir, if I could direct your attention to Table 2 of this article, which is on the second page on the bottom right-hand corner.
There is a table there rating various second generation antipsychotics and their association with metabolic abnormalities, correct?
A Yes.
Q And the assessments that they give there are for Weight gain, Risk for diabetes, and Worsening lipid profile, correct?
A Yes.
Q In the legend at the bottom they note that a plus sign indicates that there is an increased effect; a minus sign indicates there is no effect and a D indicates that there is discrepant results, correct?
A Yes.
Q And with respect to Weight gain, it shows that Olanzapine and Clozapine are given three pluses and the others have lesser numbers, correct?
A Yes.

David Thomas Noesges (January 11, 2008)

With respect to the Risk for diabetes, it shows that there are pluses, meaning that there is an increased effect, shown in this table for Clozapine and Olanzapine and there are no pluses besides -- beside any of other drugs, correct?
A For risk for diabetes, that's correct.
Q Exactly. Okay. The same thing holds true with respect to Worsening lipid profile, there are plus signs given for Clozapine and Olanzapine, but not for any of the other drugs, correct?
A Yes.
Q If I could direct your attention to the fifth page which is also page 600 in the article.
That is the page that has the Summary in the right-hand column?
A Yes.
Q I would like to direct your attention to the second full paragraph in the fourth line down on that paragraph it states, quote, Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have immediate effects. Aripiprozole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia. Do you see that language, sir?
A Yes.

David Thomas Noesges (January 11, 2008)

127:17 Q And that conclusion of the American Diabetes
18 Association and the American Psychiatric
19 Association contradicts Lilly's claims of
20 comparable rates --
21 MR. BOISE: Object to the form.
22 QUESTIONS BY MR. SUGGS:
23 Q -- of diabetes, correct?
24 MR. BOISE: Object to the form of the
25 question, mischaracterizes the document.
128: 1 THE WITNESS: It's important to note, I'm not
2 a clinical expert and rely on my medical colleagues
3 to answer that question but that's certainly not
4 consistent with our conclusions.

David Thomas Noesges (January 11, 2008)

128:25 Q Before October of 2007 did Lilly ever instruct its
129: 1 sales force to tell physicians that Lilly believed
2 that the rates of diabetes with Zyprexa were higher
3 than with other drugs?
4 MR. BOISE: Object to the form of the
5 question.
6 THE WITNESS: No, I don't believe that was
7 ever a specific message that our representatives
8 were instructed to communicate to physicians.

David Thomas Noesges (January 11, 2008)

129:12 Between October of 2007 and the present has
13 Lilly ever instructed its sales force to tell
14 physicians that the rate of diabetes with Zyprexa
15 is higher than with other drugs?
16 A No.
17 Q I'm going to hand you what's been previously marked
18 as -- well, it's been previously marked in several
19 other depositions; but it does not have a uniform
20 number on it.
21 I'm going to have to mark it again here as
22 Exhibit 6.
23 (Deposition Exhibit 6 marked for
24 identification.)
25 QUESTIONS BY MR. SUGGS:
130: 1 Q This is a March 28, 2007, letter from FDA to Eli
2 Lilly.
3 Do you recall ever seeing this document
4 before, sir?
5 A Yes, I have.
6 Q When did you see it?

David Thomas Noesges (January 11, 2008)

130:11 THE WITNESS: I saw it within the last week.
12 QUESTIONS BY MR. SUGGS:

Q After you stopped your responsibilities for Zyprexa, correct?
A Yes.
Q Okay. If I can direct your attention to the -- about the middle of the first page of Exhibit 6. There is a heading entitled "Updated Information on Risks of Weight Gain, Hyperglycemia, and Hyperlipidemia."
Do you see that, where I'm at, there?
A Yes, I do.
Q And the paragraph below that, in the middle of the paragraph third line down, there is a sentence that starts off, "In particular" -- do you see where I'm at there?
A Yes.

David Thomas Noesges (January 11, 2008)

Q Sentence goes on to state, quote, "In particular, we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine."
Do you see that language, sir?
A Yes, I do.

David Thomas Noesges (January 11, 2008)

Q You were the executive sales director for Zyprexa in the western region?
A I was the executive sales director for neuroscience including responsibility for Zyprexa in the western region, yes.
Q And under you, you had how many sales folks who were out selling Zyprexa?
A I had approximately 700 sales representatives.
Q 700 sales representatives.
They would call on, roughly, how many doctors?
A Each of them calls on between a hundred and probably a hundred and ninety doctors.
Q So we are talking thousands, like 70,000 doctors?
Am I doing my math right?
A Yes, I think that's right.
Q Okay. So you had hundreds of sales representatives who were calling on thousands, tens of thousands, of doctors selling Zyprexa?
A Yes.

David Thomas Noesges (January 11, 2008)

Q Were you aware that the FDA in this communication took the position that the Zyprexa's labeling was deficient with regard to information about weight gain, hyperglycemia and hyperlipidemia?

David Thomas Noesges (January 11, 2008)

134:12 mischaracterizes the document.
13 THE WITNESS: No, I was not.

David Thomas Noesges (January 11, 2008)

134:13 THE WITNESS: No, I was not.

David Thomas Noesges (January 11, 2008)

135:16 Q Did anyone ever tell you in March of 2007 that the
17 FDA had written to the company saying that they
18 believed that the labeling was deficient and that
19 they felt, that they, the FDA felt, the physicians
20 could not make reasonable treatment decisions until
21 they had such information?
22 MR. BOISE: Object to the form,
23 mischaracterizes the document.
24 THE WITNESS: No.

David Thomas Noesges (January 11, 2008)

136: 1 Q Okay. Was the first time that you ever learned
2 that there had been the communication of those
3 positions to the company when you saw this letter
4 for the first time last week?

David Thomas Noesges (January 11, 2008)

136: 7 MR. SUGGS: I'm going to hand you what we'll
8 have marked as Exhibit 7.
9 (Deposition Exhibit 7 marked for
10 identification.)
11 QUESTIONS BY MR. SUGGS:
12 Q Which, for the record, is a copy of an October 5,
13 2007, Dear healthcare provider letter, and you
14 have, I'm assuming, have seen this document
15 before, sir, is that correct?
16 A Yes, I have.
17 Q And would you agree with me that this letter to
18 healthcare professionals informs them of a change
19 in Lilly's label?
20 A Yes. This is a letter to healthcare professionals
21 informing them of a change in our label for Zyprexa
22 and Symbyax.
23 Q And the change in the label was to add additional
24 language in the warning section regarding
25 hyperglycemia, correct, that was one part of it?
137: 1 A These label updates included warnings for weight
2 gain, hyperlipidemia, and updated information
3 in the warning for hyperglycemia.

David Thomas Noesges (January 11, 2008)

138:23 Q Well, my question, sir: Was it your understanding
24 or did anyone inform you that this label change was
25 at the specific request of FDA?
139: 1 MR. BOISE: Object to the form, foundation,
2 beyond the scope.
3 THE WITNESS: My understanding is that the FDA
4 asked for additional information and opened a
5 dialog with our medical and regulatory colleagues
6 in response to our new drug application for
7 Symbyax, which ultimately led to a label change.
8 QUESTIONS BY MR. SUGGS:
9 Q Did anyone inform you that the FDA said that a
10 label change was necessary in order to protect the
11 public health?
12 MR. BOISE: Object to the form, foundation.
13 THE WITNESS: No, I don't recall anyone
14 communicating that to me.

David Thomas Noesges (January 11, 2008)

141: 2 Q If I could direct your attention to the third page
3 of the document.
4 A Okay.
5 Q Hyperglycemia section of the new changed label, the
6 last sentence in the first paragraph states, quote,
7 While relative risk estimates are inconsistent, the
8 association between atypical antipsychotics and
9 increases in glucose levels appears to fall on a
10 continuum and olanzapine appears to have a greater
11 association than some other atypical
12 antipsychotics.
13 Do you see that language there?
14 A Yes.
15 Q Sir, that statement is inconsistent with Lilly's
16 prior positions, correct?
17 MR. BOISE: Object to the form of the
18 question, foundation.
19 THE WITNESS: No, that statement is not
20 inconsistent with our prior positions.

David Thomas Noesges (January 11, 2008)

145:16 Does Lilly still take the position that the --
17 that the rates of diabetes between the various
18 antipsychotic drugs are comparable?
19 MR. BOISE: Object to the form of the
20 question, asked and answered.
21 THE WITNESS: We no longer have a message that
22 our sales representatives are presenting with regard to
23 comparable rates, but it is, in fact, our position
24 that the clinical data do not show a differential
25 risk of diabetes with Zyprexa relative to the other
146: 1 antipsychotic agents.

David Thomas Noesges (January 11, 2008)

146: 5 If a physician were today to ask a sales rep,
6 Are the rates of diabetes higher with Zyprexa than
7 with other antipsychotic drugs, the sales rep would
8 tell him, There is no that evidence to show that;
9 is that correct?
10 MR. BOISE: Object to the form, incomplete
11 hypothetical.
12 THE WITNESS: No, the sales representative,
13 under those circumstances, would be instructed to
14 offer the doctor a medical letter from our medical
15 department to answer that question.

David Thomas Noesges (January 11, 2008)

146:25 Q I understand that, sir, but we have already seen
147: 1 before there were some sell sheets, we looked at
2 those brochures, the color documents, where, in
3 fact, the sales reps were provided with materials
4 which they could show and discuss with physicians
5 addressing this issue of whether the rates were
6 comparable or whether there were consistent
7 differences and so forth.
8 Is it your testimony that sales reps would no
9 longer be permitted to use those brochures?
10 MR. BOISE: The brochures previously marked as
11 4 and 5 --
12 MR. SUGGS: Yes.
13 MR. BOISE: -- could the sales reps use these
14 brochures today?
15 MR. SUGGS: Yes.
16 THE WITNESS: No, sales representatives would
17 not be able to use those brochures today.
18 QUESTIONS BY MR. SUGGS:
19 Q And is it your testimony that if a physician asked
20 a sales rep whether the rates of diabetes are
21 comparable between Zyprexa and the other drugs, the
22 sales rep would be instructed to tell the doctor, I
23 cannot discuss that with you, but I will send you a
24 medical letter?
25 A What the drug sales representatives should do if
148: 1 they get that question is to indicate to the doctor
2 that they would like to send a medical letter to
3 them, which we think can best answer that question
4 for them.
5 Q Well, suppose the doctor says, Well, gee, Joe, you
6 know, I remember when you were in my office in 2001
7 and 2002 and 2003 and you were talking about how
8 there were comparable rates and there were no
9 consistent differences. I want you to tell me
10 right now on the spot, you know, are you saying now
11 that still that Zyprexa has comparable rates of
12 diabetes? What would the sales rep do in that?
13 Would he say, I can't answer and walk out?
14 MR. BOISE: Objection, incomplete
15 hypothetical, lack of foundation.
16 THE WITNESS: No, sir, what the doctor would
17 be -- what the sales representative would be
18 instructed to do is to politely indicate to the
19 doctor, Look, I would like to provide you all of
20 the medical information that we have available and

the medical letter to answer the question.

David Thomas Noesges (January 11, 2008)

153: Q I'm going to hand you what I will have marked here as Exhibit 8, which is a copy of a document entitled "LillyUSA SALES GOOD PROMOTIONAL PRACTICES, UNSOLICITED QUESTIONS ON OFF-LABEL INFORMATION OR UNAPPROVED PRODUCTS."
Do you recognize this document, sir?
A Yes, I do.
Q What is it?
A It is a portion of the company's good promotional practices with an effective date listed here on January 15th, 2004.
Q Okay. This particular portion has to deal with unsolicited questions on off-label information, correct?
A Yes.
Q And it notes -- as part of this document it indicates the scope of this policy, correct?
A Yes.
Q And it says, "This GPP applies to all sales personnel and sales support personnel in LillyUSA and all sales activities that take place in the United States or with US Healthcare Professionals," correct?
A That's correct.

David Thomas Noesges (January 11, 2008)

154: Q Okay. And then there is a policy statement which says, "It is the policy of Eli Lilly and Company to comply with FDA regulations that prohibit the promotion of any unapproved...product; or indication, dosage form and, slash, or dosing schedule for any marketed product, with any customer by sales and marketing personnel, or other Lilly personnel or representatives in a promotional context."
Was that your understanding of the policy?
A Yes, it is.

David Thomas Noesges (January 11, 2008)

155: Q But, in any event, throughout the time you were involved with Zyprexa, was it the policy of Eli Lilly and Company to comply with FDA regulations that prohibit the promotion of any unapproved new product or indication?
A Yes, it was.
Q Okay. And if I could direct your attention down to the Definitions section.
There is a definition of Off-label Information there.
Do you see that?
A Yes.
Q And the definition of Off-label Information is,

quote, Any information about a Lilly product that is not contained in or is not consistent with the package insert labeling approved by the FDA. Examples include, but are not limited to, indications, dosage forms, dosing schedules, combination therapy, and safety information.
Do you see that language, sir?
A Yes, I do.
Q And that would have been a correct definition of off-label information regardless of whether it was the year 2000, the year 1996, the year 2003, or 2007, correct?
MR. BOISE: Object to the form, foundation, beyond the scope.
THE WITNESS: Yes. Well, I would want to consult the specific language, which could have changed slightly. The concept of what constitutes off-label information would have been consistent.

David Thomas Noesges (January 11, 2008)

Q And it says, "Sales Personnel MAY NOT:," quote, "Proactively discuss, present, or promote information concerning unapproved new products or off-label information about approved products with any customer or health care professional."
Did I read that correctly?
A Yes.
Q And, sir, that was -- sales personnel were prohibited to do that in 2000 and in 2001 and throughout the times Zyprexa has been on the market, correct?
A Yes, that is correct.

David Thomas Noesges (January 11, 2008)

Q Okay. And so if, in fact, a sales rep gave safety information, which is one of the examples here, that was not contained in or was not consistent with the package insert labeling approved by the FDA, that would, by definition, be off-label information, correct?
A Yes, that's correct.

David Thomas Noesges (January 11, 2008)

Q Okay. And similarly this document refers to the indications of the package insert, correct?
A Yes.

David Thomas Noesges (January 11, 2008)

Q Would you agree, sir, as someone in charge of marketing and sales that doctors look to the indication section of the label to see if the drug

is appropriate to use for the proper treatment of the disease?
A. Yes, I believe that's one source doctors may use to make that decision.
Q. Okay. And the diseases for which the drug is indicated or appropriate to treat are listed in the indication section of the label, correct?
A. The indication section of the label indicates -- those disease states are indication for which the drug has received FDA approval for promotion.

David Thomas Noesges (January 11, 2008)

Q. Okay. You know, sir, that Zyprexa was never approved for the treatment of anxiety, correct?
A. Yes, that's correct.
Q. It was never approved for the treatment of irritability, correct?
A. Zyprexa never had an indication for the treatment of irritability -- irritability, no.
Q. Zyprexa was never approved for the treatment of disruptive sleep, correct?
A. Zyprexa never had an indication for the treatment of disruptive sleep.
Q. Zyprexa was never approved for the treatment of mood swings, correct?
A. Zyprexa never had an indication for the treatment of mood swings, but certainly mood swings are an element of the symptoms of bipolar disorder.
Q. Zyprexa never -- was never approved for the treatment of complicated mood symptoms?
A. Again, we never had a specific indication for complicated mood symptoms, but those are symptoms

David Thomas Noesges (January 11, 2008)

Zyprexa was never approved for dementia associated with Alzheimer's, correct?
A. No, sir, it was not.
Q. I'm going to hand you what's been previously as Plaintiffs' Exhibit 4121.
For the record this exhibit is entitled "ZYPREXA - Primary Care Strategy and Implementation Overview."
The first section is entitled "Background." It states, Following several months of study by the LillyUSA Zyprexa Brand Team, the affiliate approved the recommendation that Lilly actively promote Zyprexa to selected current primary care prescriber targets. Key decisions included: Launch will occur in October 2000, promotion will be handled via the Primary Care, dash, Neuroscience sales sleeve, and funding in 2000 would be incremental to existing brand opex.
Do you see that language, sir?
A. I must not be reading from the same portion of the document where you are.
Q. Under the first paragraph under the Background section.

A Okay. Sorry.

David Thomas Noesges (January 11, 2008)

Q Midway down on the first page it states, "Most PCPs" -- that refers to primary care physicians, correct?
A Yes.
Q "Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers. Many PCPs will refer patients in need of psychotropic treatment to a specialist rather than treat that patient. Key barriers to uptake include PCP's lack of training in this category, limited time with patients, and an aversion to perceived risk. Zyprexa's primary indications - schizophrenia and bipolar - are not viewed as PCP-treated conditions, so there's not a specific indication for Lilly reps to promote in the PCP segment."
Do you see that language, sir?
A Yes, I do.
Q When it says Zyprexa's primary indication was schizophrenia and bipolar, at that time in 2000 those were indeed the only indications for Zyprexa; isn't that correct?
A Yes, that's correct.
Q And then in the paragraph below that it states, Position: Zyprexa: The safe, proven solution in mood, thought, and behavioral disorders.
Do you see that?
A Yes, I do.
Q And then about the middle of the page -- pardon me, middle of the paragraph it refers to "Mental disorders."
Do you see that in quotes?
A Yes, I do.
Q "'Mental disorders' is intentionally broad and vague, providing latitude to frame the discussion around symptoms and behaviors rather than specific indications."
Do you see that language, sir?
A Yes, sir, I do.
Q And, in fact, as you previously testified, Zyprexa was not indicated for mood, thought, and behavior disorders, correct?
MR. BOISE: Object to the form, mischaracterizes testimony.
THE WITNESS: Zyprexa is indicated at this time frame for schizophrenia and Bipolar I disorder.
QUESTIONS BY MR. SUGGS:
Q But Lilly reps at this time -- after this time promoted Zyprexa for the treatment of symptoms and behaviors rather than specific indications; is that correct?
MR. BOISE: Object to the form, foundation.
THE WITNESS: No, sir. That is not correct.
QUESTIONS BY MR. SUGGS:
Q Well, let's look at what's been previously marked as between 1926, which for the record bears the date June 2002 at the top of the first page.

And I will represent to you, sir, that the database provided to us by Lilly indicates that this document was actually generated on May 1, 2002, and Lilly has represented to us in answers to interrogatories that this document was in the knowledge management database.

And, sir, do you have any information to dispute those representations?

A No, sir, I have no reason to dispute the date that you provided me.

Q Okay. If I could direct your attention to page 3. In the right-hand column about the middle of the page is bold heading ZYPREXA in Primary Care, and the beginning part of that paragraph states, quote, ZYPREXA was originally launched to the primary care audience by the Sigma sales force in November of 2000.

What was the Sigma sales force, do you know?

A Sigma was a primary care sales force that among their responsibilities included Zyprexa promotion to primary care physicians.

Q It goes on to state, "It has gained over 12 share points since that time. As the current market leader in primary care, ZYPREXA will continue to revolutionize the way complicated mood disorders are treated by primary care physicians."

Do you see that language, sir?

A Yes, sir, I do.

Q And as we have talked about before, Zyprexa was not indicated for complicated mood disorders, was it, sir?

David Thomas Noesges (January 11, 2008)

THE WITNESS: Zyprexa was indicated for schizophrenia and bipolar disorder.

QUESTIONS BY MR. SUGGS:

Q If I could direct your attention to page 5. And this is basically walking the sales rep through the use of a brochure, correct?

A Yes. This is a message example for sales representatives to use to help them in terms of how they communicate to physicians.

Q What we see here on this page in the upper right-hand corner and on the succeeding pages is an image of the brochure that was being used, correct?

A Yes.

Q And then the rest of the text on the page is a description provided by Lilly's marketing folks as to how to use that brochure, correct?

A Yes.

Q For example, on page 5 here, they show the front cover of the brochure -- and by the way, do you recall what this particular brochure was called?

A I don't know that it had a name.

Q Okay. But anyway we see the picture of the doctor and the patient on the first page. It looks like the patient is fording a river by stepping on various stones, correct? And the doctor is there to hold her hand as she gets over there, right?

A Yes, that appears to be what -- what the diagram depicts.
Q They have a suggested call opener there, correct?
A Yes.
MR. BOISE: Object to form.
THE WITNESS: Yes.
QUESTIONS BY MR. SUGGS:
Q And what's a "call opener"?
A In this context the call opener is simply an introductory statement for the sales representative to make during the call to the doctor.
Q And the sales rep was to say, "Doctor, you treat patients who present with complicated mood symptoms. Many of these patients are struggling to gain control of symptoms like anxiety, irritability, disruptive sleep, and mood swings. I would like to talk about how ZYPREXA can help you help your patients gain control of these complicated mood symptoms," correct?
A Yes, sir, that's correct.
Q No mention of schizophrenia or the acute manic phase of Bipolar I disorder?
MR. BOISE: Object to the form of the question. Object to the form of the question.
THE WITNESS: There's no mention of that in this specific sentence, no.

David Thomas Noesges (January 11, 2008)

Q Sir, one of the things that Lilly did was to have what they call "patient profiles."
Do you remember that?
A Yes, sir, that's correct.
Q And one of the patient profiles was of a character that they transcribed as or named Donna, correct?
A This is going back a long way and the names don't have a particular resonance with me. I would have to look at the profile to regain familiarity with it.
Q If you look at page 7 --
A Okay.
Q -- there is a description there, Patient Profile #1: Donna, correct?
A Yes.
Q And she is described as a single mom in her mid-30s, presents in drab clothing and seems ill at ease.
That's what the brochure says, correct?
MR. BOISE: Object to the form. That's part of what it says.
QUESTIONS BY MR. SUGGS:
Q Do you see the brochure there under the name "Donna"?
A Yes.
Q It says, quote, single mom in her mid-30s presents in drab clothing and seems ill at ease. Below that there is a quote, apparently from the fictional character Donna, I feel so anxious and irritable lately, end quote.
A Yes, I see that.
Q And below that for the history it says, Reports she

has been seeing -- pardon me, sleeping more than usual, has trouble concentrating at work and at home.

Now, sir, Zyprexa was approved, as we have talked about before, for the acute manic phase of Bipolar I disorder, correct?

A Yes, sir.

David Thomas Noesges (January 11, 2008)

Q Well, sir, just as a matter of common sense and as someone who has been in the pharmaceutical industry for, lo, these many years and had responsibility for the marketing of Zyprexa, was it your understanding that acute manic phase patients with Bipolar I disorder have trouble sleeping more than usual?

MR. BOISE: Object to the form of the question.

THE WITNESS: Again, I'm not a clinical expert and would defer to my medical colleagues; but in my experience it would not at all be unusual for a patient in acute manic phase to have difficulty sleeping.

QUESTIONS BY MR. SUGGS:

Q Sir, the difficulty that she describes here in this fictional report is that she has been reporting that she has been sleeping more than usual.

People in the manic phase of Bipolar Disorder I, they hardly sleep at all; isn't that right?

MR. BOISE: Object to the form of the question.

THE WITNESS: Again, you are asking me to make a clinical assessment, but in my experience bipolar disorder is very complex and by definition has -- includes depressive elements and manic elements of the disorder.

QUESTIONS BY MR. SUGGS:

Q Aren't manic patients the patients that are usually bouncing off the walls?

MR. BOISE: Object to the form of the question, beyond the scope.

QUESTIONS BY MR. SUGGS:

Q You don't find them sleeping all day; they are the ones that are bouncing off the walls; isn't that true?

MR. BOISE: Object to the form of question.

THE WITNESS: You are asking me to make a characterization that I would defer to a clinician to make about a patient.

David Thomas Noesges (January 11, 2008)

Q Mr. Noesges, I'm going to hand you what's been previously marked as Plaintiff's Exhibit 1962.

And for the record I'll represent that the database provided to us by Lilly indicates that this document was dated September 4, 2002, and further that Lilly's represented to us in answers

to interrogatories that it was in the knowledge management database.

And, I would assume, sir, based on your prior testimony that you don't have any basis to dispute those representations; is that correct?

A That's correct.

Q Okay. The title on the first page is "Hyperglycemia, slash, Diabetes: Sell Sheet Implementation" and as we discussed previously a sell sheet is a brochure that can be discussed with and shown to a physician, correct?

A This is a promotional material that can be used promotionally by sales representatives with physicians.

Q Okay. This one on the second page -- or this document indicates on the second page, "Proper implementation is key! Our goal and focus is on creating a market with Donna. The competition wins if we are distracted into talking about diabetes. So, stand strong against their ploys and answer the AOC concisely and with confidence!"

Did I read that correctly?

A Yes.

Q And the AOC that is being referred to is the diabetes area of concern, correct?

A Yes.

Q On the following page there is directions for handling the diabetes AOC, correct?

A Yes.

Q Below the heading states, "This is a highly competitive driven issue. Therefore, we will NOT proactively address the diabetes concern, but rather only when it arises from an MD."

Do you see that language, sir?

A Yes, I do.

Q And that was indeed the policy of Lilly at that time in 2002, was it not?

MR. BOISE: Object to the form of the question.

THE WITNESS: That was the instructions that were being provided to sales representatives through this particular sell sheet implementation guide.

David Thomas Noesges (January 11, 2008)

Q Okay. And then if you turn to the following page the heading is "What are the facts to convey and where do you find them within the sell sheet?"

And then they are laid out there, three different points that are in the sell sheet, correct?

A Yes, that's correct.

Q And the first point it's emphasized that patients with mental illness are two to four times more likely to develop diabetes, correct?

A That statement is bolded in the first step -- first item.

Q The second item it notes, "As the 'Diabetes Care' company, Lilly takes this issue very seriously and will continue to offer solutions. (Not written on

the sell sheet but use as a segue to the next point)," correct?
A Correct.
Q And the third thing was: "When you look at various agents to treat patients with mental illness, the rate of treatment-emergent diabetes is comparable across agents," correct?
MR. BOISE: You are asking that's what the statement says?
QUESTIONS BY MR. SUGGS:
Q That's what the statement says.
A Yes, that's what the statement says.
Q This is another iteration or example of the comparable rates message back in the 2002 time period, correct?
MR. BOISE: Object to the form, vague.
THE WITNESS: This is a third point in this guideline for a sell sheet which says, "When you look at various agents to treat patients with mental illness, the rate of treatment-emergent diabetes is comparable across agents."
QUESTIONS BY MR. SUGGS:
Q Okay. I would like to show you another section of the Lilly Good Promotional Practice guidelines and we'll mark this as Exhibit 9.
(Deposition Exhibit 9 marked for identification.)
QUESTIONS BY MR. SUGGS:
Q And for the record the title of this Good Promotional Practice says, quote, Definition of a Sales Call and Call Notes.
And you are familiar with call notes, are you not, sir?
A Yes, sir, I am.
Q It indicates that the scope of this promotional practice is to apply to "all sales personnel and sales support personnel in LillyUSA and all sales activities that take place in the United States or with US Healthcare Professionals," correct?
A Yes, sir, that's correct.
Q And the policy statement was that, quote, It is the policy of LillyUSA that all sales personnel appropriately document sales calls with Healthcare Professionals in the call tracking system; is that correct?
A Yes, that's what it says.
Q What was the call tracking system?
A This is referring to basically the sales representatives' computer database that was available to them in this time frame, which would have been effective June 1st, is what this document is referring to -- to put their -- to document calls they were making on healthcare providers.
MR. BOISE: just so the record is clear it's June 1st, 2004.
Q And, in fact, this call system existed before 2004, correct?
A Yes, it did.
Q Okay. Can you describe for us, generally, what is involved in this call system or call note system?
A Depends on the time frame. While that system has been in place, the process of gathering call notes has changed over time.

Q Okay. Well, is it fair to say that the sales rep is expected to -- shortly after his calling on a particular physician is expected to go to a computer database and enter information about the particular sales call that he had?
A Yes, that's correct.
Q And all of that information is to go into a centralized database, correct?
A The sales representative inputs the data into their computer laptop which then is stored centrally, but I don't know the details of how -- how that information gets stored.

David Thomas Noesges (January 11, 2008)

197:16 Q Okay. Directing your attention back to Exhibit 9.
17 A Yes.
18 Q There is a Definitions section there and sales call
19 is defined as a face-to-face discussion about Lilly
20 products between a healthcare professional and a
21 Lilly sales representative, correct?
22 A Yes, it is.
23 Q And a call note is defined as a business record
24 documented within a call system that accurately
25 reflects all aspects of the sales call, correct?
198: 1 A Yes.
2 Q Okay. And then below that there is a section
3 entitled "Information and Procedures" and there's
4 some bulleted points below that, correct?
5 A Yes.
6 Q The second bulleted point states, "The goal of the
7 sales call is to appropriately influence a
8 Healthcare Professional using the approved Lilly
9 product information to allow him or her to choose
10 the best therapy for his or her patients and
11 ultimately to increase" the "sales of Lilly
12 products," correct?
13 A Yes, that's correct.
14 Q And then on the following page there is a bullet
15 point which states, "For each sales call and/or
16 sample drop, the sales representative must
17 accurately document the interaction in the
18 Structured Call Note system in Premier."
19 Do you see that language?
20 A Yes, I do.
21 Q What is "Premier"?
22 A Looks like this was a typo here. It's probably
23 referring to Premier Force which is the name of the
24 sales representatives' computer database to enter
25 calls, again, in this time frame, 2004.
199: 1 Q And the structured call note system, was that a
2 particular program within that Premier that is
3 being referred to there?
4 A Yes.
5 Q And it goes on to say, "If applicable, unsolicited
6 questions or medical letter requests must be
7 documented within the SCN," or structured call note,
8 "system according to policy, GPP 02-004 Unsolicited
9 Questions on Off-Label Information or Unapproved
10 Products."
11 Did I read that correctly?

A Yes, you did.
Q And that is the good promotional practice that we referred to earlier in Exhibit -- trying to find the number here. If you find it before I do, let me know.
A Exhibit 8.

David Thomas Noesges (January 11, 2008)

Q I would like to show you some call notes that have been produced to us in the Alaska litigation, and I'll mark this next as Exhibit 10.
(Deposition Exhibit 10 marked for identification.)
QUESTIONS BY MR. SUGGS:
Q Which I'll represent to you is a page of call notes pulled from the sample that Lilly has produced to us in the Alaska litigation. And it would appear this particular page has call notes that were generated by Margaret Williams, several by her, and also by a Thea Jung.
Do you see that?
A Yes, I do.

David Thomas Noesges (January 11, 2008)

Q If I could direct your attention to the bottom call note by Thea Jung. In the text of the Action -- or I guess it's actually the text of the Reaction section it states, "Did full Z detail with/both. Dr. T said to just keep reminding him about Z because it's not 'stuck in' his head yet. Dr. B said she misunderstood and thought Z was just for bipolar or schizophrenia and was really excited to hear that it was applicable to her practice for 'complicated mood.'"
Do you see that, sir?
A Yes, sir, I do.
Q And, sir, that indicates that, in fact, this doctor, after hearing the presentation by the Lilly sales rep, thought Zyprexa was for something other than bipolar or schizophrenia, correct?
MR. BOISE: Object to the form of the question.
THE WITNESS: No, sir, it doesn't indicate that to me at all. Again, it's difficult. These are shorthand notes; but if you are asking me to interpret this, the rep seems to be reflecting that the doctor was excited to hear that it could be applicable for her practice for what she described -- or he or she described as complicated mood disorder. It does not refer at all to the sales representative having suggested that.
QUESTIONS BY MR. SUGGS:
Q Well, it says, "Dr. B said she misunderstood and thought Z was just for bipolar or schizophrenia and was really excited to hear that it was applicable to her practice for, quote, complicated mood, end quote," correct?

18 A Yes, that's what the document says.

David Thomas Noesges (January 11, 2008)

204:11 Q I'm handing you what we have marked as Exhibit 11.
12 This is another collection of --
13 MR. BOISE: Did you hand me one, David?
14 MR. SUGGS: I'm sorry.
15 MR. BOISE: That's okay.
16 QUESTIONS BY MR. SUGGS:
17 Q -- of call notes.
18 This is another collection of call notes from
19 those that were produced to us in the Alaska
20 litigation. I would like to draw your attention

David Thomas Noesges (January 11, 2008)

205: 1 Q I would like to direct your attention to the first
2 call note on the first page, which appears to be
3 call notes of Margaret Williams, regarding her
4 meeting with Dr. Kendrick Blais, Fairbanks, Alaska,
5 and the notes say, quote, Doc initially said any
6 pats who needed ZYP were referred to a psych, but
7 after detail realized he had pats who could benefit
8 from ZYP and that ZYP wasn't just for
9 schizophrenics. Was impressed with how safe ZYP is
10 and how much ZYP has been used for elderly patients
11 and how ZYP reduces hostility, agitation, improves
12 cognition. Then went over ZYP in bipolar mania.
13 Do you see that language, sir?
14 A Yes, sir, I do.
15 Q That indicates that this doctor was under the
16 impression that this category of elderly patients
17 with hostility and agitation was different than the
18 schizophrenics and different than bipolar mania,
19 correct?
20 MR. BOISE: Object to the form of the
21 question.
22 THE WITNESS: Again, these are shorthand
23 notes. It's difficult to tell what was noted here,
24 but the rep seems to be indicating that the doctor
25 describing just, as in here, some impressions
206: 1 around Zyprexa's usefulness in elderly patients.
2 QUESTIONS BY MR. SUGGS:
3 Q And, sir, Zyprexa was never approved for the
4 treatment of hostility in elderly patients, was it,
5 sir?
6 MR. BOISE: Object to the form.
7 THE WITNESS: Zyprexa does not have an
8 indication for hostility in elderly patients.
9 QUESTIONS BY MR. SUGGS:
10 Q And Zyprexa was never indicated for the treatment
11 of agitation in elderly patients, correct?
12 MR. BOISE: Object to the form, foundation.
13 THE WITNESS: Zyprexa does not have a specific
14 indication for agitation in elderly patients.
15 QUESTIONS BY MR. SUGGS:
16 Q And, in fact, Zyprexa was never indicated or
17 approved for the treatment of cognition or for

improving cognition, correct?
MR. BOISE: Object to the form.
THE WITNESS: Improvement of cognition is certainly a symptom of schizophrenia as can be hostility and agitation, but there is not a specific indication for cognition.

David Thomas Noesges (January 11, 2008)

207: 9 There has been a black box warning in the
10 Zyprexa label since 2004 with respect to the
11 elderly, correct?
12 A Yes, that's correct.
13 Q That did not exist in 2002 when this call note was
14 made, correct?
15 MR. BOISE: Object to the form, foundation.
16 THE WITNESS: No, I do not believe it did.
17 QUESTIONS BY MR. SUGGS:
18 Q Was Zyprexa indicated for the treatment of patients
19 whose symptoms were aggravated by a SSRI?
20 MR. BOISE: Object to the form.
21 THE WITNESS: Zyprexa's indication, as we have
22 discussed before, was for schizophrenia and bipolar
23 disorder.
24 QUESTIONS BY MR. SUGGS:
25 Q Didn't sales reps in Alaska, in fact, promote
208: 1 Zyprexa as being especially good for patients whose
2 symptoms were aggravated by an SSRI?
3 MR. BOISE: Object to the form of the
4 question, foundation.
5 THE WITNESS: Sir, what I can describe to you,
6 as I have before, is what our marketing messages
7 were on a given time frame, but I would have to
8 know what time frame you were describing and then I
9 could indicate to you what the company approved
10 message was.
11 QUESTIONS BY MR. SUGGS:
12 Q Let me show you another set of call notes, which
13 I'll mark as Exhibit 12.
14 (Deposition Exhibit 12 marked for
15 identification.)
16 MR. SUGGS: Did I give you a copy?
17 MR. BOISE: Not yet.
18 MR. SUGGS: Sorry.
19 MR. BOISE: While you are shuffling, this has
20 been marked as Exhibit 12, is a grouping of seven
21 pages of call notes.
22 MR. SUGGS: Yes.
23 Q If I could direct your attention to the first call
24 notes -- the first call note on the first page,
25 these appear to be call notes from Margaret
209: 1 Williams, dated May 17, 2002, with respect to a
2 meeting with Dr. Kathryn Flores in Soldotna,
3 Alaska, text which says in part, "Also got in a
4 decent ZYP recap, reminded doc that ZYP is a great
5 mood stabilizer, especially for patients whose
6 symptoms were aggravated by an SSRI."
7 Do you see that language, sir?
8 A Yes, sir, I do.

210:25 Q Sir, the labeling for Zyprexa never stated that it
211: 1 was good especially for patients whose symptoms
2 were aggravated by an SSRI, did it, sir?
3 A No, sir, it did not.
4 Q If I could direct your attention to the call note
5 that is second from the bottom, this is another
6 Margaret Williams' call note dated June 6th, 2002.
7 Under the Action section it states, quote,
8 Actually got in a decent ZYP detail for patients
9 with unresolved symptoms, patients who fail on an
10 SSRI, patients could be suffering from complicated
11 mood order, perhaps bipolar, ZYP is an excellent
12 mood stabilizer, very safe, easy to dose?
13 Do you see that language, sir?
14 A Yes, sir, I do.
15 Q Zyprexa was never indicated for patients who fail
16 on an SSRI, was it?
17 MR. BOISE: Object to the form of the
18 question.
19 THE WITNESS: No, sir, Zyprexa does not have a
20 specific indication for patients who fail on an
21 SSRI.

Exhibit 12
Susan Kay Schuler

Susan Kay Schuler (February [redacted] 2007)

5: 3 Q Ma'am, please state your name.
4 A Susan Schuler.

Susan Kay Schuler (February 1, 2007)

6:22 Q Okay. You are an employee of Eli Lilly; is that
23 correct?
24 A That's correct.

Susan Kay Schuler (February 1, 2007)

7:18 How long have you been employed by Eli Lilly?
19 A About six-and-a-half years.
20 Q It's -- so I'm accurate, you were hired in 2001?
21 A I was hired in 1999 and worked until February 16
22 of 2001. Left the company until the end of 2001. Was
23 rehired for January 1 of 2002.
24 Q And you've been a continuous employee since 2002
25 until present?
8: 1 A That's correct.
2 Q And what nature of employment were you doing with
3 Eli Lilly during your brief employment from 1999 to February
4 of 2001?
5 A Long-term care. Neuroscience.
6 Q Did that involve the antipsychotic drug Zyprexa in
7 any way?
8 A That's correct.
9 Q How so?
10 A We -- I was a sales rep for the product of Zyprexa
11 and Prozac, working with medical directors for the long-term
12 care.

Susan Kay Schuler (February 1, 2007)

9:14 When you terminated employment -- when you left
15 Eli Lilly in 2001 and returned in 2002 -- I'm sorry for
16 stating it that way -- was there any change in your job
17 description?
18 Did you return with the same job description in
19 2002?
20 A When I came back in 2002, I was neuroscience
21 retail, not long-term care.
22 Q And please explain to me what the difference would
23 be, in your own words.
24 A Long-term care is calling on medical directors for
25 long-term care facilities. And neuroscience retail is
10: 1 calling on private psychs and community mental health
2 centers.
3 Q Okay. And what type of training and education did
4 you have prior to 1999, prior to your employment with Eli?
5 A Two weeks at home. And it was all the testing of
6 the products. And then followed by four straight weeks at
7 Indianapolis for training, all day long. Typically we
8 started at 8:00 a.m. and we'd go until 5:00 or 6:00, and we
9 even worked on weekends. And then returning, working with a

mentor, and additional training with my mentor for several weeks. And then I was on my own.

Susan Kay Schuler (February 1, 2007)

Q So I can get a timeline going, when would you have first detailed Zyprexa?
A July of 1999.
Q Okay. And are you detailing Zyprexa today?
A Yes.

Susan Kay Schuler (February 1, 2007)

Q As if you were explaining to the jury, tell me what it means to "detail" Zyprexa.
A We have information that we are trained on at a district meeting, and then we would go through the materials from our detail piece that that company had provided.
Q And to what type of doctors would you have detailed Zyprexa?
A Well, in 1999, it was medical directors for long-term care, and they also had private jobs. And in addition to that, I currently call on private psychs. But prior to that, I was with private psychs and community mental health center psychiatrists.

Susan Kay Schuler (February 1, 2007)

Q If you were to detail Zyprexa this week and a doctor was to ask you, Do I need to be concerned with Zyprexa causing diabetes, what would be your response?
A It does not cause diabetes. There isn't any information or scientific information regarding Zyprexa causing diabetes.
Q Is what you just gave me a verbatim?
A No.
Q Is it based on your own background --
A Training.
Q -- and belief?
Training.
And can I ask what training you would have received that would have led you to that answer.
A Direct meeting training.
Q Training that was provided by Eli Lilly?
A Correct.

Susan Kay Schuler (February 1, 2007)

Q If the doctor were to ask you during your detailing this week, I need a yes or no answer, does Zyprexa cause weight gain, what would be your answer?
A No.
Q And is that answer a verbatim?
A No.
Q What would you base that answer on?

21: 1 A A detail pie[redacted] that we have worked with in th[redacted]
2 past saying that, yes, lower body mass index individuals may
3 gain weight. And some higher body mass index may not gain
4 weight. And some individuals on Zyprexa have actually lost
5 weight.
6 **Q And your knowledge of that is based on internal**
7 **Eli Lilly --**
8 A Branded material.
9 Q **-- branded material.**
10 **"Branded material" means produced by Eli Lilly?**
11 A The company. That's correct.

Susan Kay Schuler (February 1, 2007)

21:21 Since you started detailing in 1999, would the
22 answer you just gave me about Zyprexa's connection with
23 weight gain, would it have remained the same over the course
24 of time?
25 A Yes.

Susan Kay Schuler (February 1, 2007)

22:25 A minute ago I asked you if a doctor were to ask
23: 1 you this week, while detailing, Does Zyprexa cause diabetes,
2 and you gave me an answer.
3 And if you recall the answer -- and I'm not trying
4 to change that answer in any way -- but my question is:
5 Would an answer to that question have remained the same over
6 time since 1999?
7 A Yes.

Exhibit 13
Sharp, Pharm.D.

Michelle Sharp PharmD (November 3, 2006)

21:15 Q. Good morning.
16 A. Good morning.
17 Q. Would you state your full
18 name for the record, please?
19 A. Michele Lynn Sharp.

Michelle Sharp PharmD (November 3, 2006)

22: 4 Q. And what's your present
5 occupation?
6 A. I am a pharmacist.
7 Q. And you're employed by Eli
8 Lilly, correct?
9 A. That's correct.

Michelle Sharp PharmD (November 3, 2006)

22:14 Q. What's your job title?
15 A. Manager of U.S. Regulatory
16 Affairs.

Michelle Sharp PharmD (November 3, 2006)

28:14 Q. Okay. When did your job
15 change after that?
16 A. In January of '97.
17 Q. Is that when you switched
18 over to the Regulatory Department?
19 A. Yes.
20 Q. And what were you doing in
21 the Regulatory Department at that time?
22 A. I worked in the labeling
23 area.
24 Q. And what drugs did you deal
29: 1 with?
2 A. Initially in that role I
3 covered many marketed products that we had
4 for Lilly.
5 Q. Okay. Did you have
6 responsibility for Zyprexa at that time?
7 A. Not in 1997.
8 Q. Okay. Did there come a later
9 time when you did?
10 A. Yes.
11 Q. When was that?
12 A. Sometime in 1998 is when I
13 had that responsibility.

Michelle Sharp PharmD (November 3, 2006)

30:11 Q. And when you said that you
12 were, had responsibility for the labeling of
13 Zyprexa, what responsibility exactly do you

have?
A. In the labeling -- in the labeling group you help facilitate the labeling process.
Q. So if someone came along and said, "Hey, we need to make a change in the labeling," you would work with them in terms of getting that written up and then submit it to FDA?
A. You would have responsibility for gathering the cross-functional group of people that would evaluate the proposed labeling. You would help with an assistant to draft up where the words and the location of the labeling. And you would also help ensure that all the appropriate people per our policies and procedures reviewed that labeling. And you would also help, again with an assistant, work with preparing that submission package.
And then, at the time in which you were ready to print that labeling to put in packaging, you would work with our manufacturing area and the packaging area to ensure that the labeling was typeset appropriately and ready for the printers.
Q. Okay. And who was it that would give you the assignment to sort of trigger all of that?
A. Typically, there would be a regulatory scientist that would place a call with you to tell you that there's been some discussion and that we need to get a group of people together.

Michelle Sharp PharmD (November 3, 2006)

Q. So it was your testimony that someone within the, the regulatory scientist would place a call and tell you that there's been some discussion and that we need to get a group of people together; is that correct?
A. Yes.

Michelle Sharp PharmD (November 3, 2006)

Q. Who would the regulatory scientist be that would contact you about getting a labeling change done?
A. During the time frame in which I was the labeling associate, so in the 1998 time frame, that would have been Al Webber.
Q. Okay. And for how long were you in that position?
THE WITNESS: In the labeling position?
MR. SUGGS: Right.
A. Until November of 1999.

Q. And then who took it over then?
A. I believe it was Gail Uminger who followed me.
Q. Okay. But you continued to have responsibilities for Zyprexa labeling after November of 1999, didn't you?
A. Yes. In a different role.
Q. What was that role?
A. That was the regulatory scientist role.
Q. So did you then jump up to -- okay. Prior to November of 1999 some regulatory scientist would call you up and tell you, "Hey, we need to get the ball rolling with the labeling change," right?
A. That's correct.
Q. After November of 1999, you stepped into that role where you were the regulatory scientist and you told people, "Hey, you need to get the ball rolling," right?
A. Yes. That's correct.
Q. Okay. And what was your title then after November of 1999 when you were in that position?
A. Associate Regulatory Consultant.
Q. Okay. And for how long did you have that responsibility?
A. With that title, January 2001.
Q. Okay. And regardless of what the title was, how long did you have that responsibility for being the, the regulatory person who would trigger the labeling change?
A. May 2005.
Q. Okay. So it would be fair to say that between December 1999 through 2005, you would have been the regulatory person who would trigger the wheels moving to get a labeling change accomplished with respect to Zyprexa, correct?
A. There were also other regulatory scientists that had responsibility for Zyprexa during that time frame.
Q. Okay. But you had that responsibility yourself, correct?
A. I was one --
Q. Okay.
A. -- of a team of them, yes.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. There was a labeling -- we'll talk about this in more detail -- but in May of 2000 there is a labeling change with respect to Zyprexa. Do you recall that?
A. Yes, I do.
Q. And you were the regulatory

15 scientist who was involved with that project,
16 correct?
17 A. Yes, I was.

Michelle Sharp PharmD (November 3, 2006)

38: 3 Q. Between May of 2000 and
4 September 2003, there were no other
5 significant labeling changes with the
6 labeling of Zyprexa pertaining to
7 hyperglycemia or diabetes, were there?
8 A. Not within the United States.

Michelle Sharp PharmD (November 3, 2006)

38:15 Q. Okay. So it would be fair to
16 say that you were the regulatory scientist
17 most involved with -- significantly -- well,
18 with any labeling changes in connection with
19 Zyprexa that related to hyperglycemia or
20 diabetes between 2000 and 2003, correct?
21 A. Yes, that's correct.

Michelle Sharp PharmD (November 3, 2006)

39:21 Q. In addition to dealing with
22 labeling issues, did you have any other
23 responsibilities with respect to Zyprexa
24 between 1999 and 2004?
40: 1 A. Okay. Yes. They included
2 sending reports to FDA through an annual
3 report process. Included submitting to the
4 FDA supplemental NDAs for new indications.

Michelle Sharp PharmD (November 3, 2006)

40:13 A. Okay. I also reviewed
14 promotional material for the U.S.
15 marketplace.
16 Worked with the team to
17 discuss interactions that we would have with
18 FDA on various clinical plans or programs
19 that we were working on.
20 That -- I would say that
21 covers, from a high level perspective, the
22 types of activities I was involved in.

Michelle Sharp PharmD (November 3, 2006)

44: 1 Q. Okay. It was your
2 understanding that the success of Zyprexa was
3 critical to the financial health of Lilly; is
4 that correct?

A. You know, Zyprexa's one of many products that we market in our company.
Q. What's your biggest selling product?
A. It is Zyprexa.
Q. And what was Year X?
A. Year X was described as a year where there were going to be patent expiries that occurred in our company.
Q. Regarding one particular drug in particular -- Prozac. Correct?
A. That's correct.
Q. And Prozac had been one of your biggest selling drugs, correct?
A. It was one of our top selling drugs.
Q. And when did the patent go off for Prozac?
A. You know, I can't recall the exact, the exact date; it was in the early 2000 timeframe.
Q. Do you recall it was 2001?
A. That could be correct.

Michelle Sharp PharmD (November 3, 2006)

Q. You know that Lilly sales of Zyprexa are in excess of $3 billion, right?

Michelle Sharp PharmD (November 3, 2006)

A. That sounds correct.
Q. And what's the total sales of the company?
A. I couldn't say.
(Whereupon, Deposition Exhibit(s) 2197 previously marked, was presented to the witness.)
Q. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 2197. For the record, this is a Draft Chronology of FDA Interaction Re Glucose, Triglycerides and Pancreatitis, purporting to be prepared by Michele Sharp on April 24, 2003. Do you recognize this document?
A. Yes, I do.
Q. And did you, in fact, prepare this chronology on or about April 24, 2003?
A. Yes, I believe so.

Michelle Sharp PharmD (November 3, 2006)

Q. As you look at this now, do you see any inaccuracies that are stated in this chronology?

A. Not that I can tell, no.
Q. Okay. And the chronology refers to the Zyprexa USPI. Am I correct that USPI stands for United States package insert?
A. Yes.
Q. Okay. This would, probably, be a good time to talk a bit about what a package insert or the labeling consists of. You would agree with me, would you not, that FDA regulations set forth different parts, or different components that must be included in a United States labeling of drug products?
A. That's correct.
Q. Okay. And would you agree that within that labeling scheme there is a hierarchy regarding side effects and adverse reactions?
A. The regulations specify an order in which the package insert must follow.
Q. Okay. And with respect to discussing side effects and adverse reactions, there is, indeed, a section of the labeling called adverse reactions, correct?
A. That's correct.
Q. And it's towards the back of the labeling, correct?
A. As the regulations dictate, yeah, that's where the location is.
Q. And in that section of the labeling there's a listing of the adverse reactions that occurred during premarketing clinical trials, correct?
A. That's correct.
Q. And by listing those adverse reactions that occurred in clinical trials, the drug company is not saying and not admitting that those adverse reactions were caused by the drug, correct?
A. It's providing a list of the adverse reactions as they were reported in the clinical trials.
Q. And there is no statement in there about causation or anything like that with respect to those adverse reactions, correct?
A. That's correct.
Q. Okay. And the adverse reactions section also lists adverse reactions that were reported after the drug was introduced to the market and those are referred to as post-introduction reports; is that correct?
A. That's correct.
Q. Okay. And again, the fact that something is listed in the labeling, in the adverse reaction section of the labeling and the post-introduction reports, is not an indication to a physician who reads that that there's a causal link between the taking of the drug and the adverse reaction, correct?
A. That's correct.

Q. Okay. There's another section within the labeling that can also discuss adverse reactions and side effects, and that's the precautions section. Are you familiar with that?
A. Yes.
Q. Okay. And would you agree with me that if an adverse reaction is discussed in the precautions section in addition to being discussed in the adverse reaction section, that that discussion in the precaution section is a heightened, a heightened way of dealing with the adverse reaction in terms of bringing it to physicians' attention?

Michelle Sharp PharmD (November 3, 2006)

A. The precaution section is an area where there's, tends to be more descriptive information about the safety information that you're providing and may include description on something to make the prescriber aware of that safety information.
Q. And in addition to that, it can also tell the physician what he or she may do to try to prevent an adverse reaction or a side effect from occurring, correct?
A. It can provide some further description to help the physician in treating that patient with that medication.
Q. Okay. So it would be fair to say that the precaution section is certainly a more fulsome discussion of adverse reactions than if it is merely listed in the adverse reaction section, correct?
MR. LEHNER: Object to the form.
A. Again, it can be a more descriptive description provided helping, guiding the physician.
Q. Okay. And then there's another section within the labeling where adverse reactions and side effects can be discussed and that's in the warning section, correct?
A. That's correct.
Q. Okay. And the warning section is just what the name implies, it, actually, warns the physician about the risk of serious adverse reactions that are associated with the drug, correct?

Michelle Sharp PharmD (November 3, 2006)

A. It's an area of the labeling where a description on safety information that has met a reasonable evidence of association, a place for that type of safety

information to reside.
Q. Okay. And you're aware that FDA regulations state that the labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with the drug and that a causal relationship need not have been proved, correct?
A. Based on my recollection of the regulation on the warning section that sounds -- that sounds correct.
Q. I read you the language right out of the regulation. And you were aware of that legal requirement back in 1999, were you not?
A. Yes, I was.

Michelle Sharp PharmD (November 3, 2006)

54:24 You would have expected that
55: 1 the other people in the Regulatory Affairs
2 Department who were dealing with Zyprexa in
3 that 1999-2004 time frame would have also
4 been aware of that legal requirement,
5 correct?
6 A. Yes.
7 Q. Okay. Refer back to
8 Exhibit 2197 if you would, the chronology.
9 It only refers to interactions with the FDA
10 here in the United States; is that correct?
11 A. Yes, that's correct.
12 Q. And it doesn't discuss what
13 happened in other countries; is that right?
14 A. No, it does not.
15 Q. Okay. And the chronology
16 starts in September of 1999, correct?
17 A. Yes.
18 Q. And you were familiar with
19 what was going on in the Zyprexa labeling in
20 other countries in 1999, were you not?
21 A. Yes.
22 (Whereupon, Deposition
23 Exhibit(s) 4864 previously
24 marked, was presented to the
56: 1 witness.
2 MR. SUGGS: Let me show you
3 what's been previously marked as
4 Plaintiff's Exhibit 4864. For the
5 record, this is a document entitled
6 Reporter's Revised Assessment
7 Report, Review of the Data On
8 Olanzapine and Risk of Diabetes
9 Mellitus. It appears to have a date
10 of February 14, 2003.
11 QUESTIONS BY MR. SUGGS:
12 Q. And I'm going to be asking
13 you really only questions about the first two
14 pages on this document but I noticed you were
15 thumbing through it briefly. Do you
16 recognize the document?

A. Yes, I recognize it.
Q. And can you tell us what it is, please?
A. This is a report that's been prepared by the European Rapporteur in response to a submission that we had made. I'm not sure what our submission date was. It looks like we submitted information in response to a request that the European regulators had asked of us in September of 2002.
Q. Okay. And when you talked about this being the European reporter?
A. Um-hum.
Q. Was this -- the document refers to the reporter as being Dr. Markku Toivonen from Finland; is that correct?
A. Yes, that's correct.
Q. And was he part of the European regulatory agency that is the equivalent of the FDA here in the U.S.?
A. Yes.
Q. And was that organization that he was with called the EMEA?
A. Yes.
Q. Okay. And I'm blocking on the full name of that acronym. Do you recall what EMEA stands for?
A. European Medical Evaluation Agency, I think. Something similar to that if not exactly that.
Q. I don't feel so bad.
Okay. So this was an individual employed by the EMEA who was responding to or reporting on some material that you had provided to that agency, correct?
A. Yes, I think that's right.
Q. Okay. And I also noticed that there's a reference to the CPMP?
A. Um-hum.
Q. What is that? Is that a division or part of the EMEA?
A. Yes, it is.
Q. And what's that -- Committee For Proprietary?
A. I don't recall what the acronym stands for but, essentially, it's the clinical component of the EMEA that reviews scientific information about the medical products available in Europe.
Q. Okay. The document also refers to the MAH, and that's the Medical Authorization Holder, which in this case would be Lilly, correct?
A. Yes, that's correct.
Q. Okay. And then there's one other, one other acronym I need to ask you about in the -- you see how there's a Table 1 at the bottom of the first page entitled

Hyperglycemia and Related Disorders in the Olanzapine EUSPCs, do you see that?
A. Yes.
Q. Okay. If we can -- what does SPC stand for?
A. Summary of Product Characteristics.
Q. And is that what they call the labeling in Europe?
A. Yes. That's their label.
Q. So if we were to translate that table there into the U.S. terminology it would be Hyperglycemia and Related Disorders in the Zyprexa European Label, would that be a fair statement of what they're talking about there?
A. Yeah, I think that is.
Q. Okay. And it notes that in that table that there was a section of the European label that was for special warnings and special precautions for use, that being Section 4.4, correct?
A. That's correct.
Q. And there was another section, 4.8, regarding undesirable effects, correct?
A. That's correct.
Q. Okay. And -- oh, another question I meant to ask you about. I'll represent to you that when the documents were produced to us by Lilly they also produced to us a computer database which sometimes indicates dates of documents and from whom they were produced within the company.
And this particular document, the database indicated that it was produced from your files or that you were custodian of the document. Does that --
A. That's possible.

Michelle Sharp PharmD (November 3, 2006)

Q. Are you, as part of your normal job duties, are you responsible for maintaining various files relating to regulatory activities such as indicated in this particular exhibit?
A. I would say certain files, such as FDA correspondence.
Q. Okay.
A. I would feel like I'm a custodian of that type of file. But this type of file, I would not say that I'm a custodian of this type of document.
Q. But did you keep documents such as this in your personal files?
A. Sure.
Q. Okay. Back to that Table 1.
A. Um-hum.
Q. With respect to the special warnings and special precautions for use, it

indicates that there was a language in the European label that stated, quote, "Hyperglycemia or exacerbation of preexisting diabetes has been reported in very rare cases during Zyprexa treatment. In some cases a prior increase in body weight has been reported which may be a predisposing factor. Appropriate clinical monitoring is advisable in diabetic patients and in patients with risk factors for the development of diabetes mellitus." Did I read that correctly?

A. Yes, you did.

Q. And it indicates that that language was submitted in December of 1998, correct?

A. Yes, that's correct.

Q. And that language would have been submitted by Lilly; is that correct?

A. By my colleagues in Europe, yes.

Q. Okay. And was it your recollection that Lilly had been requested to provide some language regarding hyperglycemia and diabetes in the European label prior to the time that such language was, actually, submitted in December of 1998?

A. You know, I don't recall the specifics in 1998 but my recollection was it was a request of the European regulators.

Q. It was not something that Lilly voluntarily showed up on the doorstep of EMEA and said, "Hey, guess what, we want to make a label change about hyperglycemia," right?

Michelle Sharp PharmD (November 3, 2006)

A. Again, I think it was a request by the European regulators.

Q. And the table also indicates that that language was ultimately approved by EMEA on July 19, 1999, correct?

A. Yes, that's correct.

Michelle Sharp PharmD (November 3, 2006)

Q. The purpose of having this language about hyperglycemia and diabetes in the special warnings and special precautions for use section of the label was to draw the attention of physicians to the association of hyperglycemia and exacerbation of diabetes with the use of Zyprexa, correct?

Michelle Sharp PharmD (November 3, 2006)

A. I'm not sure exactly the

purpose. My understanding, it's to provide the scientific information within their label to healthcare providers.

Q. Well, isn't it common practice for physicians in Europe to regard the language regarding special warnings and special precautions as special and something that needs to be paid attention to?

Michelle Sharp PharmD (November 3, 2006)

65:24 A. You know, I'm not an expert
66: 1 in the European regulations so I can't really
2 speak to the requirements or standards behind
3 this section in the European label.
4 Q. You don't deny that the
5 purpose of placing such language in a special
6 warnings and special precautions for use was
7 to heighten physician's awareness of the
8 issue, do you?

Michelle Sharp PharmD (November 3, 2006)

66:11 A. I think that within the
12 European label it's an area to provide a
13 descriptive, descriptive information about
14 the safety information.
15 Q. What does the word "special"
16 mean to you?
17 A. Again, I'm not an expert in
18 European regulations, so I don't know why
19 they choose these words to name their
20 sections of their label.
21 Q. Is "special" different from
22 just "ordinary?"
23 A. Again, I don't have the depth
24 of experience in Europe to know why, what
67: 1 Europeans, why they would have chosen these
2 words for their sections, what they chose.

Michelle Sharp PharmD (November 3, 2006)

68: 6 Q. I'm going to hand you what we
7 will mark as Sharp 1, which for the record is
8 a copy of the 2000 Physician's Desk Reference
9 section on Zyprexa.
10 (Whereupon, Deposition
11 Exhibit(s) 1 duly received,
12 marked and made a part of the
13 record.)
14 MR. SUGGS: And in your copy
15 I've highlighted in yellow the
16 sections of the labeling and also a
17 couple of other sections.
18 QUESTIONS BY MR. SUGGS:
19 Q. But before we start turning
20 to the substance, are you familiar with the

term PDR or Physicians' Desk Reference?
A. Yes, I am.
Q. And can you tell the jury what that is?
A. The PDR is a reference text that is bound and includes product information from various products that are marketed in the United States.
Q. And would you agree with me that, essentially, what the PDR does is replicate the package insert text in a big thick volume for various drugs?
A. It replicates the text that's available at the time of the publishing of that textbook, yes.
Q. Okay. And would you agree with me that physicians often use the PDR, if they have a question about what the label of a particular drug says they will often go to the PDR to read what the label says, correct?
A. That's one source they use, yes.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. If I could direct your attention to the bottom right-hand corner of the first page of the exhibit, it states -- and I've highlighted that section for you -- this product information was prepared in June 1999. Current information on these and other products of Eli Lilly may be obtained by direct inquiry to Lilly Research Laboratories, and it gives the address and telephone number, correct?
A. Yes.
Q. And it was not uncommon for, for information that was contained in the 2000 PDR to have actually been prepared in 1999, correct?
A. With publishing schedules that's possible, yes.
Q. Okay. And on the second page of Sharp Exhibit 2 --
MR. LEHNER: Sharp Exhibit 1.
MR. SUGGS: I'm sorry.
Better mark it.
QUESTIONS BY MR. SUGGS:
Q. -- is the warning section and, also, the precautions section, correct?
A. Yes.

Michelle Sharp PharmD (November 3, 2006)

There was no language regarding hyperglycemia or diabetes in either the warnings or precautions section of the Zyprexa labeling back in 1999 nor 2000, correct?

A. That's correct.
Q. And, in fact, you know that there was no such language in those sections of the labeling in 2001 or 2002, correct?
A. That's correct.
Q. And there was, there was a labeling change, we'll talk about this in more detail, which did add language to the warning section of the Zyprexa label in 2003, correct? September of 2003, correct?
A. Yes, that's correct.
Q. But that would have come too late in the year to make it into the initial 2004 PDR, correct?
A. I'm not sure of the publishing schedule but that's possible.

Michelle Sharp PharmD (November 3, 2006)

72:23 Often when a drug company
24 makes a change in the label to add language
73: 1 about warnings, the company will also send
2 out a doctor -- pardon me -- a letter to
3 health care providers that's often referred
4 to as a Dear Doctor Letter or a Dear
5 Healthcare Provider letter, bringing their
6 attention to that label change, correct?
7 A. That's one way in which it's
8 communicated, yes.
9 Q. Okay. And the Dear Doctor
10 Letter regarding the September 2003 label
11 change did not actually go out until March
12 of 2004; is that correct?
13 A. There was a Dear Doctor
14 Letter sent on that warning labeling change
15 in 2004, yes.

Michelle Sharp PharmD (November 3, 2006)

74:10 Q. In March of 2004, correct?
11 A. Yes, that's correct.
12 Q. Okay. If I could direct your
13 attention to the adverse reaction section it
14 begins on Page 3 of this Sharp Exhibit 1,
15 correct?
16 A. Yes, it does.
17 Q. But there is no mention of
18 diabetes or hyperglycemia until the following
19 page on Page 4, where it shows up in, towards
20 the bottom of the middle column in a listing
21 of adverse events that occurred during
22 premarket evaluation of olanzapine; is that
23 correct?
24 A. Yes, that's correct.
75: 1 Q. Okay. And in that section
2 there is a listing of adverse events that
3 were exhibited by study subjects in the
4 premarketing clinical trials. And they have
5 them broken out by those that were adverse

reactions of body as a whole, cardiovascular system, digestive system, endocrine system, metabolic and nutritional orders, musculoskeletal system, nervous system, respiratory system, skin and appendages, special senses, urogenital system; is that correct?

A. Yes, that's correct.

Q. And in each of those sections there are multiple adverse reactions listed, correct?

A. Yes, that's correct.

Q. And diabetes is mentioned in the adverse event section regarding the endocrine system, correct?

A. Yes, it is.

Q. There it states, quote, "infrequent-diabetes mellitus and rare-diabetic acidosis," correct?

76: A. Yes, that's correct.

Q. And diabetic acidosis is -- can you describe that for the jury, what that is?

A. There's also a terminology called diabetic ketoacidosis, this is kind of like a synonym to that, where there's a lot of ketones and the patient is in kind of an acidic state.

Q. Basically, that is, I guess, sort of a more acute state of someone who has diabetes, correct? If someone develops acidosis as a result of being diabetic that means they're really in a bad, bad, way, need to receive medical attention, correct?

A. Yeah. I believe they have really high blood sugars and are in a serious state at that point, yes.

Q. And if that's left untreated and progresses it could proceed to diabetic coma, correct?

A. Yes, to the best of my knowledge I think that's right.

Q. And diabetic coma can proceed

77: ultimately to death?

A. Yes, if the patient's left untreated I think it can lead to death.

Q. And then in the metabolic and nutritional orders there's a reference to hyperglycemia as being infrequent, correct?

A. Yes, that's correct.

Q. Okay. And then there's a final section of the adverse reactions portion of the labeling I want to talk about, and that's over on the far right column on the same page, there's a heading there for post-introduction reports?

A. Yes, that's correct.

Q. And there is no mention of diabetes in that section, correct?

A. That's correct.

Q. And by July of 1999, the drug would have been, Zyprexa would have been on the market for almost three years at that

point, correct?
A. Yes. Almost. In September of that year.
Q. Okay. Now there is one thing that's listed in the post-introduction reports and that's priapism, correct?
A. Yes.
Q. And priapism is a prolonged male erection, correct?
A. Yes.

(Whereupon, Deposition Exhibit(s) 998, previously marked, was presented to the witness.

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 988. For the record, Exhibit 988 is a document entitled Census of Spontaneous Reports For Olanzapine During the First Two Years of Marketing 9/27/96 to 9/30/98. It was authored by Ken Hornbuckle and Man Fung, in the Worldwide Pharmacovigilance and Epidemiology Department of Eli Lilly and Company.

QUESTIONS BY MR. SUGGS:
Q. Do you recognize this particular document?
A. No, I do not.
Q. Okay. Do you recognize the names of Ken Hornbuckle and Man Fung?
A. Yes, I do.
Q. And did you work with them in the Pharmacovigilance Department?
A. They were individuals that I've interacted with, yes.

MR. SUGGS: Okay. If I could direct your attention to Page 22. If you look in the bottom right-hand corner there are, unfortunately, two page numbers. I direct your attention to the very bottom right-hand corner where it, actually, says Page 22.

THE WITNESS: Do I have the right page?

MR. SUGGS: Yes, you do.

THE WITNESS: Okay.

QUESTIONS BY MR. SUGGS:
Q. And it indicates there that in the two years of -- well, let me back up for a second.

At the very top of the page there's a heading entitled Sexual Dysfunction and below that is a subcategory for sexual function abnormal and then below that there's a reference to priapism, correct?
A. Yes.
Q. Now, priapism, as we just talked about before in Sharp Exhibit 1, was the one and only adverse reaction that was listed in the post-introduction reports

section of the 2000 PDR.
And this document, Exhibit 988, indicates that in the first two years of marketing there had been 26 reports of priapism; is that correct?
A. Yes, that's correct.
Q. And if we look at Page 14 of Exhibit 988, there's a section regarding blood sugar elevation, correct?
A. Yes, that's correct.
Q. And by the way, all these reports that we're talking about here are adverse events that were reported to the company, correct, in connection with the use of Zyprexa; is that your understanding?
A. Yes, that's my understanding.
Q. Okay. And it's generally accepted in the pharmaceutical industry that not all of the adverse events that, actually, occur with the use of a drug get reported, correct?
A. Yes, that's correct.
Q. It's generally assumed, in fact, that the reporting rate of adverse events is somewhere on the order of 1 percent to 10 percent, correct?
A. No. I'm not sure what that range is so I can't really confirm that's one to 10 percent.
Q. Have you ever heard that range referred to?
A. I'm not sure that I've heard of that one to 10 percent number.
Q. In any event, it's your understanding that the number of adverse events that actually get reported is only a fraction of what, actually, happens out in the real world, correct?
A. Yes, I believe that. That's my understanding.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. Directing your attention back to Page 14. In that section there is a table showing the number of adverse event reports for -- relating to blood sugar elevation, correct?
A. Yes.
Q. And that includes reports for hyperglycemia, which is high blood sugar, correct?
A. Yes.
Q. Diabetes mellitus, diabetic acidosis, diabetic coma, ketosis, and glucose tolerance decreased, correct?
A. Yes.
Q. Okay. And then at the bottom there's a reference to unduplicated reports, correct?
A. Yes.

Q. And it shows that by the end of this time period, that time period being September of 1998, there had been 194 unduplicated reports of those adverse events, correct?
A. Yes.
Q. So there had only been about two dozen reports of priapism and they were included in the post-introduction reports in labeling, correct?
A. Yes.
Q. But there had been about 200 reports of blood sugar elevation and those were not listed in the post-introduction reports, correct?
A. That's correct.
Q. Is priapism life threatening?
A. You know, I'm not a trained medical professional. Based on my knowledge I don't think that it is.

Michelle Sharp PharmD (November 3, 2006)

Q. And can diabetes be life threatening?
A. Yes, I believe diabetes, when severe enough, progressing to ketoacidosis coma, can be life threatening if not treated.
Q. And if not treated it can also result in blindness, correct?
A. There are complications that are associated with diabetes, and I believe blindness is one of them.
Q. And also other complications include having to have your hands or feet amputated, correct?
A. Neuropathies, I think, can also occur with diabetes which if severe enough can -- I don't know if it can cause amputations. I'm just not sure of the cascade of events.
Q. You've never heard of people having limbs amputated from diabetes?
A. I think it's because of the neuropathies that occur as a complication of diabetes. That sounds familiar.
Q. Okay. Was Lilly more concerned about Zyprexa patients getting prolonged erections than it was about them developing diabetes?

Michelle Sharp PharmD (November 3, 2006)

A. I don't think you can say that, no.

Michelle Sharp PharmD (November 3, 2006)

88: 8 Q. Okay. [illegible]t you were aware
9 that Lilly's competitors were attacking
10 Zyprexa about the risk of hyperglycemia and
11 diabetes due to weight gain, correct?

Michelle Sharp PharmD (November 3, 2006)

88:14 A. I'm aware of statements that
15 competitors were making in the marketplace
16 about Zyprexa.
17 Q. And they were making
18 statements repeatedly attacking Zyprexa,
19 telling doctors that there was a higher risk
20 of diabetes and hyperglycemia with Zyprexa
21 because Zyprexa patients gain more weight
22 than other, than with the use of other drugs,
23 correct?
24 A. I'm aware that competitors
89: 1 were making attacks in the marketplace about
2 our product.

Michelle Sharp PharmD (November 3, 2006)

89: 7 Q. If you had included reports
8 of hyperglycemia and diabetes in the
9 post-introduction section of the adverse
10 reactions in the labeling that would have fed
11 right into the attacks on Zyprexa that it was
12 already facing in the marketplace; isn't that
13 right?

Michelle Sharp PharmD (November 3, 2006)

89:16 A. You know, we don't make our
17 labeling decisions based on the attacks in
18 the marketplace. We make our labeling
19 decisions based on the data and research and
20 analysis that's conducted about our products.
21 Q. In fact, you have your
22 marketing people review the labeling changes
23 and -- to make sure it's okay with them,
24 isn't that right?

Michelle Sharp PharmD (November 3, 2006)

90: 1 A. No. Our marketing people
2 review the labels that they have awareness
3 about the changes that are going to be
4 occurring within the label. So they have
5 awareness to be able to address questions
6 from their customers.
7 Q. Well, in fact, your marketing
8 people, your marketing department revises the
9 labeling as it's being drafted; isn't that
10 right?

Michelle Sharp PharmD (November 3, 2006)

90:13 A. The marketing people are
14 asked to provide their perspectives on the
15 labeling changes that is being discussed and
16 proposed by the medical team.
17 Q. And, in fact, they change,
18 sometimes, the language that's in the draft;
19 isn't that right?

Michelle Sharp PharmD (November 3, 2006)

90:22 A. They can provide their
23 perspectives to make us aware, yes.
24 Q. When they change the language
91: 1 in the label, the reason why they do that is
2 to protect their position in the marketplace;
3 isn't that right?

Michelle Sharp PharmD (November 3, 2006)

91: 6 A. No. They're providing
7 perspectives from the healthcare providers
8 out there in the marketplace that we can
9 understand and appreciate how those customers
10 will read the language and understand the
11 language.
12 Q. You're not denying that the
13 marketing department sometimes revised
14 language in label changes with the express
15 purpose of minimizing Lilly's exposure to
16 competitive attacks, are you?
17 A. The members of the marketing
18 team do provide us their perspectives, and
19 may make suggestions on the wording of the
20 labeling. They may do that, yes.
21 Q. And they do that with the
22 specific purpose of minimizing exposure to
23 competitive attacks, correct?

Michelle Sharp PharmD (November 3, 2006)

92: 2 A. No. I don't believe they're
3 doing it to minimize competitor attacks.
4 MR. SUGGS: Okay. We'll go
5 into that in more detail. I'll show
6 you a document about that later and
7 we can talk about that a little bit.
8 But let's get back to where we are,
9 here.
10 QUESTIONS BY MR. SUGGS:
11 Q. I'd like to direct your
12 attention to exhibit, back to 2997, that's
13 the chronology. And it notes that in
14 September of 1999, Lilly received a request

from FDA to include pancreatitis in post-introduction reports -- strike that.

In September of 1999, Lilly received a request from FDA to include pancreatitis in the post-introduction reports section of the Zyprexa U.S. package insert, correct?

A. Yes, that's correct.

Q. And did you have an understanding that pancreatitis is related to diabetes?

A. I think that, believe they're both connected through endocrine disorders.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. And a couple months later in December 1999, Lilly responded to that request by saying that the data did not support inclusion of pancreatitis in the labeling but that Lilly would continue to monitor the adverse event reports, correct?

A. Yes, that's correct.

Q. Okay. So, basically, FDA says, "We want this in the labeling," and you came back and you said, "We don't think it belongs there but we'll continue to look at the situation," correct?

Is that a fair summary?

A. I believe we took a look at the adverse event reports and all the information that we had at that point in time and the medical team interpreted that data and said, "This data does not support its inclusion at that point in time; however, we will continue to monitor for that."

Michelle Sharp PharmD (November 3, 2006)

A. Yes, that's correct.

Q. Okay. But then, ultimately, the label was revised in January of 2002, almost two years later, to include pancreatitis under the post-introduction reports section that had originally been requested by the FDA two years before, correct?

A. Yes, that's correct.

Michelle Sharp PharmD (November 3, 2006)

Q. Directing your attention back to Exhibit 2197, the chronology that you prepared of interactions that Lilly had with FDA about glucose, triglycerides, and pancreatitis, it notes that on May 9, 2000, Lilly submitted a revised Zyprexa package

insert with addition of random blood glucose measures in the laboratory changes section and diabetic coma in post-introduction reports section; is that correct?

A. Yes, that's correct.

(Whereupon, Deposition Exhibit(s) 4858, previously marked, was presented to the witness.)

QUESTIONS BY MR. SUGGS:

MR. SUGGS: Let me hand you what's been previously marked as Exhibit 4858 which purports to be a copy of a May 9, 2000, letter from Lilly, specifically, George T. Brophy, the Director of U.S. Regulatory Affairs to the Food and drug Administration.

98:1 QUESTIONS BY MR. SUGGS:

Q. And do you recognize this document?

A. Yes, I do.

Michelle Sharp PharmD (November 3, 2006)

98:11 Q. And is this indeed the May 9, 2000, submission that Lilly made to the FDA about revising the Zyprexa package insert?

A. Yes, I believe it is.

Q. And up in the upper right-hand corner of the exhibit in bold letters it notes that this is a Special Supplement Changes Being Effected; is that correct?

A. That's correct.

Q. And there's a particular section of the FDA regulations which is, actually, referred to in the text of the letter, for the record it's 21CFR

99:1 Section 314.70, paren, C, paren, two, paren, small I, that allows a drug company to change a label without prior FDA approval to add or strengthen a contraindication, warning, precaution, or adverse reaction; is that correct?

A. Yes, I believe that's what that regulation says.

Q. So basically the regulation says, "Hey, drug company, if you want to strengthen a warning or you want to strengthen a contraindication or an adverse reaction or precaution, anything that's going to heighten safety information, you can do that on your own without prior FDA approval," correct?

A. That regulation allows you to add or strengthen safety information, adding that safety information to the labeling, and the regulatory process that you can do that under is this regulation.

Q. Okay. Now, when you do that

you still submit what you've done to the FDA and they can then look at it and get back to you on whether they agree with it or not. But at least in the interim, because the purpose of this is to get safety information out to prescribing doctors, you're able to do that without the prior FDA approval, correct?

A. Yes. It allows you to implement that safety information in labeling and then allows the FDA to review that information.

Q. Okay. And in fact, this label change was implemented virtually immediately, was it not?

A. Yes, I believe it was.

Q. Okay. And so, the change to the label would have been made -- I'm assuming that there was also something sent to the publication that prints the PDR that we were looking at earlier about changing the label? That would have been done, too, correct?

A. When it was time for the next publication of the PDR we would have sent the labeling that was in effect at that point in time.

Q. Okay. And the detail people, the sales people for Zyprexa, they would have been informed of the labeling change, correct?

A. Yes, they would have.

Michelle Sharp PharmD (November 3, 2006)

There are two changes that were made in the label in May of 2000 that related to diabetes, correct?

A. Yes, that's correct.

Q. Okay. The letter lists three items. Item 1 doesn't relate to diabetes but Items 2 and 3 both deal with the issue, correct?

A. That's correct.

Q. Okay. And let's talk about the last one first. In Item No. 3, Lilly changed the label to add to that post-introduction report section of the adverse reactions that we were looking at before that prior to this time only mentioned priapism, the prolonged erection, to change that section so that it then read, quote, Adverse events reported since market introduction which were temporally but not necessarily causally related to Zyprexa therapy include the following: Diabetic coma and priapism, end quote. Correct?

A. Yes, that's correct.

Q. Okay. And then the other change was in the adverse reaction section in the laboratory changes section of that part of the labeling to include an analysis of

data that Lilly had do[illegible] regarding blood glucose levels, correct?
A. Yes, that's correct.
MR. SUGGS: Oh, I forgot to do something. Can you pull out Exhibit 988? You've got it there.
THE WITNESS: This one?
MR. SUGGS: Right. Will you go back to Page 14?
QUESTIONS BY MR. SUGGS:
Q. Exhibit 988, which is the compilation of adverse event reports prepared by Ken Hornbuckle and Man Fung, indicates that Lilly had been aware of reports of diabetic coma back as early as late 1996, early 1997; is that correct?
A. It looks like there was a case reported between September of '96 and March of '97 according to this table.
Q. Um-hum. And there was another report that came in sometime between April of '97 and September of 1997, correct?
A. That's what this report shows, yes.
Q. Okay. So Lilly had been aware of reports of diabetic coma about three years before the label was changed in May to report that in the post-introduction reports section of the adverse reactions part of the label, correct?
A. Based on this report it appears that we had received an adverse event report during that September '96-March '97 and another report in April of '97 to September of '97.

Michelle Sharp PharmD (November 3, 2006)

Q. And there were almost 200 reports of blood sugar elevation, at least by September of 1998, correct?
A. That's what this report indicates, yes.
Q. And, in fact, you know that after September of 1998, Lilly continued to receive reports of blood sugar elevation, including reports of hyperglycemia and diabetes, correct?
A. Yes. I believe we did receive additional reports.
Q. Okay. If I could refer you back to Exhibit 4858, which is the May 2000 label change. Item No. 2 in that exhibit shows the language that you were adding about the blood glucose in the laboratory changes section of the adverse reaction part of the label, correct?
A. That's correct.
Q. And can you read that language that was added into the record, read it aloud so the jury can hear it?

A. "In the olanzapine clinical trial database as of September 30, 1999, 4,577 olanzapine-treated patients representing, approximately, 2,255 patient years exposure, and 445 placebo-treated patients who had no history of diabetes mellitus, and whose baseline random blood plasma glucose levels were 140 milligrams per deciliter or lower were identified.

Persistent random glucose levels greater than or equal to 200 milligrams per deciliter, suggestive of possible diabetes, were observed in 0.8 percent of olanzapine-treated patients, placebo 0.7 percent.

Transient, i.e., resolved while the patients remained on treatment, random glucose levels greater than or equal to 200 milligrams per deciliter were found in 0.3 percent of olanzapine-treated patients, placebo 0.2 percent.

Persistent random glucose levels greater or equal to 160 milligrams per deciliter but less than 200 milligrams per deciliter, possibly hyperglycemia, not necessarily diabetes, were observed in 1 percent of olanzapine-treated patients, placebo 1.1 percent.

Transient random glucose levels greater than or equal to 160 milligrams per deciliter but less than 200 milligrams per deciliter were found in 1 percent of olanzapine-treated patients, placebo, 0.4 percent."

Q. And when you boil all that down, essentially, what it's saying is that there's really not that much difference in the blood glucose levels between the patients who were exposed to Zyprexa and the patients who received placebo, correct?

Michelle Sharp PharmD (November 3, 2006)

A. This language reports the analyses that was collected in our clinical trial database and reports out the percentage of patients and the categories that were specified.

Q. Well, and in fact, this language would have been reassuring to physicians, correct?

Michelle Sharp PharmD (November 3, 2006)

A. I don't know what any one physician would, how they might interpret this language. This is reporting the analyses that were conducted at the time.

Q. Do you recall that the FDA

believed that that language was reassuring to physicians?
A. FDA did respond to this labeling supplement and in that response they indicated that it might be reassuring to physicians.
Q. And, in fact, they made you take that language out in October of 2000, correct?
A. Yes. In that correspondence they requested that this be deleted from the labeling.

Michelle Sharp PharmD (November 3, 2006)

110:13 saying. You were aware that Zyprexa was
14 facing pressure in the marketplace because
15 your competitors were alleging that Zyprexa
16 increased the risk of hyperglycemia and
17 diabetes, and you were aware of that before
18 this label change was made, correct?
19 A. I don't recall the specific
20 time points but I was made aware of
21 discussions that occurred in the marketplace.
22 Q. Um-hum. And you, personally,
23 were involved in the drafting of the language
24 that became this label change. Is that not
111: 1 correct?
2 A. I was involved in discussions
3 with the medical team that put this language
4 together, yes.
5 Q. Okay. In fact, you were one
6 of the principal draft persons, were you not?
7 A. I worked with the medical
8 team that put this language together, yes.
9 Q. And the other people that
10 were on the medical team included Charles
11 Beasley, Bruce Kinon, Barry Jones, and Paula
12 Trzepacz; is that correct?
13 A. Yes, I believe those were
14 physicians that I worked with.
15 (Whereupon, Deposition
16 Exhibit(s) 7012 previously
17 marked, was presented to the
18 witness.
19 MR. SUGGS: Okay. I'm going
20 to hand you what's been previously
21 marked as Plaintiff's Exhibit 7012.
22 For the record this is a March 27,
23 2000, e-mail written by Michele
24 Sharp to Robert Baker, Charles
112: 1 Beasley, Alan Breier, Bruce Kinon,
2 Kenneth Kwong, Paula Trzepacz with
3 copies to John Roth, Michele Sharp,
4 herself. And the subject was
5 Proposed Zyprexa U.S. Package Insert
6 Revision -- Hyperglycemia.
7 QUESTIONS BY MR. SUGGS:
8 Q. Did I accurately describe the
9 document?
10 A. Yes. This is an e-mail that

I sent to the individuals that you listed.
Q. Okay. And you note in the first paragraph of your e-mail that "Following a meeting on Friday, March 24 with Charles, Barry, Bruce and Paula, a new proposal for the Zyprexa U.S. package insert change with regards to hyperglycemia was developed. These words are in alignment with the core data sheet wording."
Did I read that correctly?
A. Yes, you did.
Q. What's the core data sheet?
A. The core data sheet is a labeling document that represents the safety information that should be incorporated in the local labels for the various countries that market Zyprexa.
Q. Okay. And then in the following paragraph you note that you're attaching the adverse reaction section of the label with the new words in large font and you're asking the recipients of this e-mail to review that language and then get back to you with any suggestions, correct?
A. Yes, that's correct.
Q. Okay. And then at the very bottom you state, quote, "Following your review I am planning to send the proposed text to our marketing colleagues in preparation for next Tuesday's April 4 meeting Weight Gain and Hyperglycemia Advisory Group. Please let me know if you will not be attending the April 4 meeting."
Did I read that correctly?
A. Yes, you read that correctly.
Q. And what was the Weight Gain and Hyperglycemia Advisory Group?
A. You know, I don't recall the specifics of that group. With the text that's here, I believe it was made up of marketing colleagues and the medical colleagues that I've communicated to here.
Q. Okay. And who was it that headed that cross-functional group?
A. You know, I don't recall the specifics of this group today, so I'm not sure who was the head of that.
Q. Do you recall that meeting?
A. I do not.
Q. Okay. Am I correct that all of the people that were listed as recipients in your e-mail had a medical background?
A. Other than John Roth and myself the recipients in the "to" did have a medical background.
Q. Okay. And then as we noted before you indicated after you heard back from them you were then going to send this on to the Marketing Department for review, correct?
A. Yes. I would be sending that to the marketing group.
(Whereupon, Deposition

Exhibit(s) 5796 previously marked, was presented to the witness.

MR. SUGGS: Okay. Next I'm going to hand you what's been previously marked as Plaintiff's Exhibit 5796. For the record this is an e-mail chain. The very top one on the first page is from Robert Baker to Charles Beasley dated April 6, 2000. But the bottom chain, pardon me, the beginning of the chain appears to be an e-mail from Robert Baker to Jack Jordan with a copy to Paula Trzepacz.

QUESTIONS BY MR. SUGGS:

Q. And who was Jack Jordan?

A. Jack Jordan was the Marketing Director.

Q. Was he the Marketing Director for Zyprexa or the Marketing Director for Zyprexa and other drugs as well?

A. I believe just for Zyprexa.

Michelle Sharp PharmD (November 3, 2006)

116:23 Q. Okay. And Robert Baker was a physician who had responsibilities regarding
117: 1 the issue of whether or not Zyprexa increased the risk of diabetes, correct?

A. He was one of the physicians that was reviewing data and information that we had, yes.

Q. And do you recall that he had a particular focus on hyperglycemia and diabetes; whereas, Dr. Kinon had a particular focus on weight gain?

A. Yeah, that's my recollection.

Q. Okay. And in this e-mail, Dr. Baker sends at the bottom on April 5th -- strike that.

At the bottom of the first page of this exhibit Robert Baker sends an e-mail to Jack Jordan with a copy to Paula Trzepacz, and who is she?

A. She was a medical director.

Q. Okay. And the subject is Proposed Label Changes, correct?

A. Yes.

Q. And he says, "Dear Jack, Attached is a draft of the proposed label revision incorporating the changes that the
118: 1 U.S. team is suggesting. Please forward if you agree." He goes on to note in the following paragraph "The draft we received from Michele/Charles, et al. looked excellent. In addition to minor rewording we suggested three substantive changes" and he goes on to describe what those changes are, correct?

A. Yes.

Michelle Sharp PharmD (November 3, 2006)

118:20 Q. Would it be fair to say that
21 you and Charles Beasley took the lead on
22 crafting this language?
23 A. I would say Charles had the
24 lead in analyzing the data, interpreting it,
119: 1 and describing the label wording that would
2 be appropriate. I took the lead in helping
3 with the labeling process, both internally
4 and interacting with FDA.

Michelle Sharp PharmD (November 3, 2006)

120:16 Q. Okay. So Jack -- it would be
17 fair to say that Jack Jordan's e-mail is
18 going to both medical people and to marketing
19 people, correct, and regulatory people?
20 A. Yes, that's correct.
21 Q. He says, "Michele, we've just
22 finished reviewing the label change.
23 Attached is our proposal. Aligns with
24 information Dr. Beasley wanted in the label
121: 1 and minimizes our exposure to, quote,
2 inappropriate, end quote, competitive
3 attacks." Did I read that correctly?
4 A. Yes, you did.
5 Q. And what did you understand
6 Jordan to mean when he put the word
7 inappropriate in quotation marks?
8 A. You know, I'd have to ask
9 Jack, but as I read this, I think he was
10 saying or intending to mean here that the
11 competition was not accurately stating what
12 the data reflected with respect to
13 olanzapine.
14 Q. And clearly, it was his view
15 that the proposal that they made was going to
16 be effective in minimizing Lilly's exposure
17 to competitive attacks, correct?
18 A. I think as I read this e-mail
19 I think he's saying that by accurately
20 reflecting the data as we know it in 2000,
21 that would provide physicians the information
22 as we knew it in 2000.
23 Q. Well, he indicates in his
24 e-mail that they had, actually, revised the
122: 1 language, correct? He says "attached is our
2 proposal?"
3 A. Those are the words he used,
4 yes.
5 Q. Okay. And he said that their
6 proposal that the marketing department had
7 come up with aligns with information
8 Dr. Beasley wanted in the label and minimizes
9 our exposure to inappropriate competitive
10 attacks, correct?
11 A. Right.
12 Q. And Jack Jordan had no

medical background, did he?
A. Not that I'm aware of.
Q. And the competitive attacks that Lilly was facing at this point in time were attacks that Zyprexa increased the risk of hyperglycemia and diabetes, correct, isn't that what he was referring to?
A. I'm not sure of the specific attacks he's referring to, but in the context of this e-mail, I imagine they were the hyperglycemia attacks he was referring to.

Michelle Sharp PharmD (November 3, 2006)

123:16 Q. Okay. And this process for making the label change that, actually, occurred in May of 2000, actually began much earlier in February of 2000 with a proposal by the Product Team and Pharmacovigilance; isn't that correct?
A. Well, it, actually, begins with the data and analyses that are conducted and then following that then there was a
124: 1 discussion about the label.
Q. And do you recall that, in fact, there was a proposal by the Product Team and Pharmacovigilance in February of 2000 to change the label?
A. Yeah. There was a proposal taken to the Global Product Labeling Committee.

Michelle Sharp PharmD (November 3, 2006)

124:15 Q. You were a member of the Product Team, Zyprexa Product Team in 2000, were you not?
A. I did not report structurally through the Product Team but I did support the regulatory efforts and needs for that product team in 2000.
MR. SUGGS: Let me show you what's been, what we will now mark as Sharp 2.
125: 1 (Whereupon, Deposition Exhibit(s) 2 duly received, marked and made a part of the record.)
MR. SUGGS: For the record, Sharp 2 is a document entitled 2000 Integrated Product Plan, Zyprexa Product Team.
QUESTIONS BY MR. SUGGS:
Q. Do you recognize this document?
A. Yes, I do.
Q. And what is it?
A. It's a product plan that crosses the clinical research that's being

conducted, the registration activities that are being planned, the -- our understanding of the, the marketplace at that point in time.
Q. Was this an annual type of document that was prepared?
A. Yes. I believe it was prepared annually.
Q. And who was it that would have prepared this?
A. It was prepared by a cross-functional team of people.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. And so it sounds like this Zyprexa product team would have been formed in January of 1995 before Zyprexa even went on the market, correct?
A. Yes, that's correct.
Q. Because it didn't go on the market until, what, September of '96?
A. That's correct.
Q. Okay. It refers to the Product Group President being Gary Tollefson, correct?
A. Yes.
Q. And what was the Product Group President?
A. He was a member of a more senior management team that had responsibility for more than one product.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. So when we get up to Gary Tollefson we're talking pretty senior executives, correct?
A. He's a senior executive, yes.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. But if, what we've got here is the 2000 Integrated Product Plan, just based generally on how these types of things would have been prepared, can you tell us, would this have actually been prepared sometime in 1999, early 2000, or when?
A. As I recall, we worked on these documents in the first quarter of a year. So as best I can recall, the 2000 would have been looked at in the first quarter of 2000.
Q. Okay. So sometime before April of 2000, correct?
A. You know, I can't recall the exact time. That's my best recollection it

would have been in the first quarter sometime.

Q. Okay. If I could direct your attention to the third page. There's a heading at the top entitled "charter." What does that refer to?

A. I believe this section is laying out kind of the scope or charter of this specific product team and what they will be charged to work on from the company.

Q. Okay. And the very first thing underneath that section is a subheading entitled 1.1 In Scope-Funded. What does that refer to?

A. That means that the corporation has identified this as work that this team is working on and has received the appropriate -- I shouldn't say has received -- it has identified that funds will be provided to work on this body of work.

Q. Okay. And then below that are several bulleted points, correct?

A. Yes, that's correct.

Q. And the very top one is Olanzapine Compound Support. And then there's a sub-bullet point underneath that that says Hyperglycemia, Weight Gain, CIV, Annual Report, Alert Safety Responses, et cetera, correct?

A. Yes, that's what it says.

Q. And then -- and the CIV that's referred to there is, means clinical investigator's brochure, correct?

A. Yes, that's correct.

Q. Because at this point in time Lilly was still conducting some studies in connection with Zyprexa. You had outside investigators who were involved in those studies, and from time to time there was a clinical investigator's brochure would be prepared that would then be supplied to those people who were conducting the research, correct?

A. As part of the regulations to conduct clinical research in this country you need to provide a clinical investigator brochure for those investigators and that's exactly what we were doing.

Q. And the annual report that's referred to, there's an annual report to the FDA which you're required by the federal regulations to report adverse reactions, new information in the published literature about safety issues and so on and so forth, correct?

A. Yeah. The regulations tell you all the information that needs to be provided for annual reports. That's the type

of information that was provided.
Q. Okay. Do you know what would have been redacted below that?
A. No. I don't recall what was in this document in 2000, no.
Q. Okay. The second bulleted item is, "Support the schizophrenia and bipolar franchises worldwide," correct?
A. Yes.
Q. Below that is "Support the use of olanzapine in patients with Alzheimer's disease," correct?
A. Yes.
Q. There was no indication for patients with Alzheimer's disease for Zyprexa, was there?
A. In 2000, we were conducting quite a fair amount of research with respect to those patient populations. That's what this bullet is referring to.
Q. My specific question is there was no indication for -- by the way, let's back up here for a second so we're clear to the jury about this.
The labeling also has a section titled the "indications" section, correct?
A. Yes, that's correct.
Q. And in that section of the labeling it states what medical conditions the drug may be used for, correct?
A. Yes, that's correct.
Q. Okay. And at this point in time in 2000, what was listed was treatment of schizophrenia, correct?
A. Yes, that's correct.
Q. And was -- at that time?
A. There was a second indication.
Q. Was there an indication for the acute manic phase of bipolar disorder?
A. That's correct.
Q. Okay. But there was no indication for Alzheimer's disease, was there?
A. No, there was not.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. If I could direct your attention to the bottom of page, the second page there, the bottom of the third page. There's a section entitled Strategic Intent. Do you see that?
A. Yes.
Q. And the very beginning of that section it says "Zyprexa will become the No. 1 selling psychotropic in history," correct?
A. Yes.
Q. And what's a psychotropic?

A. Psychotropic is a descriptor for a class of drugs.
Q. Okay. And so it was your intent, Lilly's intent, that Zyprexa would be the No. 1 selling psychotropic drug in history, correct?
A. That's what this document says, yes.

(Whereupon, Deposition Exhibit(s) 990, previously marked, was presented to the witness.

MR. SUGGS: I'm going to hand you what's been previously marked as Plaintiff's Exhibit 990. For the record, Exhibit 990 is a document which on the first page bears the label Attachment E.

And then on the second page it has a heading at the top below a confidential label, that says Olanzapine Labeling Change On Hyperglycemia for February 21, 2000 GPLC Meeting.

QUESTIONS BY MR. SUGGS:
Q. Do you recognize this document?
A. Yes, I do.
Q. And how is it that you recognize it?
A. This is a document that was provided to GPLC, February 2000, in a meeting that I would have participated in.
Q. Okay. And would you tell the jury what GPLC means?
A. It stands for the Global Product Labeling Committee.
Q. And who were the members of that committee?
A. It's made up of senior level individuals in our medical component, our regulatory component, our quality component, as well as a legal representative sits on that committee.
Q. Okay.

Michelle Sharp PharmD (November 3, 2006)

Q. And how often did the Global Product Labeling Committee meet?
A. They have scheduled standing meetings twice a month. Not always, you know, used of course, if there are not topics to bring, but that's their standing schedule.

Michelle Sharp PharmD (November 3, 2006)

The proposal that is reflected in Exhibit 990, would have been the

proposal of the Zyprexa Product Team which is listed here in Sharp Exhibit 2, correct?
A. That's correct.
Q. Okay. And then the PHV that's referred to there is the Pharmacovigilance, correct?
A. That's correct.

Michelle Sharp PharmD (November 3, 2006)

151:11 Q. Okay. And do you recall what the Global Product Labeling Committee decided with respect to this proposal?
A. As I recall, they agreed to incorporate the information into the core data sheet.
Q. Okay. If I could direct your attention to Page 2 of this exhibit. In that first box under the proposal of the Product Team and Pharmacovigilance there's a section in italics that describes the new statement. Do you see that?
A. Yes, I do.
Q. And I'll represent to you
152: 1 that we've had testimony from several witnesses that there's some bizarre little box that shows up in there instead of a greater-than or less-than sign. And I'll represent to you that we've had testimony from Lilly witnesses who are involved in this tell us that that should state, quote, "random glucose greater than or equal to 160 milligrams per deciliter in patients with baseline random glucose less-than or equal-to 140 milligrams per deciliter has been occasionally seen in clinical trials." Would you agree that that's what the new statement was that was proposed?
A. Yes, I think so.
Q. Okay. And, in fact, that language is not in the May 2000 label change that was made, correct?
A. Those exact words are not in the May 2000 but the concept is represented in the May 2000 submission.
Q. If I could direct your attention to the middle box on that first page it says "How has this proposal arisen."
153: 1 And below that it states, quote, "Recent review of random glucose levels of patients in olanzapine clinical trials reveal that the incidence of treatment-emergent hyperglycemia in olanzapine group, paren, 3.6 percent, was higher than that in the placebo group, 1.05 percent. For common events, incidences from clinical trials provide more meaningful information." Did I read that correctly?
A. Yes, you did.
Q. And what does the phrase "treatment-emergent hyperglycemia" mean?
A. My understanding is that

hyperglycemia is reported or represented through lab values following treatment being given in that patient.

Q. Okay. And at least this document indicates that the incidence of treatment-emergent hyperglycemia in the olanzapine group was about three and-a-half times higher than in the placebo group, correct?

A. It says in the olanzapine group it was 3.6 percent, in the placebo group it was 1.05 percent.

Q. And if you divide the incidence of the placebo group into the incidence of the olanzapine group it works out to be about three and-a-half times higher, correct?

A. Yeah, that looks right.

Michelle Sharp PharmD (November 3, 2006)

Q. And there was never any label change that advised physicians that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in Zyprexa users as compared to placebo group, correct?

Michelle Sharp PharmD (November 3, 2006)

A. This exact statement was not included in labeling.

Michelle Sharp PharmD (November 3, 2006)

Q. Isn't it true that the Zyprexa label never warned physicians that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in Zyprexa users as compared to placebo users?

A. The Zyprexa label included the safety information analyses that we conducted.

MR. SUGGS: Again you're not answering my question. I want a yes or no to this question.

Could you read it back to her please?

(The Court Reporter read the requested material, as set forth herein above.)

MR. LEHNER: Same objection to the form.

QUESTIONS BY MR. SUGGS:

Q. Lilly never told doctors that, correct?

A. We provided doctors the

safety information that we knew at the time.
Q. You did not tell doctors that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in Zyprexa users. It's a very simple question.
A. We provided safety information --
Q. Would you please tell the jury the answer.
Would you please quit trying to dodge the question and just tell the jury, look at the camera and tell them whether it's true, that Lilly never told doctors that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in Zyprexa users?
A. We conducted numerous analyses on this trial, clinical trial data, and we provided in the 2000 labeling supplement to FDA those analyses and safety information in the labeling that represented those analyses.
Q. And the analyses that you presented in the May 2000 labeling said there was, essentially, no difference between placebo users and Zyprexa. And, in fact, FDA came back five months later and said this language is reassuring and made you take it out, isn't that right?

Michelle Sharp PharmD (November 3, 2006)

A. We provided in May 2000, the analyses that we had conducted in this clinical trial data set. FDA did review that information and indicate in their letter that we should delete that information as there was additional information that they need to look at.
Q. And, in fact, the data that was included in the May 2000 label change said there was, essentially, no difference between the incidence of hyperglycemia in Zyprexa users as compared to placebo users, correct?

Michelle Sharp PharmD (November 3, 2006)

Q. Can you answer that question?
A. We conducted numerous analyses on these clinical trial data and we provided the safety information in the labeling at that point in time in May of 2000.
MR. SUGGS: If I could direct your attention back to Exhibit 4858. I'm sorry, that's the wrong --
THE WITNESS: Which one is

4858?
MR. SUGGS: It's the May 9, 2000, label change.
THE WITNESS: Okay.
QUESTIONS BY MR. SUGGS:
Q. In that second paragraph, in the laboratory changes section. Six lines down, actually, five lines down, this label change that you made in May of 2000 said quote, "Persistent random glucose levels greater-than or equal-to 200 milligrams per deciliter, suggestive of possible diabetes, were observed in .8 percent of olanzapine-treated patients and .7 percent in placebo," correct?
A. Yes, that's correct.
Q. Virtually no difference between .7 and .8, correct?
A. That's correct.
Q. You go on to say, "Transient, i.e., resolved while the patients remained on treatment, random glucose levels greater than 200 milligrams per deciliter were found in .3 percent of olanzapine-treated patients and placebo was .2 percent." Correct?
A. Yes, that's correct.
Q. Again, virtually no difference between .2 and .3 percent correct?
A. Yes, that's correct.
Q. It goes on to say, "Persistent random glucose levels greater-than or equal-to 160 milligrams per deciliter but less than 200 milligrams per deciliter, possibly hyperglycemia, not necessarily diabetes, were observed in 1.0 percent of olanzapine-treated patients, placebo, 1.1 percent," correct?
A. Yes.
Q. Again, virtually no difference between 1.0 percent and 1.1 percent, correct?
A. That's correct.
Q. There's nothing in this language to indicate what was found in Exhibit 990, that the incidence of treatment emergent hyperglycemia in the olanzapine group was three and-a-half times higher than in the placebo group, correct?
A. Yes, that exact sentence is not included in this labeling.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. Do you recall any other meetings of the Global Product Labeling Committee after May of 2000 that dealt with the Zyprexa labeling?
A. Sure.
Q. Okay. And which ones do you recall?
A. There were numerous ones that

occurred after May of 2000. I couldn't state all of them.
Q. Okay. Meetings of the Global Product Labeling Committee that dealt with Zyprexa labeling?
A. Yes.

Michelle Sharp PharmD (November 3, 2006)

163: 8 Were there any changes in the
9 Zyprexa labeling with respect to
10 hyperglycemia or diabetes in the U.S. between
11 May of 2000 and September of 2003?
12 A. No.

Michelle Sharp PharmD (November 3, 2006)

172:14 Q. Okay, here we go. If I could
15 direct your attention back to the chronology
16 which I put on the top of your pile, which is
17 Exhibit 2197.
18 If you could drop down to the
19 May 10 reference, May 10, 2000, it says that
20 "Lilly received a letter dated May 1, 2000,
21 requesting extensive safety information on
22 hyperglycemia, new onset diabetes, nonketonic
23 hyperosmolar coma, diabetic ketoacidosis, and
24 weight gain from preclinical, clinical and
173: 1 post-marketing sources." Did I read that
2 correctly?
3 A. Yes.
4 (Whereupon, Deposition
5 Exhibit(s) 775, previously
6 marked, was presented to the
7 witness.)
8 MR. SUGGS: And I'm going to
9 hand you what has been previously
10 marked as Plaintiff's 775. And for
11 the record, this purports to be a
12 letter dated May 1 from Russell Katz
13 at FDA addressed to Eli Lilly and
14 Company to the attention of Gregory
15 T. Brophy.
16 THE WITNESS: Yes.
17 QUESTIONS BY MR. SUGGS:
18 Q. And would you agree with me
19 that this is the letter that was referred to
20 in the chronology you prepared regarding the
21 FDA's May 1 request for information regarding
22 hyperglycemia and diabetes?
23 A. Yes, that's correct.
24 (Whereupon, Deposition
174: 1 Exhibit(s) 778, previously
2 marked, was presented to the
3 witness.)
4 MR. SUGGS: Okay. And next
5 I'm going to hand you Plaintiff's
6 Exhibit 778.
7 (Whereupon, Deposition

Exhibit(s) 3680, previously marked, was presented to the witness.)

MR. SUGGS: And I now get to unload what I've been lugging around, which is Plaintiff's Exhibit 3680, which is a 668-page document. I don't have to lug it around anymore.

Okay. The first document I handed you is Exhibit 778, which purports to be a July 31, 2000, letter from Gregory Brophy to the FDA enclosing Lilly's response to FDA's May 1, 2000, letter requesting information with olanzapine.

QUESTIONS BY MR. SUGGS:

175: Q. And do you recognize this document?

A. Yes, I do.

Michelle Sharp PharmD (November 3, 2006)

180: Q. Okay. Very good.

Directing your attention again to Page 3 of Exhibit 778, you note that in the second full paragraph, quote, "The results from the analysis of our clinical trial safety database, Section 6, and review of our spontaneous case reports, Section 7, served as the basis for the safety labeling change submitted on May 9, 2000." Did I read that correctly?

A. Yes, you did.

Q. Okay. And the May 9, 2000, labeling that's referred to there is what we

181: have talked about extensively as Exhibit 4858, correct?

A. Yes, that's correct.

Q. Okay. Can I direct your attention to Exhibit 990, which was the original February 2000 proposal for a labeling change that went to the Global Products Labeling Committee.

And if I could direct your attention in particular to Page 4 of that document. There's a box entitled Literature Reports?

A. Yes.

Q. And you see in the second paragraph in that section it states, quote, "Dr. Daniel Casey from Oregon presented in a seminar at Lilly at the end of 1999. He performed chart review of 136 veteran patients who had been exposed to olanzapine therapy for at least four months, average of 1.4 a year. Of the 39 patients who had normal fasting glucose levels before olanzapine therapy, seven, 18 percent, had fasting glucose levels of 126 milligrams per

182: deciliter or higher during olanzapine

therapy, paren, threshold that met the 1998 ADA diagnostic criteria for diabetes."
Do you see that language?
A. Yes.
Q. Were you familiar with Dr. Casey's presentation?
A. No, I don't believe I was.
Q. Okay. Do you recall anyone telling you that any physician had done a chart review and found that 18 percent of the people who had normal fasting glucose levels before using Zyprexa wound up having levels that were diagnostic for diabetes?
A. I don't recall any conversation on this.
Q. Okay. If I could direct your attention now to the very thick document, Exhibit 3680, and in particular if you could turn to Page 29. And they're numbered at the bottom right-hand corner, and also in the upper right-hand corner, and the numbers coincide, which is nice.
There's a section there, 2.8,
183: which is Olanzapine and Hyperglycemia In Patients. Do you see where I'm talking about?
A. Yes.
Q. And in that section is a description of various literature reports of Zyprexa and hyperglycemia in patients, correct?
A. Yes.
Q. And there's no mention, whatsoever, of Dr. Casey's finding of 18 percent of the people being exposed to Zyprexa developing fasting glucose levels diagnostic for diabetes, is there?
A. I don't see Dr. Casey's name mentioned on this page, no.
Q. And you said that Dr. Beasley was the person, the head medical guy who would have been in charge of preparing this document, correct?
A. Yes. He would have overseen the medical team that would have put this together.
Q. And he was also the guy who
184: signed off on and reviewed the February 2000 proposal, Exhibit 990, which discusses Dr. Casey's finding of 18 percent of the people exposed to Zyprexa developing fasting glucose levels diagnostic for diabetes, correct?
A. Yes. He was involved in the review of that document.
Q. And were you aware that Dr. Casey was a consultant for Eli Lilly?
A. I don't know what relationship that Lilly had with Dr. Casey.

185:12 Q. Am I correct that the new
13 drug application for Zyprexa was submitted in
14 about September of 1995?
15 A. That sounds right, yes.
16 Q. And the FDA approved the new
17 drug application in September of 1996?
18 A. Yes, that's sounds right.

Michelle Sharp PharmD (November 3, 2006)

185:24 In Exhibit 778, when we were
186: 1 talking about the note to the reviewer on the
2 second page of the document. I believe you
3 testified earlier, just a little while ago,
4 correct me if I'm wrong, that the Phase 2 and
5 Phase 3 data from the olanzapine NDA would be
6 in Section 5, correct? In Section 5 of this
7 Exhibit 3680?
8 A. With respect to the topic
9 that FDA's asking for information, yes --
10 Q. Which was hyperglycemia.
11 A. -- I do believe that
12 Section 5 includes the information from the
13 Phase 2 and 3 studies.
14 Q. Okay. And this would have
15 been the data that was submitted to the FDA
16 in the NDA back in September of 1995,
17 correct?
18 A. And data that was submitted
19 to the NDA after September of 1995.
20 Q. Okay. Well, good point.
21 Would it be fair to say then that in
22 Exhibit 3680, and in particular in Section 5
23 of Exhibit 3680, would contain all of the
24 data that Lilly had submitted to FDA up to
187: 1 that point in time regarding hyperglycemia
2 and diabetes and the other information that
3 was called for and described in FDA's May 1,
4 2000, letter request?
5 A. Looking at the table of
6 contents in this document, it appears to me
7 that we are submitting data related to
8 hyperglycemia, diabetes, weight gain, the
9 information that FDA requested, that had been
10 submitted to -- we have more than one NDA
11 with Zyprexa, so to at least one of the NDAs.
12 Q. Okay. That's another good
13 point. You had several NDA's for the Zyprexa
14 molecule, I'm presuming for various
15 indications and dosages and so on so forth,
16 correct?
17 A. For different dosage forms,
18 yes.
19 Q. Okay. This document 6880 was
20 intended by Lilly to collect in one place and
21 submit to FDA all of the data that had been
22 previously been submitted in whatever, with
23 whatever NDA, to the FDA in this July 31,
24 2000, submission with respect to diabetes,
188: 1 hyperglycemia, and so forth; is that correct?
2 A. To my knowledge, yes, that's

what we submitted.
Q. Okay. If I could direct your attention to page 49 of Exhibit 3680. That is the beginning of Section 5, is it not?
A. Yes.
Q. I'll represent to you that I've looked through this section and I was unable to find any language in here that would indicate that Lilly had found a statistically significant increased incidence of high glucose in Zyprexa users as compared to Haldol users.
I don't expect you to read through page by page here, but sitting here today, do you recall whether or not Lilly had informed FDA prior to July of 2000 of finding a statistically significant increased incidence of high glucose in Zyprexa users as compared to Haldol?
A. I can't say. I don't know.
Q. Okay. If I could direct your attention to Page 67. On that page is Table 5.17, which is described as incidence of high or low blood glucose at any time in NDA 20-592 active controlled integrated database acute phase. Do you see that?
A. Yes.
Q. And the NDA 20-592 is the Zyprexa NDA, correct?
A. Yes.
Q. Okay. And there's a -- in that table is data regarding the incidence of high glucose nonfasting and also low glucose nonfasting, correct?
A. Yes.
Q. And it's a comparison between olanzapine and H-A-L stands for Haldol, correct?
A. Yes.
Q. And Haldol is a first generation antipsychotic drug, correct?
A. Yes.
Q. And at least according to this table, 5.17, the percent of high glucose was 2.2 percent in the Zyprexa patients and 1.2 percent in the Haldol patients, and that was not statistically significant, correct?
A. Yes, that's correct.
Q. And the reason we say it's not statistically significant, because in order for it to be statistically significant convention says that the P value that's shown there in the right-hand column should be less than .05, correct?
A. Yes, that's correct.
Q. And here it's shown as .108, correct?
A. That's correct.
MR. SUGGS: Okay.
(Whereupon, Deposition Exhibit(s) 1605, previously marked, was presented to the witness.)

MR. SUGGS: I'm going to hand you what's been previously marked as Plaintiff's Exhibit 1605.

QUESTIONS BY MR. SUGGS:

Q. For the record, Exhibit 1605 is a computer printout dated June 19, 1995, regarding treatment emergent abnormal high or low laboratory values at any time F1D-MC-HGAJ acute phase, correct?

A. Yes.

Q. And the HGAJ study was the largest of the clinical studies that was submitted in the Zyprexa NDA, was it not?

A. Yes, I believe that's right.

Q. Had about 1900 patients in it?

A. That sounds about right, um-hum.

Q. And this particular printout, as I noted before, is dated June 19, 1995, which would have been several months before the new drug application was submitted to FDA, correct?

A. Yes.

Q. Okay. If I could direct your attention to the second to last page which is Page 11. There's a section in this printout referring to "glucose nonfasting low and high" at about the middle of the page. Do you see that?

A. Yes.

Q. And again, there's a comparison between olanzapine and Haldol, correct?

A. Yes.

Q. And in this printout it shows that there was a statistically significant higher incidence of high glucose in the Zyprexa users as compared to the Haldol users, correct?

A. Yes.

Q. The P value was .03, less than .05, correct?

A. Yes, that's right.

Q. Have you ever seen this printout before?

A. Yes, I think I've seen it before.

Q. When did you see it?

A. Well, I -- I would have seen it in reviewing the NDA at some point.

Q. Is it your testimony that this printout was part of the NDA?

A. I can't say for sure but it appears to be an appendix in the HGAJ study report and that study report was part of the NDA.

Q. Okay. Fair to say that Lilly was aware of a statistically significant increased incidence of high glucose in Zyprexa users as compared to Haldol users in this study as early as June of 1995, correct?

Michelle Sharp PharmD (November 3, 2006)

193:10 A. Lilly was aware of this
11 specific analyses and its result.

Michelle Sharp PharmD (November 3, 2006)

194:19 Q. Isn't it true that Lilly
20 never advised physicians that their own
21 clinical studies had shown that Zyprexa users
22 had a statistically significant increased
23 incidence of high blood glucose as compared
24 to Haldol users? Simple question of fact.
195: 1 I'm not asking your opinion as to whether
2 they should have or not. But just as a
3 matter of fact, they did not do that, did
4 they?

Michelle Sharp PharmD (November 3, 2006)

195: 7 A. Again, this is one analyses
8 in many, many, analyses and data we looked
9 at.

Michelle Sharp PharmD (November 3, 2006)

195:19 Q. And you know there is nowhere
20 in the Zyprexa label at any time from 1996 up
21 through the present where Lilly warned
22 physicians or advised physicians that their
23 own clinical studies had found a
24 statistically significant increased incidence
196: 1 of high blood glucose as compared to Haldol
2 users. That is not in the labeling now and
3 never has been, correct? Yes or no?
4 A. Labeling's dependent on
5 multiple analyses and interpretation of that
6 data. One single analyses does not drive
7 labeling.
8 Q. I'm not asking for your
9 opinion as to whether it should be there or
10 whether it shouldn't be there. My only
11 question is was it there or was it not? Just
12 answer the factual question. I'm not calling
13 for your opinion.
14 Did Lilly ever in its
15 labeling between 1996 and the present ever
16 advise physicians that Zyprexa users had a
17 statistically significant increased incidence
18 of high blood glucose as compared to users of
19 Haldol, yes or no?
20 A. Again, this is a single
21 analyses. The label decisions are made up
22 more than just a single analyses.
23 Q. Is that a yes or a no?
24 A. Again, it's a single

197: 1 analyses.
2 Q. Is that a yes or a no? Can
3 you please answer the question? I'll bring a
4 motion if I have to with the Court to make
5 you answer the question. But could you
6 please just tell the jury, yes or no, did you
7 ever tell doctors that?
8 A. I can't say whether this
9 analyses was in medical letters that were
10 provided to doctors or not.

Michelle Sharp PharmD (November 3, 2006)

197:24 Q. It is a fact, is it not, that
198: 1 Lilly never advised physicians in the Zyprexa
2 label that in their own clinical studies they
3 had found a statistically significant
4 increased incidence of high blood glucose in
5 Zyprexa users as compared to users of Haldol.
6 You never said that in the labeling did you
7 ever, yes or no?
8 A. Labeling is based on more
9 than one specific analyses not a specific
10 analyses.
11 Q. I'm not asking for your
12 opinion. Was it there or was it not?
13 A. Again labeling is based on
14 more than just a specific analyses.

Michelle Sharp PharmD (November 3, 2006)

199:16 Q. It is a fact, is it not, that
17 Lilly never advised physicians in the Zyprexa
18 label that in their own clinical studies they
19 had found a statistically significant
20 increased incidence of high blood glucose in
21 Zyprexa users as compared to users of Haldol.
22 You never said that in the labeling ever, did
23 you, yes or no?
24 A. This analyses was not,
200: 1 specifically, described in the label.
2 Q. That is a no, correct?
3 A. Correct.
4 Q. Thanks.
5 If I could direct your
6 attention to Page 165 of 3680.
7 MR. LEHNER: 165?
8 MR. SUGGS: Um-hum.
9 QUESTIONS BY MR. SUGGS:
10 Q. This is a table showing a
11 category called analysis of the incidence of
12 IGT or diabetes by treatment, correct?
13 A. Yes.
14 Q. And IGT stands for impaired
15 glucose tolerance, correct?
16 A. Yes.
17 Q. Okay. And when we're at this
18 point in the exhibit we are in Section 6 of
19 the report to FDA, correct?

A. Yes.
Q. Which you told the FDA was the analysis of your clinical trial safety database that was the -- served as the basis for the safety labeling change submitted in May of 2000, correct?
A. Yes, that's correct.
Q. And on -- beginning on Page 178 and continuing through Page 182 is a discussion section which, essentially, discusses that analysis, correct?
A. Yes, that's correct.
Q. And would Dr. Beasley have been the person primarily responsible for writing that section of this report?
A. Yes.
Q. Okay. In the first paragraph of that discussion at the bottom of Page 178, the paragraph starts off by saying, quote, "The results of these analyses indicated that the rate of development of treatment emergent markers of deficient glucose homeostasis temporarily associated with olanzapine treatment did not differ from the rates associated with placebo, haloperidol, or risperidone," correct?
A. That's correct.
Q. And haloperidol is the same as Haldol that we discussed previously, correct?
A. Yes.
Q. And risperidone is another atypical antipsychotic that goes by the trade name Risperdal, correct?
A. That's correct.

Michelle Sharp PharmD (November 3, 2006)

Q. So what Dr. Beasley was saying in this discussion paragraph was that there was no difference in the rates of glucose events between Zyprexa and placebo, Haldol or Risperdal, correct?
MR. LEHNER: Same objection.
A. Yes.
Q. Okay. And in the second full paragraph in this section, which is at the top of Page 179, he states, quote, "These results do not suggest a causal relationship between the use of antipsychotic agents, at least for olanzapine, haloperidol, risperidone, and the development of IGT and/or diabetes among patients with schizophrenia and related disorders." Did I read that correctly?
A. Yes.
Q. So Dr. Beasley and Lilly were saying there's no causal relationship between Zyprexa and diabetes?
A. That's right.
Q. Okay. By the way, back to

the first paragraph in that section which you agreed with me Dr. Beasley was saying that there was no difference in the rates of glucose events between Zyprexa and placebo, Haldol or Risperdal. If indeed that is correct wouldn't that also indicate that at least up until July of 2000, the date of this document, Lilly did not advise FDA that the clinical data up to that point showed a statistically significant increased incidence of high blood glucose as compared to Haldol or placebo?

Michelle Sharp PharmD (November 3, 2006)

A. The analyses from the HGAJ study was provided to FDA.

Q. That wasn't my question.

A. So we did inform FDA of that statistical significant difference. This report, this specific section in the discussion is providing results from the integrated clinical analyses that were conducted following the HGAJ study report.

Q. And in this report Lilly is telling FDA at this point in time, July 2000, that there is no difference in hyperglycemia between Zyprexa and placebo or Haldol or Risperdal, correct?

A. Lilly is reporting the result of an integrated analyses that was conducted to look at the comparisons between these three, olanzapine versus placebo, Haloperidol, and risperidone.

Q. And was telling the FDA there was no difference, Zyprexa did not have any higher incidence of hyperglycemia than any of those other drugs, correct?

A. Based on those analyses that are provided under Section 6, yes.

Q. Okay. In that paragraph where, on the following page where Lilly was saying that these results do not suggest a causal relationship between the use of antipsychotic agents, at least for olanzapine, haloperidol and risperidone. Am I correct that even today Lilly is asserting that there is no causal relationship between the use of Zyprexa and the development of diabetes?

Michelle Sharp PharmD (November 3, 2006)

A. In my role today I don't work closely with the medical team that supports olanzapine, but based on what I know today, yes.

(Whereupon, Deposition Exhibit(s) 6998, previously marked, was presented to the witness.)

MR. SUGGS: Okay. I'm going to show you a couple of exhibits. The first of which is Plaintiff's Exhibit 6998.

Let me put a rubber band around this one so it doesn't get mixed up.

(Whereupon, Deposition Exhibit(s) 1452, previously marked, was presented to the witness.)

MR. SUGGS: And I'm also going to hand you what's been previously marked as Plaintiff's Exhibit 1452.

For the record, Exhibit 6998 is an October 9, 2000, e-mail from Robert Baker to Charles Beasley and others regarding meeting with endocrinologic consultants.

And Exhibit 1452 is a string of e-mails, the first -- well, the one that's at the top of Page 1 is an e-mail dated October 10, 2000, from Dr. Robert Baker to Charles Beasley and others.

And, Ms. Sharp, I recognize that you are not copied on any of these e-mails.

If I could direct your attention first to Exhibit 6998. In that e-mail are there the names of any individuals there who were in the regulatory affairs department?

A. No. Let me just check one more time. No, I don't see anyone.

Q. Okay. And it's the people in the regulatory affairs department who communicate with FDA, correct?

A. Yes, primarily, yes.

Q. If I could direct your attention to the first paragraph of Robert Baker's e-mail on October 9, 2000, he says, "For your information, the Lilly diabetes endocrine group held an academic advisory board meeting this weekend in Atlanta. They kindly allotted two hours for discussion of olanzapine potential hyperglycemia risks, and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the topic."

Were you ever informed of that meeting?

A. I don't recall the specifics or any information from this meeting.
Q. Okay. Dr. Baker then goes on to say in the second paragraph of the second sentence, "They were, however, concerned by our spontaneous AE reports and quite impressed by the magnitude of weight gain on olanzapine and implications for glucose." Do you see that language?
A. Yes.
Q. Dropping down a couple of lines Dr. Baker said, where he says "Citing methodological questions." Do you see where I'm at?
A. Yes.
Q. He says, quote, "Citing methodological questions at least the vocal members were not reassured adequately by our analyses such as the finding that the relative risk was not higher than comparative drugs. Disconcertingly, one member compared our approach to Warner Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class." Do you see that language?
A. Yes.
Q. Did anyone ever inform you that outside endocrine consultants were citing methodological questions and saying that they were not reassured adequately by Lilly's analyses of the hyperglycemia data?
A. No, I don't recall them telling me this, but these are consultants helping the medical team here so.
Q. And, obviously, if people in the Regulatory Affairs Department were not told about these concerns by the outside endocrine consultants, the Regulatory Affairs People would not be even capable of communicating that information to FDA, correct?
A. You know, I had many discussions with the medical team and they would share with me and bring forward information that was important for us to share with FDA.
Q. Did they share this with you?
A. You know, without having further context around this, I don't really know what this e-mail is referring to.
Q. Okay. Let me give you some more context. If I could direct your attention to Exhibit 1452. The last physical page is an e-mail from John Holcombe to Robert Baker and others. And in the last paragraph of his e-mail he's referring to that advisory group of endocrinologic consultants and says "Our advisory group is Who's Who in diabetes." Do you see that reference in the last paragraph?
A. Yeah, I see a sentence that says that.
Q. Okay. And, in fact, Eli

Lilly has been manufacturing and selling diabetes drugs for many decades, correct?
A. Yes, we have.
Q. And Eli Lilly has, indeed, a Who's Who group of outside consultants on the issue of diabetes, correct?
A. As John Holcombe suggests we do. I can't speak for that, for him.
Q. Do you know who John Holcombe is?
A. He is an endocrinologist that works at our company.
Q. And you would expect him to know whether the advisory consultant group to the company was a Who's Who or not, don't you?
A. I can't really speak for him. If that's what he thinks that's what he thinks.
Q. You don't have any basis to dispute his assessment that this outside advisory group was a Who's Who of diabetes, correct?
A. No, I don't.
Q. Okay. You said you wanted some more context so I'd like to direct your attention to Page 6 at the bottom.
This is from an e-mail from -- in an e-mail from Thomas Brodie to Robert Baker and Eugene Theim. Do you know any of those individuals?
A. I know Robert Baker, I don't know the other two.
Q. Okay. Anyway, Mr. Brodie goes on to says in his e-mail, "Robert, clearly this group of endocrinologists who spoke up, and I would rate those who did speak up as the leaders of the pack, are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes. I can only hope that you and all the team who attended the NADAB meeting are gaining the ear of senior leadership and articulated this finding. Although the board's recommendation is probably not the way Lilly, typically, does business, they made a strong point that unless we come clean on this it could get much more serious than we might anticipate." Do you see that language?
A. Yes, I see that language.
Q. And is it fair to say that no one at the company advised you back in 2000 that this Who's Who group of endocrinologists had expressed those types of concerns?

A. I'm not sure what they're objecting to exactly.
Q. Okay. Let's give you some

more context. Direct your attention to Page 5. In the second full paragraph on that page starts off by saying "These guys." Do you see that?

A. Yes.

Q. By the way, this is in an e-mail from Charles Beasley to Alan Breier with copies to Robert Baker, Paul Berg, Scott Clark, John Holcombe, Roland Powell, Alvin Rampey and Roy Tamura, correct?

A. Yes.

Q. And Alan Breier was the head of the Zyprexa Product Team, correct?

A. Yes, at the time of this e-mail he was.

Q. And Charles Beasley was the lead physician on the Zyprexa Product Team, was he not?

A. Yes, he was a physician on the team.

Q. Okay. And in his e-mail in the second paragraph Beasley writes to Breier and says, "These guys were really concerned about the weight gain, not only because of a diabetes risk but all the other potential health risks."

And in the middle of the paragraph he writes, "They believe we should aggressively face the issue and work with physicians to address methods of reducing weight gain."

Did they ever tell you that those physicians were concerned about that?

Michelle Sharp PharmD (November 3, 2006)

A. You know, this is a discussion between consultants and our physicians, and our physicians learning how to understand the way that they looked at it today and how they may do additional analyses. So I'm not sure, I'm not sure that I should be apprised of this at this point in time.

Q. Well, whether you should be or shouldn't we'll leave to the jury but my question is were you aware of it? Did Dr. Beasley, or anyone else, make you aware that these outside consultants were advising you to, quote, "aggressively face the issue?"

A. I don't recall being part of these conversations that were going on here.

Q. Okay. Let's drop down to the following paragraph. Starts off that paragraph by saying, "On the diabetes side the concern was about the use of categorical analyses." Do you see that sentence?

A. Yes, I do.

Q. And the studies and submissions that you had made to FDA that we've been talking about, Exhibit 3680, and

the label change that you folks did in May of 2000, those were all based on the use of categorical analyses, correct?
A. That's correct.
Q. Okay. And then in about the middle of the paragraph Dr. Beasley says, "The problem is the arbitrary nature of the cut points and the potential for big shifts depending on those cut points, and the fact that we chose the cut points, not really, they came from ADA website. They, specifically, referred to the data as being," quote, "tortured," end quote. Do you see that language?
A. I see those words in this document, yes.
Q. And my question to you is did Dr. Beasley or anyone else ever inform you that this outside group that was a Who's Who of diabetes referred to your categorical analyses which you submitted to the FDA as being tortured?

Michelle Sharp PharmD (November 3, 2006)

Q. Calls for a simple yes or no. Did they tell you that or did they not?
A. I was not part of these discussions so I was not aware of this exchange of information that was occurring.
Q. And if you were never told that this outside group of Who's Who endocrinologists referred to the categorical analysis as being tortured you could not have communicated that to the FDA, correct?

Michelle Sharp PharmD (November 3, 2006)

A. If the medical team didn't provide me additional information to send to FDA then I would not have sent it.
Q. Well, since FDA wanted to know the information that you guys had about hyperglycemia, and you've got this outside group of consultants who your own people describe as being a Who's Who of diabetes, don't you think if you were going to be honest with the FDA that you should have told them, that the company should have told them, that, hey, we've had outside consultants look at this and they think the data's tortured?

Michelle Sharp PharmD (November 3, 2006)

Q. If you're interested in honesty shouldn't you have provided that to the FDA?

Michelle Sharp PharmD (November 3, 2006)

229:21 A. We provided FDA the analyses
22 that we conducted and we continued to conduct
23 analyses after this October 2000 exchange of
24 information, and we shared that additional
230: 1 information with FDA.
2 Q. You didn't tell them that
3 this outside group of consultants had severe
4 questions about your analysis, correct?

Michelle Sharp PharmD (November 3, 2006)

230: 7 A. Don't know that it's
8 information that you would share with FDA. I
9 think you'd take the advice that you're given
10 and continue to conduct research,
11 understanding outside perspective.
12 Q. If an outside expert refers
13 to data being tortured is that a good thing
14 or bad thing?
15 A. You know, FDA is reviewing
16 this data independent as well and using their
17 own consultants, too, so.
18 Q. That isn't my question. My
19 question to you is if you have a group of
20 outside consultants review your data
21 analysis, and they tell you that they think
22 your analysis tortured, is that a good thing
23 or bad thing?

Michelle Sharp PharmD (November 3, 2006)

231: 2 A. I think it depends on -- this
3 is a perspective of some consultants.
4 It's --
5 Q. Did Dr. Beasley appear to be
6 happy about this reaction?
7 A. I have no idea. I don't
8 recall -- I wasn't involved in this and I
9 don't recall a reaction by Dr. Beasley about
10 this.
11 Q. We know from Dr. Baker that
12 he said, "Unfortunately, this consultation
13 reinforced my impression that hyperglycemia
14 remains quite a threat for olanzapine and may
15 merit increasing even further medical
16 attention and marketing focus on the topic."
17 Isn't that what was said in
18 the earlier exhibit?

Michelle Sharp PharmD (November 3, 2006)

231:21 A. I wasn't involved in this so
22 I can't provide anymore information.

Q. It would be fair to say that no one, not Dr. Beasley, not Dr. Cavazzoni, not Dr. Breier, not any of the people that we've seen mentioned on this chain of e-mails, ever suggested to you that the Regulatory Affairs Department contact the FDA and advise them of this meeting that you'd had with consultants, or that Lilly had had with consultants; isn't that correct?

Michelle Sharp PharmD (November 3, 2006)

Q. Yes or no, did they suggest that you contact FDA about this meeting with the consultants, yes or no?
A. I wasn't involved in this and wasn't made aware of the discussions or requests to contact FDA.
Q. And no one ever advised you to contact FDA about it, correct?

Michelle Sharp PharmD (November 3, 2006)

A. These individuals did not tell me to contact FDA regarding this meeting.

Michelle Sharp PharmD (November 3, 2006)

MR. SUGGS: I'm going to hand you what's been previously marked as Plaintiff's Exhibit 3567. For the record, this document has a cover page with the label Attachment Three and then attached to that is a manuscript entitled Random Blood Glucose Concentrations in Patients with Schizophrenia Treated with Typical and Antipsychotic Agents: An Analysis of Pooled Data from Double-blind, Randomized, Controlled Clinical Trials with the authors being David Allison, Patrizia Cavazzoni, Charles Beasley, Paul Berg, Nitai Mukhopadhyay -- I'm sure I mangled that -- Craig Mallinckrodt, Robert Baker, John Holcombe, Cindy Taylor, Alan Breier and John Buse.
QUESTIONS BY MR. SUGGS:
Q. Did I describe that accurately?
A. Yes, you read the authors right.
Q. Okay. And is this the, in fact, the manuscript that was referred to in the prior exhibit -- 4815?

A. Yeah, it was one of the attachments for the May 21, 2001, submission.
Q. Okay. And this was, according to Exhibit 4815, a manuscript that had been submitted to the "American Journal of Psychiatry," correct?
A. Yes.
Q. And it was not published, however, was it?
A. I don't believe at that time that it was.
Q. In fact, to this day it's never been published, has it?
A. I do not know.
Q. If I could refer back to your chronology, Exhibit 2197. On the second page you note that on April 12 Lilly submitted a report on Japan hyperglycemia cases?
A. Yes.
Q. And I presume that you also informed FDA that the Japanese regulatory authority in April of 2002, insisted that Lilly not only change its label in Japan to warn about diabetes but also required Lilly to send out a letter to Japanese doctors alerting them to the change; is that correct?
A. Yes, that's correct.
Q. And do you recall that the Japanese regulatory authority require that the letter have a bold red box around it with a large font title at the top stating that it was emergency safety information?
A. Yes. That's the format they use in Japan for Dear Doctor Letters.

(Whereupon, Deposition Exhibit(s) 320, previously marked, was presented to the witness.)

MR. SUGGS: Let me show you what's been previously marked as Plaintiff's Exhibit 320. Unfortunately, that stamp is cut off. I don't have any highlighting on this. I'll use this for the official record.

QUESTIONS BY MR. SUGGS:
Q. And is this a copy of the English translation of the Japanese Dear Doctor Letter?
A. Yes, I believe it is.
Q. And it has a big bold title Emergency Safety Information at the top, correct?
A. Yes, it does.
Q. And then it has in the text of the first page a big box which has three numbered points, correct?
A. Yes.
Q. And each of those has in large font a warning: No. 1, "Do not administer to patients with diabetes mellitus and those who have a history of diabetes mellitus," correct?

A. Yes.
Q. Point No. 2 is "During administration of this product observe sufficiently with such as measurement of blood glucose." Did I read that correctly?
A. Yes.
Q. The translation isn't the smoothest English language but there it is.
Point 3, "Explain sufficiently to the patient and family members," correct?
A. Yes.
Q. After this point in time -- by the way, this is dated April 2002, correct?
A. Yes.
Q. There was no change made to
272: 1 the United States labeling to reflect the
2 changes that were incorporated in what was
3 required by the Japanese, correct?
4 A. No, these changes were not
5 made in the U.S.
6 Q. And, in fact, when Lilly
7 talked about the Japanese label change it
8 stated that it was in complete disagreement
9 with the Japanese regulatory authority in
10 requiring that label change, correct?
11 A. We did not agree with this
12 labeling change, correct.

Michelle Sharp PharmD (November 3, 2006)

272:16 Did the Global Products
17 Labeling Committee meet after April 2002 to
18 discuss the Japanese label change?
19 A. Yes, they did.
20 Q. And the Product Team met with
21 the Global Product Labeling Committee,
22 correct?
23 A. Yes, they did.
24 Q. And do you recall when that
273: 1 would have been?
2 A. It was shortly after this
3 that I recall. I don't remember the exact
4 date.

Michelle Sharp PharmD (November 3, 2006)

273: 7 The Zyprexa Product Team met
8 with the Global Product Labeling Committee
9 and told that committee that Lilly should not
10 change the label here in the U.S., correct?
11 A. The Zyprexa Product Team
12 representatives said to the Global Product
13 Labeling Committee that we do not feel a
14 change is warranted to the core data sheet
15 which, in effect, is not warranted for the
16 U.S. label.
17 Q. Okay. I'd like to review,

generally, the situation that existed after April of 2002, with respect to the Zyprexa label as it stood, not only in Japan but also here in the U.S. and over in Europe. And to do that I'd like to hand you what's been previously marked as -- shoot, not showing up in the copy here. I represent to you that this has been previously marked as Plaintiff's Exhibit 4436. For some reason I'm having a problem with the number being cut off. Oh, no, there it is. It does have a number on it. I thought I made a mistake and I was wrong.

(Whereupon, Deposition Exhibit(s) 4436, previously marked, was presented to the witness.)

MR. SUGGS: For the record, this is a document entitled Psychotropic Label Overview for DM. In the upper left-hand corner it has a stamp saying it's a draft and it also has a stamp on the right-hand side on every page thereafter indicating it's confidential.

QUESTIONS BY MR. SUGGS:

Q. And if I could direct your attention to the fifth page. On that page is a chart entitled Zyprexa Label Overview For DM. Do you see that?

A. Yes.

Q. And DM stands for diabetes mellitus, correct?

A. Yeah, I believe so.

Michelle Sharp PharmD (November 3, 2006)

In this chart is a series of columns. One column has a listing of various components of labeling, such as black box, contraindication, warning, precaution, adverse reaction, post introduction reports, correct?

A. Yes.

Q. And then the other column refer to the U.S., the EU, which would be Europe, correct?

A. Correct.

Q. Australia, Japan and Canada. And by looking at this table we can see that in -- by the way, this document, I will represent was apparently prepared in May of 2003, the database that was produced to us by Lilly indicates that that was the date the document was prepared. And it shows that the table that's on Page 5 here, that in Japan diabetes was a contraindication for Zyprexa but none of the other countries had that as a contraindication; is that correct?

A. That's correct.

Q. And you would agree that that

was the situation that also would have obtained back in April of 2002, correct, after the Japanese label change?

A. Yes, I believe so.

Q. Okay. This table also indicates that there was a warning for diabetes in Europe and also in Japan, but not in the other countries, correct?

A. Yes.

Q. And there's an asterisk there noting that in the European label warnings and precautions are in one paragraph, correct?

A. It's one section in Europe is what it's referring to.

Q. Okay. And then if we go down to the precaution level of the label we see that there were precautions in Europe, and Australia, and Japan, and Canada, but not in the U.S., correct?

A. Yes, that's correct.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. And would you agree that the situation that is reflected there in this chart would have been applicable as of, say, June of 2002?

A. I think that's probably right.

Q. Okay. Now we know from some of the other documents that we looked at earlier that the European label that had the special precautions and warnings about diabetes back as early as 1999 -- do you recall that discussion that we had?

A. Yes, I recall that.

Q. Okay. And we know that at least in April of 2002, Japan had not only a precaution and a warning but also a contraindication, correct?

A. That's correct.

Q. Do you know whether or not prior to that April 2002 label change, Japan had had a warnings section about diabetes?

A. I don't recall. I don't believe that they did.

Q. Okay. Do you recall whether they had a precaution section?

A. I don't recall what their initial label was when they were approved on the market and what was included in that label. So I'm not sure.

Q. Okay. Was it your impression that the label change the Japanese required in April of 2002 was a significant step up from what it had been before that time?

279:16 A. There were -- the label
17 change that occurred in April 2002 in Japan
18 did include more descriptive information than
19 had previously occurred in the label.
20 Q. Well, and it wasn't only
21 descriptive information, they had specific
22 categories that had not been there before,
23 such as contraindication and warning,
24 correct?
280: 1 A. Yes, that's correct.
2 Q. Okay. Do you know when it
3 was that Canada and Australia required their
4 precautions?
5 A. I believe both of those
6 occurred after the European labeling change
7 but I don't remember the years that it
8 occurred.
9 Q. Is it your recollection that
10 those in Australia and Canada requiring
11 precautions would have occurred sometime
12 after 1999 but before the April 2002 label
13 change?
14 A. I believe so.

Michelle Sharp PharmD (November 3, 2006)

302:10 MR. SUGGS: Let me hand you
11 what's been previously marked as
12 Plaintiff's Exhibit 439.
13 For the record this is a
14 September 15, 2003, letter from --
15 strike that.
16 For the record this is a
17 September 11, 2003, letter from
18 Russell Katz at FDA to Eli Lilly in
19 the attention of Gregory T. Brophy
20 in the Regulatory Affairs
21 Department.
22 THE WITNESS: That's correct.
23 QUESTIONS BY MR. SUGGS:
24 Q. You've seen this document
303: 1 before, have you not?
2 A. Yes, I have.
3 Q. Okay. AND in the second
4 paragraph of this letter the FDA notes that,
5 "After reviewing the available data
6 pertaining to the use of atypical
7 antipsychotic medications and diabetes
8 mellitus adverse events, we have concluded
9 that the product labeling for all atypical
10 antipsychotics should be updated to include
11 information about these events," correct?
12 A. Yes, that's what it says.
13 Q. And they went on to say,
14 "While we acknowledge that the relationship
15 between atypical antipsychotic use and
16 diabetes mellitus adverse events has not been
17 completely described, we believe the safe use
18 of Zyprexa can be enhanced by informing
19 prescribers and patients about these events.
20 Increased attention to the signs and symptoms

atypical antipsychotics including Zyprexa."
Did I read that correctly?
A. That's correct.
Q. And in fact, Lilly had been aware of reports of ketoacidosis and diabetic coma for at least five years before this, correct?
A. There were reports that reported to us, yes.
Q. At least five years before September of 2003, correct?
A. Yes. I believe there was a case that we discussed earlier in 1997.
Q. Okay. Now in the last sentence of that first paragraph, the language that was mandated by the FDA at that time said, quote, "The available data are insufficient to provide reliable estimates of differences in hyperglycemia-related adverse event risk among the marketed atypical antipsychotics." Did I read that correctly?
A. Yes, you did.
Q. And Lilly was very happy with that last sentence, was it not?

Michelle Sharp PharmD (November 3, 2006)

307:11 A. This is the opinion of the FDA regulators based on the data that they've reviewed. I wouldn't characterize it as us being happy.
Q. Well, Lilly had, at this point, been claiming for years that the rates of hyperglycemia were comparable between Zyprexa and other atypical antipsychotics, had it not?
A. We analyzed data comparing the atypical antipsychotics and provided that data to FDA and our interpretation of the data is that they were comparable.
Q. And you had been making that
308: 1 claim for years at this point, correct?
A. Based on the data that occurred at each of the time points, yes.
Q. And, in fact, Lilly still makes that claim today, correct? Or at least of the last time you worked on the product drug?
A. To my knowledge based on the last time that I worked with the drug, yes.
Q. But in December of 2003, a couple of months after this, FDA sent you a letter telling you to take out that sentence, which said that there was not sufficient data to provide reliable estimates of differences between the marketed antipsychotics; isn't that correct?
A. FDA sent us a revision to the language in December of '03, right.
(Whereupon, Deposition Exhibit(s) 4871, previously

marked, was presented to the witness.)
MR. SUGGS: And I'm going to hand you what's been previously marked as Plaintiff's Exhibit 4871.
And this exhibit is a December 16, 2003, letter from Russell Katz to Dr. Michele Sharp.

Michelle Sharp PharmD (November 3, 2006)

Q. In this letter the FDA again sets forth the language that they are mandating with respect to a warning about hyperglycemia and diabetes, correct?
A. Yes, that's correct.
Q. And they show the changes that they make -- pardon me -- that were made between their letter to Dr. Brophy in September and this letter two months later in December 2003, correct?
A. Yes, they do.
Q. And in this letter they struck out that sentence that said, quote, "The available data are insufficient to provide reliable estimates of differences in hyperglycemia-related adverse event risks among the marketed atypical antipsychotics," correct?
A. Yes, that sentence is struck.

Michelle Sharp PharmD (November 3, 2006)

Q. What happened between the September 2003, letter from FDA and the December FDA letter was that in November of 2003, there was a consensus development conference of the American Diabetes Association, American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity which concluded that, indeed, you could tell that there were differences between the rate of diabetes with atypical antipsychotics, and that, in fact, Zyprexa was one of the worst offenders; isn't that right?

Michelle Sharp PharmD (November 3, 2006)

A. I believe that was the opinion of the physicians that were involved in that ADA consensus that you refer to.
(Whereupon, Deposition Exhibit(s) 2368, previously marked, was presented to the witness.)

MR. SUGGS: Let me hand you what's been previously marked as Plaintiff's Exhibit 2368.

For the record, this is a publication entitled Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. It was published in February 2004.

QUESTIONS BY MR. SUGGS:

Q. Do you recognize this document?

A. Yes, I do.

Michelle Sharp PharmD (November 3, 2006)

If I could direct your attention to the first page, the top of the middle column -- let me back up even further than that.

In the left-hand column on the first page about five lines from the bottom it says, "Presentations were also made by a representative from the U.S. Food and Drug Administration, and by representatives from the AstraZeneca, Bristol-Myers Squibb, Janssen, Lilly and Pfizer pharmaceutical companies. In addition, before the conference, the consensus panel was given copies of most of the known peer-reviewed English language clinical studies published in this area as well as additional articles from animal studies; other papers and abstracts were reviewed at the conference." Do you see that language?

A. Yes, I do.

Michelle Sharp PharmD (November 3, 2006)

Q. Okay. And if I could direct your attention to the third page. In the middle column about ten lines down there's a sentence that starts off "despite limitations." Do you see where I'm at?

A. Yes.

Q. It says, "Despite limitations in the study design, the data consistently showed an increased risk for diabetes in patients treated with clozapine or olanzapine compared with patients not receiving treatment with FGAs" -- which is first generation antipsychotics -- "or with SGAs" -- which is second generation antipsychotics. Correct?

A. Yes, that's what it says.

Q. If I could direct your attention to Page 5, in the Summary section. The second paragraph -- well, in the first paragraph about four lines down it says, "One

constellation of adverse effects is an increased risk for obesity, diabetes, and dyslipidemia." Do you see that language?
A. Yes, I see that.
Q. And in the second paragraph it states, quote, "These three adverse conditions are closely linked and their prevalence appears to differ depending on the SGA used. Clozapine and olanzapine are associated with the greatest weight gain and highest appearance of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate effects. Aripiprazole and ziprasidone are associated with little or no associated weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as the other agents." Do you see that language?
A. Yes.
Q. And you clearly understood after being informed of this, the findings of the consensus development conference were contrary to the message of comparable rates of diabetes that Lilly had been proclaiming for some years at that point, correct?

Michelle Sharp PharmD (November 3, 2006)

A. This publication is not consistent with the labeling that FDA required Zyprexa and all the atypical antipsychotics to include in their labeling.

Michelle Sharp PharmD (November 3, 2006)

Q. The consensus development conference publication concluded that Zyprexa had higher rates of diabetes than other drugs, correct?
A. That's correct.

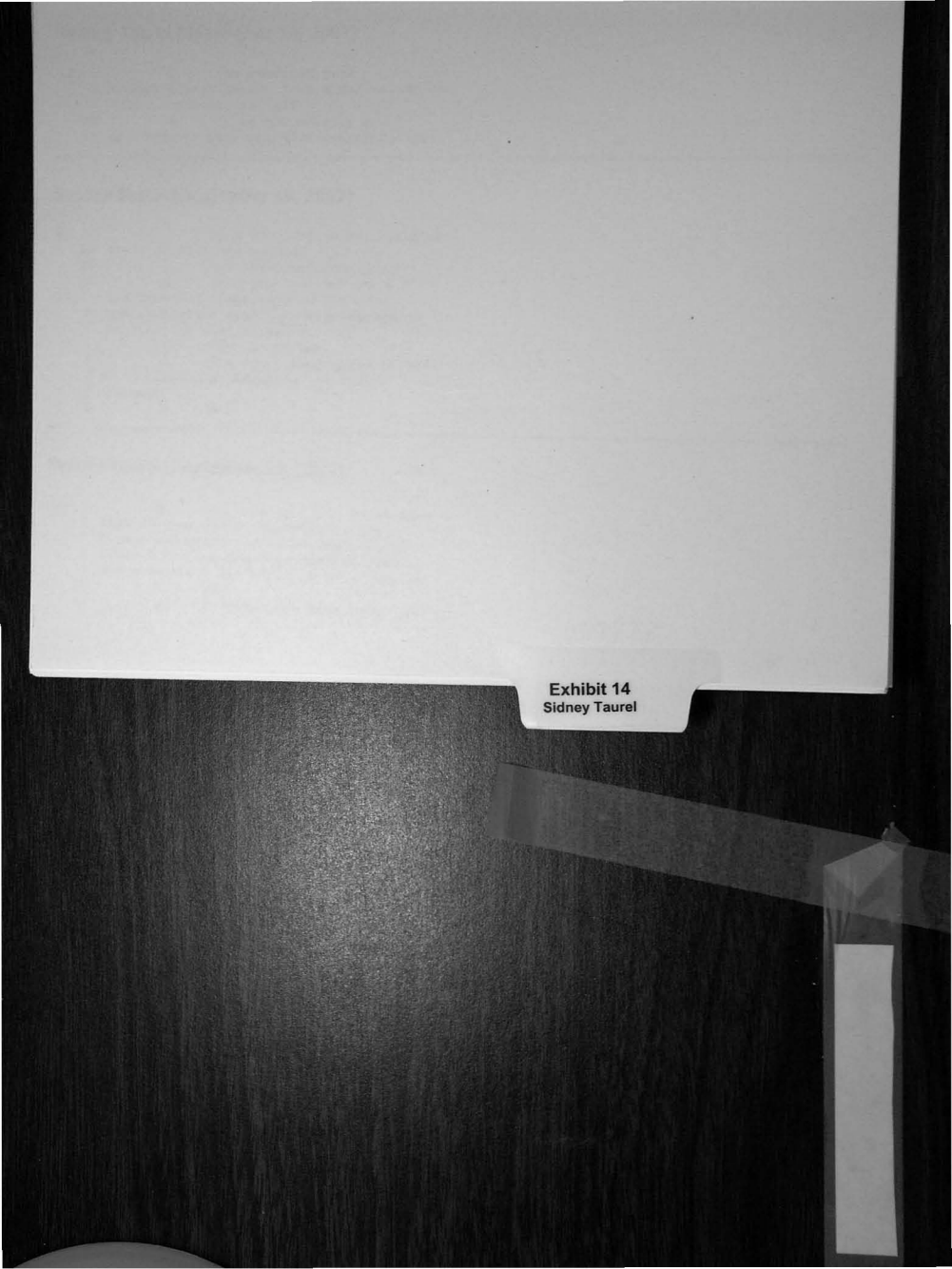
Exhibit 14
Sidney Taurel

Sydney Taurel (September 19, 2007)

10:12 Q. Would you state your full
13 name for the record, please.
14 A. Sidney Taurel.
15 Q. You are currently the Chief
16 Executive Officer and Chairman of the
17 Board of Eli Lilly; is that correct?
18 A. Correct.
19 Q. I'm sure you're aware that
20 Harry Truman had a sign on his desk in
21 the Oval office when he was President
22 that said "The buck stops here." Do you
23 have that same philosophy of management?

Sydney Taurel (September 19, 2007)

11: 2 THE WITNESS: I certainly
3 agree that I'm overall responsible
4 for the company, yes, and have
5 ultimate accountability for the
6 company.

Sydney Taurel (September 19, 2007)

12: 7 Q. You received your
8 undergraduate degree from a university in
9 Paris, correct, in 1969?
10 A. It is not exactly a
11 university, it's called a county college.

Sydney Taurel (September 19, 2007)

12:21 What was your major field of
22 study at that university?
23 A. Business administration.
24 Q. Then you came to the U.S.
13: 1 and received a Master's of business
2 administration from Columbia University
3 in 1971; is that correct?
4 A. That's correct.
5 Q. And you joined Lilly in 1971
6 as a marketing associate; is that
7 correct?
8 A. Yes.

Sydney Taurel (September 19, 2007)

14: 5 Q. And then in 1993, after more
6 than 20 years with the company, you
7 became executive vice president of Eli
8 Lilly & Company and president of its
9 pharmaceutical division; is that correct?
10 A. Yes.
11 Q. I assume you were based in

Indianapolis then?
A. Yes.
Q. And you became a U.S. citizen in 1995; is that correct?
A. Correct.

Sydney Taurel (September 19, 2007)

In 1996, the same year that Zyprexa came on the market, you were promoted to President and Chief Operating Officer; is that correct?
A. I was promoted to President and COO in 1996, yes.
Q. When you said "COO," that stands for Chief Operating Officer?
A. Yes.

Sydney Taurel (September 19, 2007)

Q. In July of 1998 you became Chief Executive Officer; correct?
A. Yes.
Q. Okay.
And by that point, you'd been with the company for over 25 years, correct?
A. Yes. I joined in 1971.
Q. Okay.
Today you've been with the company for over 36 years, correct?
A. Correct.

Sydney Taurel (September 19, 2007)

Q. With respect to 2006, what was your income from Lilly?
A. Base salary in the range of $1.6 million or so, bonus, which was, again, based on 125 percent of base salary at target. So, again, it could vary between zero and a higher number. The target is like 2.1 million or so. And then again an equity program in the same range, 6 million or so.
Q. Okay.
What did the bonus turn out to be in 2006?
A. I believe it was 2.7 million.
Q. So, you had the one -- salary, the bonus and also the equity value that you just discussed in 2006, correct?
A. They're -- both a salary and the bonus were paid. In terms of the equity, the stock option part is worth, I

believe, 0 or thereabo[illegible] right now due to the price of the stock, and the performance award did have a payout.
Q. How many shares of Lilly stock do you presently own?
A. I do not remember the exact number. It's in the range of, I believe, $45 million or so. Most of my equity is in the company.

Sydney Taurel (September 19, 2007)

Q. At any time up to the present, has the board of directors or its public policy and compliance committee addressed the issues of whether Zyprexa can cause diabetes?

Sydney Taurel (September 19, 2007)

THE WITNESS: We have reviewed at the board several times the data on Zyprexa, and that data shows that there's no causality with diabetes.
BY MR. SUGGS:
Q. Okay.
So, the members of the board have been informed by the company that there is no evidence showing that Zyprexa causes diabetes, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Yes.

Sydney Taurel (September 19, 2007)

Q. Okay.
I'm assuming that the board has been informed by Lilly executives that the Zyprexa label adequately warns about the risk of diabetes, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: The Zyprexa label reflects all of the best information that the company and the regulators have about Zyprexa.
BY MR. SUGGS:
Q. And has the board been informed by the company that there was no

off-label promotion of Zyprexa?
A. Yes.

Sydney Taurel (September 19, 2007)

Q. Am I correct that so far Eli Lilly has paid out over $1.2 billion to settle thousands of lawsuits by individuals who claimed that Lilly negligently failed to warn them about the risk of Zyprexa?
MS. GUSSACK: Objection.
THE WITNESS: We have settled a large number of cases, yes. I don't recall exactly the amount of the settlement.
BY MR. SUGGS:
Q. Did the board of directors authorize the settlement of those claims?
A. Yes.
Q. Okay.
MR. SUGGS: I'm marking as Taurel Exhibit Number 2 a copy of a New York Times article published on December 17, 2006.
- - -
(Whereupon, Deposition Exhibit Taurel-2, "Eli Lilly Said to Play Down Risk of Top Pill," (Berenson) New York Times, December 17, 2006 (4 pages), was marked for identification.)
- - -
BY MR. SUGGS:
Q. The headline states, "Eli Lilly Said to Play Down Risk of Top Pill."
The first two paragraphs of this article state, "The drug maker Eli Lilly has engaged in a decade-long effort to play down the health risks of Zyprexa, its best-selling medication for schizophrenia, according to hundreds of internal Lilly documents and e-mail messages among top company managers.
"The documents, given to The Times by a lawyer representing mentally ill patients, show that Lilly executives kept important information from doctors about Zyprexa's links to obesity and its tendency to raise blood sugar - both known risk factors for diabetes."
Do you see that language, sir?
THE WITNESS: I see it, yes.
BY MR. SUGGS:
Q. And did --
I'm assuming that when that article was published, it was probably noticed by the members of the board of directors, correct?

Sydney Taurel (September 19, 2007)

59:16 A. I believe that they paid
17 attention to it. It was a very important
18 article obviously.
19 Q. Okay.
20 Did the board of directors
21 or its public policy and compliance
22 committee investigate those allegations
23 that I just read?

Sydney Taurel (September 19, 2007)

60: 1 THE WITNESS: Could you
2 repeat the question.

Sydney Taurel (September 19, 2007)

60:21 My question was, did the
22 board of directors or its public policy
23 and compliance committee investigate
24 those allegations?

Sydney Taurel (September 19, 2007)

61: 2 THE WITNESS: No, they did
3 not do an investigation because
4 they trust and they rely on the
5 report that -- and the compliance
6 systems that we have in place and
7 have been following this issue for
8 a long time. And we're satisfied
9 that all of the information that
10 we have had over the years on
11 Zyprexa has been appropriately
12 reflected in our label and shared
13 with doctors.

Sydney Taurel (September 19, 2007)

62:19 Q. Let's shift our discussion
20 back in time to 1996.
21 Before Zyprexa came on the
22 market in 1996, Lilly's biggest selling
23 product was an antidepressant drug called
24 Prozac; is that correct?
63: 1 A. Yes.
2 Q. Pharmaceutical companies
3 often use the term "molecule" to refer to
4 what those of us not in the business
5 would think of as a drug, correct?
6 A. Usually when it's a chemical

compound, it's called a molecule. When it's a biotech compound, it's called a protein.
Q. Okay.
Lilly had a monopoly on Prozac because the drug molecule was patented, correct, at least for some period of time?
A. Yes.
Q. Okay.
But Lilly knew that that patent was going to expire at some point after 2000, correct?
A. It is correct that we expected the patent to expire sometime after 2001.
Q. Okay.
When a patent on a drug
64: 1 expires, then other drug manufacturers can step in with generic versions of that same molecule and sell the drug/molecule at a cheaper price, correct?
A. Yes.
Q. Okay.
When generic manufacturers are able to sell the same molecule, sales and profitability of the original patent drug typically go down, correct?

Sydney Taurel (September 19, 2007)

64:12 THE WITNESS: Yes.
BY MR. SUGGS:
Q. In the case of Prozac, there was some uncertainty as to exactly when the patent was going to expire due to some technical legal issues, isn't that correct?

Sydney Taurel (September 19, 2007)

64:20 THE WITNESS: There was litigation regarding the patent, and so there was uncertainty as to what exact date generics might appear on the market.
65: 1 BY MR. SUGGS:
Q. Because of that uncertainty, Lilly referred to the time when the Prozac patent was going to go off patent as year X, correct?
A. Yes.
Q. Because you just didn't know exactly when that was going to be, right?
A. That is correct.
Q. Okay.
Lilly knew that year X was going to be a critical year for the company because it anticipated that

whenever year X did happen, the company was likely to face a big drop in revenues, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Well, the patent expiration of a major product is always an important event in the life of a company, so, we appropriately prepared ourselves for this event several years ahead of time.

BY MR. SUGGS:

Q. That was especially the case with respect to Prozac because Prozac was a -- it was a blockbuster drug, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: It was an important source of revenue for the company, and we prepared for its patent expiration.

BY MR. SUGGS:

Q. In fact, I think your sales of Prozac at its peak were on the order of several billion dollars a year, correct, in sales?

A. I believe that the total sales of Prozac reached about $2.6 billion.

Q. Per year?

A. Yes.

Q. As you said, for several years in the late 1990s, Lilly had been preparing to deal with that year X situation, correct?

A. Yes.

Sydney Taurel (September 19, 2007)

MR. SUGGS: For the record, I've handed the witness an exhibit that was previously marked Zyprexa MDL Plaintiffs' Exhibit Number 5913 in this Alaska litigation and continue to use the same numbers.

Sydney Taurel (September 19, 2007)

Q. This is a Xerox copy of Lilly's 2000 Annual Report. Is that correct, sir?

A. Yes.

Q. The report begins with a letter from yourself to the shareholders, correct?
A. Yes.
Q. In the second paragraph of your letter, you state "For several years, we have been preparing for the expiration of the U.S. patents that have protected our exclusive rights to our top-selling product, Prozac. Due to uncertainty over the exact timing of this event, we have referred to it as "Year X."
We just talked about that situation.
A. Right.
Q. You then go on and state, "In January 1999, a federal district court had affirmed our 2003 Prozac patent. Last August, we were very surprised when a federal appeals court reversed that ruling." Did I read that correctly?
A. You read that correctly.
Q. So, at least up until the summer of 2000, I guess it would have been August of 2000, you had been expecting that your Prozac patent was going to last through 2003?

Sydney Taurel (September 19, 2007)

THE WITNESS: We were -- we knew that the patent would expire. We were engaged in legal proceedings, and one as is explained here at the federal court level in 1999, and if that decision had been upheld on appeal, the patent would have actually expired in 2003. And beyond that, there was a so-called six months pediatric exclusivity, so, it was 2004. Our planning, however, included various scenarios. So, we were ready for whatever the final outcome was.
BY MR. SUGGS:
Q. Okay.
If I can direct your attention to the bottom of the first page there in the left-hand column, the last paragraph in that column starts off by saying "For a number of years, we have also implemented contingency plans that would help us overcome any Year X outcome we might face. For instance, we have invested aggressively in our products with the strongest growth potential."
Correct?
A. Yes. The first sentence you

just read exemplifies [illegible]t I just told you, that we are looking at various scenarios, yes.

Q. Okay.

Zyprexa was one of your products with a very strong growth potential, correct?

A. Yes. I believe this sentence and the next one describes some of the main actions that we took to get prepared for Year X, which included developing products in our pipeline, licensing molecules from other companies, as well as developing our existing pipeline of -- our existing portfolio of products with new indications and so forth.

Q. Okay.

In the right-hand column on that same page, there's a heading in bold print, "Strong product line fuels growth." Do you see that?

A. Yes.

Q. In the second paragraph below that it states -- starts off by saying, "Zyprexa exemplifies our growth opportunities."

Is that correct?

A. Yes.

Q. That was one of the products in which you invested in most aggressively, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: This is one example of the types of investment that we made. As I mentioned earlier, we made investments -- we doubled our R&D efforts to bring more new products to the market, and indeed between 2000 and 2005, we ended up launching eight new products, which was a record for the company. We also invested in the existing products, and we also brought in some products from the outside.

BY MR. SUGGS:

Q. If I can direct your attention to the following page.

In the second paragraph in the left-hand column, it starts off by saying, "Intense competition is a fact of life throughout the pharmaceutical industry. To meet that competition, we significantly elevated our marketing investments in 2000 with the goal of making our growth products available to more patients throughout the world. More specifically, we added some 2,000 sales

representatives worldwide, an increase of more than 20 percent. We recruited scores of experienced marketing professionals to support our growing product line."

Did I read that correctly?

A. Yes, sir.

Sydney Taurel (September 19, 2007)

Q. If I can direct your attention back to the previous page in the right-hand column, the second paragraph under the heading "Strong product line fuels growth."

In particular, the last three or four lines of that paragraph, it states, "In 2000, our sales of Zyprexa were $2.3 billion, a 25 percent increase. During the fourth quarter, this neuroscience blockbuster surpassed Prozac as our top-selling product." Do you see that language?

A. Uh-huh.

Q. That is an accurate statement, is it not?

A. Yes.

Sydney Taurel (September 19, 2007)

Q. Well, and of all the products that the company had on the market, in 2001, Zyprexa was bringing in more revenue than anyone else, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I think I've answered.

BY MR. SUGGS:

Q. The answer to that is yes, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Zyprexa in 2000 was our second product. In 2001, after the patent expiration of Prozac, became the number one product.

Sydney Taurel (September 19, 2007)

83:24 Did Dr. Tollefson tell you
84: 1 that in December of 1998, before Zyprexa
2 even went on the market, that an advisory
3 board of outside consultants hired by
4 Lilly had told him and Dr. Beasley that
5 the weight gain associated with the use
6 of Zyprexa might result in increased
7 risks of hyperglycemia and diabetes?

Sydney Taurel (September 19, 2007)

84:11 Q. Did Dr. Tollefson tell you
12 about that?
13 A. I do not recall.

Sydney Taurel (September 19, 2007)

96: 8 Q. I'm going to hand you what
9 has previously marked as Exhibit 8262.
10 For the record, this is a chain of
11 e-mails. The one I will be asking you
12 questions about is on the bottom of the
13 first page. It's from Alan Breier to
14 more than a dozen people dated November
15 9, 1999.
16 A. (Witness reviewing
17 document.)
18 Q. Have you ever seen this
19 document before, Mr. Taurel?
20 A. Not at the time, no.
21 Q. I'm sorry, not at --
22 A. Not at 1999. I'm not on the
23 list here of recipients.
24 Q. Have you seen this document
97: 1 since that time?

Sydney Taurel (September 19, 2007)

97: 8 THE WITNESS: I've seen it
9 in the context of privileged
10 information from my lawyer.
11 BY MR. SUGGS:
12 Q. Okay.
13 The author of the e-mail
14 that I directed your attention to is Mr.
15 Alan Breier. We've talked about him
16 before. At the time, he was head of the
17 Zyprexa product team, correct?
18 A. Again, I do not recall
19 exactly when the switch was made from Dr.
20 Tollefson to Dr. Breier.
21 Q. Okay.
22 I notice that Steven Paul is
23 one of the addressees of the e-mail. He
24 was a senior executive within the company
98: 1 at the time, was he not?
2 A. Yes.

Q. As was M. Lechleiter, who's cc'd, he was a senior executive, correct?
A. Dr. Lechleiter was a senior executive, yes.
Q. Was he already President and Chief Operating Officer of the company at that time?
A. No.
Q. Do you recall what his title was back at that time?
A. I believe he was executive vice president of the pharmaceutical products, so he had the overall responsibility for development of pharmaceutical products.
Q. Okay.
Also cc'd is an August M -- is it Watanabe?
A. Watanabe.
Q. Watanabe. He was a senior executive within the company, was he not?
A. Yes.
Q. Okay.
How many --
Were there any individuals that are listed there who were members of the policy committee at that time?
A. Yes.
Q. Which ones?
A. Dr. Watanabe, Dr. Lechleiter.
Q. Any others?
A. That's it.
Q. Okay.
Dr. Breier starts off his e-mail by saying, "Olanzapine-associated weight gain and possible hyperglycemia is a major threat to the long-term success of this critically important molecule." Do you see that language, sir?
A. Yes, I can read it.
Q. And although you are not copied on this e-mail, were you aware that olanzapine-associated weight gain and possible hyperglycemia was regarded by Dr. Breier and others as a major threat to the long-term success of Zyprexa?

Sydney Taurel (September 19, 2007)

THE WITNESS: I was aware that around that time, 1999/2000, there were concerns about weight gain and potential hyperglycemia association with Zyprexa and that we wanted to elucidate this, yes.

Sydney Taurel (September 19, 2007)

100:14 Did you agree that weight
15 gain and possible hyperglycemia were
16 major threats to Zyprexa?
17 A. Not per se. I think the
18 important thing was to elucidate whether
19 there was an association, and for in the
20 case of weight gain, we knew there was,
21 and make sure that we inform physicians
22 appropriately.
23 Q. So, you would have disagreed
24 then with Dr. Breier when he said that
101: 1 "Olanzapine-associated weight gain and
2 possible hyperglycemia is a major threat
3 to the long-term success of Zyprexa"?
4 You would not have agreed with that, is
5 that a fair statement?

Sydney Taurel (September 19, 2007)

101: 7 THE WITNESS: I would put it
8 in different words. I think our
9 responsibility is to provide
10 regulatory authorities and
11 physicians with the most
12 appropriate and clinically
13 relevant information that we have.
14 Our long-term success depends on
15 our credibility and depends on our
16 ability to show both the efficacy
17 and side effects of products.
18 That's how I would have put that
19 issue.
20 BY MR. SUGGS:
21 Q. Did you say that your
22 long-term success depends on your
23 credibility?
24 A. I believe so. Our long-term
102: 1 success depends very much on the
2 reputation that we have, which is based
3 on the application of our policies, the
4 ethics with which we conduct our business
5 and so on.
6 Q. I couldn't agree with you
7 more, sir.
8 Dr. Breier goes on in his
9 e-mail to state, "In addition, it could
10 be argued that Eli Lilly, with its
11 strengths in neuroscience, metabolism,
12 endocrinology and diabetology is better
13 positioned than any other institution to
14 elucidate the mechanisms and developed
15 treatments for this side effect." Do you
16 see that language, sir?
17 A. Yes.
18 Q. Lilly had been very closely
19 involved, very deeply involved in the
20 manufacture and sale of anti-diabetic
21 drugs for decades at this point, correct?
22 A. Correct.
23 Q. Lilly had within its stable
24 of employees a number of physicians and

103: 1 other scientists who [illegible]e deeply
2 knowledgeable about diabetes and the
3 risks of that disease, correct?
4 A. Correct.
5 Q. Dr. Breier goes on to say,
6 "Thus, we have formed a cross-functional
7 action team to meet these challenges.
8 Success of this effort will contribute to
9 securing the future of olanzapine and the
10 financial health of our company, and
11 likely spur the development of next
12 generation antipsychotic drugs (i.e.
13 olanzapine without the weight gain) and
14 drugs for obesity."
15 Did I read that correctly?
16 A. You read that correctly.

Sydney Taurel (September 19, 2007)

105: 3 I believe you testified
4 previously that you were indeed aware
5 that your competitors were essentially
6 attacking Zyprexa in the marketplace and
7 saying that the weight gain associated
8 with Zyprexa would lead to the
9 development of hyperglycemia and
10 diabetes, correct?

Sydney Taurel (September 19, 2007)

105:13 Q. You were aware that your
14 competitors were alleging that, correct?

Sydney Taurel (September 19, 2007)

105:16 THE WITNESS: I was aware
17 that our competitors were focusing
18 a lot of their detailing efforts
19 on attacking Zyprexa, and, yes,
20 alleging that the weight gain that
21 we did see and reported was
22 causing potentially both
23 hyperglycemia and diabetes.
24 BY MR. SUGGS:
106: 1 Q. Okay.
2 And the fact that Zyprexa
3 was under attack in the marketplace by
4 your competitors did not relieve Lilly of
5 its obligation to provide complete and
6 truthful information to doctors about the
7 risks and benefits of Zyprexa, did it,
8 sir?
9 A. Absolutely not.
10 Q. Lilly had an obligation to
11 tell doctors the truth, the whole truth
12 and nothing but the truth about the risks
13 and benefits of Zyprexa, correct?

Sydney Taurel (September 19, 2007)

106:16 THE WITNESS: Our
17 responsibility is to inform
18 doctors in an accurate and
19 clinically meaningful way of both
20 benefits and risks of our drugs.
21 BY MR. SUGGS:
22 Q. And you had an obligation to
23 do that even if it hurt sales, correct?
24 A. As I mentioned earlier, I
107: 1 believe that our long-term success as a
2 company is dependent upon our ability to
3 be reliable and trustworthy with our
4 customers.
5 Q. I couldn't agree with you
6 more, sir.

Sydney Taurel (September 19, 2007)

107:22 Q. Were you aware that FDA
23 regulations permit a drug company to
24 change the label to strengthen warnings
108: 1 without prior FDA approval?
2 A. Yes, I'm aware of that.
3 Q. Okay.
4 Were you aware that FDA
5 regulations require a drug company to
6 issue a warning in the warnings section
7 of the labeling as soon as there's
8 reasonable evidence of an association
9 between the drug and a serious adverse
10 reaction and that causation need not be
11 proven? Were you aware of that, sir?

Sydney Taurel (September 19, 2007)

108:22 THE WITNESS: Just the use
23 of the word "reasonable" means
24 that there is interpretation, and,
109: 1 therefore, that this would require
2 discussion with the regulators.
3 And my understanding is that we
4 have been sharing all of the data
5 that we have on Zyprexa with
6 regulators, both in the U.S. and
7 elsewhere, and reflecting those
8 discussions in the label. Now,
9 when we had a very specific side
10 effect which was very clear, we
11 went ahead and put that on the
12 label immediately. That was the
13 case of cardiovascular events
14 sometimes in -- after 2000.

Sydney Taurel (September 1[illegible]2007)

109:16 Q. Sir, you understood that the
17 reason why information in the product
18 label is so important is because
19 physicians need to use the information in
20 the label to decide whether the potential
21 benefits of the drug outweigh its risks,
22 correct?
23 A. I do.

Sydney Taurel (September 19, 2007)

110:10 It would be wrong for Lilly
11 to try to spin the data about potential
12 safety problems regarding Zyprexa in an
13 attempt to protect profits, correct?

Sydney Taurel (September 19, 2007)

110:15 THE WITNESS: We do not spin
16 data. We share the data that we
17 have with regulators and with
18 physicians through various means.
19 BY MR. SUGGS:
20 Q. If Lilly did, in fact, spin
21 information or spin the data about a
22 safety problem in order to protect
23 profits, you would agree that the company
24 should be punished for that, correct?

Sydney Taurel (September 19, 2007)

111: 2 THE WITNESS: Lilly did not
3 spin data, and we do not put
4 profits before patients. As I
5 mentioned earlier, the long-term
6 viability of the company depends
7 on its reputation and its
8 reliability. This is a solemn
9 mission that we have and that I
10 personally take extremely
11 seriously.

Sydney Taurel (September 19, 2007)

112: 7 Q. Last month I was on a
8 Northwest Airlines flight, and I saw an
9 article featuring you in the August 2007
10 edition of their Northwest Airlines World
11 Traveler magazine. I'm assuming you are
12 familiar with that?
13 A. Yes.
14 Q. It's about six or seven
15 pages long, had five or six different

photos of you in ther very complimentary article.

MR. SUGGS: I'll have that marked as Taurel Exhibit Number 3.

Sydney Taurel (September 19, 2007)

Q. If I can direct your attention to Page 48, which is the -- By the way, the title of the article is "Global Citizen." It begins on Page 48. In the right-hand column in the beginning of the second full paragraph you state, "'The first thing I think any leader should be judged by is a very strong set of values?'"

Do you see that?

A. Yes.

Q. Is that an accurate quotation?

A. That's an accurate quotation, something I believe very strongly, as I just told you.

Q. If I could direct your attention to Page 53. In the middle column of that page at the very bottom there's a quote that says, "'The company was founded on its respect for people, integrity and pursuit of excellence,' he says. 'Those are not just words on a card. If you talk to just about any employee, they will relate what we do to be consistent with those values.'"

Did I read that correctly?

A. Yes.

Q. Was that an accurate quotation of what you told the reporter?

A. Yes.

Q. If the company does not act consistently with those values, should it be punished?

Sydney Taurel (September 19, 2007)

THE WITNESS: The company acts consistent with those values.

BY MR. SUGGS:

Q. If it doesn't, should it be punished?

Sydney Taurel (September 19, 2007)

THE WITNESS: I don't know how to answer that question. It is a hypothetical question. The company does not -- abides by those values in everything that we

do.
BY MR. SUGGS:
Q. Is it consistent with Lilly's values to spin data to gain a competitive advantage?

Sydney Taurel (September 19, 2007)

115: 9 THE WITNESS: We do not spin data to get competitive advantage.
BY MR. SUGGS:
Q. Would Lilly be acting with integrity if it spins data to gain a competitive advantage?

Sydney Taurel (September 19, 2007)

115:16 THE WITNESS: We do not spin data.

Sydney Taurel (September 19, 2007)

116:17 If an Alaska jury were to return a punitive damage verdict of $100 million, would that convince you that Lilly acted improperly and needed to change its ways?

Sydney Taurel (September 19, 2007)

117: 1 A. No. I am confident that Lilly is acting appropriately. We have in place a philosophy, policies, procedures, an organization, trained people to ensure that we act appropriately.
Q. Would a verdict of $500 million convince you that Lilly acted improperly and needs to change its ways?

Sydney Taurel (September 19, 2007)

117:11 THE WITNESS: My answer is the same.

Sydney Taurel (September 19, 2007)

117:14 Q. How about if the Alaska jury were to return a punitive damage verdict in the amount of $1 billion, would that have any effect on your behavior?

Sydney Taurel (September 19, 2007)

117:20 THE WITNESS: It is not a
21 question of money.

Sydney Taurel (September 19, 2007)

117:24 I'm going to show you what's
118: 1 previously been marked as Exhibit 9281.
2 For the record, Exhibit 9281
3 is a February 6, 2004 e-mail from Alan
4 Breier to US Medical. And in particular,
5 sir, I'm going to direct your attention
6 to the language in Dr. Breier's e-mail
7 under the bolded heading "Principles."
8 A. (Witness reviewing
9 document.)
10 Q. Have you seen this document
11 before, sir?
12 A. I've been shown this
13 document by counsel.
14 Q. Okay.
15 Did you receive a copy of it
16 back in 2004?
17 A. No.
18 Q. In that section that I
19 pointed your attention to regarding
20 principles, Dr. Breier starts off by
21 saying, "Making medicine for people
22 facing illness is a much different and
23 higher calling than making consumer
24 products for other markets. We do not
119: 1 sell soap! It therefore requires a
2 different and higher code for conducting
3 our business."
4 Do you agree with that, sir?
5 A. Very much so.
6 Q. Okay.
7 If you drop your attention
8 down to about the third line from the
9 bottom, Dr. Breier has a sentence which
10 starts off, "we are particularly
11 challenged." Do you see that?
12 A. Yes.
13 Q. It says, "We are
14 particularly challenged when it comes to
15 presenting our data in a completely
16 objective, unbiased manner because of our
17 passion for our molecules and the belief
18 that 'spinning' data is sometimes
19 necessary to gain a competitive
20 advantage. If we do not abandon the
21 'spinning' mentality, we will not restore
22 confidence in our medical research and
23 rebuild the public trust our industry
24 compromised." Do you see that language?
120: 1 A. I do.

Sydney Taurel (September 19, 2007)

122: 3 Q. What does the word "abandon"
4 mean to you, sir?
5 A. It means to leave behind.
6 Q. It means to stop doing
7 something that you're already doing,
8 right?

Sydney Taurel (September 19, 2007)

124: 3 What Dr. Breier was talking
4 about in this e-mail was abandoning or
5 leaving behind the spinning of data in
6 order to gain a competitive advantage.
7 Isn't that the subject of his e-mail
8 there?

Sydney Taurel (September 19, 2007)

124:10 THE WITNESS: I do not
11 agree. The subject of his e-mail
12 is to talk to all medical
13 colleagues about the principle --
14 ethical principle of medical
15 research. And part of his message
16 relates to issues of public trust
17 that the industry is suffering
18 from.
19 BY MR. SUGGS:
20 Q. Sir, in fact, Eli Lilly
21 itself was regarded by your customers, by
22 payors and doctors who used your product
23 as spinning the data about Zyprexa.
24 Isn't that true, sir?

Sydney Taurel (September 19, 2007)

125: 2 THE WITNESS: No.

Sydney Taurel (September 19, 2007)

125: 4 Q. Let me hand you what's been
5 previously marked as Exhibit 3223. For
6 the record, Exhibit 3223 is an e-mail
7 from Jerry Clewell to Virginia Stauffer
8 with copies to a bunch of people,
9 probably, I'm guessing, two dozen people.
10 My first question -- by the way, the
11 e-mail is dated January 14, 2004, and the
12 subject is "Re: Annals of Pharmacotherapy
13 Recent articles of interest 2004."

Sydney Taurel (September 19, 2007)

Q. I'd like to direct your attention to section 1 down at the bottom of the first page, has a bold heading there that says, "Selection of atypical antipsychotics for the management of schizophrenia." Do you see that?
A. If I can ask for a minute to read the document.
Q. Sure.
A. Thank you.
Q. I'm only going to be asking questions about the first e-mail which continues over to the following page.
A. (Witness reviewing document.)
Q. Sir, have you read the e-mail that I directed your attention to?
A. Yes. I'm just trying to understand the context by reading the attachment which you provided to me.
(Witness reviewing document.)
Q. Thank you. If I could direct your attention to the -- by the way, since you've read this entire e-mail, including the attached e-mails that I did not direct your attention to, you're fully aware that this e-mail chain is discussing Zyprexa, correct?
A. Yes.
Q. Okay.
In Jerry Clewell's e-mail on the second page, his last paragraph starts off "As a company." Do you see where I'm at?
A. Yes.
Q. He states, "As a company, we all need to do a much better job of proactively listening to payers (and other customers) concerns, and proactively communicating important information such as adverse effect label changes without a tone of minimizing their importance" (for example, "weight gain, diabetes, CVA)." Do you see that language, sir?
A. Yes.

Sydney Taurel (September 19, 2007)

A. Pharmacy benefit managers.
Q. And what he's saying there is that as a company, y'all needed to do a "much better job of proactively listening" to those types of people, your customers, "and proactively communicating important information such as adverse effect label changes without a tone of

minimizing their importance." Correct?
A. That's what Mr. Clewell is saying.
Q. The weight gain and diabetes that he's referring to there were side effects of Zyprexa, were they not?
A. No.

Sydney Taurel (September 19, 2007)

Q. Well, sir, at the time this e-mail was written in June of -- pardon me, January of 2004, the company had just changed its label to discuss hyperglycemia and diabetes in the label of Zyprexa; isn't that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: You referred to diabetes, and I said no. And that continues to be correct even with your reminding me that in 2003 that there was a change in the label.
BY MR. SUGGS:
Q. So, it's your position that diabetes is not a side effect of Zyprexa, correct?
A. Diabetes has been observed in a very few cases of people taking Zyprexa, that is correct.

Sydney Taurel (September 19, 2007)

After Mr. Clewell pointed out that he thought that everyone needed to do a better job of "proactively communicating important information such as adverse event label changes without a tone of minimizing their importance," he goes on to say, "Payers and clinicians have clearly articulated that this is an area where Lilly has lost its scientific integrity and therefore exposed us to great skepticism when we need to communicate the positive benefits of our products." Do you see that language, sir?
A. I do see that language.
Q. Did anybody tell you that this is an area where Lilly had lost its scientific integrity?
A. No. This is the personal opinion of Dr. Clewell, whom I don't know, but does not reflect the behavior of the company. For example, when he

mentioned CVA, CVAE, 's saying we were not proactive. Well, we had a "Dear Doctor" letter which followed our changes being effected, a change in our label, which were proactively decided upon and implemented.

Q. If I could direct your attention back to the New York Times article -- by the way, have you ever seen this document before?

A. No.

Q. Okay.

If I can direct your attention back to the New York Times article which was Exhibit -- I forget which number.

MS. GUSSACK: Exhibit 2.

BY MR. SUGGS:

Q. Exhibit 2. Did you read this article when it came out?

A. Yes.

Q. If I can direct your attention to the last page, the third paragraph up from the bottom has a quote from a Dr. James Phelps. He says, "'From my personal experience, at first my concerns about weight gain with this drug were very significantly downplayed by their field representatives,' said Dr. James Phelps, a psychiatrist in Corvallis Oregon. 'Their continued efforts to downplay that, I think in retrospect, was an embarrassment to the company.'" Do you see that language, sir?

A. Yes.

Sydney Taurel (September 19, 2007)

I'm going to hand you what's been previously marked as Exhibit 918.

For the record, Exhibit 918 is an e-mail from Alan Breier to Gerhard Mayr and several other individuals. It's dated November 24th, 1999. And my first question to you is, sir, have you ever seen this document before?

A. (Reviewing document.)

I do not recall.

Q. We've talked about Dr. Breier and who he was. There's some new names here I want to ask you about. The e-mail is addressed to Gerhard Mayr, Gino Santini, Lorenzo Talarigo, with copies to John Lechleiter, Roland Powell, Gary Tollefson. Did the people to whom the e-mail was addressed directly, Mr. Mayr, Mr. Santini, Mr. Talarigo and Mr. VanDenBergh, did they report directly to you at that time?

A. Not all of them, no.

Q. Did some of them?

A. Yes. Mr. Mayr reported to me.
Q. What was his position at the time?
A. I believe he was executive vice president for pharmaceutical operations.
Q. Who else reported directly to you in this group of people at that time?
A. Dr. Lechleiter.
Q. Okay.
Directing your attention to the text of Dr. Breier's e-mail, we have had testimony that the "John" referred to in the first word of the e-mail refers to Mr. Lechleiter. In his e-mail, he says, "John asked me to overview the topic of olanzapine-associated weight changes (OWC). I want to emphasize to you that OWC has been and continues to be a top priority for the Zyprexa Product Team. Although it is a significant issue for us, perhaps our only major clinical Achilles heel, and our competitors have robustly focused on it (reminiscent of anxiety, and," then there's something that was blacked out there or whited out, "the fact is Zyprexa offers the best combination of efficacy, safety and ease of use of any available treatment for psychosis and acute mania." Do you see that language, sir?
A. Yes.
Q. Had you been informed back in 1999 that Dr. Breier was of the view that weight gain -- olanzapine-associated weight gain was perhaps the drug's only major clinical Achilles' heel?

Sydney Taurel (September 19, 2007)

THE WITNESS: I was aware around that time that we were paying a lot of attention to the issue of weight gain. We were trying to elucidate what it meant. I think we discussed earlier a specific effort in that area.
BY MR. SUGGS:
Q. Did Mr. Mayr or Mr. Lechleiter discuss the matters addressed here with you?
A. I do not recall a specific conversation, but I was generally aware of those issues.
Q. If I can direct your attention to the market research section of the e-mail. There are about ten or so bulleted items below that heading. Do you see that?

A. Yes.
Q. The fifth bulleted item starts off "'Outliers.'" Do you see that?
A. Uh-huh.
Q. It says, "'Outliers' are the main concern for physicians; 20-pound increase is viewed as" a "threshold for concern (Fact: two-thirds of olanzapine-treated patients gain less than 20 pounds)." Do you see that, sir?
A. Yes.
Q. And if two-thirds gain less than 20 pounds, then one-third gains more than 20 pounds; correct? Is that your understanding?

Sydney Taurel (September 19, 2007)

147:22 THE WITNESS: That's an implication you can make from what's written here, yes.
148: 1 BY MR. SUGGS:
Q. Did Dr. Breier or Dr. Tollefson ever inform you that in the largest clinical study that was done prior to FDA approval, it was found that the average weight gain of people using Zyprexa for a year was 24 pounds?

Sydney Taurel (September 19, 2007)

148: 9 THE WITNESS: I do not recall those numbers, no. I don't have such a detailed knowledge of the results of clinical trials.
BY MR. SUGGS:
Q. The next bulleted item states, "Olanzapine is viewed to have more associated weight gain than risperidone, seroquel, and traditional neuroleptics." Those other drugs were competitors of Zyprexa, were they not?
A. Yes.
Q. And then it goes on to say in parenthesis, "Fact: the order of weight gain among antipsychotics is: Clozapine greater than olanzapine,
149: 1 greater than seroquel, greater than risperidone, greater than traditional neuroleptics." Do you see that, sir?
A. I see that.
Q. In essence, the fact of the matter was that, indeed, olanzapine did have more weight gain than Seroquel, Risperdal and traditional neuroleptics, correct?
A. I cannot comment on the veracity of this. I can confirm that

this is what's written in this paper.
Q. Wouldn't you expect Dr. Alan Breier to be telling the truth to Gerhard Mayr, Gino Santini and Mr. Lechleiter?
A. Yes, I would.
Q. His boss at that time was Gary Tollefson, correct?
A. I believe that's correct, yes.
Q. You'd expect him to be telling the truth internally to people in the company, right?
A. Yes. You asked me to
150: comment on whether I had knowledge of that fact, and I don't, except for what's written here.
Q. Okay.
If I could direct your attention to the third bullet point in the bottom of that section, the one that starts off, "Physicians view." It says, "Physicians view EPS as something they can address with dose adjustment but not OWC." Do you see that?
A. Yes.
Q. "EPS" refers to extrapyramidal symptoms, correct?
A. Yes.
Q. Extrapyramidal symptoms were one of the big drawbacks of traditional neuroleptic drugs, correct?
A. Yes.

Sydney Taurel (September 19, 2007)

151:21 What Dr. Breier is saying here is physicians viewed extrapyramidal symptoms as something they could address with dose adjustments, but not olanzapine
152: weight change, correct?
A. That's what he's saying, yes.
Q. Then he goes on to say in parenthesis, "Fact: OWC" or olanzapine weight change "is not dose dependent," right?
A. Correct.
Q. So, the fact of the matter was exactly what physicians were

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Sydney Taurel (September 19, 2007)

152:11 thinking, correct?

Sydney Taurel (September 19, 2007)

152:13 THE WITNESS: The fact that

he's quoting h e seems to confirm, yes, hat physicians are saying. And that is -- my understanding is if you are likely to gain weight on olanzapine, you find out fairly soon, and it is -- I don't know for sure whether it's dose-dependent or not, but --

BY MR. SUGGS:

Q. Well, according to Dr. Breier, who you would expect to know, he said it was not dose-dependent, correct?

A. Okay.

Q. The last bullet point in that section refers to "blanket detailing." Do you see that?

A. Yes.

Q. Now, "blanket detailing" means that you go and -- by the way, detailing is a pharmaceutical industry term that means sales promotions, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Visits to physicians by our sales representatives so they can discuss our products.

BY MR. SUGGS:

Q. Right. And "blanket detailing" refers to discussing an issue with all of -- all physicians, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I don't know. This could mean saying the same thing to all physicians. And I think what maybe Mr. -- Dr. Breier is saying here, again, I'm not Dr. Breier, so, I don't know exactly what his intention is here, but is that we need to adapt, adjust the message and information we give to the needs and concerns and questions of physicians. Blanket detailing would be saying the same thing to everyone.

BY MR. SUGGS:

Q. In fact, what he says here in quotes is, "Blanket detailing will be damaging since many physicians do not see olanzapine weight change as an issue." Correct?

A. That's what's written here, yes.

Q. Were you advised that Lilly was telling doctors that weight gain was

manageable for most patients?

Sydney Taurel (September 19, 2007)

THE WITNESS: What time are you talking about?
BY MR. SUGGS:
Q. Say the 2001 time period?
A. I think around that time, we were trying to help physicians deal with the issue of weight gain by offering wellness programs so that if the issue would be raised, they could help their patients avoid issue of weight gain.
Q. You knew for a fact, the company knew for a fact that those didn't work; isn't that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: No.
BY MR. SUGGS:
Q. Let me hand you what's been previously marked as Exhibit 1110. For the record, this is what appears to be a PowerPoint presentation. It has on its first page the title "Issues Management Planning Weight Gain." If I could direct your attention, sir, to the second page, there is a section in the middle with a bold font and enlarged font that says "Our Position." Do you see where I'm referring to, sir?
A. Yes.
Q. It states under "Our Position," "Weight gain can occur with Zyprexa as with other anti-psychotics and mood stabilizers. For most patients, this can be managed allowing them to receive the overwhelming benefits Zyprexa offers." Do you see that language, sir?
A. Yes.

Sydney Taurel (September 19, 2007)

Q. I would direct your attention to the third page, sir, and there's a heading there that says "Marketplace Feedback." Do you see where I'm at?
A. Yes.
Q. The first bullet point there states, "Only 50% of MDs feel weight gain is manageable for Zyprexa versus 87% for Risperdal and Seroquel and 92% for Geodon." Do you see that language, sir?
A. Yes.

Q. Would y have been informed of that back in Novem er of 2001?
A. Not that specific information, no.
Q. By the way, I'll represent to you that the database that has been provided to us indicates that this document was prepared on November 29, 2001, and that in the bottom left-hand corner of this document there is that date printed on every page except the very first page.
If I could direct your attention in that same section to the third bullet point, it says, "'It is laughable when Lilly comes in and tries to talk about weight gain.'" Do you see that, sir?
A. Yes.
Q. Were you ever informed that physicians were giving feedback to Lilly that they thought it was laughable when the company came in and tried to talk about weight gain?
A. No.
Q. If I can direct your attention to the bottom bullet point in that section. It states, "'I am more excited about the Risperdal than Zyprexa depot because of weight gain and diabetes.'" Do you see that language, sir?

Sydney Taurel (September 19, 2007)

Q. After noting that -- after stating this quote where apparently someone said "I am more excited about the Risperdal than Zyprexa depot because of weight gain and diabetes," the document then goes to say in parenthesis, "group then makes fun of diet and exercise solutions provided by Lilly)."
Do you see that language, sir?
A. I do.

Sydney Taurel (September 19, 2007)

Were you informed that anyone was giving feedback to Lilly in the form of making fun of diet and exercise solutions that were being provided by the company?
A. No, on the contrary. My understanding, the majority of the feedback that we were receiving from our customers was that this was very helpful, and they really appreciated it. It was a

very unique approach. Given the fact that many of these products had similar issues of association with weight gain, we're the only company providing proactively help to psychiatrists who are not used to treating physical disease. We were helping them to deal with their physicians -- with their patients. So, I have to assume that this is not representative.

Q. Okay.

So, your answer is no, no one ever told you about that, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: My answer is that the preponderance of feedback that we are receiving from what I was told was that the solutions for wellness were very appreciated by our customers.

Sydney Taurel (September 19, 2007)

Q. Sir, is it fair to say, then, that no one ever told you that physicians were regarding Lilly's weight loss programs as laughable attempts? It's a simple yes or no question. Either somebody told you about that or they didn't.

Sydney Taurel (September 19, 2007)

THE WITNESS: Your premise is that doctors are saying that as if it were the majority of doctors. And the answer to that is no.

BY MR. SUGGS:

Q. Sir, if, in fact, Lilly knew that weight loss programs only work approximately five percent in normal volunteers, then it would be false to tell doctors that weight gain with Zyprexa was manageable for most patients; isn't that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not know the exact message which was given to physicians. This program was helpful. It was something that

met a need that they had, because for many patients under Zyprexa, they saw weight gain. So, this was helping them deal with the potential issue. And even if that premise is true, it only helps five percent of the patients, it's very important.
BY MR. SUGGS:
Q. But, sir, your company was telling Doctors that Zyprexa weight gain was manageable for most patients; isn't that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not know that.
BY MR. SUGGS:
Q. Isn't that exactly what this document says?

Sydney Taurel (September 19, 2007)

A. Well, this is a planning document, as I see the title. What we said to the doctors in visits to them was in accordance with the label. It is -- all the messages to physicians go through a very involved process of medical, regulatory and legal review. So, there's a distinction between what you see in a planning document and actually what we say to physicians.

Sydney Taurel (September 19, 2007)

Q. Are you familiar with what the sales reps went out and told doctors?
A. No, not in detail.
Q. Are you going to deny that doctors were told that weight gain was manageable for most patients?

Sydney Taurel (September 19, 2007)

THE WITNESS: I have no knowledge of exactly what went on in every detail with doctors.

Sydney Taurel (September 19, 2007)

Q. Were you informed that in

early 2002, Lilly's medical department concluded that the incidence of treatment emergent hyperglycemia was about three-and-a-half times higher in Zyprexa users as compared to placebo?

A. No.

Q. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 990.

For the record, this is a document, the first page of which says, "Attachment E," and above that it says, "Confidential, Do Not Forward - To be distributed only by Global Operations Labeling Department." Are you familiar with an organization or a group known as the global operations labeling department, Mr. Taurel?

A. Not specifically. I do know that we have groups of people who deal with labeling.

Q. On the second page, there is a reference to -- well, the title at the top of the page is: "Olanzapine Labeling Change on Hyperglycemia For 2/21/2000 GPLC Meeting." Do you see that?

A. Yes.

Q. What does GPLC stand for in Lilly?

A. It would be the global product labeling committee, I assume. This is the body that reviews label changes, labels in general.

Q. And if I could direct your attention to the middle -- there's a series of boxes in this document. The middle has a title "How has this Proposal Arisen." Do you see that language?

A. Yes.

Q. Below that it states, "Recent review random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment-emergent hyperglycemia in olanzapine group (3.6%) was higher than that in the placebo group (1.05%). For common events, incidences from clinical trials provide more meaningful information." Do you see that language, sir?

A. Yes.

Q. It is your testimony that you were not informed of that back in 2000?

A. Yes.

Q. If I can direct your attention to the following page, pardon me, Page 4, there's a box towards the top of the page that says -- that's titled "Literature Reports." Do you see that, sir?

A. Yes.

Q. There's two paragraphs in

there. The bottom paragraph starts off by referring to a Dr. Casey. Do you see where that begins?
A. Yes.
Q. It says Dr. -- by the way, do you know Dr. Daniel Casey?
A. No.
Q. That paragraph states, "Dr. Daniel Casey from Oregon presented in a seminar at Lilly at the end of 1999. He performed chart review of 136 veteran patients who had been exposed to olanzapine therapy for at least 4 months (average of 1.4 year). Of the 39 patients who had normal fasting glucose levels before olanzapine therapy, seven (18%) had fasting glucose levels of 126 milligrams per deciliter or higher during olanzapine therapy (threshold that met the 1998 ADA diagnostic criteria for diabetes)." Do you see that language, sir?

173: A. Yes.

Sydney Taurel (September 19, 2007)

174: Q. Were you informed back in early 2000 at around the date of this document, which is February 2000, that this Dr. Casey had found that 18 percent of the people who had normal fasting glucose levels before starting Zyprexa developed fasting glucose levels that were diagnostic for diabetes?

Sydney Taurel (September 19, 2007)

174: THE WITNESS: The answer is no. I would not be informed of every clinical trial, especially one with only 136 patients.

Sydney Taurel (September 19, 2007)

175: Q. I'll represent to you that we've had testimony from, I believe, Dr. Breier and others that the label change that was implemented in May of 2000 essentially said that there was not much difference in the blood sugar levels between Zyprexa users and placebo. Would you dispute whatever their testimony is on that?

Sydney Taurel (September 19, 2007)

175:18 THE WITNESS: I'm not sure
19 whether you have characterized
20 that testimony appropriately.
21 Therefore, I cannot comment on
22 that specif -- on your -- I cannot
23 answer your question specifically.
24 I have no reason to doubt that Dr.
176: 1 Breier said exactly the truth.

Sydney Taurel (September 19, 2007)

176: 5 You were aware that there
6 was a label change in May of 2000,
7 correct?

Sydney Taurel (September 19, 2007)

176: 9 THE WITNESS: Not at the
10 time.

Sydney Taurel (September 19, 2007)

176:14 Q. Okay.
15 When did you become aware of
16 it?

Sydney Taurel (September 19, 2007)

176:17 A. I became aware of it
18 following the publication of the New York
19 Times allegation.
20 Q. That was the first that you
21 were aware that there had been a label
22 change back in 2000?
23 A. Yes.

Sydney Taurel (September 19, 2007)

177:14 Q. Okay.
15 The record, I think, clearly
16 shows from the testimony of any number of
17 witnesses that in May of 2000, Lilly made
18 a change to the Zyprexa label regarding
19 hyperglycemia.

Sydney Taurel (September 19, 2007)

177:23 Q. And that in October of 2000,
24 the FDA made the company take out that
178: 1 language. I'll represent that to you.

Sydney Taurel (September 19, 2007)

178: 6 Q. **Is it your testimony that**
7 **you, as you sit here today, that you're**
8 **unaware of that?**
9 A. No. My testimony is that I
10 was unaware of it -- I was unaware of the
11 exchange with the FDA at the time. I've
12 become aware of it, and I believe your
13 characterization is not correct. I think
14 that the FDA asked us to eliminate some
15 words, but there was still some data
16 which remained, I believe.
17 Q. **When was it that you became**
18 **aware that the FDA wanted you to take the**
19 **language out of the label that had been**
20 **put in without prior FDA approval in May**
21 **of 2000?**
22 A. Again, after the publication
23 of the New York Times article.
24 Q. In 2006?
179: 1 A. Yes. 7. Well, 6 or 7. I'm
2 sorry. It was late December/early
3 January.
4 Q. **The article we were looking**
5 **at as Exhibit 2 was published on December**
6 **16, 2006.**
7 **Were you aware that Lilly**
8 **attempted to get an article published in**
9 **a scientific journal regarding its**
10 **analyses that formed the basis of that**
11 **label change and that that article was**
12 **rejected?**

Sydney Taurel (September 19, 2007)

179:15 Q. **For publication?**
16 A. No. We have a policy to
17 share and publish our data whenever
18 publications are interested in publishing
19 them. And for those that are not being
20 published, we now have our clinical trial
21 registry where the results of the trials,
22 whether they are positive or negative,
23 are being shared.
24 Q. **Were you aware that when the**
180: 1 **analysis behind Lilly's May 2000 label**
2 **change was presented to a group of**
3 **outside experts in October of 2000, that**
4 **those outside experts were concerned**
5 **about it?**

Sydney Taurel (September 19, 2007)

180: 7 THE WITNESS: No.
8 BY MR. SUGGS:
9 Q. **Were you told that a group**
10 **of outside experts told representatives**

of the company in October of 2000 that they were concerned about Lilly's approach to marketing Zyprexa?

Sydney Taurel (September 19, 2007)

THE WITNESS: Do you have a document that can help me understand what you are talking about?
BY MR. SUGGS:
Q. Sure do. I'd be happy to show it to you.
I'm going to hand you two e-mails, sir, one of which is labeled Exhibit 6998, which is an e-mail from Robert Baker to a number of individuals dated October 9, 2000. I'm also going to hand you what's been previously marked as Exhibit 1453, which is an e-mail chain, the most recent of which is on the top of the first page from Robert Baker to Charles Beasley dated October 10, 2000.

Sydney Taurel (September 19, 2007)

Q. Have you completed reading the exhibits?
A. Yes.
Q. I first direct your attention to Exhibit 6998, which is the e-mail from Robert Baker to Charles Beasley and others. Do you recognize the names of any of the people who were on this e-mail other than Bruce Kinon?
A. Yes.
Q. Who else do you know?
A. Robert Baker, Charles Beasley, Alan Breier, Patrizia Cavazzoni, John Holcombe, Jack Jordan, John R. Richards, Mauricio Tohen and Paula Trzepacz.
Q. So, you knew most of the people who got this e-mail then?
A. Yes.
Q. In the first paragraph, Dr. Baker states: "FYI: The Lilly diabetes/endocrine group held an academic advisory board meeting this weekend in Atlanta. They kindly allotted two hours for discussion of olanzapine's potential hyperglycemia risks, and Charles Beasley, Chris Bomba, Patrizia Cavazzoni, Suni Keeling, and I attended. Unfortunately, this consultation reinforced my impression that hyperglycemia remains quite a threat for olanzapine and may merit increasing even further medical attention and marketing focus on the

topic." Do you see that language, sir?
A. Yes.
Q. Were you aware of that meeting at the time?
A. No, I was not.

Sydney Taurel (September 19, 2007)

Directing your attention to the following paragraph, Dr. Baker goes on to state: "On the positive side, like other endocrinologists, they were not impressed with the Newcomer findings. They were however concerned by our spontaneous AE reports, and quite impressed by the magnitude of weight gain on olanzapine and implications for glucose." Do you see that language, sir?
A. Yes.
Q. And were you ever informed -- by the way, at the beginning of the e-mail letter, it refers to the "Lilly diabetes/endocrine group." Was there a group within the company that dealt specifically with diabetes and endocrine issues?
A. Yes. There is a group -- yes, we are in the diabetology field because of our products, insulin and others, and I think that's what they are referring to here.

Sydney Taurel (September 19, 2007)

Were you aware that the company had an outside advisory board that they met with periodically to get their input on scientific matters?
A. Not specifically, but I'm generally aware that we have advisory boards for most therapeutic areas in which we work so that we can get outside input from opinion leaders.
Q. And I'm assuming that it's the company's intent to have the most well qualified people they can get on those boards, correct?
A. Yes.
Q. And it's the company's intent that those outside advisors will give you as unbiased and straightforward view of the science as they possibly can, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: We consult

with these consultants, with these opinion leaders, to get their views on our data, on new products and other things.
BY MR. SUGGS:
Q. And you expect them to give you the best possible expertise they can, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Yes, we expect them to use their knowledge and expertise in their advice to us.

Sydney Taurel (September 19, 2007)

Q. You want their bald, unvarnished truthful assessment of the matter, right? That's why you have them, right?
A. Yes.
Q. Okay.
Did anyone inform you, as Dr. Baker notes here, that they, referring to that advisory board, were concerned by your spontaneous adverse event reports and quite impressed by the magnitude of weight gain on olanzapine and implications for glucose? Did anybody ever tell you that back in 2000?
A. No. As I mentioned, I was

Sydney Taurel (September 19, 2007)

Q. I direct your attention to the next exhibit, which is Exhibit 1453. Even though I described it generally, I noted that it was an e-mail chain. I'd like to direct your attention to the last physical page, which I believe is the first e-mail in time. This was an e-mail from Thomas Brodie to Robert Baker with a copy to Eugene R. Thiem or Thiem. Do you know -- besides Dr. Baker, do you know either Mr. Brodie or Mr. Thiem?
A. No.
Q. It's again referring to the meeting with the endocrinologic consultants, and Mr. Brodie starts off by saying, "Robert...clearly, this group of Endocrinologists (who spoke up and I would rate those who did speak up as the leaders of the pack) are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes. I can only hope that you and all of the

team who attended the DAB meeting are gaining the ear of senior leadership and articulating this finding." Do you see that language, sir?

A. I do.

Q. Apparently no one saw fit to gain your ear about that; is that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I trust that the senior leadership that Mr. Brodie is referring to here would include our senior scientists, not the business people like myself, and that they would have been made aware of this.

BY MR. SUGGS:

Q. Do you know whether, in fact, the senior scientists were made aware of this?

A. No, I do not.

Sydney Taurel (September 19, 2007)

Q. Let me restate the question.

You would agree that the senior scientific leadership of the company certainly should have been made aware of these comments from the advisory board members, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I would expect that all the people dealing with Zyprexa, all the people -- the leadership of our medical group should be aware of these, yes. I'm not sure whether the -- like the head of R&D should necessarily be aware of this. As I saw this string of e-mails, it's a series of exchanges of ideas, of analysis to make and more work to do on the product. So, I trust that everyone in the leadership was aware that we were pursuing those things.

BY MR. SUGGS:

Q. If I can direct your attention to the balance of that paragraph in Mr. Brodie's e-mail. He states, "Although the board's recommendation is probably not the way Lilly typically does business, I do

believe they made a very strong point that unless we come clean on this, it could get much more serious than we might anticipate." Do you see that language, sir?

A. I do.

Q. It's your testimony that no one back in 2000 ever informed you that Mr. Brodie or the outside advisory board were of the view that Lilly needed to come clean on this issue; is that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: This is language used by Mr. Brodie, and it is his own perception of things. If I read the string of e-mails here, I can see that he deals with suggestions and opinions and advice given by our consultants. And as I understand it, we took to heart many of these suggestions, for example, investigating further whether there was a direct correlation between Zyprexa and diabetes through studies that they suggested here, and have found no such direct correlation.

Sydney Taurel (September 19, 2007)

I take it back. I would like to direct your attention to the second page. Towards the bottom of the page, there's an e-mail from Charles Beasley dated October 10, 2000 to Alan Breier with copies to others. At that point in time, Mr. Breier would have been head of the Zyprexa product team, correct?

A. I believe so.

Q. You testified, I think earlier, that he was one of the people that you relied on to keep you informed of scientific matters regarding Zyprexa, correct?

A. Not exactly. I would rely on the head of R&D to inform me periodically, and then once in a while we would have reviews of the policy committee, in which case Dr. Breier would make the presentation typically.

Q. If I could direct your attention to the second paragraph of Dr. Beasley's e-mail to Dr. Breier. He starts off by saying, "These guys were really concerned about the weight gain."

198: 1 Do you see where I'm referring to?
2 A. Yes.
3 Q. It says, "These guys were
4 really concerned about the weight gain,
5 not only because of a diabetes risk but
6 all the other potential health risks."
7 Were you aware that there were other
8 potential health risks associated with
9 weight gain besides diabetes?

Sydney Taurel (September 19, 2007)

198:12 THE WITNESS: It is well
13 known that diabetes -- I'm sorry
14 -- that weight gain has
15 potential -- increases the risk of
16 heart disease and other things.
17 BY MR. SUGGS:
18 Q. You knew that back in 2000,
19 correct?
20 A. Yes. It's common knowledge.
21 Q. Drop down a couple of lines,
22 there's a sentence that starts off, "When
23 they." Do you see where I'm at?
24 A. Yes.
199: 1 Q. Dr. Beasley says, "When they
2 understood that this is seen in non-
3 psychotic 'normals' and animals on fixed
4 diets (less concern with animals) and
5 that olanzapine is the worst offender,
6 other than clozapine, they advocated a
7 different marketing strategy than we are
8 taking. They believe we should
9 'aggressively face the issue' and work
10 with physicians to address methods of
11 reducing weight gain." Do you see that
12 language, sir?
13 A. Yes.
14 Q. I assume it's your testimony
15 that you were never informed back in 2000
16 of those suggestions by the outside
17 advisory board with respect to Zyprexa;
18 is that correct?

Sydney Taurel (September 19, 2007)

199:20 THE WITNESS: As I mentioned
21 earlier, I was not aware
22 specifically of an advisory board
23 meeting. However, I am aware that
24 during the period of time, we were
200: 1 continuously getting information
2 from the market and continuously
3 trying to elucidate this question.
4 As I mentioned earlier, we started
5 to implement our wellness program,
6 and I think that is -- I'm not
7 sure whether temporally it exactly
8 corresponds to this, but I would

not be surprised that, you know, when they say we should work with physicians to address methods of reducing weight gain, that's exactly what we did. We took their advice.

BY MR. SUGGS:

Q. If I could direct your attention to about the third line from the bottom of that paragraph. Dr. Brier states, "There does not seem much to say about scientific analyses of weight gain, we know it's a weighty problem. When you translate 1-2% gain of 40 plus kilos into the absolute number based on 5 million patients, the number is 50,000 to 100,000. 100,000 people putting on 90 pounds of weight is a lot." Do you see that language, sir?

A. I do.

Q. Were you informed that there was that many people who were gaining that order of magnitude of weight?

A. Not specifically, no. I did not know the exact numbers.

Q. If I could direct your attention to the following page. The last paragraph of Dr. Beasley's e-mail states, "With regard to the marketing side of this issue of impaired glucose tolerance/diabetes, the message was clear. Don't get too aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents until we are sure of the facts and sure that we can convince regulators and academicians. W-L with Rezulin was the example. Sounds exactly like what Dan Casey was saying." Do you see that language, sir?

A. I do.

Sydney Taurel (September 19, 2007)

Q. They were clearly saying, "Don't get too aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents until we are sure of the facts," correct?

A. That's what it says here.

Sydney Taurel (September 19, 2007)

This meeting in October of 2000 occurred several months after the Federal Appeals Court held that the Zy -- pardon me, that the Prozac patent was to expire in 2001, correct?

A. Yes.

Q. Okay.

That legal decision had a profound impact on Lilly's financial well-being, didn't it, sir?

MS. GUSSACK: Objection.

THE WITNESS: I think we talked about that earlier. It's a decision for which we had been prepared and which led us to the development of several new products and licensing of others and so on.

BY MR. SUGGS:

Q. Sir, do you recall that the day that that Federal Court ruling was announced publicly that Lilly's stock plunged by almost one-third in a day, wiping out over $36 billion in equity?

A. I sure do. I still have the scar tissue.

Sydney Taurel (September 19, 2007)

Q. I went on Wall Street Journal online and had a chart drawn of Lilly's stock between the dates of August 1, 2000 and August 10, 2000, August 10, 2000 being the date of the outside advisory board meeting that we had referred to in the prior exhibits. And it indicates that there was a quite dramatic drop in the stock price in early August there on the day of the announcement from, it looks like something -- the stock value is something over $105 per share, dropping down to about $75 per share. Is that accurate?

A. Yes.

Q. That was a one day drop?

A. Yes. It was an unexpected decision by the appeals court.

Q. Okay.

Sydney Taurel (September 19, 2007)

Q. Do you recall that it was the Federal Appeals Court decision in August of 2000 which resulted in the Prozac patent expiring a year later in August of 2001?

A. Correct.

Q. Okay.

According to this document, 80 percent of the patients who had been on Prozac switched to this cheaper generic . Is that an accurate statement to your recollection?

Sydney Taurel (September 19, 2007)

208: 5 THE WITNESS: Again, there
6 is a time frame around this, and I
7 don't recall how long it took for
8 the reduction of 80 percent.
9 BY MR. SUGGS:
10 Q. The following sentence in
11 this document notes that "Sales of the
12 molecule dropped faster than the company
13 had expected, and by the fourth quarter
14 of 2001 sales declined 66 percent." Do
15 you see that language?
16 A. Yes.
17 Q. Is that accurate to your
18 recollection?
19 A. I have no reason to think
20 otherwise. I don't remember
21 specifically.

Sydney Taurel (September 19, 2007)

209:15 Q. Mr. Taurel, back in 2001,
16 was there a global management team?
17 A. A global management team?
18 Q. Yes.
19 A. Throughout the history of
20 the company, there has been a global
21 management team.
22 Q. Who was on the global
23 management team back in 2001?
24 A. I'm not sure. This is a
210: 1 very loose term, global management team.
2 To what are you referring?
3 MR. SUGGS: I'm going to
4 hand you a document. We actually
5 have to put a sticker on this one.
6 This will be Taurel number 5.

Sydney Taurel (September 19, 2007)

210:14 Q. For the record, this is a
15 document produced by Lilly that bears the
16 Bates Number ZY206198660. It's a
17 one-page document. And the first
18 paragraph says, "Chairman Sidney Taurel
19 presented the company's 2002 priorities
20 to the global management team on December
21 14, stressing their importance as Lilly
22 works to become 'the pharmaceutical
23 growth company of the decade.'"
24 Does that help at all in --
211: 1 A. Yes. This refers to all the
2 people who have the title of manager and
3 above inside the company. And typically
4 once a year I would discuss in a video or
5 even a live conference the company's
6 priorities for next year.
7 Q. Okay.
8 And I presume this probably

would have been given our presentation, sometime in December of 2001; is that correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Yes. This says December 14.

Sydney Taurel (September 19, 2007)

Q. How big was the global management, the group that you would have presented this to?

A. I believe there are about 5,000 people more or less who are at the management level. Whether all of them listened in to this isn't clear. Typically I make the presentation to a live audience of a few hundred, and then the rest is broadcast in various locations.

Q. Okay.

So, this message -- the message that you delivered there would have been broadly spread throughout the corporation; correct?

A. Yes.

Q. Okay.

According to this document, "Taurel emphasized that to weather Year X," which we've talked about before, "and outgrow its competition, Lilly must," and there's a list of bulleted up items, correct?

A. Yes.

Q. Very first thing is "Maximize sales of Zyprexa" correct?

A. Yes. I note that it is a

Sydney Taurel (September 19, 2007)

Q. Well, do you recall that at least up through 2004, Zyprexa brought in approximately $16.1 billion in income before taxes?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not. We typically -- I mean, I'm unaware of measurements of income before taxes by product.

MR. SUGGS: Let me hand you what we'll mark as Taurel Exhibit

5 6.

Sydney Taurel (September 19, 2007)

215:15 Q. For the record, this is a
16 document that bears the legend "Company
17 Confidential ,"and below that, "Summary
18 of Historical Analysis - Zyprexa," and
19 then there's a word that's apparently
20 redacted, "April 6, 2003." It consists
21 of a page of text on the first page
22 followed by what appear to be several
23 pages of tables thereafter.

Sydney Taurel (September 19, 2007)

216:20 Q. Are you familiar with the
21 term "IBT"?
22 A. Yes.
23 Q. Does that stand for income
24 before taxes?
217: 1 A. Yes, sir.
2 Q. What is your understanding
3 of what that term means?
4 A. Income before tax is what
5 you get after you calculate sales, deduct
6 the cost of products sold, and deduct the
7 various operating expenses.
8 Q. Okay.

Sydney Taurel (September 19, 2007)

218: 1 Q. Directing your attention to
2 the text in the first page of this
3 exhibit, it says, "Zyprexa was first
4 launched in late 1996. The estimated R&D
5 spend to first launch was $195 million.
6 Since then, Lilly has spent approximately
7 $750 million plus on R&D for Zyprexa's
8 multiple indications.
9 "On a cumulative IBT basis,
10 Zyprexa will bring in approximately $16.1
11 billion in IBT through 2004."
12 Do you see that language?
13 A. I do see that language, yes.
14 Q. Is it your understanding
15 that that would be a correct statement?
16 A. I have no basis to say yes
17 or no.

Sydney Taurel (September 19, 2007)

219:20 Q. Continuing on in the text of
21 this document, it goes on to state,
22 "Sales and IBT have greatly exceeded the

pre- launch PMC valuations for Psychosis and Schizophrenia combined. Through 2004, Sales and IBT will be approximately $14.3 billion and $9.2 billion, respectively, above the initial PMC valuations." Do you see that language?

A. Yes.

Q. Now seeing that phrase "PMC valuations" in that context, does that help you understand what they're referring to there?

A. No.

Q. Very first sentence of the next paragraph starts off by saying, "Zyprexa clearly exceeded all expectations." Do you see that?

A. Yes.

Sydney Taurel (September 19, 2007)

Q. If I can direct your attention to the following page. It bears the title at the top, "Zyprexa - Revenue and Cost Summary Estimated 1981 through 2002 and Forecasted 2003 through 2004." And the numbers that are expressed there in that chart are in the millions. And do you see that towards the bottom of the chart, the second to last entry there is the total IBT impact?

A. Yes.

Q. Would that be your understanding that the number there states the income before taxes for that particular year?

A. The income before taxes of what?

Q. Zyprexa.

A. That's what this document seems to indicate, but I have no understanding of the assumptions which are behind this document.

Q. If I can direct your attention to the columns for 2003 and 2004. 2003 indicates that there was $3 billion in income before taxes in 2003, or at least that was projected, apparently, and it was projected $3.4 billion in income before taxes for 2004. Do you know whether those projections were met?

A. No.

Q. Do you know what the total IBT impact was for last year, 2006?

A. No. As I mentioned earlier, we do not track the specific profits linked to a specific product because it is very complex to do.

Q. Apparently somebody attempted to here, though?

A. Some financial wizard did

that, yes.
Q. Do you recall when we were discussing the meeting that some individuals within Eli Lilly had with the outside advisory board in October of 2000 that the outside consultants told Lilly to come clean on the diabetes issues? Do you remember that that language was used in the e-mail?

Sydney Taurel (September 19, 2007)

THE WITNESS: I'm looking at the e-mail here.
BY MR. SUGGS:
Q. You can look at the very last page. And do you see where Mr., I believe it was Brodie, who wrote the e-mail, noted that the outside consultants were telling Lilly to come clean on the issue?
A. There must be another e-mail. The one you are mentioning to Mr. Brodie that does not say that. Oh, I'm sorry, it's right there.
Q. I thought so.
A. I'm sorry.
Q. Mr. Brodie wrote, "Although the boards recommendations is probably not the way Lilly typically does business, I do believe they made a very strong point that unless we come clean on this, it could get much more serious than we might anticipate."
You recall that, correct?
A. Yes.
Q. In an earlier e-mail in that chain, the company was advised that they should "aggressively face the issue." Do you recall that?
A. I recall that there was an exchange of various -- or a chain of e-mails discussing the various pieces of advice that we got from this advisory committee, yes.
Q. Well, just so there's no confusion, on that page 2 on that Exhibit 1453, in Dr. Beasley's e-mail, the second paragraph, 6 lines down, he notes "They believe we should 'aggressively face the issue' -- and that phrase is in quotes in his e-mail -- "and work with physicians to address methods of reducing weight gain." Do you see that language, sir?
A. I do.

Sydney Taurel (September 19, 2007)

Q. Sir, if you could direct

your attention again to the last page of Exhibit 1453. This is Mr. Brodie's e-mail. He starts off by saying, "Robert...clearly this group of endocrinologists (who spoke up and I would rate those who did speak up as the leaders of the pack) are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes." Do you see that?

A. I see that.

Sydney Taurel (September 19, 2007)

Do you recall being informed that the sales force was trained and taught and instructed not to bring up the issue of diabetes unless the doctor brought it up first?

Sydney Taurel (September 19, 2007)

THE WITNESS: No.

Sydney Taurel (September 19, 2007)

Q. Let me show you what's been previously marked as Plaintiff's Exhibit 1962.

A. Thank you.

Q. I'll represent to you, sir, that -- by the way, this document is dated September 4, 2002, according to the database that was provided to us by Eli Lilly. And if that's the correct date, it must have been about two years after your advisory board met with Lilly in October of 2000, correct?

Sydney Taurel (September 19, 2007)

Q. In any event, if, in fact, this document is dated September 24, 2002, as was represented to us in an electronic database provided to us by Lilly, that date would be about two years after the meeting that we referred to in the prior exhibit, correct?

A. I'm just checking the date. Yes. Yes. Right.

Q. Sir, I will also represent to you that in Answers to Interrogatories in the Alaska litigation, Lilly has stated that this document was maintained in something called the knowledge

management database and made available to sales representatives so they would know what information it provided to physicians. I'll make that representation to you.

A. May I just note that what I see in the title is "For Internal Use Only, Not For Use in Detailing."

Q. Yes. That's exactly what it says on the first page.

231:

A. Okay.

Q. This contains --

Well, do you see the title of this document is "Hyperglycemia/Diabetes: Sell Sheet Implementation"?

A. Yes.

Q. Would you direct your attention to the follow page?

A. (Witness complies.)

Q. It bears a title at the top, "Proper implementation is key! Our goal and focus is on creating a market with Donna. The competition wins if we are distracted into talking about diabetes. So, stand strong against their ploys and answer the AOC concisely and with confidence!" Do you see that?

A. Yes.

Q. Were you aware that your sales force was instructed that the competition wins if you are distracted into talking about diabetes?

Sydney Taurel (September 19, 2007)

232:

THE WITNESS: I was not -- I'm not aware of communications to the sales force. I note once more that this says very clearly this is not for use in detailing.

BY MR. SUGGS:

Q. I would agree with you completely, sir. That meant that this was something that they weren't supposed to give the doctors because they didn't want the doctors to know what was said in here; isn't that correct, sir?

Sydney Taurel (September 19, 2007)

232:16

Q. They didn't want the doctors to know that it was the company's position that the competition was going to win if you were distracted into talking about diabetes?

Sydney Taurel (September 19, 2007)

232:22 THE WITNESS: I need to read
23 this.

Sydney Taurel (September 19, 2007)

233: 7 Q. Sir, I would like to direct
8 your attention to Page 3.
9 A. Can I first read the
10 document in its entirety.
11 Q. Sir, I don't think you need
12 to do that in order to answer the
13 question that I'm going to pose to you.
14 Let me pose the question, and if you
15 think you do need to read the entire
16 document to answer this question, I would
17 be happy to let you do that just as we
18 previously agreed. On Page 3 at the top,
19 it says, "Handling the Diabetes AOC:
20 This is a highly competitive driven
21 issue. Therefore, we will NOT
22 proactively address the diabetes concern,
23 but rather only when it arises from an
24 MD." Do you see that language, sir?
234: 1 A. Yes.

Sydney Taurel (September 19, 2007)

234:14 Q. Sir, were you informed that
15 the sales force was instructed that
16 diabetes was a highly competitive driven
17 issue and that "Therefore, we will NOT
18 proactively address the diabetes concern,
19 but rather only when it arises from an
20 MD"? Did you or did you not become aware
21 that that instruction was given to your
22 sales force?

Sydney Taurel (September 19, 2007)

235: 4 Q. Can you answer that
5 question, Mr. Taurel?
6 A. Not without reading the
7 document.
8 Q. It is your testimony to the
9 jury that you have to read this entire
10 document in order to answer the question
11 that I posed to you? Is that correct?

Sydney Taurel (September 19, 2007)

236:23 Q. My question, sir, was, were
24 you informed that the sales force was
237: 1 instructed that diabetes was a highly
2 competitive driven issue and, "Therefore,

we will NOT proactively address the diabetes concern, but rather only when it arises from an MD"?
A. I was not specifically informed of what is in this document.

Sydney Taurel (September 19, 2007)

Q. Sir, do you recall that the sales force was instructed that "Patients treated with Zyprexa, risperidone, haloperidol, divalproex, and ziprasidone in clinical trials had comparable rates of diabetes and hyperglycemia"?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not know exact instructions to the sales force, and I don't know what you are referring to. What date are you talking about, and what are you referring to?
BY MR. SUGGS:
Q. What I was referring to in particular was a document dated November 14, 2002 according to the database that was provided to us by Eli Lilly. I'm referring to Plaintiff's Exhibit 1901. It bears a title "Hyperglycemia/Diabetes Data on Demand Resource Guide."
I will represent to you that in Answers to Interrogatories, Lilly told us that this document was maintained on the knowledge management database for sales representatives. That's the document that I was referring to.
Sir, if I could direct your attention to the first bullet point on the first page. It says, "Patients treated with Zyprexa, risperidone, haloperidol, divalproex, and ziprasidone in clinical trials had comparable rates of diabetes and hyperglycemia, even when the data was analyzed in 3 different ways." Do you see that language, sir?
A. Yes.
Q. Was it your under --
It was your understanding, was it not, that Lilly consistently told physicians that the rates of diabetes between the various antipsychotics was comparable, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: We share with

physicians the information that we have at the time we have it, and we have had a chance to analyze it and get the whole body of evidence.

BY MR. SUGGS:

Q. Sir, your answer is not responsive to my question.

A. And in 2002, I believe that this reflected our analysis of the body of evidence that we had, and, in fact, this conclusion is -- was confirmed by the FDA in September of 2003 when they decided there that should be a class label for these products.

Q. Sir, in fact, the statement that the rates of hyperglycemia and diabetes are comparable is, in fact, generally accepted as being a false statement at this point in time, isn't that correct, sir?

Sydney Taurel (September 19, 2007)

THE WITNESS: That is your statement. I'm sorry. I do not agree with that.

BY MR. SUGGS:

Q. Have you heard of something called the Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes?

A. Yes, I have.

Q. Did you review that at the time it came out?

A. Yes.

Q. I'm going to hand you what's been previously marked as Exhibit 2368.

A. Thank you.

Q. Which, for the record, is a copy of an article entitled "Consensus Development Conference on Antipsychotic Drugs on Obesity and Diabetes." Was this the document that you were referring to, sir?

A. That was the document that you were referring to.

Q. Okay.

This is the document that you indicated that you, yourself, had read before, correct?

A. No. I did not exactly read the document, but I was aware of this statement.

Q. You were aware that this was a consensus statement by the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists and the North American Association For the Study of Obesity, correct?

A. Yes. I'm aware of the process they use, which was to bring together experts from those groups, and they spent two days discussing the data on Zyprexa.
Q. In fact --
A. I'm sorry, on antipsychotics.
Q. In fact, employees of Lilly attended and made presentations at that conference; correct?
A. I believe that's correct.

Sydney Taurel (September 19, 2007)

243:20 Q. Sir, this consensus statement by those medical organizations that we talked about before concluded that "Clozapine and olanzapine are associated with the greatest weight gain
244: 1 and highest occurrence of diabetes and dyslipidemia," correct?

Sydney Taurel (September 19, 2007)

244: 5 THE WITNESS: Can you point me to the --
BY MR. SUGGS:
Q. Sure. The summary section, sir, on Page 5, right-hand column, the second full paragraph, four lines down. "Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia." Did I read that correctly, sir?
A. Yes.
Q. It goes on to state, "Risperidone and quetiapine appear to have intermediate effects." Did I read that correctly?
A. Yes.
Q. And it goes on to say -- I can never pronounce this correctly -- "Arip --
A. Aripiprozole.
245: 1 Q. Thanks. "Aripiprozole and ziprasidone are associated with little or no significant weight gain, diabetes or dyslipidemia, although they have not been used as extensively as the other agents." Did I read that correctly?
A. That's what's written here, yes.
Q. That was the conclusion of those medical organizations, correct?
A. That was the conclusion of the group of people that they gathered during two days on this issue, yes.

Sydney Taurel (September 19, 2007)

249:20 or anything else. I'm just asking, isn't
21 it true that even after the consensus
22 statement came out with those conclusions
23 that we stated before, Lilly has
24 consistently maintained that the rates of
250: 1 diabetes among the various antipsychotic
2 agents are comparable? It's either a yes

Sydney Taurel (September 19, 2007)

250: 8 Q. Did you or did you not
9 continue to make those statements?

Sydney Taurel (September 19, 2007)

250:12 THE WITNESS: I don't know
13 for sure, but whatever we did was,
14 I'm sure, informed by the best
15 science available.
16 BY MR. SUGGS:
17 Q. So, your answer is you don't
18 know?
19 A. Correct.

Sydney Taurel (September 19, 2007)

252: 1 Q. Sir, I'm going to hand you
2 what's been previously marked as Exhibit
3 3192, which, for the record, is an e-mail
4 from Vicki Poole Hoffmann to Thomas
5 Hardy, Sara Kollack, copies to Michael
6 Baker and Michael Overdorf. I believe
7 you previously testified that you know
8 Dr. Baker.
9 A. Correct.
10 Q. Do you know any of the other
11 individuals?
12 A. Michael Overdorf.
13 Q. Who is Michael Overdorf?
14 A. Right now I think he's
15 somewhere in the UK. He's an employee of
16 the company in the marketing area.
17 Q. I'll note for the record
18 that this e-mail is dated March 10, 2004,
19 and I would direct your attention to the
20 second paragraph that starts off "I
21 think," and in particular, the language
22 at the beginning which states, "I think
23 we should delete most of the third
24 paragraph and all of the fourth as they
253: 1 are defensive and attempt to show that
2 there is no differential risk of"
3 diabetes mellitus or "DM among atypicals
4 in spite of the differences in weight

gain. Our advisors have told us that this position is making us look foolish." Do you see that language, sir?
A. I do.
Q. It's your testimony that no one ever told you that Lilly's advisors told the company that that position was making Lilly look foolish?

Sydney Taurel (September 19, 2007)

THE WITNESS: That's what this said in this e-mail. I have no basis to assess that this is what our advisors, indeed, told us, and no one has told me that specifically.

Sydney Taurel (September 19, 2007)

Q. I'm going to hand you another Wall Street Journal chart. I went on the Internet apparently on September 14 and had the Wall Street Journal stock charting program draw a chart of Lilly's stock performance as compared to the Dow Jones Industrial five years back from November -- or September 14. So, it would have been from September 2002 through September of 2007, and we'll mark this as Exhibit 7.

- - -

(Whereupon, Deposition Exhibit Taurel-7, Wall Street Journal On-line excerpt (1 page), was marked for identification.)

- - -

BY MR. SUGGS:
Q. Would you agree with me, sir, that this chart indicates that starting around a couple of months into 2004, the Dow Jones Industrial Average continued on an upward slope, and that at that point there is the beginning of a fairly wide divergence between the Dow Jones Average and the Lilly stock value?
A. Yes.

Sydney Taurel (September 19, 2007)

Were you informed that the "Dear Doctor" letter of the Zyprexa label change went out in March of 2004?
A. The label change of what -- I'm sorry.
Q. There was a "Dear Doctor" letter regarding the Zyprexa label change

which included warning language regarding hyperglycemia that went out in March of 2004. Were you aware of that, sir?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not recall. I know that there was a change in September '03, I believe. Early '04 I recall CVAE "Dear Doctor" letter and changing the label.

BY MR. SUGGS:

Q. Did no one inform you that Lilly did not send out a "Dear Doctor" letter warning -- or advising physicians of the change in the warning regarding hyperglycemia until March of 2004?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do not recall that.

Sydney Taurel (September 19, 2007)

Q. Okay.

I want to switch gears for a while to talk about what Lilly was warning foreign doctors about as compared to what was it was telling US doctors about. Would it be fair to say that the U.S. market for Zyprexa was the most profitable market as compared to the rest of the world?

A. The U.S. market is the largest market for pharmaceutical products, that's correct, yes.

Q. Prior to 2003, there was no mention in the U.S. label in the Warnings section regarding hyperglycemia or diabetes, correct?

A. I believe that's correct. Those observations that we had in our clinical trials were elsewhere in the label.

Q. And you do recall that there was mention of hyperglycemia and diabetes in the European label before that time, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I don't believe that's correct.

BY MR. SUGGS:
Q. Do you recall that in April of 2002, the Japanese regulatory authority required Lilly to issue a warning about diabetes occurring with Zyprexa?

Sydney Taurel (September 19, 2007)

259:14 THE WITNESS: I believe that
15 the Japanese authorities mandated
16 a black box warning or their
17 version thereof mentioning
18 instances of ketoacidosis. This

Sydney Taurel (September 19, 2007)

260: 6 Q. Sir, I'm going to hand you
7 what has been previously marked as
8 Exhibit 320, which I will represent to
9 you is a translation of the Japanese
10 "Dear Doctor" letter. I believe the
11 translation or the document was certainly
12 produced to us by Lilly. Have you seen
13 this document before?
14 A. No. But I'm aware of the
15 change in label which occurred in '02 in
16 Japan.
17 Q. According to this document,
18 which is dated April of 2002, there were
19 three major elements to the warning over
20 in Japan, correct?
21 A. Say that again. I'm sorry.
22 Q. According to this document
23 and the numbered items in the box that
24 you see there, there were three major
261: 1 elements to the warning in Japan,
2 correct?
3 A. Yes.
4 Q. The first was: "Do not
5 administer to patients with diabetes...
6 and those who have a history of
7 diabetes..." correct?
8 A. Yes.
9 Q. The second part was "During
10 administration of this product" -- I'm
11 just reading what's written here --
12 "observe sufficiently with such as
13 measurement of blood glucose." Correct?
14 A. Right.

Sydney Taurel (September 19, 2007)

262: 1 And the third element of the
2 warning was to "Explain sufficiently to
3 the patient and family members," correct?
4 A. Correct.

Q. Do you recall that about ten days after this label change went into effect that the policy committee of Lilly had a meeting where the safety of Zyprexa was discussed?

Sydney Taurel (September 19, 2007)

THE WITNESS: No.
BY MR. SUGGS:
Q. Let me hand you what's been previously marked as Plaintiff's Exhibit 4051. For the record, this is a document entitled "Policy Committee Meeting." It's dated April 12, 2002, "Zyprexa Safety Overview."
A. Okay.
Q. We have had previous testimony, I believe by Dr. Breier, that this was a preread that was provided to the policy committee in advance of this meeting.

Sydney Taurel (September 19, 2007)

A. (Nodding.)
Q. And you're nodding your head. Apparently that's ringing bells with you, too?

Sydney Taurel (September 19, 2007)

THE WITNESS: I have no reason to disbelieve Dr. Breier. I know that we had periodic reviews of Zyprexa and all information we had about Zyprexa, but I have no knowledge as to whether this was a preread or --
BY MR. SUGGS:
Q. Did you --
A. -- something else.
Q. Did you make it a practice to attend every policy committee meeting?
A. Oh, yes. I was the chairman of the policy committee, and I definitely attended all meetings, yes.
Q. I thought that was probably the case.

Do you recall who the other members of the policy committee were at that time besides yourself?
A. I think Gerhard Mayr, Charlie Golden. We had the executive vice president of pharmaceutical operations. We had Mayr. We had the CFO. We had the executive vice president

of product development.
Q. Can you give me the names?
A. John Lechleiter; the executive vice president of R&D, I am not 100 percent certain whether it was still Dr. Watanabe or Dr. Paul.
Q. When you say you are still not sure, that would be in terms of who was the executive vice president of R&D?
A. In April of 2002, there was a transition from one to the other, and I don't remember the exact date.
Q. If I could direct your attention to Page 2. In the introductory paragraph, about three lines up from the bottom there's a sentence that starts off "A side effect." Do you see that?
A. Yes.
Q. "A side effect that is associated with Zyprexa is weight gain and the sequelae of weight gain." Do you see that?
A. Yes.
Q. Now, "sequelae" means an aftereffect or secondary result, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: I generally suppose that's the definition of sequelae.
BY MR. SUGGS:
Q. That's the dictionary definition.
A. Okay. I trust you.
Q. Diabetes, high cholesterol and heart disease are all sequelae of weight gain, correct?
A. I don't know that.
Q. When you got this e-mail, or, pardon me, this preread that said "A side effect that is associated with Zyprexa is weight gain and the sequelae of weight gain," what was your understanding of what was being referred to there?

Sydney Taurel (September 19, 2007)

Q. Diabetes was clearly a sequelae of weight gain, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: No, no. I wouldn't say that. Because that would imply that everybody who

17 gains weight w[illegible] become diabetic.

Sydney Taurel (September 19, 2007)

269:14 Q. Under the weight gain
15 section, it states, "Five atypical
16 antipsychotic agents are associated with
17 more weight gain than most traditional
18 neuroleptic agents in the following
19 order," "Clozaril greater than Zyprexa,
20 greater than Seroquel, greater than
21 Risperdal," correct?
22 A. Yes.

Sydney Taurel (September 19, 2007)

295: 7 Q. Sir, do you recall that in
8 March of 2007, the FDA informed the
9 company that it was concerned about the
10 adequacy of the Zyprexa label?
11 A. I'm aware we received a
12 letter -- an approvable letter for
13 Symbyax from the FDA which had some
14 comments about their concerns on the
15 label.

Sydney Taurel (September 19, 2007)

295:16 MR. SUGGS: I'm going to
17 hand you what we'll mark as Taurel
18 Exhibit 9.

Sydney Taurel (September 19, 2007)

296:13 Q. -- which I'll describe for
14 the record as a letter from FDA to Eli
15 Lilly with attachments. It has several,
16 what appear to be fax imprint dates at
17 the top of the pages, the earliest of
18 which is March 28, 2007. It also bears
19 the date of March 28, 2007 with a stamp
20 for G. Brophy. I don't see any other
21 dates on here. I'll also represent this
22 document does not have a Lilly Bates
23 Number on it.

Sydney Taurel (September 19, 2007)

297: 6 Q. Mr. Taurel, is this letter
7 that I've handed you as Exhibit 9 the
8 letter that you were referring to?
9 A. Yes, approvable letter for
10 Symbyax.

Q. It refers to -- by the way, is Mr. Brophy, is he in the regulatory affairs of Eli Lilly?
A. Yes, Dr. Brophy, yes.
Q. This refers to a supplemental new drug application regarding a drug product called Symbyax, correct?
A. Yes.
Q. Symbyax is a combination of both olanzapine and fluoxetine, correct?
A. Correct.
Q. Olanzapine is the generic name for Zyprexa, and fluoxetine is the generic name for Prozac, correct?
A. Correct.
Q. Lilly was seeking approval from the FDA to market this combination drug with those two drugs in it for the treatment of treatment-resistant depression; is that correct?
A. Correct.
Q. According to the letter, it appears that a number of submissions had been made by Lilly to FDA in 2006 and early 2007, correct?

Sydney Taurel (September 19, 2007)

Q. If you look at the first two paragraphs.
A. It appears that way, yes.
Q. And about midway through the first page, there is a heading entitled "Updated Information on Risks of Weight Gain, Hyperglycemia, and Hyperlipidemia," correct?
A. Yes.
Q. Okay.
About the middle of that paragraph -- actually, it's the second sentence, the FDA stated, "In particular, we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine."
Did I read that correctly?
A. Yes.

Sydney Taurel (September 19, 2007)

let me back up for a second. When was it that you became aware of this letter?
A. Shortly after we received it.
Q. Did Mr. or Dr. Brophy bring it to your attention?

A. No, not directly.
Q. Who did?
A. I think it was mentioned at the end of one of our policy and strategy committees when we go around the table and each member of the committee talks about the issues of relevance.
Q. Do you know who it would have -- strike that.
Do you know who would have brought that issue up?
A. It would have been the head of R&D, Dr. Paul.
Q. If I could direct your attention to the following page. Let me back up for a second.
Was this -- you said just a moment ago that you were first made aware of this letter in a policy committee meeting that would have occurred shortly after the corporation received the letter, correct?
A. Yes, I believe so.
Q. So, obviously, all of the other folks who were on the policy committee, I'm assuming they would have been informed of this as well, correct?
MS. GUSSACK: Objection.
THE WITNESS: They would have if they were present. Not everyone attends every meeting.
BY MR. SUGGS:
Q. Were copies of this letter distributed by Mr. or Dr. Paul at the meeting, or did he just verbally inform you of it?

Sydney Taurel (September 19, 2007)

THE WITNESS: As I mentioned, I don't have specific recollection of how I learned about this. I believe it was at a PSC meeting. That would be the normal process by which I would learn about something like this. And, no, I do not recall at that time Dr. Paul sending a copy of this. That would not be a normal process.
BY MR. SUGGS:
Q. Did you at some time shortly thereafter actually receive a copy of this document?
A. No. I've received a copy actually more recently.
Q. Maybe I was a little unclear in my previous questions. I think it's your testimony that you were aware of this letter shortly after it was written.
A. Correct.

Q. When did you actually first see it?

Sydney Taurel (September 19, 2007)

THE WITNESS: I've been shown this letter in a privileged conversation recently.

BY MR. SUGGS:

Q. For the first time?

A. Yes.

Q. Okay.

If I could direct your attention to the second page, there's a reference to data in the first full paragraph on the second page, correct?

A. The paragraph starting with "Regarding data displays"?

Q. Yes.

They note within the paragraph that -- they state in the second sentence, "For example, we note that your proposed Symbyax label includes information only on proportions of patients who are relatively normal at baseline with regard to random blood glucose (less than 140 milligrams per deciliter), i.e., 2.9% of such patients receiving OFC had on-treatment levels greater than or equal to 200 milligrams per deciliter compared to .3% of placebo-treated patients." Do you see that language, sir?

A. Yes.

Q. Okay.

Now, that would --

By the way, the OFC that's referred to there is the combination of olanzapine and fluoxetine, correct?

A. Yes.

Q. Okay.

That data is indicating that there was roughly a ten times higher incidence of people getting blood levels greater than 200 milligrams per deciliter who were exposed to the combination drug as compared to placebo-treated patients, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: It says that the patients -- it talks about proportions of patients who are relatively normal at baseline with regard to random blood glucose, which is 2.9 percent of such patients receiving OFC had on-treatment levels higher than

200 milligram compared to .3 percent of placebo-treated patients.
BY MR. SUGGS:
Q. So, the rate for the patients who received the combination drug was about ten times higher than the people who received placebo, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: Again, the observation is 2.9 percent of patients receiving OFC had on-treatment levels of higher than 200 milligrams and 0.3 percent of placebo-treated patients.
BY MR. SUGGS:
Q. 2.9 percent is about ten times higher than .3 percent, correct?
A. More or less. That's not precise.
Q. They went on to note -- they say, "However, we note that 46% of patients who were borderline to high at baseline (140 to 200) had such on-treatment levels compared to only 5% of placebo-treated patients." Do you see that language?
A. I do.
Q. So there again, with respect to those people who had borderline to high levels at the outset, their rate or incidence of going above 200 milligrams per deciliter was, again, about ten times higher than those folks who were exposed to placebo, correct?

Sydney Taurel (September 19, 2007)

A. That's what this says, yes.
Q. And 46 percent is about ten times higher than 5 percent, correct?

Sydney Taurel (September 19, 2007)

THE WITNESS: No. It's incorrect. It is about 9.2 percent times --
BY MR. SUGGS:
Q. That's fine. It is over 9 times higher, correct?
A. Yes. But as the next

Sydney Taurel (September 19, 2007)

309:10 Q. The FDA goes on to note:
11 "We were troubled that this important
12 finding was not included in your proposed
13 label." Do you see that language?
14 A. Yes.

Sydney Taurel (September 19, 2007)

310:12 Q. Directing your attention to
13 -- well, do you see towards the bottom of
14 the page there's a heading entitled "Post
15 Marketing Commitments"?
16 A. Yes.
17 Q. In the paragraph just above
18 that, it states, "Our overall goal is to
19 improve labeling with regard to these
20 findings so that clinicians will be
21 better informed on what the risks are for
22 their patients. They cannot make
23 reasonable treatment decisions until they
24 have such information. We do not feel
311: 1 that current labeling for either Symbyax
2 or Zyprexa provides sufficient
3 information on these risks, and we fully
4 intend to insure that these labels are
5 enhanced with the best available
6 information to characterize these risks."
7 Do you see that language, sir?
8 A. Yes.

Sydney Taurel (September 19, 2007)

313:22 Q. As we sit here today on
23 September 19, the Zyprexa label does not
24 warn physicians of the data that's
314: 1 referred to in the second paragraph of
2 the FDA letter on Page 2, correct?
3 A. That is correct.

Sydney Taurel (September 19, 2007)

321:18 You have that annual report
19 in front of you, do you not, sir?
20 A. Yes.
21 Q. And I just am going to go
22 over a couple of things in it and make
23 sure we're communicating. This is your
24 letter to the shareholders that was
322: 1 signed by you, right?
2 A. Yes.
3 Q. And I figure a Chairman of
4 the Board, President, Chief Executive
5 Officer probably doesn't write his own
6 letters, that somebody writes them for
7 him, and then he has to approve the
8 letters he writes. That's what I'm
9 figuring.

Sydney Taurel (September 19, 2007)

322:13 Q. Is that right?
14 A. It's an iterative process.
15 I'm being helped by a speech writer,
16 indeed, but there's a lot of my own
17 thinking, obviously, in this.
18 Q. That's what I figured. So,
19 when you put your name on it, you agreed
20 with it?
21 A. Yes.
22 Q. Okay.
23 That's what I figured.
24 And it said in your own
323: 1 letter, "Last August, we were very
2 surprised when a federal appeals court
3 reversed that ruling." And that was a
4 ruling on the patent, right?
5 A. Correct.
6 Q. You told Mr. Suggs, and I
7 think Ms. Gussack knew about this and
8 y'all kind of shared a chuckle, you still
9 have the scars from what happened in the
10 stock price after that happened, right?
11 A. Correct.
12 Q. Your stock price dropped
13 from over 100 down to the low 70s, high
14 60s in a matter of a day or two, right?

Sydney Taurel (September 19, 2007)

323:17 THE WITNESS: I think the
18 figure was 105 or so to 75 or so.
19 BY MR. ALLEN:
20 Q. Yes, sir. I got this chart
21 right there. It's from August 1st to
22 October the 10th, and it had a straight
23 line drop. You said you had scars from
24 that?
324: 1 A. What's the number? I'm
2 sorry. Just to be specific, if you can
3 push your slide a little bit.
4 Q. What do you need?
5 A. Okay. 75. You said the
6 high 60s and the stock price fell to $75
7 the day of the --
8 Q. Right. It was just a
9 straight line plunge though when the
10 Prozac lost its patent protection.
11 A. Clearly.
12 Q. And then it got down to the
13 75, and then it went down a little
14 further, and it's tracked back up a
15 little bit, right?
16 A. Yes.
17 Q. Now, over $30 billion of
18 value was lost when that happened,
19 correct?
20 A. Yes.

Q. That's what you said in your letter, "Given this turn of events involving a product with U.S. sales of $2.2 billion, you may well ask whether Lilly can successfully navigate the next several years. My response is a strong 'Yes.'" That's your response, right?
A. Yes.
Q. So, you were telling the shareholders, we can respond to this dramatic drop in price, and we can continue doing business successfully as we have in the past, right?

Sydney Taurel (September 19, 2007)

BY MR. ALLEN:
Q. Right?
A. You said we can continue to do business as we have in the past. That's not exactly what I say there, but I'm saying we can successfully navigate the next several years, yes.
Q. You said that strongly, you're not even worried. My strong response is yes, right?
A. Yes.

Sydney Taurel (September 19, 2007)

You said, "My response is a strong 'Yes.' We fully recognize the magnitude of our challenge." So, this was a challenge of some magnitude.
A. Yes, sir.
Q. It says, "And we are prepared not only to manage the short term challenges of Year X but also to embark soon thereafter on a period of renewed growth." I've underlined "growth" there, right?
A. Yes.
Q. What's growth mean? I think I know what it means, but I want you to tell the jury what you meant when you said "a period of renewed growth."
A. Well, we were at that point in the late stage development of eight new products -- nine new products, which was a record in the history of our company and, frankly, a record in our industry as well. And those products were going to be launched in the years following the Zyprex -- I mean, the Prozac patent expiration, and that was going to bring a lot of growth to the company.
Q. Well, in fact, you explain it, and here's why I'm confident. One of

your reasons you were confident is
"Strong product line fuels growth."
Didn't you say in your letter, "Zyprexa
exemplifies our growth opportunities"?
Didn't you say that, your words, your
letter?
A. I said that, but if you read
the whole letter, you'll see that I talk
about not just Zyprexa, but other
products, as well as newer products that
were not yet on the market.
Q. Mr. Taurel, I'm not here to
argue about the whole letter. I'm here
to talk about Zyprexa, and I just want to
make clear that you said in your letter
that you signed to the shareholders that
Zyprexa exemplified, set an example as
one of your growth opportunities in your
company; is that right?

Sydney Taurel (September 19, 2007)

Q. "Exemplifies our growth
opportunities." Did I read that right?
A. It means it's one of the
examples of one of the growth
opportunities that we had, yes.
Q. Right. So, just there's no
confusion, you were telling the
shareholders in the 2000 annual report
following the loss of the Prozac patent
protection that Zyprexa exemplified one
of your areas for opportunity for growth,
right?
A. That is correct.
Q. Now, what were the
indications for Zyprexa at the time in
2000, 2001? I can help you out. They
were schizophrenia and bipolar mania,
correct?
A. I have to remember when the
bipolar mania --
Q. Let's just assume it is. I
have the package insert. Here, I'll help
you out.
A. I'm sorry.
Q. I'll put up here on the
board. You can have a copy. We don't
need to spend a lot of time on it. 2001
Physicians' Desk Reference. Do you see
it's on the board, sir? I'm going to
help you out. We're going to go straight
to it. We're going to go to indications.
A. All right.
Q. Indications are
schizophrenia, bipolar mania, right?
A. Right. I don't remember

When Prozac lost its patent protection, you were telling the shareholders Zyprexa exemplifies our growth opportunities and Zyprexa was indicated for two things, schizophrenia and bipolar mania, correct?

A. Correct.

Q. As a matter of fact, in that same letter, you said, "In 2000, our sales of Zyprexa were $2.3 billion, a 25 percent increase. During the fourth quarter, this neuroscience blockbuster surpassed Prozac as our top-selling product." Right?

A. Right.

Q. And then not to beat a dead horse, I hope, you skip over here to Page 9 of that annual report. It has a little heading. I don't have a color copy. It says, "So, what now," and it says, "Our newer products will stand as our front line against inevitable generic competition for Prozac. Introduced throughout the last half of the 1990s, they'll be the key" -- don't you use the word "the key," sir? That's your word, right?

A. Yes.

Q. "They'll be the key to our ability to produce earnings growth during that time and resume our strong performance thereafter." Did I read that correctly?

A. Yes, sir.

Q. Okay.

So, the front line against the generic competition for Prozac are the products that were introduced during the last half of the '90s, and that would include, and the first one listed in the annual report is Zyprexa, correct?

A. Correct.

Q. By the way, I saw there, you've led an interesting life. You were born in Morocco; is that right?

A. Yes.

Q. Spanish citizen?

A. Yes.

Q. I think you've gone to school in France, and your family is from Spain, and you've practiced and done your career all over the world, isn't that right?

A. I've lived in several countries, yes.

Q. I was born and raised in Galveston Texas, and I spent my entire life in about a 300 mile square area. Okay? So, I'm going to try to use some of the words, just common sense words and see if I understand what you're writing here in this report. Okay? Do you understand me?

What you're saying here is that the key to protecting our earnings is to get growth in our products that we developed in the last half of the '90s, right?

Sydney Taurel (September 19, 2007)

THE WITNESS: That's not the word I used. You said "protect" our earnings, and I'm saying "produce earnings growth."

BY MR. ALLEN:

Q. That's even better. You did better than I did. You were going to produce earnings growth from these products that you developed in the '90s?

A. Following a decline which we had in 2002 due to the Prozac patent expiration.

Q. Well, in fact, you don't list the drugs in any type of alphabetical order, you introduce -- the first drug you talk about is Zyprexa, right? Is that correct?

A. Yes.

Q. Down here you said, "Introduced as a therapy for schizophrenia in 1996, Zyprexa was approved in the U.S. last year for additional indications of acute mania associated with bipolar disorder and the maintenance of treatment response in schizophrenia." Did I read that correctly?

A. You did.

Q. So, what you're saying is what we just discussed, the two indications, and the only two FDA-approved indications for Zyprexa at the time Prozac went off patent were schizophrenia and bipolar mania, right?

Sydney Taurel (September 19, 2007)

THE WITNESS: Schizophrenia had actually two different indications. It was first schizophrenia short term therapy and then the maintenance of treatment response in schizophrenia.

BY MR. ALLEN:

Q. Right. Two disease states. Two diagnoses, schizophrenia and bipolar mania, right?

Sydney Taurel (September 19, 2007)

335:18 THE WITNESS: Again, yes.
19 BY MR. ALLEN:
20 Q. Thank you, sir.
21 It says, "We're exploring
22 broader uses for Zyprexa in schizophrenia
23 and other key segments of the
24 antipsychotic market, including bipolar
336: 1 depression and the psychotic or
2 behavioral disturbances that accompany
3 dementia." Did I read that right?
4 A. You did.
5 Q. Now, I know it's clear as a
6 bell and you know you can tell me right
7 now, Zyprexa has never been approved for
8 the treatment of dementia either in the
9 past or as we sit here today, has it?

Sydney Taurel (September 19, 2007)

337: 4 A. That is correct.

Sydney Taurel (September 19, 2007)

346: 4 Q. So, easy question. I think
5 this is going to be the easiest question.
6 In 2000, 2001 or up until today, has
7 Zyprexa ever been approved for the
8 treatment of Alzheimer's psychosis?
9 A. No.
10 Q. Okay.
11 In 2001, up until today, has
12 Zyprexa ever been approved for the
13 treatment of dementia?
14 A. No.
15 Q. Okay.
16 So -- and we're going to get
17 to it in more depth in just a second, but
18 it's improper for a company to promote
19 Zyprexa for treatment of dementia or
20 Alzheimer's psychosis, true?

Sydney Taurel (September 19, 2007)

347: 1 A. Yes. We did not promote
2 Zyprexa for dementia or Alzheimer's.

Sydney Taurel (September 19, 2007)

347: 6 Q. See, I think you did, and
7 I'm going to be honest with you, I think
8 the company did do that. I'm saying it
9 is illegal for a company to promote a
10 drug for an indication that has no FDA
11 approval; is that true?

Sydney Taurel (September 19, 2007)

348: 7 THE WITNESS: The answer to
8 that is yes.
9 BY MR. ALLEN:
10 Q. Thank you, sir.
11 Now, on that point, and I
12 think this is a series of just easy
13 questions. I think it's a series of
14 easy, easy questions.
15 From the time of Zyprexa's
16 approval in 1996 -- is that when it was
17 approved?
18 A. Yes.
19 Q. -- up until today, if we sit
20 here in September of 2007, has Zyprexa
21 ever been approved by the FDA for the
22 treatment of anxiety?
23 A. No.
24 Q. Has it ever been --
349: 1 Has Zyprexa ever approved
2 here in the United States for the
3 treatment of general anxiety disorder?
4 A. No.
5 Q. Has Zyprexa ever been
6 approved for signs or symptoms of
7 hostility?
8 A. This is not an indication.
9 Q. That's what -- I didn't
10 think it was.
11 Has it ever been approved
12 for symptoms of irritability, Zyprexa?
13 A. The FDA typically does not
14 approve products for symptoms.
15 Q. That's a good point. So, it
16 hadn't been approved for the symptom of
17 irritability?
18 A. Neither would any product be
19 approved for symptoms of irritability. I
20 don't think that's a classified disease.
21 Q. Good point.
22 Has Zyprexa ever been
23 approved for memory problems, for the
24 treatment of memory difficulties?
350: 1 A. No.
2 Q. Has Zyprexa ever been
3 approved for attention deficit disorder
4 or hyperactivity disorder?
5 A. No.
6 Q. Has Zyprexa ever been
7 approved for the management of social
8 phobias?
9 A. No, there's no indication.
10 Q. Sir?
11 A. There's not an indication.
12 Q. If there's no indication
13 approved by the FDA, a drug company can't
14 promote the drug for that, right?
15 A. Right.
16 Q. Thank you. That's all I
17 need to know.

Sydney Taurel (September 19, 2007)

358: 8 Q. Now, you made a good point a
9 little while ago. You said, Mr. Allen, I
10 think you said there's something like
11 40,000 employees, right?
12 A. We have 41,000 employees
13 today.
14 Q. You clearly can't go around
15 every day and talk to 40,000 employees
16 and see what they're doing, right?
17 A. Obviously.
18 Q. That's just common old
19 sense. That's why you have to have a
20 senior management team. Don't you have a
21 senior management team?
22 A. We do.
23 Q. And some of the people on
24 that team would include the medical
359: 1 director of the entire company now, Dr.
2 Alan Breier, right?
3 A. Yes.

Sydney Taurel (September 19, 2007)

359: 7 Q. Mr. Santini, right?

Sydney Taurel (September 19, 2007)

359:11 Q. He's a member of the senior
12 management team?
13 A. Are you talking about today?
14 Q. Yes, sir, today.
15 A. Yes, those people are part
16 of the senior management council.
17 Q. What was Mr. Santini's job
18 back in 2001?
19 A. I do not recall exactly.
20 Q. He was on the senior
21 management team, wasn't he?
22 A. Yes, he would have been.
23 Q. Yes, sir, I thought so. All
24 right.
360: 1 Then you have the senior
2 managers, and they have people that work
3 for them, some executives that are put in
4 charge of particular products, and you
5 have all kinds of cross-functional teams.
6 And then you have things like sales
7 forces and different departments,
8 regulatory and things of that nature,
9 right?

Sydney Taurel (September 19, 2007)

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360:13 Q. Isn't that how your company
14 works, it has all kinds of departments on
15 different levels?

Sydney Taurel (September 19, 2007)

360:17 THE WITNESS: Generally,
18 yes.
19 BY MR. ALLEN:
20 Q. That's all I can do, sir. I
21 don't have time, an hour and 15 minutes,
22 to get into the detail, but I want the
23 jury to understand that you're the head
24 of the company, and you have people
361: 1 working there for the company doing their
2 job, right?
3 A. Correct.
4 Q. The guy that was doing the
5 job that was in charge of the product
6 team for Zyprexa was Dr. Alan Breier,
7 right?
8 A. When?
9 Q. Well, in 2000.
10 A. I do not recall exactly. We
11 went from Dr. Tollefson to Dr. Breier. I
12 do not recall at what time exactly the
13 responsibilities changed.
14 Q. That's a fair answer. The
15 head of the Zyprexa product team, there's
16 two people that you can recall. One was
17 Dr. Gary Tollefson, and Dr. Breier took
18 over from him?
19 A. Correct.
20 Q. After Dr. Breier did his job
21 on the Zyprexa product team, he's
22 promoted, wasn't he?
23 A. Yes. He has become the
24 chief medical officer.
362: 1 Q. So we can clearly say that
2 when we look at what Dr. Breier did at
3 Eli Lilly, Eli Lilly thought he did a
4 good job, and whatever he did was worthy
5 of a promotion, correct?

Sydney Taurel (September 19, 2007)

362: 9 Q. It was worthy of a
10 promotion, right?
11 A. We make promotion of people
12 based on a series of criteria, their
13 performance at the job, their leadership
14 skills, their adherence to our values,
15 how they relate to other people, to the
16 extent -- or how they are viewed in the
17 external world and many other criteria.
18 Q. You listed some of the
19 criteria there in your answer, did you
20 not? You listed some of those criteria
21 you considered in your answer, did you

not?
A. Yes.
Q. One of the criteria I thought you listed was did he, Dr. Breier, adhere to our company values, right?
A. Yes.
Q. And you can tell this jury when we look at what Dr. Breier did in regard to Zyprexa, he adhered to the company values, right?
A. Yes.
Q. No question about it.
Now, back on that issue of the growth strategy. Do you remember Zyprexa was going to be one of your growth opportunities? Do you remember that?
A. Yes.
Q. I have this for you and your lawyer, and this is an agenda.
MS. GUSSACK: Is this going to be marked as an exhibit?
MR. ALLEN: Yes, it is. Nina, and I am very good at this usually, but it says it is Exhibit Number 05846.

Sydney Taurel (September 19, 2007)

Q. I'm going to show you something. This is an agenda, Zyprexa PCP launch meeting, October 25 and 27, 2000 in Orlando, Florida. Do you see that heading up there?
A. Yes.
Q. Now, first of all, I'm sure that as head of the entire company you were familiar with the fact that in October of 2000, this was after, by the way, Prozac had the decision losing its patent protection, correct?
A. Yes.
Q. It was following the time, as you said, I carried the scars with me 'til today, that Zyprexa's or Eli Lilly's stock had dropped from above 100 to the 70s, right?
A. Correct.
Q. Y'all lost over, and we'll do the math later, over $30 billion into equity value since August, right?
A. Right.
Q. So, I'm sure -- and your annual report said Zyprexa was going to be one of the ways you were confident that you were going to grow the company, correct?
A. Yes. One of the ways, yes, that's what I said.

Sydney Taurel (September 19, 2007)

367: 1 Q. All right. Now, I take it
2 then in October of 2000, when it said
3 "Zyprexa PCP launch meeting," you were
4 aware Zyprexa was being launched to the
5 primary care physicians in October of
6 2000?
7 A. Yes.
8 Q. And this was part of the
9 Zyprexa growth strategy, was it not?
10 A. Yes.

Sydney Taurel (September 19, 2007)

370: 2 Q. My question is, and it still
3 hasn't been answered. Between August of
4 2000 and October of 2000, had there been
5 any change in the indications for
6 Zyprexa?
7 A. I believe I answered that.
8 Q. What is that answer?
9 A. No.
10 Q. Thank you. And the
11 indications were schizophrenia and
12 bipolar mania, right?
13 A. Yes.
14 Q. And it would be improper and
15 illegal and contrary to FDA regulations
16 to promote in an off-label fashion,
17 right?

Sydney Taurel (September 19, 2007)

370:21 Q. Right?
22 A. Yes.
23 Q. Thank you, sir.
24 Now, one of the people at
371: 1 this -- did you go down to Orlando for
2 the PCP launch?
3 A. I do not recall going.
4 Q. You don't recall if you went
5 down there?
6 A. No.
7 Q. Did you send a corporate jet
8 down there with Mr. Santini and Dr.
9 Breier on it?
10 A. I would not send a jet.
11 They would travel on their own.

Sydney Taurel (September 19, 2007)

372:17 Q. Now, somebody else at this
18 PCP launch was Dr. Breier, who was the
19 olanzapine, that's Zyprexa, product team
20 leader, right?

A. Right.
Q. And it says he's going to speak in the general session about "Medical Framing." Do you know what that means, "medical framing"?
A. Not exactly, no.
Q. Do you have any general knowledge of what that means?
A. We talk about medical aspects relating to olanzapine, I would think.
Q. He's going to speak, and some other people are going to speak, it looks like Dr. Hay and Dr. Hurley. Who are those two gentlemen?
A. I don't know.
Q. That's fine. Also at the PCP launch at the general session, Zyprexa sendoff, you had Mr. Gino Santini, president, US operations; is that right?
A. That's what this agenda says, yes.
Q. So, senior management was present for the PCP, primary care physician launch, right?
A. Some members of senior management were present, yes.
Q. Yes, sir. Well, not every member, but Mr. Santini, for example, right?
A. Yes.
Q. He was going to give the "General Session - Zyprexa Sendoff," correct? Right?
A. Correct.
Q. Now, when you found out that they were doing off-label promotion, they were training the sales reps down there to do off-label promotion, did you take any disciplinary action?

Sydney Taurel (September 19, 2007)

THE WITNESS: They were not sending sales reps to do off-label promotion, as you allege.
BY MR. ALLEN:
Q. If you found out about it, would you take disciplinary action?

Sydney Taurel (September 19, 2007)

THE WITNESS: That would not happen because we have processes inside the company to ensure that our promotion is in accordance to the label.
BY MR. ALLEN:

Q. At this launch, they're down there talking to the sales representatives of the company, right?
A. Yes.
Q. And as you said in the answer several hours ago to Mr. Suggs, the sales representatives are trained before they go out to detail and talk to doctors, right?
A. Yes.
Q. And I would assume that the sales reps are going to utilize the training they receive in launch meetings such as this, correct?

Sydney Taurel (September 19, 2007)

375:21 Q. Correct? That's why you're having this big meeting?

Sydney Taurel (September 19, 2007)

376: 1 Q. Isn't that the case?
A. The sales representatives get trained at the meetings. Yes. They have role plays, and then they go out and share the information that they receive at the meeting with physicians.
Q. That's exactly correct. And your company recognizes that some sales reps may not be able to make it to the meeting, and then some sales reps need to be reminded about what took place at the meeting, and so they record what took place. Don't you record the sales meeting -- the PCP launch meeting?

Sydney Taurel (September 19, 2007)

376:16 THE WITNESS: I don't know.
BY MR. ALLEN:
Q. You don't know?
A. No.
Q. Do you know that sales reps get video or audio cassette tapes that they can listen to about what happened at the PCP meeting?
A. I'm not sure about specific
377: 1 procedures which are used in our sales and marketing operation.
Q. That's okay. That's understandable. So, you probably haven't ever -- I guess you've never read nor seen what was actually said to the sales reps down at that PCP meeting. Is that what you're telling me?
A. I did not see it at the

time.
Q. Well, that's a better question. You are going to help me out a lot. Have you ever known as you sit here today on September 19, 2007 what the sales reps were told by Dr. Breier, for example, at the primary care physician launch?

Sydney Taurel (September 19, 2007)

377:22 Q. Do you know what they were told?
A. I found out from my lawyers recently.
378: 1 Q. Are you going to discipline Dr. Breier?

Sydney Taurel (September 19, 2007)

378: 6 Q. Sir?
Do you have any plans to discipline Dr. Breier?
A. I don't.
Q. Okay.
Well, here, I found out in a document that y'all gave me, it's Exhibit Number 04007. I will not read any, what do you call those, Bates Numbers. This is a "Zyprexa Audio Program Number 3, Post-Meeting Communications Campaign Cassette Version." "Eli Lilly & Company, Viva Zyprexa Post-Meeting Campaign," "Cassette Version 12/1/00." Do you see that, sir?
A. Yes.
Q. Now, just to put this in context, and we have this, and we may or may not talk about it depending on time,
379: 1 but we have -- the launch meeting that took place down there in the PCP launch was called Zyprexa launch meeting viva Zyprexa. Did you know that?
A. Not at the time.
Q. Do you know that now?
A. No.
Q. Did you know you had a song, Eli Lilly Zyprexa song?
A. No.
Q. Have you ever learned that?
A. No.
Q. I'll come back to the Viva Zyprexa Song when we have time, if we have time. But at this Viva Zyprexa launch meeting, a recording was made and put on a cassette tape for the sales representatives. Did you know that?
A. Can you ask the question again?

Q. Yes, sir. At the launch meeting in October 2000, did you know a tape was made of what happened at the launch meeting?
A. Not at the time.

Sydney Taurel (September 19, 2007)

Q. When did you learn that a tape recording was made of the events at the PCP launch? When? September of 2007 is when you learned that?
A. Yes.
Q. Okay.
Before that time, you did not know that; is that correct?
A. Yes.
Q. Okay.
You know, earlier we talked about -- you've read --
You've had a lot of documents shown to you today, haven't you? A lot of documents have been shown to you?
A. Today?
Q. Yes, sir.
A. Yes.
Q. There's reasons why people put things in writing, isn't it? You put things in writing for a reason, don't you?

Sydney Taurel (September 19, 2007)

Q. Well, again, I haven't been schooled in Paris. I was schooled in Galveston, Texas. But the reason things are put in writing is to memorialize what happens, right? Isn't that one of the reasons we put things in writing?
A. I suppose one of many, yes.

Sydney Taurel (September 19, 2007)

Q. No. I'm sorry. I didn't mean to argue with you. I'm talking about business. You said there's many reasons we put things in writing. Can you tell the jury some of the many reasons you put things in writing in business? To memorialize what happened?
A. Or what plans are or if -- there are many, many, many different reasons. We write an annual report, for example, we have to put this in writing to report back to our shareholders. We have filing with the SEC or with various

regulatory agencies. [redacted] put in writing all of our documents to the FDA. We do that with our registry of clinical trials, many, many different reasons.

Q. The reason is because you don't have to rely upon your memory of what happened ten years ago, five years ago, two months ago, or even a week ago. You put it down in writing so we can see what happened, right?

Sydney Taurel (September 19, 2007)

THE WITNESS: Again, that's not the only reason why you put things in writing.

BY MR. ALLEN:

Q. But it is one of the reasons, isn't it?

A. Yes.

Q. I mean, you ask for written reports on your desk. That's part of your protocol at your company. You have certain written reports you receive on a weekly basis, don't you?

Sydney Taurel (September 19, 2007)

Q. Don't you?

A. No.

Q. No?

A. Not on a weekly basis.

Q. How about monthly basis?

A. I have certain reports I do receive on a monthly basis.

Q. You ask for them to be in writing?

A. Yes.

Q. Thank you, sir.

A. Data, for example, charts, figures and so forth are put in writing, yes.

Q. The best evidence of what happened five years ago would not be your recollection, but what somebody put down in writing about the event at the time it transpired, correct?

Sydney Taurel (September 19, 2007)

Q. Let me give you an example, and then we're going to move on. I thought this was a simple kind of question we all could agree upon.

You didn't go down to Atlanta to the diabetes advisory board meeting, did you?

A. No.
Q. You said you heard about it, right?
A. Not at the time.
Q. Not at the time. You've heard about it since then?
A. Yes.
Q. But the people that were there kept notes and prepared e-mails and memoranda on it, right?
A. I don't know.
Q. Well, you've seen some today, haven't you?
A. I --
Q. Not that exhibit.
A. Memoranda? No. You've shown me the agenda.
Q. Oh, no. I think we're talking about two entirely different things, but let's move on.
A. I'm sorry. What were you talking about?
Q. I was talking about the diabetes advisory committee that met back in 2000.
A. Oh, I'm sorry. I thought you were on the -- still on the primary care physician launch.
Q. Well, we're getting back to it. But do you recall seeing the e-mails about that, the diabetes advisory meeting in Atlanta?
A. Yes. I saw that earlier today.
Q. You weren't there?
A. No.
Q. The best evidence of what happened is by the people who were there who took notes and wrote down in their e-mails what happened, right?

Sydney Taurel (September 19, 2007)

What would be a better evidence of what happened in Atlanta in the fall of 2000, what you say now or what the people who were there wrote down at the time?

Sydney Taurel (September 19, 2007)

Q. What would be the best evidence?
A. I couldn't say anything today because I was not at that meeting.
Q. That's good. That was on another subject. Now, back to Viva Zyprexa. They didn't just write down what happened, they recorded what

happened. You learned that this month, September 2007, right? Sir?
A. Yes.
Q. I'm not -- we don't have time to read the whole thing, but it says this is a cassette tape and it has a program announcer: "This program is for internal use only and is not to be used in detailing. Insert: Viva Zyprexa song." And it goes on to say "The purpose of this program is to provide you with some of the highlights and insights from the Orlando launch meeting in October. In addition to being a productive, high energy meeting, it produced" -- and I need to zoom in on this.
389: A. Can you tell me where it is --
Q. Yes, sir. It's the very first paragraph right there.
A. Okay. Thank you.
Q. -- "high energy meeting, it produced several pearls of wisdom" -- what's a pearl of wisdom?
A. An insight, a new idea.
Q. -- "that we've captured here on tape." So, they captured these pearls of wisdom that occurred down in Orlando on tape, right?
A. That's what it says here.
Q. "Our intent" -- now, "Our" is your company, right?
A. I don't believe that we can say that whoever is talking represents necessarily the company.
Q. It's Jim Delisle, and I think if we look back on this -- I think we had Mr. Delisle -- can't remember. We'll find him later.
A. Never heard the name.
390: Q. Well, I think he was hired by y'all to do this, but it doesn't matter, this is y'all's tape you gave the sales reps. We'll quibble about that later.
"Our intent is to spark a memory or two, and strengthen your selling efforts." Now, is that generally what you want to do when you're training sales reps, is to spark their memories about your meetings on what they were trained so it will help them sell the product?

Sydney Taurel (September 19, 2007)

390:17 Q. Is that what you were trying to do for sales reps?
A. We bring sales reps to meetings of that type to inform and

educate them about everything that we know about a product, about how to communicate with physicians about that product.

Q. So, you're training, and you did better than I did, to educate them, to train them and to tell them how to communicate with physicians, right?

Sydney Taurel (September 19, 2007)

A. We tell them everything that we know about the product and information on the label and so on so that they can appropriately communicate with physicians.

Sydney Taurel (September 19, 2007)

Mr. Taurel, we're back on the record, and we're going to go over this audio transcript of what the Zyprexa product team leader said at the primary care launch in Orlando to the sales reps. Dr. Breier, you personally know Dr. Breier, do you not?

A. I do.

Q. As the medical director of the entire company now, how often do you interact with Dr. Breier?

A. Oh, I see him every three months when we have the meetings of the senior management council, and beyond that, periodically. I don't know how many times.

Q. I'm just assuming that he could not have been promoted to the medical director of the entire company unless you approved it. Did you have to approve that promotion?

Sydney Taurel (September 19, 2007)

THE WITNESS: I do approve promotions to vice president level.

BY MR. ALLEN:

Q. He's on the vice president level?

A. Yes.

Q. So, when he is promoted to his current position from his position when he was product team leader for Zyprexa, you had to approve that promotion?

A. That's correct.

Q. Let's see what he said to

the sales reps back in Orlando in the fall of 2000. Now, putting this in context again, Mr. Taurel, this was when Zyprexa was representing one of your growth opportunities, right, for your business, correct?

A. Zyprexa was and is an important product for the company.

Q. Well, but, we saw --

You specifically said in the 2000 annual report Zyprexa represented a growth opportunity for your company?

A. That's correct.

Q. Now, we're not going to read everything he says. Let's go down here where he says to the sales reps "Now, why don't we go on and talk about some specifics around Zyprexa, and sort of what the future looks like. And I said that Zyprexa is a very, very special molecule.

"Let's go to the first one: growing sales in the elderly. How many people, in their own lives and their own families, have been touched by Alzheimer's disease. Parents, grandparents, uncles, aunts, best friends. Yeah, so have I. Is there a more tragic illness? That illness takes what we all consider to be human and begins to erode that, month after month after month in a very progressive way. And the need for better treatment in Alzheimer's and other elderly conditions is so paramount and so key, and what you're going to see, and you'll see it with your own eyes, is that Zyprexa is an optimally suited molecule for this disorder."

Did I read that correctly?

A. That's what's written here.

Q. Was Zyprexa approved for the treatment of the elderly and Alzheimer's in October of 2000 when Dr. Breier was telling the sales reps this?

A. I do not believe that Dr. Breier is saying it was approved, neither is he telling them to talk about this indication. He was talking about planning for the development of that indication through clinical trials.

Sydney Taurel (September 19, 2007)

Q. Now, Dr. Breier is talking to the sales reps and he says, "Zyprexa is an optimally suited molecule." When something is optimally suited, that means it's the very best, doesn't it, optimal, the very best?

Sydney Taurel (September 19, 2007)

THE WITNESS: I believe taken in context, which is a large sales meeting where Dr. Breier is conveying his enthusiasm for the product that he's responsible for, he's talking about the characteristics of the molecule which might make it a good agent for Alzheimer's. And indeed we were at that point doing clinical trials to find out whether the characteristic that he's referring to and ideally suited and optimally suited were going to be indeed proven in clinical trials.

BY MR. ALLEN:

Q. Well, does he say anything about it's going to be proven in clinical trials, or is he talking directly to the sales representatives at the time of the launch in primary care in Orlando in October of 2000?

Sydney Taurel (September 19, 2007)

THE WITNESS: Dr. Breier is not the sales manager. Dr. Breier is the head of the product -- was the head of the product team, and so what he was talking about was all of the potential indications for the product. He was not giving them instructions as to what to do the next day in the field.

BY MR. ALLEN:

Q. You're saying that's what he said, but you may -- he's not a sales manager, but look what Dr. Breier says. "And there is a huge amount of business in the elderly." It looks like Dr. Breier was actually focusing on the business in the elderly, wasn't he?

Sydney Taurel (September 19, 2007)

Q. Isn't that what he's saying? He's talking about the business we can generate in the elderly, correct?

Sydney Taurel (September 19, 2007)

A. The pharmaceutical company is successful if it serves patients well,

and if it does that well, the business will come as well. And he's referring here to two things. He's talking about elderly patients, he's talking about their symptoms, he's talking about how difficult -- patients with Alzheimer's, he's talking about the symptoms and how potentially Zyprexa could help those patients, which we believed at the time. And he is saying if you do that, then the business is there, the potential sales results will be there.

Q. He's saying --

You know what, it's pretty interesting to me how you know now as you sit here today what Dr. Breier was saying other than what's on the words on the paper. You weren't at this meeting, were you?

A. I'm putting this in the context of --

Q. Sir, answer my question. Were you at this meeting?

A. I wasn't at the meeting.

Sydney Taurel (September 19, 2007)

Other than with your lawyer, have you ever read these comments by Dr. Breier in your entire life?

Sydney Taurel (September 19, 2007)

THE WITNESS: No.

Sydney Taurel (September 19, 2007)

Q. Other than have you ever listened to these comments on the audiotape?

A. No.

Q. Have you ever seen them on the video that was taken?

A. No.

Q. Okay.

But what you can say is that the audience of Dr. Breier, when these statements were made, was the sales representatives for the company. You can say that as a fact, right?

Sydney Taurel (September 19, 2007)

THE WITNESS: There were sales representatives and I'm sure

other people al from medical, from regulatory, marketing, et cetera.
BY MR. ALLEN:
Q. What y'all were trying to do right then in October of 2000, continuing to 2001, was to get doctors to prescribe Zyprexa for Alzheimer's psychosis and dementia, weren't you?
A. No.

Sydney Taurel (September 19, 2007)

402:16 THE WITNESS: Absolutely not.
BY MR. ALLEN:
Q. Absolutely not. Well, let's look at the last thing on the last page when we fade out on the tape. It says, "And, you'll be hearing from us again in February as we prepare for the upcoming National Sales Meeting in Dallas." Do
403: 1 you see that?
A. Yes.
Q. So, your company has national sales meetings, right?
A. Periodically, yes.
Q. Have you ever been to any?
A. I've been to a few.
Q. Did you go to the one in Dallas in 2001?
A. No.
Q. They took a tape of that, too. Have you ever looked at what happened down there in Dallas?
A. No.

Sydney Taurel (September 19, 2007)

404: 3 Weren't they still telling the sales representatives in the national sales meeting to promote Zyprexa for the elderly and people with Alzheimer's?

Sydney Taurel (September 19, 2007)

404:10 Q. Weren't they still doing that?

Sydney Taurel (September 19, 2007)

404:13 THE WITNESS: You have to give me evidence that they did say that.
BY MR. ALLEN:

Q. You want some evidence. Here's some evidence. It's Exhibit Number 01079.

Sydney Taurel (September 19, 2007)

404:22 Q. This is Mr. Bandick. Do you remember -- you've seen Mr. Bandick's name. He's Zyprexa brand manager.
405: 1 A. Yes.
Q. He's at the Eli Lilly National Sales Meeting, March 13, 2001. Okay? Do you see that, sir?
A. Yes.

Sydney Taurel (September 19, 2007)

405: 8 It's in Dallas, we learn that. And I want to go back -- let's go to Page 3 of what Mr. Bandick told the people back then, the sales reps at the national sales meetings. "Dollars pay the bills and boost the stock price, so let's look at dollar growth." You see that, sir?
A. Where is it?
Q. Right here. It's on the screen. I have it up on the screen. It's right in the middle of the page.
A. Okay, but I'm trying to get the context.
Q. Right there in the middle.
A. I've never seen this document before, so I would like to read
406: 1 the rest as well.
Q. Well, we don't have time. We'll just get back to the -- you want to see evidence of whether what the sales reps were being told about the elderly. I think that's what you asked for.
Do you remember a person called Martha? Do you remember a person called Martha, sir? Do you know who that is?
A. No.
Q. Do you know that patient profiles were used by your sales teams to promote Zyprexa?
A. Not at the time.

Sydney Taurel (September 19, 2007)

407: 3 Did you learn that patient profiles were used to promote Zyprexa by the sales force in September of 2007? Is that when you learned it?
A. Yes.

Sydney Taurel (September 19, 2007)

409:15 Q. The evidence will show that
16 a patient profile y'all used to promote
17 Zyprexa was Martha. Now, here's what Mr.
18 Bandick said. "What's the first thing
19 you notice about Martha? She's old.
20 That does two things. First, it
21 reinforces Zyprexa as a nursing home
22 drug. Our mission is to build" --
23 A. I'm sorry. Where are you?
24 Q. Page 13, the bottom. Right
410: 1 there at the bottom, Page 13. Right
2 there on the big screen, it's huge
3 letters.
4 You've got Page 13, sir?
5 Here, let me have it. I can give it to
6 you right there?

Sydney Taurel (September 19, 2007)

410:13 Q. It's a talk being given by
14 Mr. Bandick to the sales force.
15 A. Right. I want to see what
16 he said just before he said this, if I
17 may.
18 Q. Okay.
19 A. (Reviewing document.)
20 Q. While you're doing this,
21 sir, I'm going to ask a question. Did
22 Mr. Bandick tell the sales force, "What's
23 first thing you notice about Martha?
24 She's old. That does two things. First,
411: 1 it reinforces Zyprexa as a nursing home
2 drug. Our mission is to build a primary
3 care franchise, and let our
4 long-term...team drive the nursing home
5 business." Did I read that correctly?
6 A. Yes.
7 Q. Was Zyprexa approved as a
8 drug to treat patients in nursing
9 homes --
10 MS. GUSSACK: Objection as
11 to form.
12 BY MR. ALLEN:
13 Q. -- that had Alzheimer's and
14 dementia?

Sydney Taurel (September 19, 2007)

411:18 THE WITNESS: Zyprexa was
19 approved to treat schizophrenia
20 and bipolar mania, and those
21 indications are prevalent not only
22 in younger patients, but also in
23 older patients. It is,
24 unfortunately, a disease that you

412: 1 don't cure from and, therefore,
2 people go through old age with
3 those diseases.
4 BY MR. ALLEN:
5 Q. Well, that's funny. Look
6 what he says next. That isn't what he
7 says at the time. That's what you're
8 saying now.

Sydney Taurel (September 19, 2007)

412:11 Q. He says, "Second, it limits
12 the perception of behavioral
13 disturbances -- agitation, tension,
14 anger, hostility all show up in primary
15 care in a variety of packages."

Sydney Taurel (September 19, 2007)

412:18 Q. He doesn't say it shows up
19 in schizophrenia, does he?

Sydney Taurel (September 19, 2007)

412:23 THE WITNESS: You're on Page
24 14.

Sydney Taurel (September 19, 2007)

413: 1 MR. ALLEN: Same page.
2 BY MR. ALLEN:
3 Q. He doesn't speak --
4 As a matter of fact, he
5 doesn't speak about schizophrenia or
6 bipolar mania in any regard when he's
7 talking about this, does he? He talks
8 about it being a nursing home drug,
9 driving it to the nursing home for
10 patients with symptoms in a variety of
11 packages. Isn't that correct?
12 A. That's what he says here.

Sydney Taurel (September 19, 2007)

418: 8 Q. Do you recall a consensus
9 statement being published by the American
10 Diabetes Association after June of 2003?
11 A. I do not recall the exact
12 date, but we talked about it earlier
13 today.
14 Q. Yes, sir, you do. You
15 recall that there was a consensus
16 statement that was published, right?

17 A. Yes, I do.

Sydney Taurel (September 19, 2007)

423: 8 I'm going to give you Exhibit 03109.
9 When the consensus panel published its
10 result, it was considered at Eli Lilly to
11 be a corporate crisis, wasn't it?

Sydney Taurel (September 19, 2007)

424:13 A. This is the wording that Dr.
14 Heath is using. I would not endorse it.
15 Q. Well, Dr. Heath, he is
16 sending this e-mail to John Holcombe and
17 others. Do you know any of the people?
18 Paula Trzepacz, you said you know her.
19 She's in issues management, right?
20 A. I know --
21 MS. GUSSACK: Objection.
22 THE WITNESS: -- she's a
23 physician.
24 BY MR. ALLEN:
425: 1 Q. You knew Mr. VanDenBergh.
2 He's on the -- he's a senior manager of
3 Eli Lilly, right?
4 A. Yes. I see that he's copied
5 on this memo, yes, on this e-mail.
6 Q. Here's what Dr. Heath says.
7 "Dear all, If you are not aware at the
8 time you read this, you will soon know
9 that we have been asked by Messrs.
10 Lechleiter" -- now, what position did Mr.
11 Lechleiter hold in January of 2004?
12 A. I do not recall.
13 Q. Was he president?
14 A. No, not yet. I don't recall
15 whether he was still in charge of
16 pharmaceutical products or if he was in
17 charge of sales and marketing.
18 Q. He was on the senior
19 management team, subsequently at least
20 promoted to President and Chief Operating
21 Officer, the number two man at the
22 company, right?
23 A. Yes.
24 Q. "If you are not aware at the
426: 1 time you read this, you will soon know
2 that we have been asked by Messrs.
3 Lechleiter and Santini to gear up for a
4 major assault on Zyprexa, because of the
5 ADA consensus statement copied below.
6 This is regarded as potentially a
7 corporate-level crisis." Did I read that
8 correctly?
9 A. Yes.

Exhibit 15
Gary Tollefson, M.D.

Gary Tollefson, M.D. (Novemb[illegible]6, 2006)

11: 9 Q. Now, would you state your
10 full name for the record, please?
11 A. Gary Dennis Tollefson.

Gary Tollefson, M.D. (November 6, 2006)

13: 6 Q. Okay. And you were formerly
7 employed as an executive at Eli Lilly,
8 correct?
9 A. Correct.
10 Q. Okay. Pardon me. I'm
11 fighting off a bit of a cold today.
12 Your employment with Lilly
13 and your involvement with the drug Zyprexa is
14 going to be the focus of my questioning but
15 before I get to that I'd like to ask you some
16 questions about your background.
17 A. Sure.
18 Q. You are a medical doctor,
19 correct?
20 A. Yes.
21 Q. You also hold a Ph.D. in
22 Psychopharmacology; is that correct?
23 A. Yes.
24 Q. And I believe you went to
14: 1 undergraduate graduate, graduate school, and
2 medical school at the University of
3 Minnesota; is that correct?
4 A. That's correct.
5 Q. In what years did you receive
6 your respective degrees?
7 A. Got a bachelor's degree in
8 psychology, summa cum laude, University of
9 Minnesota, 1973. Degree in medicine,
10 University of Minnesota 1976, and a Ph.D. in
11 Psychopharmacology, 1980.
12 Q. And after finishing
13 medical school I believe you did your
14 internship at St. Paul Ramsey Medical
15 Hospital and your residency in psychiatry at
16 the University of Minnesota Hospitals in
17 Minneapolis; is that correct?
18 A. Yes, sir.
19 Q. And when did you complete your
20 residency?
21 A. Also around 1980, beginning
22 of '80.
23 Q. And I believe you're
24 board certified in psychiatry; is that
15: 1 correct?
2 A. Yes. I passed the American
3 Board of Psychiatry and Neurology exams.
4 Q. And in what year was that?
5 A. It's a good question. I'm
6 not sure that I remember. I don't recall.
7 Q. Would it have been a year or
8 two after you completed your residency, or a
9 couple years?
10 A. Probably in the very early

'80s, I suspect.
Q. Okay. And are you board certified in any specialties other than psychiatry?
A. No, sir.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Am I correct that you began working for Lilly in 1991?
A. That is correct.
Q. Okay. Can you describe your employment after you completed your medical training in 1980 up until the time you joined Eli Lilly 11 years later in 1991?
A. Well, I joined the faculty of both the University of Minnesota and the St. Paul Ramsey Medical Center as an assistant professor of psychiatry and initially had responsibility for a discipline that was called Consultation Liaison Psychiatry, as well as doing some outpatient work and research. And I did that for, approximately, five years.

And shortly thereafter, then became the Chairman of that Department of Psychiatry. Continued actively involved with teaching research and outpatient practice. And that was the case up until '91 and joining Lilly.
Q. Okay. And you left Eli Lilly in 2004; is that correct?
A. Yes, sir.
Q. What was the date that you left in 2004?
A. I believe it was April 1st.
Q. And what was your title when you left?
A. Lilly Distinguished Research Fellow and Vice President Lilly Research Laboratories.
Q. Now, at the time you left -- well, during what period of time that you were at Lilly did you have any responsibilities for Zyprexa?
A. I assumed some responsibility for Zyprexa probably towards the end of '94 into the early part of '95, somewhere in that window.
Q. Okay. And then how long did you continue to have any responsibilities for Zyprexa?
A. Up through the late fall of 2000.
Q. And what happened in late fall of 2000?
A. I no longer was in the position of Product Group President of the Neuroscience Division. Went into a different role.
Q. And what was that different

role?
A. I was for about a year a Lilly Distinguished Research Fellow I mentioned, which was a consulting role, and then became Vice President of the medical division overseeing the early phase development for new products for Neuroscience.
Q. Okay. Do you still have any professional dealings with Lilly at this time?
A. I have done occasional consulting for them.

Gary Tollefson, M.D. (November 6, 2006)

Q. You're presently on the Board of Directors of a company called Cortex, aren't you?
A. Yes.
Q. Okay. I saw in an April 7, 2006 SEC filing of Cortex which stated that you elected to take early retirement from Lilly; is that correct?
A. Correct.
Q. Is that -- and that is an accurate statement?
A. Yes.
Q. But you're not really retired?
A. Yes, I am.
Q. How many hours a week do you work?
A. I thought you asked me am I retired from Lilly? And I answered, yes, I'm retired from Lilly. Yes.
Q. Okay. But you're not really retired, are you?
A. Perhaps you'd provide me your definition of retirement.
Q. My definition of retirement is that you're not working anymore.
A. I'm retired from Eli Lilly and Company, I am working for, as you established earlier, Orexigen Incorporated as CEO and President.
Q. And is that a full-time job?
A. It is.
Q. Did anyone at Lilly encourage you to leave the company?
A. No.
Q. Okay. Before you left Lilly, were you aware that the U.S. Department of Justice was investigating allegations that Lilly illegally promoted Zyprexa for off-label uses?
A. I was not.

35:10 Q. Can you list and describe
11 briefly the various positions that you held
12 at Lilly after coming to the company in 1991?
13 A. From '91 to late '94, I was
14 an executive director, clinical
15 investigation, oversight for Prozac.
16 In late '94, early '95, became
17 the Product Team Leader for Zyprexa.
18 Continued in that role until probably
19 beginning of '99, at which time I became
20 Product Group President for the Neuroscience
21 Division, and held that through, as we
22 established earlier, the fall of 2000.
23 Q. And then what were your
24 titles after fall of 2000?
36: 1 A. As we previously said,
2 Distinguished Lilly Research Fellow and
3 Vice President Lilly Research Laboratories.
4 Q. And did you remain in that
5 position until you left in 2004?
6 A. Yes, I did.
7 Q. Okay. Between 1994 and 1999,
8 when you were the Product Team Leader for
9 Zyprexa -- well, what did that
10 role as Product Team Leader involve?
11 A. I was overseeing the global
12 clinical development and global commercial
13 planning for the molecule up to launch and
14 then in the post-approval environment as well.
15 Q. And so you would have had
16 medical people reporting to you?
17 A. Yes.
18 Q. And marketing people?
19 A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

37:21 Q. Okay. Who reported to you
22 directly regarding Zyprexa in the '94 to '99
23 time period?
24 A. I'm not sure I can recite
38: 1 everyone who reported to me.
2 Q. Okay.
3 A. But it was the senior medical
4 contributors of the team. So it would be, in
5 essence, the chief medical officer or other
6 senior medical people. So Dr. Charles
7 Beasley, Dr. Alan Breier would have been
8 involved in that way.
9
10 the head of global marketing was a gentleman,
11 Mr. James Lancaster.
12
13 oversaw implementation of different projects
14 was for a while a gentleman, Dr. Jeffrey
15 Casher, followed by Dr. Alvin Rampey.
16
17 functional homes within the product team.
18 Q. Okay. When you became
19 Product Group President in 1999, what changed
20 then in terms of what your function was?

A. So I no longer had direct responsibility for the Zyprexa Product Team. That role was taken over by Dr. Breier. The Product Group President role was overseeing the entire Neuroscience portfolio. That would include marketed products, but also products that were still in the development that had not yet been approved for marketing authorization. It had to do with the oversight of the clinical portfolio, as well as overall global commercial strategy.

Q. Okay. Between '94 and '99, how much of your time did you personally spend dealing with Zyprexa?

A. Probably 110 percent.

Q. Okay. And for the 1999 to 2000 time period, how much of your time did you spend on Zyprexa?

A. That's more difficult. Perhaps, 20 percent, guesstimate.

Q. Okay. From your perspective was there any particular person or group within your organization that was responsible for identifying any safety issues with respect to Zyprexa?

THE WITNESS: At what time frame?

MR. SUGGS: Let's talk about, let's break it up between '94 and '99 and '99-2000.

A. Well, I think the issues, it never resided in a single individual, it's a collective responsibility and obligation of the entire team.

When I was leading the team, I would say it resided, as far as maybe point people, Dr. Beasley and the chief medical officer that was Dr. Breier.

Q. Okay. And so it would be fair to say that you relied on both Dr. Beasley and Dr. Breier to keep you apprised of any potential safety issues with Zyprexa?

A. Yes.

Q. And Lilly finished conducting the clinical trials that it used to support its NDA application in 1995; is that correct?

A. The NDA was filed in '95. Typically, you know, there were clinical trials that were still ongoing at that time, and they had to be incorporated into the NDA during its review process. So there isn't a formal end point, per se. This was an ongoing process which continues today to continue to investigate and understand the molecule better.

Q. Were you involved in or did you approve the design of the Phase 3 clinical trials for Zyprexa?

A. Yes.

Q. Were you also involved in any of the Phase 1 trials of Zyprexa?

A. Most of the Phase 1 work was

done prior to my taking over the product team. There was some additional work done, it's called clinical pharmacology, that some people would designate Phase 1 that occurred during my period as product team leader. But the early exploration, quote, Phase 1 work was done principally in the latter half of the '80s, perhaps into the early '90s.

Q. Okay. Am I correct that the clinical trials that were done for Zyprexa only measured blood glucose through random blood glucose testing?

A. That was the norm for those studies that were part of the NDA, the outpatient studies. And I think there probably were clinpharm studies that might have done additional glucose analyses, but the standard protocol for the ambulatory schizophrenia trials, and I think for that matter, the inpatient studies, was to do serial random glucose.

Gary Tollefson, M.D. (November 6, 2006)

Q. Back in 1995, before Lilly submitted its NDA to the FDA, you personally reviewed the data from those studies, did you not?

THE WITNESS: What studies, may I clarify?

MR. SUGGS: The studies that were done in support of Zyprexa's new drug application.

A. I would have reviewed at least summary reports of all the studies.

Q. Okay. And when was it that you first became aware that Zyprexa might be associated with hyperglycemia and diabetes?

Gary Tollefson, M.D. (November 6, 2006)

A. I think that probably at the time of the submission there were cases of individuals that may have had hyperglycemia. And, in fact, in some of the longer term data there may have been individuals that had confirmation or new diagnosis of diabetes.

So in the sense of did anyone who was participating in a study have hyperglycemia or diabetes, it would have been during the assembly of the new drug application.

Q. Okay. Would it be fair to say that the focus of the clinical studies that were done in support of the Zyprexa new drug application were dealing with patients who had been diagnosed as schizophrenic?

Gary Tollefson, M.D. (November 6, 2006)

52:22 A. The first new drug
23 application was for schizophrenia and it
24 included, principally, individuals with
53: 1 well-diagnosed schizophrenia. But it also
2 included a smaller subset of individuals with
3 related conditions, sometimes called
4 schizoaffective disorder, schizophreniform
5 disorder. The vast majority were
6 schizophrenic.

Gary Tollefson, M.D. (November 6, 2006)

74: 2 Q. Okay. We've already had some
3 testimony from Dr. Beasley that study HGAJ
4 was the largest clinical study that was done
5 in support of the NDA; is that your
6 recollection as well?
7 A. It's the largest as far as
8 number of subjects. I think it accounted for
9 55-60 percent of the entire integrated
10 database that went into the NDA.

Gary Tollefson, M.D. (November 6, 2006)

74:16 Q. Okay. Do you recall that --
17 well, I'll represent to you we've also had
18 testimony from Dr. Beasley that in study HGAJ
19 it was found that on average, patients who use
20 Zyprexa for up to a year had 24 pounds of
21 weight gain on average. Does that square
22 with your recollection?

Gary Tollefson, M.D. (November 6, 2006)

75: 1 A. I can't speak to that. I
2 believe about 56 percent had more than a
3 7 percent increase in their body weight, and
4 I thought the mean was, approximately, five
5 kilos.
6 Q. Okay. But your recollection
7 is more than half had greater than 7 percent
8 gain in body weight, correct?
9 A. With the long-term data, yes.
10 Q. Okay. And that figure of
11 7 percent of the body weight is significant
12 because it is at that point, 7 percent, that
13 most physicians regard as clinically
14 significant, correct?
15 A. No. I think that figure is
16 used because it's an FDA definition for, my
17 understanding, a potential adverse event of
18 weight gain.
19 Q. Okay. And isn't that the
20 same as saying -- would you disagree with

Dr. Beasley and Dr. Ki[illegible] and Dr. Baker if they testified that a weight gain in excess of 7 percent was what was generally regarded as clinically significant?

Gary Tollefson, M.D. (November 6, 2006)

A. I think I'd say potentially clinically significant.

Gary Tollefson, M.D. (November 6, 2006)

Are you aware that Dr. Beasley has testified that you and he, and others, would have reviewed computer analyses of data from the HGAJ study back in June of 1995?

A. We certainly would have reviewed analyses from all the studies --

Q. Okay.

A. -- and looked at them not only individually but collectively.

Q. Okay. And so it is true as Dr. Beasley said, that you and he both would have reviewed computer printouts of data from the HGAJ study back in 1995; is that correct?

A. Amongst others.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 1605. For the record, this is a computer printout dated June 19, 1995, purporting to show Treatment-Emergent Abnormal High or Low Laboratory Values at Any Time from the HGAJ Acute Phase.

QUESTIONS BY MR. SUGGS:

Q. First, sir, do you recognize the format of this particular document?

A. Yes.

Q. Okay. And could you tell us what it is?

A. This is a so-called production mode, which is generated by the systems analysts, so it's a data output of laboratory values with patients randomization, in this case, this example, olanzapine or haloperidol, and then with a pair-wise statistical comparison made between those individual categorical lab values.

Q. Okay. And am I correct that there was an acute phase of the HGAJ study?

A. Correct.

Q. And would that have been a

relatively short-term study, six to eight weeks?
A. It was six to eight weeks. I wouldn't call that a relatively short term but six to eight weeks is -- six weeks was the duration of this study.
Q. Okay. There were other people who used Zyprexa in the context and as part of the HGAJ study for much longer periods of time, correct?
A. There was an extension that permitted more chronic administration.
Q. Okay. And in this printout showing the acute phase treatment-emergent abnormal high or low laboratory values at any time, would it be fair to say that this is purporting to show abnormal high or low laboratory values for all of the folks who
80: 1 were in the HGAJ study for the acute phase of that study?
A. Assuming that they had been randomized and taken at least one dose of study drug, yes.
Q. Okay. And if I could direct your attention to Page 11. In the middle of the page there are the results of the lab test for glucose nonfasting. Do you see where I'm at?
A. I do.
Q. It's broken out in two things, either low or high blood glucose, correct?
A. Correct.
Q. And what's done there is a comparison between olanzapine and the comparator, which in this case was Haldol, correct?
A. Yes.
Q. Okay. And what it found was that there was a statistically significant increased incidence of high glucose in the Zyprexa users as compared to the Haldol
81: 1 users, correct?
A. Yes.
Q. Okay. And we can tell that it's statistically significant by looking over at the right-hand column where there's a description of the P value, correct?
A. Yes. That refers to the statistical but not the clinical significance.
Q. Okay. And generally, it's regarded that if -- the P value is a measure of the likelihood that the difference observed is real versus just being a matter of chance, correct?
A. Relatively speaking.
Q. And there's a convention in the field of statistics that if you have a P value of .05, that means that there's a 95 percent chance that the difference that is observed is real as opposed to just being a matter of chance, correct?

A. That is correct.
Q. And there's a convention in statistics that if the P value is less than .05, then it's regarded generally and generally accepted by people in the field that that is statistically significant, correct?
A. Correct.

Gary Tollefson, M.D. (November 6, 2006)

Q. Exhibit 1604 is dated July 5, 1995, and purports to be a computer printout of Abnormal Lab Values For HGAJ All Phases. Do you recognize this document, sir?
A. It looks familiar for the formatting, yes.
Q. And does it appear to be, in fact, as I said, a printout of Abnormal Lab Values for the HGAJ Study All Phases?
A. Yes. It looks to be one HGAJ which was one of the studies in the new drug application.
Q. Okay. In fact, HGAJ, as you said before, was the largest study, correct?
A. Slightly over half the patients, yes.
Q. Okay. If I could direct your attention to Page 2, towards the bottom of the page, there is a table on that page that shows what the low limits and high limits are of the various tests that are being done, correct?
A. Correct.
Q. Okay. And at the very bottom, or not the very bottom, but second to last is a listing for nonfasting glucose, correct?
A. Yes.
Q. And it shows in the international system the low limits and high limits, correct?
A. Correct.
Q. The low limit being 2.4975 millimoles per liter and the high limit being 13.875 millimoles per liter, correct?
A. Yes.
Q. And that can be translated to -- well, that's the system, convention that used over in Europe, correct?
A. I believe it's used internationally but, yes, it's used in Europe.
Q. Okay. But here in the United States people tend to use another measuring system of blood glucose that is advocated by the American Diabetic Association, correct?
A. Right.
Q. And to convert the international system to the ADA system you multiply by 18, correct?

A. I don't have the algorithim so I can't answer that.
Q. If I represent that to you would you have any dispute with that?
A. Just that I don't know.
Q. Okay. Would you agree with me, sir, that if you take the upper limit as shown here of 13.875 millimoles per liter that translates to 247 in the ADA system?

Gary Tollefson, M.D. (November 6, 2006)

A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

Q. Dr. Tollefson, do you recall that shortly after Zyprexa was launched in October of 1996 you were accused by the FDA of making false and misleading statements about the safety of Zyprexa?

Gary Tollefson, M.D. (November 6, 2006)

A. I remember seeing a document that suggested that I may have, perhaps, overstated.
Q. Well, the FDA didn't just suggest that, they flat out said that you made false and misleading statements, didn't they?
A. I don't believe so, but I'd have to review the document.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Let me see if I can help you out here. Let me show you what's been previously marked as Plaintiff's 1169. I apologize that

Gary Tollefson, M.D. (November 6, 2006)

Q. In any event, this exhibit is a letter from Kenneth Feather, the Senior Adviser in the Division of Drug, Marketing and Advertising Communications of the FDA, to Charles Perry, Jr., Director of Pharmaceutical Communications and Compliance at Eli Lilly, and it's dated November 14, 1996.
QUESTIONS BY MR. SUGGS:
Q. Do you recall seeing this letter, sir?

A. Yes, I do.
Q. If I could direct your attention to the first page. In the first paragraph, the letter states, "This concerns a number of labeling" -- well, let me back up for a second. If the date of this is November 14, 1996, that would have been just weeks after Zyprexa was launched here in the United States; isn't that correct?
A. I believe so.
Q. Okay. Directing your attention to the first paragraph, the letter states, "This concerns a number of labeling pieces for Zyprexa identified as a multi-page detail aid, OL0026, stack grams identified as OL0077, and OL7708, a letter to the California Department of Health Sciences, assumed to be an example of similar letters to other states with an attached background, and a John Q Public letter, all submitted as required with the form FDA 2253 and also found during normal surveillance activities.
This also concerns other promotional activities such as an interactive telephone conference held on or about October 2, 1996. The Division of Drug Marketing, Advertising, and Communications, DDMAC, considers these promotional labeling pieces and promotional activities to be false and misleading and in violation of the Federal Food, Drug, and Cosmetic Act." Do you see that language, sir?
A. I do.
Q. And did Mr. Perry advise you that the FDA had written to him in early November stating that the promotional labeling pieces and promotional activities relating to Zyprexa were false and misleading?

Gary Tollefson, M.D. (November 6, 2006)

A. To my recall, Mr. Perry had mentioned to me the specific comment that was made by DDMAC on Page 4 regarding an interactive teleconference I had with stock analysts on October 2nd, 1996. I don't recall mentioning the other pieces since that would be probably a U.S. affiliate-related activity.
Q. Okay. Directing your attention to the following paragraph on Page 1, the first part of it states, "The promotional campaign, including the above identified labeling pieces and others submitted with the form 2253 is lacking an appropriate balance, thereby creating a misleading message about Zyprexa. The promotional materials emphasize efficacy data but do not provide sufficient balance relating to adverse events and cautionary

information." Do you s[redacted] that language?
A. I do.
Q. And were you advised of that by Mr. Perry?
A. I don't recall that. Again, it would not have been my area of responsibility. So it would not have been necessarily expected that he would have said that to me.

Gary Tollefson, M.D. (November 6, 2006)

Q. A physician needs to consider both the benefits and the risks of a drug before he makes the decision as to whether or not he's going to use it in his patient, correct?
A. Correct.
Q. And here in this letter to the FDA, the FDA was saying the promotional materials emphasize efficacy data but do not provide sufficient balance relating to adverse events and cautionary information, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. That is what the sentence says.
Q. And when someone does a risk/benefit analysis, what they do is they balance the risks with the benefits, correct?
A. Correct.
Q. Okay. And what the FDA was saying here was that the information you were giving was not balanced, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. It would appear that there were some materials being used where that balance wasn't optimal.
Q. Okay. If I could direct your attention to the fourth page, on this page and the following page are some items that the FDA objected to that involved you in particular, correct?
A. Correct.
Q. Okay. And at the top of the page they note that there was an interactive teleconference held on or about October 2, 1996, by Dr. Gary D. Tollefson, Vice President of Lilly Research Laboratories, correct?
A. Correct.
Q. And who were the other participants on that teleconference?

A. This was a teleconference with a number of different investors or prospective investors in the company. These were not healthcare providers.
Q. And these teleconferences that you had with those investors were ultimately written about in various press articles, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. I do not know whether they were or were not. It wouldn't be a matter of routine to do that.
Q. They noted, the FDA noted that there were about six items that they characterized you as being misleading, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. Not all of them are ascribed to being misleading. Some of them in the eyes of DDMAC were.
Q. Well, at the top of the section on Page 4 it says, "The interactive teleconference held on or about October 2, 1996, by Dr. Gary D. Tollefson, Vice President of Lilly Research Laboratories is misleading in the following particulars," correct?
A. That's what it says.
Q. And then following that there is a listing of six different items, correct?
A. That's correct.
Q. And I'm not going to go through all six of them, I'm not going to take the time to do that, but there are a couple I'd like to discuss. The first is Item 1. It states, "Dr. Tollefson states that the therapeutic effects of Zyprexa are maintained over at least one year. The approved labeling states the effectiveness of the product was only established in short-term six week studies. Therefore, for any use over six weeks, the physician should periodically reevaluate the long-term effectiveness of Zyprexa. However, this cautionary information for the indication is never presented in the teleconference." Did I read that correctly?
A. You did.
Q. And am I correct that the labeling that came out when the drug came on the market noted that the effectiveness of the product was only established in short-term six week studies?
A. The approved labeling at the time of launch, that's correct.

Q. And are you aware, sir, now that there are a number of studies which have concluded that Zyprexa is no more effective than first generation antipsychotics that cost about one tenth of what Zyprexa costs?

Gary Tollefson, M.D. (November 6, 2006)

105:23 A. I would disagree with that vehemently.
106: 1 Q. Are you saying there are no such studies?
A. I'm not saying there are no such studies, I'm saying that the burden of clinical research and, I think, the vast majority of clinicians believe that the second generation agents do offer advantages over the first generation counterparts.

Gary Tollefson, M.D. (November 6, 2006)

107:13 Q. If I could direct your attention to Item 6 -- pardon me, Item 5, in that portion of the letter the FDA stated, "When asked a question about weight gain, Dr. Tollefson's response misleadingly turned an adverse event into a therapeutic benefit. He states "So we went back and analyzed our data and saw that the vast majority of weight gain reported initially as an adverse event, in fact, was weight gain occurring in patients who had baseline before starting treatment, had been
108: 1 below their ideal body weight. So we really look at this with the majority of patients as being part of a therapeutic recovery rather than an adverse event. And that data, I think, is fairly compelling because it was included in our labeling," emphasis added. And noting that the FDA has put in bold font some of that -- what I just read, correct?
A. Correct.
Q. Okay. Then they went on to say, "The information on weight gain was indeed included in the approved labeling but as an adverse event, not a therapeutic benefit. Since the product was approved at the time of this teleconference, Dr. Tollefson knew or should have known what information the approved labeling contained and in what section it appeared. His statements were therefore, false and misleading." Did I read that correctly?
A. You read it correct.
Q. And after the FDA came out with this letter stating that you made false and misleading statements, were you punished
109: 1 in any way by Lilly after that?

Gary Tollefson, M.D. (November 6, 2006)

109: 4 A. First of all, this was a
5 teleconference, as you pointed out, with
6 investors, not with health care prescribers.
7 So I was not aware that some of the same
8 restrictions that you might use with health
9 care providers in a continuing medical
10 education forum would be applied here. So I
11 was educated that those same standards might
12 well apply in investor conferences, as well.
13 Subsequently, I did hundreds of continuing
14 medical education conferences and never
15 received any kind of critique from the FDA.
16 So was I punished? No. Was I educated
17 regarding investor conferencing? Yes. Did I
18 repeat it? No.

Gary Tollefson, M.D. (November 6, 2006)

111:22 Q. Okay. Would it be fair to
23 say that Lilly wanted Zyprexa to be a
24 blockbuster drug?

Gary Tollefson, M.D. (November 6, 2006)

112: 3 A. I don't think that anyone
4 wants a blockbuster drug. I think one wants
5 a drug that's going to benefit patients and
6 addressed unmet medical needs. To what
7 degree it does that it may or may not be
8 economically successful.
9 Q. Well, you wanted -- it was
10 the strategic intent of Lilly to have Zyprexa
11 be the largest selling psychiatric drug in
12 history; isn't that correct?
13 A. If the drug lived up to its
14 potential in delivering benefits for patients,
15 it had that possibility. So that was
16 certainly an ambitious goal but one that was
17 achievable.
18 Q. In fact, it was your intent
19 that Zyprexa would be the largest selling
20 psychiatric drug in history as early as 1997;
21 is that correct?
22 A. We definitely tried to do
23 clinical studies to demonstrate where Zyprexa
24 was beneficial in the treatment of psychosis,
113: 1 and it was then up to prescribers as to
2 whether or not they wanted to use the drug
3 and as to whether it became ultimately an
4 economic success or not.

Gary Tollefson, M.D. (November 6, 2006)

113: 9 MR. SUGGS: Let me hand you

what has been previously marked as Zyprexa MDL Plaintiff's Exhibit 6100.

For the record, this is a sixty-four page document, appears to be a PowerPoint presentation. It has a title on the first page entitled, "Zyprexa Product Team 4 Column Summary." Then below that it has the name Gary D. Tollefson, Vice President Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana.

QUESTIONS BY MR. ALLEN:

Q. Do you recognize this document, sir?

A. I do.

Q. And what is it?

A. It's an Annual Strategic Planning Exercise that each and every product at Lilly went through.

Q. Okay. And to whom would this be presented?

A. It was presented to the head of the product group area. At that time it was an individual named John Lechleiter.

Q. Okay. And did you report to John Lechleiter?

A. Let me double check the dates just so I make sure I'm characterizing this right.

Gary Tollefson, M.D. (November 6, 2006)

Q. On Page 37 there's a reference year-to-date October '97. And I was wondering if that would help you place this in time.

A. Yeah, it looks like it was probably around, as you said, '97/'98. And it's about the time, I think, that Dr. Lechleiter took over responsibility for the Pharmaceutical Product Group. So I'm thinking that that's probably -- his staff is where this document was presented.

Q. And would he have been present at that meeting, also?

A. Yes, I would imagine.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Getting back to Exhibit 6100. I believe you said you would have presented this at an annual meeting which would have been attended by Mr. Lechleiter and others, correct?

A. Correct.

Q. And what was the purpose of that annual meeting?

17 A. This w reviewing a proposed
18 product strategy and summary for the upcoming
19 business year.

Gary Tollefson, M.D. (November 6, 2006)

119: 3 Q. Okay. And if, indeed, this
4 was prepared sometime in '97, and we're both
5 assuming that it was; is that correct?
6 A. Give or take a year, I'm not
7 sure.
8 Q. Okay. It would have been
9 about a year or so after Zyprexa was on the
10 market, correct?
11 A. It appears that way.

Gary Tollefson, M.D. (November 6, 2006)

119:22 Q. Directing your attention to
23 Page 7. The title on this page is "Top 15
24 Neuroleptic Products Worldwide, MAT, Q2/97."

Gary Tollefson, M.D. (November 6, 2006)

120: 1 Is that correct?
2 A. Correct.
3 Q. And I believe you said that
4 the term "neuroleptic" is a synonym for
5 antipsychotic, correct?
6 A. Yeah. It usually refers to
7 the first generation antipsychotics.

Gary Tollefson, M.D. (November 6, 2006)

122: 6 Q. Okay. And if I could direct
7 your attention to Page 18, there's a chart
8 on that page entitled, "Disease State
9 Prioritization." Is that correct?
10 A. Correct.
11 Q. And at this point in time in
12 1997, Zyprexa was only indicated for the
13 treatment of schizophrenia, correct?

Gary Tollefson, M.D. (November 6, 2006)

122:16 A. That was the only currently,
17 or then approved indication. We were
18 exploring additional ones at that time.
19 Q. The ones you were exploring,
20 are those the ones listed in the box A on the
21 left-hand side?
22 A. "A" would indicate ones that
23 were candidates to be explored for a --

highest priority to be explored for a new indication.
Q. Okay. And those as listed here were bipolar disorder, dementia with psychosis, depression with psychotic features, dysthymia, PD with treatment-associated psychosis, schizoaffective schizophrenia, and unipolar depression, correct?
A. Correct.
Q. What's dysthymia?
A. It's a chronic low-grade depression that's not of sufficient severity to be called a major depression. So it's a low-grade depression that tends to be chronic.
Q. And what's PD?
A. This is Parkinson's Disease.

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at all. Did you become aware of efforts by the sales force to promote Zyprexa for treatment of depression and dementia associated with -- pardon me -- dementia with psychosis?

Gary Tollefson, M.D. (November 6, 2006)

A. No, I wasn't aware of that because those were not approved indications. There would be no reason to do that.
Q. If, in fact, Zyprexa was promoted for depression and dementia, or any other diseases that were not approved indications, that would be wrong, correct?

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A. I think within the confines of the Washington Legal Foundation opinion that said if a company was pursuing an indication and a physician were to inquire or have interest, that there could -- peer-reviewed materials could be shared. So in that context I believe it was acceptable. Outside of the WLF boundaries it would be inappropriate.
Q. So if a salesman approached a physician and tried to promote the use of Zyprexa without first being asked questions about the disease, if a salesman went and actively promoted Zyprexa for the treatment of diseases other than schizophrenia and later the acute manic phase of bipolar disorder which was a later indication, then that would be inappropriate, correct?

A. Yeah. I believe that they could disseminate previously approved reprints if they had received approval for dissemination, but outside of approved reprints then they could not, you're correct.
Q. Okay. If I could direct your attention to Page 34.
A. I have it.
Q. Okay. The title on that page is Strategic Intent. Zyprexa will be the world's No. 1 neuroscience pharmaceutical in history," correct?
A. Yes.
Q. Was that a strategic intent that had been developed by you or was it the consensus that that should be the strategic intent?
A. That was the strategic intent of the Marketing group.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Do you recall that by 2000 the price for Zyprexa was, approximately, $10 per 10-milligram pill?

Gary Tollefson, M.D. (November 6, 2006)

A. I would have said more around $8, but ballpark.
Q. Did there come a time that you recall that Zyprexa did reach a price of $10 a pill?
A. I don't recall that. It's possible.
Q. You just don't know for sure one way or the other?
A. Depends on, you know, how many pills you're taking.
Q. What kind of discount you can get and so forth?
A. I mean, there are a lot of variables but that's probably in the ballpark.
Q. Okay. You saw Zyprexa as a profound corporate opportunity, correct?
A. I saw it as a profound opportunity for patients and, in turn, a profound corporate opportunity as well.
Q. Okay. If I could direct your attention to the last physical page. Mine

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Gary Tollefson, M.D. (November 6, 2006)

Q. There's a summary on that page; is that correct?
A. Correct.

Q. And several bullet points?
A. Um-hum.
Q. And one of those bullet points is "Zyprexa is a profound corporate opportunity," correct?
A. Correct.
Q. And this was your presentation to your superiors, correct?
A. That's correct.
Q. Okay. Right below that is a bullet point that says "bipolar is an opportunity equal to our top NCEs." What does that stand for?
A. NCEs? New chemical entities. This would be drugs that are in development but not yet approved by a regulatory agency.
Q. Okay. And so were you saying there that if you could expand Zyprexa into treatment of bipolar disorder that that would be an opportunity that would be equal for
137: Zyprexa, that that would be an opportunity that was equal to any of the other drugs that Lilly was currently investigating?

Gary Tollefson, M.D. (November 6, 2006)

137: A. At this point we'd already initiated significant numbers of trials to pursue an indication in bipolar disorder. So this is meant to say that if we can get the indication in bipolar disorder that the value, the economic value there is equal to other drugs being developed.
Q. And Zyprexa was later approved for the acute manic phase of bipolar disorder; is that correct?
A. Both acute and maintenance.
Q. Okay. The acute portion indication was received in, what -- 2000?
A. I don't recall the exact year. That sounds directionally correct.
Q. Okay. And the maintenance indication didn't come about until January of 2004; is that correct?
A. I believe so.

Gary Tollefson, M.D. (November 6, 2006)

138: MR. SUGGS: I'm going to hand you what's been previously marked as Plaintiff's Exhibit 8479.
For the record, this is a two-page document entitled "Zyprexa Primary Care Strategy and Implementation Overview."
I will represent to you, sir, that the database that is -- that Lilly has provided us with ,the production of documents indicates

that this document was generated in August of 2000.

Gary Tollefson, M.D. (November 6, 2006)

Q. And at that point in time, were you still the Product Group President of Zyprexa?
A. Yes. I think I was probably in the final 60 days or so, but I was indeed.
Q. Okay. And do you remember the exact date that you stopped being the Product Group President?
A. No. I believe it was in October of 2000.
Q. Okay. Late in the month? Early in the month?
A. I don't know.
Q. Who succeeded you?
A. Bert VanDenBergh.
Q. Okay. If I could direct your attention to the first paragraph of this document, it's a paragraph referring to background that says, "Following several months of study by the Lilly U.S.A. Zyprexa Brand Team, the affiliate approved the recommendation that Lilly actively promote Zyprexa to selected current primary care prescriber targets. Key decisions included: The launch will occur in October 2000, promotion will be handled via the Primary Care-Neuroscience sales sleeve, 510 reps, and funding in 2000 would be incremental to existing brand opex." Do you see what I'm referring to, sir?
A. I do.
Q. And would you have had any part in approving that recommendation by the Zyprexa Brand Team to actively promote Zyprexa to primary care prescribers?
A. No, sir.
Q. Were you aware of this? Were you informed of this?
A. Yes, sir.
Q. Who was it that informed you of this?
A. I don't recall. I think -- I'm thinking it probably would have been -- this is 2000 -- Mr. Santini, who was the operational director of the U.S. Affiliate or President of the U.S. Affiliate.
Q. Do you recall when it was that he would have advised you of this?
A. I do not.
Q. If I could drop your attention -- get you to direct your attention down to the paragraph entitled "Challenges." It states: "Most PCPs currently prescribe a low volume of antipsychotics and mood stabilizers. Many PCPs," again, PCPs is

referring to primary c[redacted] physicians, would you agree?
A. Yes.
Q. Okay. It states, "Many PCPs will refer patients in need of psychotropic treatment to a specialist rather than treat that patient. Key barriers to uptake include PCPs' lack of training in this category, limited time with patients, and an aversion to perceived risk. Zyprexa's primary indications -- schizophrenia and bipolar -- are not viewed as PCP-treated conditions, so, there's not a specific indication for Lilly reps to promote in the PCP segment." Do you see that language, sir?
A. I do.
Q. And did you have any discussion with the people who were advocating marketing to PCPs regarding those challenges?

Gary Tollefson, M.D. (November 6, 2006)

A. I didn't have any discussions. I mean, the page you've given me here suggests that there are a small subgroup of individuals referred to as top deciles, PCPs, who currently were writing a large number of these prescriptions and they would appear to be the target that they're talking about.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay.
Sir, do you recall that by at least late 1999, Lilly recognized that olanzapine-associated weight gain and hyperglycemia were a major threat to the long-term success of Zyprexa?
A. I would say that I was aware that there was a perception by -- being spun by a lot of our competitors in the absence of an efficacy story that was concerning to people at Lilly.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Let me show you what has been previously marked as Plaintiff's Exhibit 8262.
For the record, this is an e-mail chain. The very top one on the first page is dated November 10, 1999, from Charles Beasley to Norma Kim Ascroft and Anna Thornton with a copy to John Krueger but there are

preceding e-mails in time.

Gary Tollefson, M.D. (November 6, 2006)

Q. And do you recognize this e-mail, sir?
A. Take a moment to look at it.
Q. Sure.
A. I do recognize it.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. And how is it -- when is the last time you saw this document?
A. I probably -- I recall seeing this during discussions with counsel that we talked about earlier. And then, of course, when it originally came out, I was one of the recipients of part of this string that, from Dr. Breier on November 9, 1999, has me as a recipient.
Q. Okay. You're referring to the e-mail that begins at the bottom of Page 1 --
A. That's correct.
Q. -- and continues on to Page 2?
A. Yes, sir.
Q. That's the one I really want to talk with you about the e-mail from Alan Breier. At this point in time, November of '99, did Alan Breier report directly to you?
A. Yes.
Q. And he was writing to Charles Beasley and a long list of other folks, correct?
A. That's correct.
Q. And did Charles Beasley also report directly to you at that time?
A. I don't think so, but I don't recall. I don't believe during that time. There was a period prior where we did and a period after where we did. I'm not 100 percent sure during this period of time, but I think not.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. You're included in the "to" list, correct?
A. Yes.
Q. Okay. And then there's a "cc" list that includes Norma Kim Ascroft, do you know who that is?
A. She was a clinical research assistant on the team. So she was working in a support role for the physicians on the team

at that point, I belie[illegible] She also had a regulatory assignment that predated that. But I think probably at this stage she was in a support position for the physicians.

Q. Okay. And also on the cc list was Alan Breier to himself, and then also John Lechleiter, correct?

A. Correct.

Q. And remind me again what was his title at that time?

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vice president in charge of the pharmaceutical product group, or area.

Q. Okay. So it's fair to say that Alan Breier's e-mail went to some pretty high-level executives of the company, yourself included, along with Dr. Lechleiter, correct?

A. Correct.

Q. Okay. And in the first sentence of his e-mail Dr. Breier says, "Olanzapine-associated weight gain and possible hyperglycemia is a major threat to the long-term success of this critically important molecule." Did I read that correctly?

A. Yes, you did.

Q. And for how long had that been regarded to be the case?

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A. I think probably that was a fairly contemporary analysis on the part of Dr. Breier because of a lot of the counter-marketing that was going on, that

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being by drugs that were in competition with Zyprexa.

Physicians were, at that point, hearing a lot of negative discussion. Back to our discussion on the risk/benefit, they were hearing only about the risk from our competitors. And I think at that point that was perceived to be a misrepresentation of the data and a threat in Dr. Breier's eyes.

Q. Is it your recollection that this competitive information that was coming out had been a fairly recent occurrence at that point?

A. I think the definition of it as a threat, yes.

Gary Tollefson, M.D. (November 6, 2006)

Q. Dr. Br[illegible]r went on to say, "In addition, it could be argued that Eli Lilly, with its strengths in neuroscience, metabolism, endocrinology, and diabetology, is better positioned than any other institution to elucidate the mechanisms and develop treatments for this side effect." Did I read that correctly?
A. Yes.
Q. And that's referring to the fact that Eli Lilly had a long history of involvement with diabetes drugs, correct?
A. That is correct.
Q. Okay. And the side effect that's being referred to there is the drug-associated weight gain and possible hyperglycemia; is that correct?
A. I read this to mean that the side effect was the weight gain.
Q. Okay. Well, he also --
A. I'm saying you could interpret it, I suppose, either way. I read it to mean he says singular side effect, I assume that to be the weight gain. Then he refers to a second side effect, possible hyperglycemia.
Q. Okay. Diabetologists are -- deal with the treatment of diabetes, correct?
A. That's correct.
Q. And he does list Lilly as having expertise -- strength, rather, in diabetology, correct?
A. That's correct.
Q. And, in fact, Lilly had been a marketer of diabetic drugs for decades at that point, correct?
A. It was one of the leading companies in providing insulin and related products for people suffering from diabetes, you are correct.
Q. Okay. And Dr. Breier goes on to say, "Thus, we have formed a cross-functional action team to meet these challenges. Success of this effort will contribute to securing the future of olanzapine and the financial health of our company and likely spur the development of next generation antipsychotic drugs, i.e., olanzapine without the weight gain and drugs for obesity." Did I read that correctly?
A. Yes.

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Q. Okay. In the following paragraph, in about the -- he refers to a meeting that's going to be occurring on November 23, 1999. Do you see that?
A. I do.
Q. And then he says, "The purpose of this meeting is for the executive

steering committee composed of Alan Breier, Jose Caro, Richard Demarchi, Chris Fibeger, Steve Paul, Greg Probst and Gary Tollefson to review the ongoing work and provide guidance for the scope and direction for future activities." Did I read that correctly?

A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. And how long did this executive steering committee -- let me back up a second.

How long did this cross-functional action team remain in existence?

A. My recollection is there were several meetings. So, probably over several months to lay out some suggested strategic interventions types of studies, further research that could be done.

Q. Okay. And is it your recollection that that is -- the length of its life was several months?

A. Yeah. I mean, it was charged again with coming up with strategic recommendations, and then the team was charged to implement the recommendations. So a short half-life was anticipated for this group.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. In Item B of his background he says "Two regulatory agencies, EMEA and Canada, have proactively asked questions about hyperglycemia and Zyprexa." Do you see that reference?

A. I do.

Q. And the EMEA is the European functional equivalent of the FDA here in the U.S; is that correct?

A. Correct.

Q. Okay. And, in fact, by this point in time, November of 1999, EMEA had already required FDA -- pardon me -- had already required Lilly to include language about hyperglycemia and diabetes in the special precautions and special warnings section of the European label; isn't that correct?

A. Yeah. I believe they had requested discussion that in very rare instances there had been an association observed but did not address whether they thought it was causally related.

Q. That language about hyperglycemia and diabetes was in the special warnings and special precautions section of

the European labeling, was it not?
A. That is correct.
Q. And you were aware of that, were you not?
A. Yes. As was the FDA.
Q. How did you become aware of that?
A. I'm sure that it was communicated both from our regulatory colleagues in their function and from the Zyprexa team, both.
Q. Okay. In Item D it's noted "That hyperglycemia and DKA are both in the U.S. label." DKA refers to diabetic ketoacidosis; is that correct?
A. Yes.
Q. And hyperglycemia and DKA were both mentioned in the adverse reactions section of the label, were they not?

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Q. My question was: There were no references to hyperglycemia or diabetic ketoacidosis in either the precautions or the warnings section of the U.S. label, correct?
A. Just in the adverse events section.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Then there's reference in Mr. Muniz's e-mail to short-term action plan. And one of those elements of the action plan was "to discuss Zyprexa label at a GPLC session and evaluate potential proactive regulatory strategies." Is that correct?
A. That's correct.
Q. Okay. And the GPLC stands for the Global Product Labeling Committee, does it not?
A. Yes.
Q. And were you a member of that committee?
A. I was on it briefly, although I don't remember the exact years. I think it was probably around 2002, 2003. I was probably on it for about a year, year and-a-half.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Well, as we saw before in Mr. Breier's e-mail on November 9th, 1999, he said that olanzapine-associated weight gain and possible hyperglycemia is a major

threat to the long-term success of this critically important molecule. Do you recall that?
A. I recall reading that.
Q. And would it be fair to say that the critical nature of Zyprexa to Lilly was becoming even more established in light of the fact that the patent on Prozac was going to be expiring?

Gary Tollefson, M.D. (November 6, 2006)

A. Well, by my recollection in 1999 that was presumed to be years away. So I don't think it was something being considered, at least not that I was aware of.
Q. Are you familiar with a term called Year X?
A. I am.
Q. And what is Year X?
A. Year X was the year that Prozac was anticipated to go off-patent.
Q. And what year was that?
A. 2004, I believe.
Q. In fact, when did it, actually, go off-patent?
A. I believe it went off in 2000.

Gary Tollefson, M.D. (November 6, 2006)

Am I correct that for some period of time you and other executives had thought that Prozac was going to be going off patent in 2004 but then ultimately it went off patent several years earlier than you had originally anticipated?
A. My recollection is that the patent was set to expire, I believe it was in 2004. There subsequently was some litigation and an appeal of the lower court rulings, and it overturned the patent unexpectedly, and I thought that was in 2000 or around that time.
Q. Okay. And so although the company had been planning on Year X for some -- well, let me make sure I get this straight.
Had Lilly been planning for the expiration of the patent on Prozac?

Gary Tollefson, M.D. (November 6, 2006)

A. Again, I'm not sure what you mean by "planning for it." It was something that people were aware of. There were significant efforts going on to bring forth a new generation of improved antidepressant

175: 1 agents that would be successors in the
2 marketplace. So in that sense there was
3 certainly preparation.
4 Q. It would be fair to say that
5 for some period of time the expiration of the
6 patent on Prozac was sort of looming out
7 there on the horizon. Would that be fair to
8 say?

Gary Tollefson, M.D. (November 6, 2006)

175:11 A. People were aware of when it
12 was anticipated to expire.
13 Q. Okay. And Lilly was -- had
14 the mindset that to deal with that they
15 needed to do something to help bring in more
16 revenue because sales of Prozac would, at
17 least dollar sales of Prozac, would decline
18 after it went off patent, correct?

Gary Tollefson, M.D. (November 6, 2006)

175:21 A. Well, typically, when a
22 branded product goes off, a patent is no
23 longer protected like that, that there is a
24 varying degree of generic substitution or
176: 1 other product substitution. So there's some
2 attrition or erosion of revenue. How fast,
3 you know, no one really knew what to expect
4 because there wasn't a very good model. But,
5 yeah, it was expected to go down, not go up.
6 Q. Okay. And then what happened
7 it was sometime in 2000, what Lilly thought
8 was going to be happening sometime, years in
9 the future, at least a couple years in the
10 future, got suddenly dumped in your lap when
11 the patent got overturned by a court appeal;
12 is that correct?
13 A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

176:16 Q. Can you recall more,
17 specifically, when in 2000 that occurred?
18 A. No. I think it was
19 probably summer or fall, but I don't recall.
20 Q. Summer or fall of 2000, okay.
21 And do you recall who it was that was
22 contesting the patent?
23 A. Not specifically. I believe
24 it was a consortium of several generic
177: 1 manufacturers.
2 Q. Okay. You said that earlier
3 that you probably had some interaction with
4 John Lechleiter about this issue of
5 hyperglycemia and Zyprexa. Do you recall how
6 often you would have had such communications

with him?
A. We met at least weekly. I would expect it was a topic that was discussed to some degree probably on a regular recurring basis.
Q. Okay. Was there a regularly established meeting that you would have with Mr. Lechleiter?
A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

178:
Q. How long would these meetings last?
A. Usually, an hour, hour and-a-half.

Gary Tollefson, M.D. (November 6, 2006)

179:
Q. Do you recognize this document, sir?
A. I don't recall it specifically, no. But as you've said, I was copied on it, so I'm sure I've seen it.
Q. And you don't have any basis to dispute that you would have received it, do you?
A. No.
Q. We've talked about Alan Breier and some of the other individuals who are listed on here, but there are some new names here, at least new for this deposition.
A. Um-hum.
Q. Can you tell us who Gerhard Mayr was and what his function was in the company?
A. He was the No. 1 person for Global Sales and Marketing.
Q. Okay. And who was Gino Santini, and what was his role in the
180:
corporation?
A. I believe he was head of the U.S. operation.
Q. And who was Lorenzo Tallarigo?
A. He was in charge -- he had, I believe, responsibility for sales and marketing in Eastern Europe and the Mediterranean region.
Q. And who is Albertus VanDenBergh?
A. He was in charge of the European, Western European operations.
Q. Okay. And then on the cc list we've talked about Alan Breier, and you, and Mr. Lechleiter, but there's another name there, Roland Powell; who was he?
A. He was in charge of European marketing for Zyprexa.

Q. Okay. And the subject of this e-mail is olanzapine-associated weight changes, correct?
A. Yes.
Q. And the first sentence says, "John asked me to overview the topic of olanzapine-associated weight changes."
Was the John there referring to John Lechleiter?
A. I would imagine.
Q. Okay. He went on to say, "I want to emphasize to you that OWC," which stands for olanzapine-associated weight changes, "has been and continues to be a top priority for the Zyprexa Product Team. Although it is a significant issue for us, perhaps our only major clinical Achilles heel, and our competitors have robustly focused on it, reminiscent of anxiety and" something's blanked out, "the fact is Zyprexa offers the best combination of efficacy, safety, and ease of use, of any available treatment for psychosis and acute mania."
Do you see that language, sir?
A. Yes.
Q. Did you also regard olanzapine-associated weight change as, perhaps, your only major clinical Achilles heel?
A. I think it was a leading adverse event and probably the one of greatest concern for the largest number of people receiving Zyprexa.
Q. Okay. Dr. Breier goes on to state, "The most critical and immediate issue is to keep the focus where it belongs. Superior treatment and outcome -- an arena where we have no peer." Do you see that language, sir?
A. I do.
Q. For the period of time that you were involved with Zyprexa, would it be fair to say that Lilly consistently took the position that Zyprexa had superior efficacy as compared to other antipsychotic drugs?

Gary Tollefson, M.D. (November 6, 2006)

A. I think the position was that there was clinical data that we had generated that demonstrated advantages of olanzapine that other drugs had not yet demonstrated and that differentiated it from other existing molecules save, perhaps, clozapine or Clozaril, a fairly unique agent.

Gary Tollefson, M.D. (November 6, 2006)

183:23 Q. Okay. The next section of
24 Dr. Breier's e-mail is headed up Market
184: 1 Research. And he has a number of bullet
2 points below that, correct?
3 A. Yes.
4 Q. And about the fifth one down
5 he says, "Outliers are the main concern for
6 physicians; 20-pound increase is viewed as
7 threshold for concern." Do you see that
8 reference?
9 A. I see the comment there, yes.
10 Q. Then he goes on to say,
11 "Fact: Two-thirds of olanzapine-treated
12 patients gain less than 20 pounds." Do you
13 see that?
14 A. Yes.
15 Q. And the converse of that is
16 about a third gained more than 20 pounds,
17 correct, although that's not stated in his
18 e-mail?

Gary Tollefson, M.D. (November 6, 2006)

184:21 A. You could infer that from
22 what he said.
23 Q. Okay. And you can infer that
24 from what you know about the characteristics
185: 1 of the drug, correct?
2 A. I mean, I don't -- I don't
3 recall the data being cut specifically at
4 20 pounds, so I can't speak to that. But
5 there -- there are probably on the order of
6 20 to 25 percent of people that would gain on
7 the order of, you know, five or more kilos.
8 Q. And, in fact, with study
9 HGAJ, the average weight gain for people who
10 used the drug for up to 12 months was
11 24 pounds, correct?
12 A. That is true, although
13 extraordinarily few discontinued the
14 treatment, but I believe that's true of their
15 weight gain.
16 Q. And that's what I was asking.
17 A. Yes.
18 Q. Okay. In his next bulleted
19 item says, "Olanzapine is viewed to have more
20 associated weight gain than risperidone,
21 Seroquel and traditional neuroleptics." Did
22 I read that correctly?
23 A. You read it correctly, yes.
24 Q. And risperidone and Seroquel
186: 1 are both second generation atypical
2 antipsychotics, correct?
3 A. Yes.
4 Q. And then Dr. Breier goes on
5 to say, "Fact: The order of weight gain
6 among antipsychotics is clozapine greater
7 than olanzapine, greater that Seroquel,
8 greater than risperidone, greater than
9 traditional neuroleptics.
10 A. That's what he says. I

wouldn't agree with it [illegible]0 percent but that is what he's stating.
Q. At least according to Dr. Breier, in fact, olanzapine did have more associated weight gain than risperidone, Seroquel, and traditional neuroleptics, correct?

Gary Tollefson, M.D. (November 6, 2006)

186:20 A. Yes.
Q. Okay. And then dropping down a couple of bullet points he states, "Physicians view EPS as something they can address with dose adjustment but not OWC."

Gary Tollefson, M.D. (November 6, 2006)

187: 2 A. Yes.
Q. And EPS refers to extrapyramidal symptoms; is that correct? Did I pronounce that correctly?
A. Extrapyramidal side effects or symptoms.
Q. And what are those?
A. There are several. These are classic side effects associated with the first generation agents. They range from a drug-induced Parkinsonism, much like if you've seen Michael Fox doing some of his advertisement for the foundation, characterized by involuntary movements, difficulty initiating movement, unstable gait. They can go to what are called acute dystonias, which are muscular contractions that cause significant disfiguration. The neck pulling back, for example, in spasm. Or the most severe and most concerning, which is a long-term irreversible one, tardive dyskinesia, which is a persistent involuntary movement, often of the jaw as if somebody's
188: 1 chewing gum or sticking their tongue out in public. These are movements of the oral facial muscles that an individual cannot control; they're involuntary and disabling.
Q. Okay. And Dr. Breier was saying in his e-mail that physicians view that cluster of symptoms or syndromes as something that they can address by adjusting the dose of the drug but they didn't think that dose adjustment would work with olanzapine weight gain, correct? At least that's what he's saying?

Gary Tollefson, M.D. (November 6, 2006)

188:15 A. I think he's inferring that

with regards to the EPS. I don't know if he's saying here that physicians do not believe they can address it with dose or he doesn't believe they can be addressed with dose. At that time, my recollection is that there was not a clear relationship between those individuals who did gain large amounts of weight and the dose that they were on.

Q. Okay. Well, in fact, that's when he goes on to say in his e-mail, "In fact, OWC is not dose dependent," correct?

A. Based on the data at that point as I understood it.

Q. Two questions: No. 1, I want to make sure I understand what Dr. Breier was saying here. Was it your understanding that Dr. Breier was saying that physicians thought that they could, perhaps, deal with EPS by adjusting the dosage but that physicians thought that they could not deal with weight gain by reducing the dosage?

Gary Tollefson, M.D. (November 6, 2006)

A. I think that's partially correct. I think the inference here is that physicians believe that with lower doses of these first generation agents that they could lower, either the risk or the severity of EPS, but they may not have perceived that they could do the same thing when it came to associated weight gain.

Q. Okay. And as we noted before, Dr. Breier then goes on to say, "Fact: OWC," the weight gain, "is not dose dependent."

And when I directed your attention to that language before I thought you said based on the data that was available at that time that was true. Did anything change? Has the data changed?

A. I'm not aware of that.

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Q. Okay. So as far as you know sitting here today, the data indicates that weight gain with Zyprexa is not dose dependent, correct?

A. The burden of literature data that I'm familiar with does not show a clear relationship between dose and eventual weight gained.

Q. Okay. And his next bullet point was "Physicians want more data." Correct?

A. Physicians always want more data, that's their nature.

Gary Tollefson, M.D. (November 6, 2006)

Q. Well, in fact, physicians want more data because they use that data to make the risk/benefit analysis that they need to make every time they prescribe a drug, correct?
A. I think that that's correct.
Q. So the more data they can have the better physicians like it, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. Assuming that it's reputable data and valid data.
Q. Okay. And physicians want to know not only about efficacy data, how well a drug works, they also want to know about the risks that are associated with the drug, correct?
A. The nature of the risks, what to do about managing the risks, putting them in perspective, yes, I would agree.

Gary Tollefson, M.D. (November 6, 2006)

Q. Now there's a phrase in the next bullet point I want you to explain to us what it is. It refers to blanket detailing. What is blanket detailing?
A. I'm not a marketing expert and I would just be guessing. I don't know what he -- you'd have to ask Dr. Breier, I guess, what he meant by it. It's not a term that I recognize as a common nomenclature.
Q. Was Dr. Breier a marketing expert?
A. Was he a marketing expert, no.
Q. Yeah.
A. No.
Q. Is it your testimony you've never heard the phrase "blanket detailing" before?
A. I'm not familiar with the term "blanket detailing," no.
Q. Well, in context here it says, "Blanket detailing would be damaging since many physicians do not see OWC as an issue." That's what it says, correct?
A. That's what it says.
Q. When you got this e-mail the message that you took from that is that if you went around talking about weight gain to everybody through blanket detailing then that was going to cause problems for you because not all physicians saw that as a problem?

Gary Tollefson, M.D. (November 6, 2006)

193:21 Q. Isn't that how you took that?
22 A. I took that as this was
23 something that Dr. Breier had said. I wasn't
24 fully sure what he meant by it.

Gary Tollefson, M.D. (November 6, 2006)

194: 1 Q. Did you ever ask him?
2 A. I did not ask him.

Gary Tollefson, M.D. (November 6, 2006)

195: 5 Q. Now we pointed out in an
6 earlier e-mail, the one from Mr. Muniz, that
7 one of the items on the -- his short-term
8 action plan was to discuss Zyprexa label at a
9 GPLC session and evaluate potential
10 regulatory strategies. Do you recall that?
11 A. I recall us talking about it
12 today.
13 Q. Okay. And do you recall
14 that, in fact, in February of 2000,
15 Dr. Beasley and Kenneth Kwong submitted a
16 proposal to the Global Products Labeling
17 Committee to revise the Zyprexa label?
18 A. I'm aware that they brought
19 in some data for the committee to look at. I
20 think the decision whether to revise and how
21 to revise it was the committee's, not
22 Dr. Kwong's or Dr. Beasley's.

Gary Tollefson, M.D. (November 6, 2006)

196: 3 MR. SUGGS: Okay. Let me
4 show you what has been previously
5 marked as Plaintiff's Exhibit 990.
6 For the record, this is a
7 document which on the first page
8 says Attachment E. It has
9 confidential stamps on every page.
10 And on the second physical page the
11 heading at the top indicates that
12 this was an "Olanzapine Labeling
13 Change On Hyperglycemia For
14 February 21, 2000, GPLC Meeting."
15 QUESTIONS BY MR. SUGGS:
16 Q. Have you seen this document
17 before, sir?
18 A. I believe so.

Gary Tollefson, M.D. (November 6, 2006)

197: 1 Q. Okay. I could direct your
2 attention to the last physical page, it
3 indicates that this was reviewed by Charles
4 Beasley and Kenneth Kwong on February 15,
5 2000. And at this point in time in February
6 of 2000, Dr. Beasley would have been
7 reporting directly to you, was he not?
8 A. I don't recall. There was a
9 period where he was jointly reporting to
10 pharmacovigilance and then on the science and
11 technical side to me. It might well have
12 been during this time, I don't recall.
13 Q. Okay. At this time you were
14 still the product team leader, correct?
15 A. Product Group President.
16 Q. Product Group President,
17 okay.
18 And would you have reviewed
19 this proposal before it was submitted to the
20 Global Product Labeling Committee?
21 A. Probably not because it was
22 coming from a different function. It was
23 coming from pharmacovigilance which was an
24 independent function within the company.
198: 1 Q. Okay. Well, if you can
2 direct your attention on the first page,
3 actually, it's the second physical page. It
4 states that this was a proposal of the
5 Product Team and Pharmacovigilance, correct?
6 A. Um-hum.
7 Q. So it was a joint submission,
8 correct?
9 A. It says that. Dr. Beasley
10 was probably functioning in a dual role. I
11 don't know who else on the team may or may
12 not have been involved with it, I'd have to
13 ask Dr. Breier, but that's the inference.
14 Q. Well, was the Product Team
15 and Pharmacovigilance, were they two
16 different entities or were they one and the
17 same?
18 A. They were two different
19 entities. Although Charles had a role, as we
20 said earlier, contributing to both groups.
21 Q. Okay. Well, at least
22 according to the form here this was a
23 proposal of the Product Team and
24 Pharmacovigilance, correct?
199: 1 A. That's what it reads.

Gary Tollefson, M.D. (November 6, 2006)

199: 2 Q. Okay. You testified just a
3 moment ago that you don't believe you would
4 have reviewed this before it was submitted.
5 Do you recall when it was that you did see
6 this?
7 A. I think I just remember it
8 being discussed after the committee had first
9 seen it, because it had created some -- some
10 discussion and dialogue about the methodology

behind it.
Q. **Okay. There had been some discussion and dialogue about the methodology behind how the form was prepared?**
A. No. About how the analysis had been conducted and whether, you know, what the criteria that were used for the analysis, the statistics used, the rigor, you know, those kinds of things.
Q. **Who was the discussion between?**
A. I remember someone from the committee, I can't tell you who, bringing it to my attention as Product Group President
200: that this issue had been discussed, that there were some concerns about the analysis, and they were going to, I think, remit it to a broader more sophisticated group to take a look at the analysis and see if they were comfortable with what Drs. Beasley and Kwong had come up with. Were they, you know, were they robust and were they valid.
Q. **Who was it that had the concerns about the analysis?**
A. The committee, as I understood it.
Q. **And who were the members of the committee at that time?**
A. I couldn't tell you. I know it was chaired by Dr. Clayman. I don't know the individual members.
Q. **And in which department is Dr. Clayman?**
A. Pharmacovigilance.
Q. **Okay. Was it usual or unusual for a member of the Product Labeling Committee to come to you after a meeting and say that there was some concern about a**
201: **proposed label change?**
A. Well, again, it wasn't my understanding that there was a -- that the committee had not advocated a proposed label change. Rather, they had looked at the analyses and there were some concerns about how the analyses had been conducted, and that they wanted to remit that back to a larger cross-functional group to validate.

Gary Tollefson, M.D. (November 6, 2006)

201:10 Q. **Okay. The actual proposal was -- is reflected in that first box at the top of Page 2, correct, refers to New Statement?**
A. This is a proposal that was made to the labeling committee.
Q. **Right.**
A. It's not the labeling committee's proposal.
Q. **I understand.**
A. Okay.

Q. And we had some testimony about this before. And I'll represent to you that that little box sign that's in that sentence in two places, we've had testimony that something must have gone goofy there because it should, in the first instance, state greater than or equal to, and the second time it occurs it should state less than or equal to.

A. Okay.

Q. So the sentence would state, "Random glucose greater than or equal to 160 milligrams per deciliter in patients with baseline random glucose less than or equal to 140 milligrams per deciliter has been occasionally seen in clinical trials."

And is that your understanding of what was proposed?

A. I don't recall a specific proposal. It seems consistent with the fact that the trials didn't exclude diabetics, so it's certainly conceivable.

Q. Okay. When you said that there was some concern expressed about the analysis, who was it that had done the analysis?

A. I don't know if it was Doctor -- I assumed it was Dr. Kwong and someone, perhaps colleagues within his area of pharmacovigilance, his particular unit, but I don't know, specifically, who conducted it.

Q. I'll represent to you that we had some testimony just on Friday, this is Monday, by Dr. Sharp that that analysis was conducted by Dr. Beasley. Does that square with your recollection?

A. Well, Dr. Beasley's not a trained biostatistician, so it would surprise me if he conducted the statistics.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. In the middle of the page there's a little box that says "how has this proposal arisen?" And the text in that box states, "Recent review of random glucose levels of patients in olanzapine clinical trials revealed that the incidence of treatment-emergent hyperglycemia in olanzapine group, 3.6 percent, was higher than that in the placebo group, 1.05 percent. For common events, incidences from clinical trials provide more meaningful information." Did I read that correctly?

A. Yes.

Q. And if you do the math, that would indicate that the -- by the way, treatment-emergent hyperglycemia refers to hyperglycemia occurring after someone has been exposed to the treatment of Zyprexa,

correct?
A. I think in this case they're referring to clinical trials. So it would have been after the point of randomization and during the conduct of the trial there was an associated event.
Q. Okay. And the event being hyperglycemia, correct?
A. In this particular case, yes.
Q. Okay. And if you do the math and the comparison between the olanzapine group and the placebo group, we see that the incidence of treatment-emergent hyperglycemia is about three and-a-half times higher in the olanzapine group than in the placebo group, correct?
A. That's what the raw numbers look like.
Q. Okay. And given the problem that you were dealing with in the marketplace at that point in time, where competitors were saying that Zyprexa had a hyperglycemia problem, if you told doctors that the incidence of treatment-emergent hyperglycemia was three and-a-half times higher in the Zyprexa group than in the placebo group, that would have presented real problems to you, wouldn't it?

Gary Tollefson, M.D. (November 6, 2006)

A. Not necessarily. I think it depends on the context of it. But it was inconsistent with earlier data we talked about where there was no difference seen between olanzapine and placebo. Thus it was something that caught one's attention and it did beg a question of why does it appear to be inconsistent with everything from the previous four and five years and, you know, a requirement to go back and look carefully to make sure mistakes weren't made unintentionally, appropriate definitions, criteria, et cetera, were used. I thought that this led them to a submission to the FDA with that three analysis subsequently.
Q. In fact it did. It led to several reports to the FDA.
And, sir, isn't it true that also as we've seen here today, we've seen computer printouts showing statistically significant increased incidence of hyperglycemia in Zyprexa users as compared to Haldol users back as early as 1995?
A. Well, I think as we said earlier that's misrepresenting the total data. You picked out one study that showed that. I agree that one study did show that. Many other studies did not show that. The totality of all the studies did not show that or corroborate that.

Q. Well, [redacted], in fact, the totality of studies that was submitted by Lilly to the FDA in 2001, showed that there was a statistically significant elevated mean levels of glucose in Zyprexa users as compared to Haldol and placebo; isn't that right?

A. That was, again, as we said, an even larger database that had accumulated by the time of that submission in 2001. And I don't know the specific numbers. That may just have been a powering phenomenon. That is, as you get more and more and more patients, as you well know with a statistical background, you may not change an incidence rate but you may have more power to detect a statistical significance just based on a larger sample size. I know that sample size was in excess of 4200 individuals at that point.

But the bottom line was by 2001, there was a significant difference. It first emerged in the data set that was submitted to FDA.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. The one study that you were referring to that did show a statistically significant increased incidence of high glucose was from the HGAJ study, correct, that's the one we were looking at earlier?

A. That is one we looked at earlier.

Q. And that was the largest study that had been done back in 1995, correct?

A. I think as we agreed earlier, it represented slightly over half of the patients that had been studied.

Q. Half of the total. How many studies had been done that were included in the NDA?

A. I don't recall. There probably were 15 studies, maybe more.

Q. Fifteen studies or more and yet study HGAJ accounted for more than 55 percent of the entire total of subjects, correct?

MR. LEHNER: Object to the form.

Q. That one study out of the 15 accounted for 55 percent of the total number of subjects studied, correct?

A. It was a large Phase 3 study. Phase 3 studies, typically, are large in number. This was done under a single protocol in multiple different countries and, yes, it did account for a large sample.

Q. I'd like to direct your attention to Page 4 of Exhibit 990.
In the second box from the top there's a reference to "Literature Reports." Do you see that?
A. I do.
Q. And in the second paragraph there there's a reference to Dr. Daniel Casey from Oregon. Do you see that?
A. I do.
Q. Do you know Dr. Casey?
A. I do.
Q. And how is it that you know him?
A. I'm a specialist in the practice of psychiatry, Dr. Casey is a psychiatrist. We've attended meetings together, we know one another, we've done research together.
Q. Okay. In that paragraph it states, "Dr. Daniel Casey from Oregon presented in a seminar at Lilly at the end of 1999. He performed chart review of 136 veteran patients who had been exposed to olanzapine therapy for at least four months, an average of 1.4 year. Of the 39 patients who had normal fasting glucose levels before olanzapine therapy, seven, or 18 percent, had fasting glucose levels of 126 milligrams per deciliter or higher during olanzapine therapy. Threshold that met the 1998 ADA diagnostic criteria for diabetes."
Do you see that language, sir?
A. I do.
Q. And were you informed of that?
A. I believe so.
Q. And do you recall how it was that you were informed of that?
A. No, I don't.
Q. Were you present at the seminar that Dr. Casey gave at Lilly at the end of 1999?
A. No, sir.
Q. Okay. Do you recall who it was that would have told you of his finding?
A. I do not.
Q. Did you ever talk with Dr. Casey about that?
A. I did on one occasion.
Q. And when was that?
A. Shortly after this. Probably in early 2000.
Q. And how did that come about?
A. I think we were having a phone conversation on another matter, which I don't recall what it was, and I did ask him about this because I wanted to understand the nature of what he observed because it was

very atypical given the incidence figures that were exceedingly high. And so I wanted to understand his methodology and his thoughts on it.

Q. Okay. And at that time Dr. Casey was a consultant for Lilly, was he not?

A. He had been a consultant for several years to the company.

Q. In fact, he was a consultant back in 1995, was he not?

A. I believe so.

Gary Tollefson, M.D. (November 6, 2006)

Q. You said that someone, some member of the Global Product Labeling Committee came to you after the February 2000 meeting and expressed some concern about the analysis that had been done that was the basis for this proposed label change; is that correct?

Gary Tollefson, M.D. (November 6, 2006)

A. I said I was informed. I thought it probably was a member of the committee, not 100 percent certain it was a committee member.

Q. Okay. I believe you said that they were going to, that the committee wanted to bring more people to bear on the issue; is that right?

A. Yes.

Q. Were additional people brought to bear on the issue?

A. That was my understanding.

Q. Who were they?

A. I don't know individual names but I believe the people who ultimately put together the comprehensive report to the FDA were the people that conducted the exercise. So it was probably multiple different functions: Senior biostatisticians, system analysts, regulatory scientists, pharmacovigilance, docs.

Q. Wasn't it, principally, Dr. Charles Beasley?

A. I don't know what "principally" means. I don't think so. I think this was a large cross-functional effort that was led by pharmacovigilance and not exclusively or uniquely by or principally by Dr. Beasley.

Gary Tollefson, M.D. (November 6, 2006)

217:24 Q. Do you recall that in May of
218: 1 2000, Lilly submitted a label change to FDA
2 on this issue of hyperglycemia?
3 A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

218: 8 MR. SUGGS: Okay. And let me
9 show you what's been previously
10 marked as Plaintiff's Exhibit 4858.
11 For the record, this is a
12 May 9, 2000, letter from Gregory
13 Brophy at Lilly to FDA. It has a
14 bold heading on the upper right-hand
15 side stating "Special Supplement
16 Changes Being Effected."

Gary Tollefson, M.D. (November 6, 2006)

218:21 Q. Do you recall that the change
22 to the label in May of 2000 to discuss
23 hyperglycemia was done under provision of the
24 FDA regulations referred to as a change being
219: 1 effected mechanism?
2 A. Yes.
3 Q. And that means that a drug
4 company may on their own without prior FDA
5 approval change the labeling if it
6 strengthens warnings, indications, adverse
7 reactions or precautions; is that correct?
8 A. I believe it can.
9 Q. Okay. And would you agree
10 with me, sir, that this letter which has
11 several numbered paragraphs, that it's
12 paragraph two, numbered two, that deals with
13 the revision to the labeling regarding blood
14 sugar levels or blood glucose levels?
15 A. It appears to be Items 2 and
16 3.
17 Q. Okay. Well, Item 3 referred
18 to the addition of diabetic coma to the
19 adverse reaction section, correct?
20 A. Correct.
21 Q. Okay.
22 A. That's a blood sugar
23 consequence.
24 Q. Right. Okay. Item No. 2
220: 1 refers to the olanzapine clinical trial
2 database, correct?
3 A. Yes.
4 Q. Okay. And whereas the
5 proposed label change that we saw in
6 Exhibit 990 noted that there was almost a
7 three and-a-half times higher incidence of
8 treatment-emergent hyperglycemia in the
9 Zyprexa group as compared to placebo, in
10 Paragraph No. 2 of Exhibit 4858, the actual
11 label change that went in, there does not
12 appear to be much, if any, difference between

blood glucose levels of Zyprexa users as compared to placebo users; isn't that true, sir?

Gary Tollefson, M.D. (November 6, 2006)

A. Based on these definitions, yes.
Q. Okay. And so there was nothing in this Paragraph 2 here that was going to cause physicians to have concern about hyperglycemia occurring after exposure to Zyprexa, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. No. I mean, I think that this says that hyperglycemic events were observed in patients receiving olanzapine. It really doesn't matter whether it was caused by the drug or not. You would still manage the issues appropriately.
Q. Let me restate the question. There was nothing in Paragraph 2 of Exhibit 4858 that would cause doctors to be concerned that the incidence of hyperglycemia with Zyprexa would be any higher than in the placebo group, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. With the exception -- it says at the end of the paragraph, transient, which meant sometimes, elevations of blood sugar are only transient. You might see them once, you won't see them again. It says "transient random glucose levels greater than 160 but less than 200 were found in 1 percent of olanzapine-treated patients, placebo 0.4%." That might be a difference.
Q. With respect to all the other language that's in there it's saying, essentially, there's not much difference between Zyprexa users and placebo users, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. Based on the analysis of the clinical trial database that's what the data said.

Gary Tollefson, M.D. (November 6, 2006)

223:11 Q. I'm not asking whether you
12 think the analysis that's in Exhibit 4858 is
13 correct or whether you think the analysis
14 that was in Exhibit 990 was correct. I'm
15 just talking about the effect of the words,
16 okay.
17 If, in fact, you had changed
18 the label in May of 2000 to tell doctors that
19 the incidence of treatment-emergent
20 hyperglycemia was three and-a-half times
21 higher in Zyprexa users as compared to
22 placebo users, that would have caused concern
23 on the part of prescribing physicians, would
24 it not?

Gary Tollefson, M.D. (November 6, 2006)

224: 3 A. I don't think I could make
4 that kind of generalization. Hyperglycemia
5 was already in as an adverse event term. Now
6 you could poll physicians, some might say,
7 "Gee, I think that means it's 8 times
8 higher," someone else might say, "I think
9 that means it's only 2 times higher." So I
10 don't think you can make that kind of
11 generalization. You want valid data in the
12 package insert. You don't want erroneous data.
13 Q. Sir, in the context of what
14 was happening in the marketplace in the
15 spring of 2000, with the attacks that Lilly
16 was facing in the marketplace by competitors
17 who were saying that, "Gee, Zyprexa has all
18 this additional weight gain. It's going to
19 increase the risk of diabetes. It's going to
20 increase the risk of hyperglycemia."
21 And that was what was being
22 said, wasn't it, by your competitors?
23 A. That is what was being said
24 by competitors.

Gary Tollefson, M.D. (November 6, 2006)

226: 8 Q. Sir, do you recall that this
9 label change that Lilly did without prior FDA
10 approval in May of 2000 got struck down by
11 FDA in October of 2000?

Gary Tollefson, M.D. (November 6, 2006)

226:14 A. I don't know that I would
15 have used the term "struck down."

Gary Tollefson, M.D. (November 6, 2006)

227:12 MR. SU[redacted]: Sir, I'm going to
13 show you what has been previously
14 marked as Plaintiff's 195. For the
15 record, this is a letter from
16 Russell Katz at FDA to Gregory
17 Brophy at Eli Lilly. It's dated in
18 the upper right-hand corner as
19 October 11, 2000.

Gary Tollefson, M.D. (November 6, 2006)

227:21 Q. Did you ever see this before,
22 sir?
23 A. I believe so.
24 Q. And when did you see it?
228: 1 A. When it came out. Dr. Brophy
2 shared it with me.
3 Q. Okay. And if I could direct
4 your attention to Item No. 3 in the letter,
5 the FDA said that they have completed the
6 review of the application. That's referring
7 back to the May 9, 2000, submission, correct?
8 A. I presume.
9 Q. And they determined that the
10 changes proposed in Items 1 and 3 were
11 approvable, correct?
12 A. I'm sorry, I'm not finding
13 that spot. May I ask where you are?
14 Q. It's in Item No. 3, the very
15 first paragraph right below that numbered?
16 A. Ah, yes, I've got it.
17 Q. Okay. The FDA said they had
18 completed review of the May 2000 application
19 and had determined that the changes proposed
20 in Items 1 and 3 were approvable, correct?
21 A. Correct.
22 Q. It was Item No. 2 that had
23 the hyperglycemia language, correct?
24 A. Correct.
229: 1 Q. Okay. And they go on to say,
2 "Before this application may be approved, it
3 will be necessary for you to submit final
4 printed labeling revised with the deletion of
5 the following paragraph, paren, changes
6 effected Item 2 above." And then they quote
7 the language of the label change that you
8 guys had made, correct?
9 A. This is the label change the
10 company submitted.
11 Q. Correct.
12 A. Yes.
13 Q. Okay. And then after quoting
14 that language the FDA then said in the
15 following paragraph, this descriptive data --
16 pardon me -- "The descriptive data that is
17 provided expresses a certain level of implied
18 safety with respect to treatment-emergent
19 hyperglycemia. This reassuring language is
20 not appropriate for submission under
21 21CFR314.70, paren, C as a special supplement
22 changes being effected." Do you see that

language, sir?
A. I do.
Q. And the reason why it was inappropriate was because a change being effected label is permitted when you strengthen a warning or a precaution or an indication or contraindication or adverse reactions, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. Yes.
Q. That's when that type of change is appropriate. And it's not appropriate when the descriptive data provides a certain level of implied safety because that doesn't strengthen the warning. It's giving a sense of implied safety; isn't that right, sir?
A. I would not agree with that. If this at that point had been accepted it would be strengthening the information for physicians by providing additional data, updated and contemporary data.
Q. Sir, that was your opinion.
A. Yeah.
Q. But the opinion of the FDA was that "The descriptive data that is provided expresses a certain level of implied safety with respect to treatment-emergent hyperglycemia." Isn't that what they said, sir?
A. That's what they said.

Gary Tollefson, M.D. (November 6, 2006)

The analysis that formed the basis of the May 2000 label change and the analysis which formed the basis of a submission that Lilly made to FDA in the summer of 2000 with respect to hyperglycemia was what is referred to as a categorical analysis.
A. I don't remember all of the detail of that. The wording that we have reviewed in this letter appears to be categorical.

Gary Tollefson, M.D. (November 6, 2006)

Q. What your group did was to establish various cutoff points and group people by where they fell within those cutoff points of blood glucose, correct?
MR. LEHNER: Object to the form.
A. My understanding was they

took cutoff points that had been articulated by the ADA and had applied them to the data set to try to determine an incident rate of clinically meaningful elevations of blood sugar.

Q. Okay. Another way of doing the analysis of blood glucose is to use what's referred to as continuous data, correct?

A. That was done as well.

Q. Okay. And with continuous data, what you do is you take everybody's readings and then you establish what the means are for various groups, correct?

A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

Q. And by "mean" we mean average, correct?

A. Yes.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 1476.

For the record, this is an e-mail chain. The very top one on the first page of the exhibit is dated March 9, 2000, from Jack Jordan to Robert Baker, Christopher Bomba, Bruce Kinon and Michael Murray.

But, sir, I want to direct your attention to the e-mail below that which is an e-mail to you, pardon me, from you to Charles Beasley, Alan Breier, Jack Jordan, Roland Powell, Robert Thompson, Dennis West and John R. and the e-mails below that.

THE WITNESS: Um-hum.

MR. SUGGS: And, sir, can I have you read in particular the text of the e-mail from Charles Beasley that's at the very bottom of the first page. Just read it to yourself first.

Gary Tollefson, M.D. (November 6, 2006)

Q. Have you finished reading it, sir?

A. I have.

Q. Okay. Would you agree with me that at the bottom of Page 1 of

Exhibit 1476, which is the beginning of Dr. Beasley's e-mail, and continuing on to the top of Page 2, that he is talking about a categorical analysis of the data?
A. It appears that way, although I find it rather difficult to get through.

Gary Tollefson, M.D. (November 6, 2006)

Q. "These are issues in which we probably should involve our diabetes and obesity colleagues."
A. I see it.
Q. Is it your understanding, sir, that at least up until this point in time, that is March of 2000, that you had not involved Lilly's diabetes and obesity colleagues in the analysis of the hyperglycemia issues?
A. I don't believe that's the case.
Q. Well, at least according to Dr. Beasley he's saying that you should involve our diabetes and obesity colleagues, correct?
A. He says that, but he's not saying that they haven't previously been involved, either.
Q. Okay. Directing your attention to that same paragraph, third line from the bottom, Dr. Beasley writes, "What I'm getting at, only my opinion, is that we need to bring more talent to bear." Do you see that, sir?
A. I do.
Q. And then I have a question for you, sir. That e-mail that Dr. Beasley wrote was responded to by Paul Berg a day later, correct?
A. Yes.
Q. Okay. And who is Paul Berg?
A. Statistician.
Q. Okay. And then somehow you get a hold of those two e-mails; isn't that right?

Gary Tollefson, M.D. (November 6, 2006)

Q. I'm trying to figure out the communication, because just above Paul Berg's e-mail is an e-mail from you to Charles Beasley, Alan Breier, Jack Jordan, Roland Powell, Robert Thompson, Dennis West and John R. Do you see that?
A. I do.
Q. How was it that you got that, got those prior e-mails?
A. Well, either, I presume, I

was either copied by Paul Berg, which would explain the flow of e-mails, or this has just been copied such that it looks that way. But, otherwise, routinely, if you're not copied or sent an e-mail you wouldn't have it.

Q. I know.

A. So it wouldn't appear on this string. So either I was copied or --

Q. That's what I thought was odd because there was no -- you weren't in the "to" line of Paul Berg's e-mail and you weren't in the "cc" line?

A. Well, it's cut off but I don't know if there was another name to the right. Ken Kwong's name is not completed but it seems unlikely there'd be yet another name, but that's the only explanation I could think of.

Q. I guess another possible explanation, and you tell me if this is true given the way the Lilly e-mail system worked, if somebody blind carbon-copied you, is that another way you would have gotten this without showing on the face of this here?

A. I suppose that's possible but unlikely coming from Paul Berg. I wouldn't have expected that but, I mean, it's possible.

Q. Okay. In any event, directing the attention to your e-mail. You tell Charles Beasley, Alan Breier, Jack Jordan, Roland Powell, Robert Thompson, and Dennis West and John R. Do you know who John R would have been? It's cut off there?

A. No.

Q. Okay. In any event, you state, "I saw the attached notes and wanted to share some relevant competitive analysis."

And then you say, "We had an academic guest in Friday who at lunch mentioned he had been at a Janssen sponsored event last week."

Am I correct that Janssen is one of your competitors?

A. Yes.

Q. And they were the manufacturer of Risperdal; is that correct?

A. Correct.

Q. Dropping down a couple of lines on the right-hand side, "Of note, the last lecture, delivered by John Neumeier, was totally out of the day's context and focused on the ills of an atypical-induced elevation of blood sugar in the 70 to 95 nanograms per deciliter range."

Q. Was that your understanding? Was that what you were saying it was in the

70 to 95 nanograms per [illegible]iliter range?
A. In that interval.
Q. Okay. You go on to say, "This was focused on Zyprexa and reportedly delivered in such a way as to cause much concern/reflection on our product. I suspect this was a field test of something we may well see more of and would encourage the team to A, be prepared with a data response and B, think more seriously about our own offensive." Do you see that language, sir?
A. Yeah.
Q. And what did you mean by "our own offensive?"
A. Well, this had occurred in the context of discussing on working with opinion leaders and working with them individually or in groups. And the company had been leaning towards individual or a small group format. And one of the things that had concerned me when I heard about this event was allegedly the competitor company brought in a very, very large number of people for a day-long meeting at their facilities to extensively show them their R & D portfolio. And then at the end of the day parachuted in this discussion on atypicals and hyperglycemia, which seemed out of context. But the more overarching issue was, you know, that looking at the competitive lay of the landscape, it appeared that other companies were aggressively trying to bring in very, very large groups of people to their corporate headquarters to, basically, create, you know, a relationship, a story, an image. And this particular data that I'd heard about seemed somewhat perplexing. So I was suggesting we need to understand it so that we could anticipate what we might hear from those competitors.
Q. Okay. Well, did Lilly establish similar-type operations?

A. I'm not aware of anything where a very large number of people were brought into the corporate headquarters for a corporate tour like this.
Q. Okay. But Lilly did, indeed, conduct numerous seminars around the country?
A. These were, typically, done on either at a local level or at a state level, where you would have moderate levels of people brought together within their own geography, as opposed to a great exodus into the corporate center.
Q. Okay. You then have a PS to your e-mail. It says Denny/Bob. I assume that's referring to Dennis West and Robert Thompson?

A. Correct.
Q. **Who were they?**
A. These were our two principal, we call them medical sciences liaisons. Their job was to go out and interact with key academic leaders -- understand, you know, what's going on in the field from their viewpoint, share with them clinical trials we were doing, perhaps create opportunities for them to do future work with us.
It was really sort of that relationship building with the key academic opinion leaders. And they each had half of the U.S. geographic academic centers in their area of responsibility.
Q. **Okay. And then you go on to say, "Denny/Bob, it may be time to call cousin Guido to visit John." Who is John? Was that a reference to John Neumeier?**
A. Yeah. I think that was my typo. Because John Neumeier, or Neumeier was someone we were working with at the University of Washington. I think this is in reference to the Wash U position, John Newcomer, St. Louis Wash U, as opposed to Seattle Wash U. So that was my typo.
Q. **Actually, when we look at your e-mail in the text there where you talk about a lecture delivered by John Neumeier, you now think that should be John Newcomer?**
A. I think it's possible. I'm just not aware of John Neumeier having done work in this area. Obviously, Dr. Newcomer has. So I'm thinking, as I read it now, I may have mistyped just because of the Washington association.
Q. **And the names both starting out with "new?"**
A. Yeah.
Q. **Okay. So who is cousin Guido that was supposed to go visit John Newcomer?**
A. That was a poor attempt at humor but, Dennis West, who was based in St. Louis, had our coverage of Wash U, and I was, basically, inviting Denny to go meet with John and see if he could understand the data that John was presenting and, you know, what additional information John might have on the subject matter that we weren't aware of.
Q. **Again, who was cousin Guido?**
A. That was a poor humor reference to Denny West.
Q. **Well, I guess I'm not understanding because your PS is to "Denny slash Bob, it may be time to call," you're saying we should substitute Denny in there to visit John?**
A. Denny West is the appropriate person to have a visit with John Newcomer.
Q. **Well, again, what's the cousin Guido part?**
A. As I said, that was a poor attempt at humor to suggest that we need to

have somebody go visit [redacted] Newcomer and understand why he was presenting some of this data on the 75 to 90 interval, which I didn't understand. So I was trying to be facetious. That's all it was.

Gary Tollefson, M.D. (November 6, 2006)

Q. Dr. Tollefson, I've got a couple follow-up questions I want to ask about that Global Products Labeling Committee. I think you said you were a member of that in 2002-2003, somewhere in that time frame?

A. Something in that time frame.

Q. Okay. At that point -- and how many members are on that committee?

A. Maybe 12 or so.

Q. Twelve or so. And is it fair to say that the people who are members of that committee are executives within the company?

A. Either management executives or senior science leaders in a discipline, but, certainly, senior members of the company.

Q. Okay. And would that also have been the case back in 2000?

A. I suspect, yes.

Gary Tollefson, M.D. (November 6, 2006)

Does the label committee have a chair of the committee?

A. When I was on it, it was Dr. Clayman as head of global regulatory. And I think that, normally, it's headed by the person leading the regulatory organization.

Q. Okay. And who was leading the regulatory organization back in 2000?

A. I'm thinking it might have been Tim Franson but I can't be 100 percent sure.

Q. And are there any marketing people on the Global Product Labeling Committee?

A. No, I don't believe so.

Q. Okay. But it is fair to say that everybody who's a member of the Global Product Labeling Committee is a fairly senior executive within the company?

A. Or scientist, yes.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Okay. I've got a

couple of exhibits I want to hand you at the same time, one of which is Plaintiff's Exhibit 6998 and the other one is Exhibit 1453.

For the record, Exhibit 6998 is an October 9, 2000, e-mail from Robert Baker to Charles Beasley, Christopher Bomba, Alan Breier, Thomas Brodie, Patrizia Cavazzoni, James Gregory, John Holcombe, Jack Jordan, Suni Keeling, Bruce Kinon, Michael Murray, John R. Richards, Eugene R. Thiem, Mauricio Tohen, and Paula Trzepacz. Subject is meeting with endocrinologic consultants.

Gary Tollefson, M.D. (November 6, 2006)

249:22 Q. Have you seen this document
23 before, sir?
24 A. Yes.
250: 1 Q. Okay. When did you see it?
2 A. The first time I saw it, I
3 believe, was during review with counsel.

Gary Tollefson, M.D. (November 6, 2006)

250:21 Q. Okay. And in the first
22 paragraph Dr. Baker writes, "FYI, the Lilly
23 diabetes/endocrine group held an academic
24 advisory board meeting this weekend in
251: 1 Atlanta. They kindly allotted two hours for
2 discussion of olanzapine's potential
3 hyperglycemia risks, and Charles Beasley,
4 Chris Bomba, Patrizia Cavazzoni, Suni Keeling
5 and I attended. Unfortunately, this
6 consultation reinforced my impression that
7 hyperglycemia remains quite a threat for
8 olanzapine and may merit increasing even
9 further medical attention and marketing focus
10 on the topic."
11 Do you see that language,
12 sir?
13 A. I do.
14 Q. Were you aware of, that there
15 was such a meeting back in October of 2000?
16 A. I don't believe so.
17 Q. Okay. Dr. Baker goes on to
18 say, "On the positive side like other
19 endocrinologists they were not impressed with
20 the Newcomer findings." Do you see that?
21 A. Yes.
22 Q. Do you take that to mean a
23 reference to Dr. John Newcomer at Washington
24 University?
252: 1 A. Yes.
2 Q. The same one that you said we
3 ought to send cousin Guido to go talk to him?
4 A. Actually, Mr. Dennis West,

but, yes, the same John Newcomer.
Q. Okay. They go on to say, "They were, however, concerned by our spontaneous AE reports and quite impressed by the magnitude of weight gain on olanzapine and the implications for glucose."
Do you see that language?
A. I do.
Q. And is it your testimony that you were not apprised of the results of that meeting?
A. I don't remember being informed of the meeting or, specifically, the results of this meeting.
Q. Okay.
A. There's nothing here that's inconsistent with, I think, some of the feedback that the company had been receiving and taking into consideration.
Q. I'm sorry, you said there's nothing here that's inconsistent with, I think, some of the feedback that the company had been receiving?
A. Yeah, from different opinion leaders, prescribers.
Q. And for how long had you been getting that type of feedback? Well, what you're talking about that you're saying is not inconsistent is the concern as reported here about the spontaneous adverse event reports and the magnitude of weight gain on olanzapine and the implications for glucose, correct?
A. No. I was saying, No. 1, not impressed with the Newcomer findings and, 2, the magnitude of the weight gain. I think those are issues that, you know, I had certainly heard about on more than one occasion when it came to prescriber issues.
Q. For how long had you been hearing that concern expressed?
A. At least two years, I would imagine.
Q. So at least 1998?
A. Probably.
Q. Okay. Dr. Baker goes on to say in this e-mail, "Citing methodological questions, at least the vocal members were not reassured adequately by our analyses, such as the finding that relative risk was not higher than comparative drugs. Disconcertingly, one member compared our approach to Warner Lambert's reported argument that Rezulin did not cause more hepatic problems than other drugs in its class." Do you see that language, sir?
A. I do.
Q. What is your understanding as to the reference to Warner Lambert there?
A. Again, I was not in attendance at the meeting, so I'm not sure what the one member was, specifically, meaning.

Q. Do you recall Warner Lambert having problems with hepatic issues in connection with its drug Rezulin?
A. I do.
Q. And do you recall that Warner Lambert argued in that situation that Rezulin did not cause more hepatic problems than other drugs in its class?
A. I wasn't directly involved with their presentation or their discussion with regulatory agencies. I'm aware of the issue, though.
MR. SUGGS: Okay. If I could direct your attention to the second exhibit I handed you, which was Exhibit 1453.
For the record, this is a chain of e-mails. The very top one on the first page is one from Robert Baker to Charles Beasley dated October 10, 2000. But, sir, I would like to direct your attention to Page 3 at the bottom. And that is an October 9 e-mail from Robert Baker to Charles Beasley and Alan Breier.

Gary Tollefson, M.D. (November 6, 2006)

Q. As we've discussed several times before, you've indicated that Dr. Beasley reported to you before this time and after this time, but you're not quite sure about whether he reported directly to you in October of 2000, correct?
A. Correct.
Q. But I believe your testimony was that Dr. Alan Breier did report to you directly at this time in October 2000, correct?
A. That's correct.
Q. Okay. And if you can turn to the following page you can see that in this e-mail from Robert Baker to Charles Beasley and Alan Breier, with copies to some other folks, he's forwarding an e-mail that he had received from Thomas Brodie. Do you see that?
A. I do.
Q. And do you know Thomas Brodie?
A. I do not.
Q. That e-mail from Thomas Brodie dated October 9, 2000, was to Robert Baker and Eugene R. Thiem. Do you know who Eugene Thiem was?
A. No.
Q. Okay. In any event, in that e-mail Mr. Brodie said, "Robert, Clearly this group of endocrinologists who spoke up, and I would rate those who did speak up as the

leaders of the pack, a[illegible]very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes. I can only hope that you and all of the team who attended the NADAB meeting are gaining the ear of senior leadership and articulating this finding. Although the board's recommendation is probably not the way Lilly, typically, does business, I do believe they made a very strong point that unless we come clean on this it might get more serious than we might anticipate."

Do you see that language, sir?

A. I do.

Q. And it's your testimony that neither Dr. Beasley or Dr. Breier informed you of this meeting or the comments and concerns of this panel of endocrinologists?

Gary Tollefson, M.D. (November 6, 2006)

A. No. I said I don't recall having had the conversation.

Q. Well, I guess --

A. Not that it didn't exist, I just don't remember it.

Q. Silly me, I thought your testimony earlier was that you were saying that you hadn't been informed. So is it your testimony now that you may have been informed but you can't recall?

A. I don't recall.

Q. Okay. So you may have been informed but you don't recall?

A. Correct.

Q. Okay. Well, if you don't recall being informed then I guess you probably wouldn't recall ever passing this information on to executives above your

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Gary Tollefson, M.D. (November 6, 2006)

Q. Correct?

A. Correct.

Gary Tollefson, M.D. (November 6, 2006)

Q. Did you regard Dr. Breier as a conscientious guy?

A. Yes.

Q. Did you expect him to bring issues of potential safety problems to your attention?

A. Yes.

Q. Would you have expected him to bring the subject of this meeting to your

attention?
A. It would make sense that he would.
Q. I mean, especially if Thomas Brodie is writing and saying "I only hope that you and all of the team who attended the meeting are gaining the ear of senior leadership and articulating this finding." You would have been senior leadership, right?
A. I would have been one of a group.
Q. But you don't recall Dr. Breier coming to you?
A. I said I don't, specifically, remember talking about this meeting, per se.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Now, I believe you said earlier that sometime in 2000 at the end of the year your job position changed, correct?
A. Correct.
Q. And remind me again what was the title change?
A. Well, right around this time in October, I mentioned that I left the role of Product Group President and went into a scientific technical position referred to as a Lilly Fellow.
Q. Okay. And did you continue to have responsibilities for Zyprexa?
A. No.
Q. Did they just stop when you made that shift?
A. Yes.
Q. Okay. And when would that shift have occurred?
A. In October.
Q. Okay. October of 2000?
A. Yes.
Q. Did not persist for any time after that?
A. That's correct.

Gary Tollefson, M.D. (November 6, 2006)

MR. SUGGS: Okay. Let me show you what's been previously marked as Plaintiff's Exhibit 5565. We have used this document before in other depositions and that number is printed out on the bottom on those, but for some reason we had a copying problem and it's not shown here.
For the record, this document consists of an e-mail chain, the very top of which is an e-mail dated

February 22, 2001, from Jared Kerr to Mark Millikan, which is forwarding an e-mail from Charles Beasley, to Ralf Dittmann with copies to Alan Breier, Patrizia Cavazzoni, Mark Millikan, and Gary Tollefson, the subject being olanzapine and hyperglycemia.

QUESTIONS BY MR. SUGGS:

Q. Have you seen this e-mail before, sir?

A. I believe so.

Q. And when did you see it?

A. When I received it.

Gary Tollefson, M.D. (November 6, 2006)

Q. Did you receive it on or about February 2001?

A. I believe that's when it was received. I would have read it in that proximity.

Q. This would have been four months after you stopped having anything to do with Zyprexa, right?

A. That's correct. Well, you said, let me correct it. You said responsibility for Zyprexa, correct?

Q. Well, did you continue to have duties regarding Zyprexa?

A. You asked me if I had responsibility for Zyprexa, I said, no. That is a correct statement.

Q. Are we playing games here with the language?

A. I'm not. You might be.

Q. What involvement did you continue to have with Zyprexa after October of 2000?

A. Good question. I was a senior technical person in the neuroscience area. I consulted on a variety of different things. But I served as a consultant. I offered a scientific opinion, scientific insight, but I wasn't a decision maker, I didn't have direct line reporting responsibility for the molecule. So it was exactly as I had told you.

Q. Okay. So people would provide you with information and then you would provide them with your opinions?

A. That could be a scenario. Again, this is coming from overseas. I don't know that Ralf Dittmann even knew that I was no longer in the role. He may have been copying me out of courtesy, I have no idea, but I did not have direct product line responsibility.

Q. What do you recall doing with respect to Zyprexa after October of 2000?

A. Very little. I mean, if I

were asked about something I might offer an opinion --

Q. Okay.

A. -- but only if it was solicited.

Q. Okay. And at least in this instance, you were copied on an e-mail regarding the subject of olanzapine and hyperglycemia, correct?

A. Yes, I was.

Q. Okay. And about a little less than a year before this point, Lilly had made a label change which said there was, essentially, no difference between Zyprexa and placebo users with respect to blood glucose. We've talked about that before.

A. That's correct.

Q. Okay. And in this e-mail, Dr. Beasley is saying starting in the third sentence of his e-mail, "Our continuous analyses show that olanzapine does result in statistically significant mean increases in random glucoses relative to placebo and haloperidol."

Do you see that language, sir?

A. I do.

Q. And do you know when that analysis was done?

A. I do not.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. After you found out that this continuous analyses showed that olanzapine does result in statistically significant mean increases in random glucose relative to placebo and haloperidol, did you suggest that since physicians had been previously told by Lilly that there really wasn't that much difference between Zyprexa and placebo that, perhaps, you ought to go out and correct the record?

Gary Tollefson, M.D. (November 6, 2006)

A. I don't think it's a correction. I think it's a subsequent, as we said earlier, expansion of the database. The database was being continually analyzed. And presumably, at least, in this analysis at this point in time that continuous difference was observed.

I vaguely remember they had some outside people in working with them, Allison and others. And it was my understanding, although I may be wrong, that they submitted that to the FDA as well.

Q. Well, when your analysis

showed a threefold difference with Zyprexa having a higher rate, a higher incidence of treatment-emergent hyperglycemia in February of 2000, you didn't issue a label change saying that.

When the label -- when you did some further analysis after being directed to do so by some executive on the Global Product Labeling Committee and the data then concluded that or the analysis then concluded that there was no difference with placebo, you did do a change being effected label change with that.

And then in February of 2001, when the analysis shows that, yes, there is, in fact, a statistically significant mean increase in blood glucose relative to placebo and haloperidol, you don't make any label change.

Is there a pattern that seems to stare at you in the face there?

A. No.

Gary Tollefson, M.D. (November 6, 2006)

Q. In February of 2001, or anytime in 2001, did anyone at Lilly propose to change the Zyprexa label to advise physicians that your continuous analyses showed that olanzapine does result in statistically significant mean increases in random glucose relative to placebo and haloperidol?

A. I wasn't directly involved with the product, I can't answer that. I know that there subsequently was a submission to the FDA with this data, and I believe it did lead to a label change, and I believe it was associated with the weight gain.

Gary Tollefson, M.D. (November 6, 2006)

Between 2000 and 2004, the only label changes that occurred in the Zyprexa label with respect to hyperglycemia were, 1, the label change that you folks did in May of 2000 that we've already discussed that the FDA made you take out later that same year, and the label change that was imposed, mandated, by the FDA in September 2003, correct?

Gary Tollefson, M.D. (November 6, 2006)

A. I believe that's correct.

Q. Sir, in your continued involvement with Zyprexa after 2000, were you ever consulted with respect to whether Lilly should make a label change to warn about hyperglycemia after the Japanese government required such a warning in April of 2002?
A. Not that I know of.

MR. SUGGS: I'm handing you Plaintiff's Exhibit 8666. For the record, this is a June 27, 2002, e-mail from Simeon Israel Taylor to Willard Dere, with copies to a number of individuals including Dr. Tollefson.

273:11 Q. Okay. Do you recall
12 receiving this e-mail on or about June 27,
13 2002?
14 A. I'd have to look at it for a
15 moment.
16 I don't remember this one,
17 no.
18 Q. Okay. Would you agree with
19 me that this appears to be some discussion in
20 this e-mail about appointing a panel to look
21 at the issue of hyperglycemia?
22 A. I'm having a hard time
23 determining what the topic for the panel is.
24 Q. Well, if I could direct your
274: 1 attention to the third page there's an e-mail
2 from Meng Tan to Willard Dere with copies to
3 other folks including yourself.
4 A. Um-hum.
5 Q. And he says, "Will, Thank you
6 for inviting me to the June 25-26 meetings on
7 Zyprexa and hyperglycemia meetings." Do you
8 see that?
9 A. I do.
10 Q. And then there's some
11 discussion about five potential candidates to
12 consider for that meeting, correct? All of
13 whom appear to be involved with diabetes
14 issues, correct?
15 A. Yes.
16 Q. Okay. And then in the
17 succeeding e-mails, there's discussion about
18 various people who might be appropriate to
19 serve on this outside consultant panel,
20 correct?
21 A. Yes.
22 Q. And then finally, the last
23 e-mail in this chain is from Dr. Simeon

Israel Taylor, correct, on the first page?
A. Yes.
Q. And who's Dr. Taylor?
A. He was a, I believe, sort of a guest researcher at Lilly on sabbatical, who had an interest in a variety of areas of internal medicine but I think inclusive of metabolic concerns.

Gary Tollefson, M.D. (November 6, 2006)

Q. Okay. Looking at his e-mail, the last part of his first paragraph -- well, actually starting at three lines or four lines up from the bottom in the middle of the line there he says, "Perhaps we should retain the right to veto panel members, but probably not to choose the members. Clearly, this approach entails some risk that we will be unhappy with the panel's findings. However, I feel that we need to deal with the scientific facts, whatever they are. Ultimately, I am expect that a fair-minded, scholarly evaluation of the available data is likely to support several conclusions." And then he lists what those conclusions are, correct?
A. Yes.
Q. And the first conclusion is "Zyprexa, like other members of the class, causes weight gain."
A. Correct.
Q. And would you agree with Dr. Taylor that Zyprexa causes weight gain?
A. Yes.
Q. Okay. And then he goes on to say in point two, "Like other causes of weight gain, Zyprexa-induced weight gain probably increases the risk of diabetes." Do you see that language?
A. That's what he says.
Q. And did you respond back to Dr. Taylor?
A. I don't recall.

Gary Tollefson, M.D. (November 6, 2006)

Q. Sir, you take the position today that Zyprexa does not increase the risk of diabetes, correct?
A. Whether it does or doesn't I think is unknown.

Exhibit 16
Denice Torres

Denice M. Torres (December 15, 2006)

31: 4 Q. Can you tell the jury your
5 name, please.
6 A. Denice Torres.
7 Q. Ms. Torres, can you tell the
8 jury where you work?
9 A. I work for a division of
10 Johnson & Johnson called Ortho-McNeil
11 Neurologics.

Denice M. Torres (December 15, 2006)

42: 5 Now, prior to coming to work
6 with Eli -- with Ortho-McNeil in January
7 of 2004, where were you employed?
8 A. Eli Lilly & Company.
9 Q. And you had worked at Eli
10 Lilly & Company since when?
11 A. 1990.

Denice M. Torres (December 15, 2006)

46:20 Q. Now, in preparing for the
21 deposition, I looked at some documents to
22 determine what your work history and
23 background was, and I'm going to go over
24 that in some more detail. But just for
47: 1 the record for the jury, what was your
2 title at the time you left Eli Lilly at
3 the end of December of 2004?
4 A. Executive director, global
5 marketing.
6 Q. Executive director of global
7 marketing for what product?
8 A. Zyprexa, and then for a very
9 short time period, Symbyax.
10 Q. Okay.
11 Symbyax is a combination
12 product of Zyprexa and what else?
13 A. Prozac.
14 Q. Prozac is also a Lilly
15 product, right?
16 A. That's correct.
17 Q. Prozac was the number one
18 selling blockbuster drug for Eli Lilly
19 until Zyprexa took over that position; is
20 that correct?

Denice M. Torres (December 15, 2006)

47:23 THE WITNESS: I think those
24 are two very separate things.
48: 1 Prozac was certainly incredibly,
2 incredibly successful in the
3 marketplace and really changed the
4 way that depression was recognized

by physicians and by consumers. Was there a transition from Prozac to Zyprexa? No. That's not --

Denice M. Torres (December 15, 2006)

After the time Prozac lost its patent protection, Eli Lilly bet the farm on Zyprexa, did they not?

Denice M. Torres (December 15, 2006)

THE WITNESS: What do you mean, "bet the farm"?
BY MR. ALLEN:
Q. You don't understand the question?

Denice M. Torres (December 15, 2006)

Isn't it a fact that after Prozac lost its patent protection, the sales of Zyprexa in the United States and worldwide were the key to Eli Lilly's corporate success?

Denice M. Torres (December 15, 2006)

THE WITNESS: They were a key.

Denice M. Torres (December 15, 2006)

Q. They weren't the key?
A. No.

Denice M. Torres (December 15, 2006)

THE WITNESS: I mean, if you look at -- I'll answer your questions to the best I can.
In terms of Lilly's short-term success, Zyprexa was very important.
In terms of long-term success, every pharmaceutical company's goal is to develop a rich pipeline. And so, you know, for a point in time, if you said for X year was Zyprexa incredibly important and pivotal to Lilly,

yes, from a short term time period. But so much of the company, in fact, much of what I did in global marketing was focused on long-term, long-term growth of the company. So, if you want -- if you're asking your question for a certain time period, yes, Zyprexa was incredibly important and really at the center of Lilly, yes.

Denice M. Torres (December 15, 2006)

THE WITNESS: You know, it was interesting. I worked on women's health before coming to Zyprexa, and I felt what I was doing was incredibly important to the company. So, I can't say that it was betting the farm because we invested a lot of money in other therapeutic areas. And so I spent -- I dedicated a good part of my life to women's health, and I felt like that was really important to the company. So, I don't think Lilly bet the farm.

Denice M. Torres (December 15, 2006)

Q. You were on the team that bet the farm, weren't you?

Denice M. Torres (December 15, 2006)

THE WITNESS: I was on a team that we dedicated our time and our careers to Zyprexa. I can't -- you know, I find it distasteful to talk about medication in the way of betting a farm. There's people's lives behind that, and I find that -- I can't characterize, you know, betting the farm in the way of talking about people's lives and about developing medications.

Denice M. Torres (December 15, 2006)

Q. That's distasteful to you?
A. Yes, it is.

56:19 Q. And you've been involved in
20 the pharmaceutical business here in the
21 United States for how long?
22 A. Since 1990.
23 Q. Can you describe for the
24 jury, please, why it is, in your words,
57: 1 "distasteful" to use the phrase "bet the
2 farm" in regard to Zyprexa sales?
3 A. You know, someone else may
4 use that term, and that would be
5 appropriate for them. I don't like to
6 talk about -- you know, there's
7 definitely a part of everything we do
8 that we have a shareholder. We're a
9 for-profit company. But in terms of, you
10 know, if you're saying everything that
11 Lilly did, which I would characterize by
12 the colloquial term, "betting the farm,"
13 was about Zyprexa, that is not what I
14 saw. I worked in other therapeutic areas
15 when Zyprexa was around. So, did Lilly
16 bet everything? No. Did the team bet --
17 did the team commit everything they could
18 to Zyprexa? If you're working on
19 Zyprexa, that's what you're going to do.
20 Q. My question to you is, you
21 told the jury clearly about
22 two-and-a-half minutes ago that the use
23 of the term "bet the farm" in relation to
24 Zyprexa was distasteful to you.
58: 1 A. It --
2 Q. Let me finish my question.
3 A. Sure.
4 Q. Why is it distasteful to
5 you?

Denice M. Torres (December 15, 2006)

58:14 A. From my standpoint, the way
15 you're characterizing it, you know, in
16 terms of basically saying Lilly, that's
17 all Lilly was doing was banking on
18 Zyprexa because it's all about -- and,
19 again, you know, maybe I'm putting words
20 in your mouth -- it's all about
21 short-term financial success, I think
22 that's inappropriate. You know, and I
23 think it mischaracterizes what the goal
24 of a pharmaceutical company is.
59: 1 Now, if you're talking about
2 in a pure bottom-line context, you know,
3 financially, were the people -- from a
4 Zyprexa team standpoint, were we, you
5 know, totally committed and did we have
6 resources to maximize the brand?
7 Absolutely. Absolutely. But, you know,
8 it's all in the context of the word
9 you're using. And I'm not, you know,
10 trying to be coy. I'm just not really

sure what you're asking me here. Would it be -- you know, would I call something like we're going to -- if it's in regard to patients betting the farm on certain patients? No. If you're talking about it from a business standpoint, fine. And I just don't -- I don't really know what you're asking me.

Denice M. Torres (December 15, 2006)

So, let me see. You graduated from Ball State. Is that in Muncie?

A. Yes.

Q. You graduated from there in 1981 with a degree in what?

A. Psychology and sociology.

Q. Okay.

After graduating from Ball State, you went to Indiana University School of Law?

A. That's correct.

Q. Did you go straight from Ball State to that law school?

A. I did.

Q. I presume if you got out on time, you got out of law school in 1984?

A. That's correct.

Q. You're a lawyer?

A. Yes.

Q. You, in fact, went to work at a law firm after you graduated?

A. I sure did.

Q. What law firm did you go to work for?

A. A firm called Smith, Haughey, Rice & Roegge.

Q. Where?

A. In Grand Rapids, Michigan.

Q. You did litigation work; is that correct?

A. I did. As a first-year lawyer, I pretty much did research for workers' compensation.

Denice M. Torres (December 15, 2006)

You're still a lawyer though, aren't you?

A. I sure am.

Q. What states are you currently licensed to practice law?

A. I keep my license up in Michigan.

Denice M. Torres (December 15, 2006)

71:17 Q. So, after finishing your law
18 job at the insurance defense firm with
19 some interim jobs, you went to work for
20 the advertising company?
21 A. Yes.
22 Q. In Grand Rapids. After
23 concluding that job, you got your
24 M.B.A. --
72: 1 A. Yes.
2 Q. -- from the University of
3 Michigan?
4 A. Yes.
5 Q. In Ann Arbor?
6 A. Yes.
7 Q. And then you went to work
8 for Eli Lilly in 1990 where you worked
9 until the end of December 2004?
10 A. That's correct.

Denice M. Torres (December 15, 2006)

73: 6 At the time you left, you
7 were marketing executive director for
8 Zyprexa global brand?
9 A. That's correct.
10 Q. You had been the managing
11 executive director of marketing for
12 Zyprexa global brand at Eli Lilly from
13 when to when?
14 A. I was promoted while I was
15 in that role, so, it was basically
16 2000 -- I can't remember if I started in
17 2000 or 2001, but about eight months or a
18 year after being in that role, I was
19 promoted.

Denice M. Torres (December 15, 2006)

75:11 Q. When did you first become
12 involved in any role in Zyprexa?
13 A. Again, I can't remember if
14 it was 2000 or 2001.
15 Q. Prior to that, what did you
16 do at Eli Lilly?
17 A. I was in the women's health
18 group.
19 Q. What products were you
20 involved with prior to 2000 when you
21 became involved in Zyprexa?
22 A. Evista, growth hormone prior
23 to that, and then I was in charge of the
24 market research group. I've been in
76: 1 managed care, new product planning,
2 business development. I was a sales
3 representative for two years.
4 Q. Where were you a sales rep?
5 A. In Chicago.
6 Q. Was that from the start --
7 when you first started with the company?

A. No. I started off, actually, in new product planning. And then from there -- I spent about a year in new product planning, global new product planning, and then was a sales representative for two years after that.

Q. Sounds like you were a sales rep sometime between about '91 and '94?

A. That's right. I think it was 1991 to '93.

Q. What products of Eli Lilly did you detail as a sales representative?

A. I had Prozac, Ceclor and Axid.

Denice M. Torres (December 15, 2006)

77:18 Prozac was, at the time you were a sales representative, that was the number one selling product for Eli Lilly, was it not?

A. Yes.

Q. It was a blockbuster product, was it not?

Denice M. Torres (December 15, 2006)

78: 3 THE WITNESS: It was a blockbuster at the time.

Denice M. Torres (December 15, 2006)

78: 6 **Q. Tell the jury, because I want them to know, and I think maybe at the time they see your testimony, they will have heard, but "blockbuster" is not a term that Scott Allen created, that's a term of art in the pharmaceutical industry, is it not?**

Denice M. Torres (December 15, 2006)

78:15 THE WITNESS: You know, I think it's a term used a lot by perhaps analysts or other people, and there's a lot of what does blockbuster mean. When Ceclor was around, Ceclor was a blockbuster, and I don't even think it sold a billion dollars. It's all relative. I can't give you a
79: 1 dollar amount, but it means a very successful product, yes.

BY MR. ALLEN:

Q. Well, Prozac was a

multibillion dollar blockbuster for Eli Lilly?

Denice M. Torres (December 15, 2006)

THE WITNESS: It was a blockbuster.
BY MR. ALLEN:
Q. Yes. It was a multibillion dollar blockbuster?
A. I don't think it actually was. I know it sold over a billion. I don't know if it ever got above that. It was -- suffice it to say, it was a very, very successful product.
Q. We know Zyprexa was a multibillion dollar blockbuster for Eli Lilly. We know that.

Denice M. Torres (December 15, 2006)

THE WITNESS: Zyprexa was a blockbuster, and it was multibillion, yes.

Denice M. Torres (December 15, 2006)

That's what made it the engine room of the company.

Denice M. Torres (December 15, 2006)

THE WITNESS: It wasn't the -- I think I've stated this several times. Zyprexa was very important to Eli Lilly & Company in terms -- by saying "engine room," engine room is what makes, you know, a train work, you know, something like that, and it was not the only -- was it in the engine room? Sure. Was it the engine room? No.

Denice M. Torres (December 15, 2006)

Q. Who is Glyn Parkin?
A. Glyn Parkin was the vice president that oversaw sales and marketing for the U.S. affiliate for Zyprexa.
Q. So, he would certainly know about the importance of Zyprexa to Eli

Lilly, would he not?

Denice M. Torres (December 15, 2006)

THE WITNESS: Yes.

Denice M. Torres (December 15, 2006)

Q. The first exhibit I need to you show you I'm going to put on the screen and see if it helps.

Denice M. Torres (December 15, 2006)

This is a document I marked as Exhibit Number 3. The court reporter will denote it as Torres-3 at the conclusion. It's a memoranda of February 25, 2003. And it just -- it is internal to Eli Lilly. It was produced to us.

Denice M. Torres (December 15, 2006)

Q. By 2003, what were Zyprexa sales worldwide?
A. I don't remember for sure, but according to this document, it says it's approaching $4 billion globally.
Q. $4 billion. Wasn't Zyprexa by early 2003 not only a $4 billion worldwide sales drug, but one of the "fastest growing" drugs in terms of percentage sales in the world?
A. That's what it says here, yes.

Denice M. Torres (December 15, 2006)

I think by 2003, I don't know if it's reflected in that document, but you can probably recall from your long experience involved in marketing, in global marketing for Eli Lilly, wasn't by 2003 Zyprexa either the third or fourth largest selling drug product in the world?
A. Yes.
Q. So, it just goes without saying, Zyprexa was a very important financial product to Eli Lilly?

Denice M. Torres (December 15, 2006)

85:22 THE WITNESS: Yes.

Denice M. Torres (December 15, 2006)

86: 1 I handed you prior to the
2 start of the deposition, I think you have
3 it in front of you as Exhibit Number 1, a
4 document entitled, that we got from your
5 files, "Restructuring of the Marketing
6 Component" of the "Zyprexa Product Team."
7 You've looked at that, have you not?
8 A. Yes, I have, sir.

Denice M. Torres (December 15, 2006)

87: 5 Q. -- and let me get down here
6 to the nitty-gritty. "Restructuring the
7 Marketing Component" --

Denice M. Torres (December 15, 2006)

87:21 "We are pleased to announce
22 the restructuring of the Marketing
23 component of the Zyprexa Product Team.
24 In July of this year the Zyprexa Product

Denice M. Torres (December 15, 2006)

88: 1 Team, led by the efforts of Denice
2 Torres, Global Marketing Director for
3 Zyprexa, embarked upon an important
4 initiative, Project Open Door. The
5 purpose of this initiative was to
6 identify action steps to: (1) achieve our
7 goal of reaching $6 billion by 2006."
8 Did I read that correctly?
9 A. That's correct.
10 Q. It goes on, and I'm skipping
11 down to the last sentence of this first
12 paragraph. "The U.S. Affiliate -- with
13 significant leadership from Glyn Parkin
14 and Jack Jordan -- was instrumental in
15 the development of the new team." Did I
16 read that correctly?
17 A. That's correct.
18 Q. Now, as I went through this
19 document, it described the members of
20 this new restructured global marketing
21 team who had as one of its goals $6
22 billion in annual sales, right?
23 A. That was one of the goals,
24 yes.
89: 1 Q. It was the number one goal.

2 It's listed number one, isn't it?

Denice M. Torres (December 15, 2006)

89: 5 THE WITNESS: It's listed in
6 a sequence of several.

Denice M. Torres (December 15, 2006)

89: 8 Q. Well, it has a number by it,
9 doesn't it?
10 A. Just as you would list
11 apples, oranges, pears, et cetera, it's
12 one of the goals. It wasn't meant to say
13 that was the primary goal and everything
14 else supported that.
15 Q. Well, it says the purpose --
16 it's misspelled "the purposed," but I
17 would assume that means purpose, "of this
18 initiative was to identify action steps:
19 (1) achieve our goal of reaching $6
20 billion by 2006." Did I read that
21 correctly?
22 A. You read that correctly in
23 terms of that is listed as number 1 in
24 the sequence of three different items.
90: 1 Q. Let's look at number 2 then.
2 Number 2: "identify drivers that produce
3 the greatest customer and affiliate
4 value." So, the number one goal, $6
5 billion in sales; and the number two goal
6 is "identify drivers that
7 produce...affiliate value."

Denice M. Torres (December 15, 2006)

90:11 Q. Is that correct?
12 A. You missed out on an
13 important word, "Customer."
14 Q. Okay.
15 Number 3 is "insure world
16 class global marketing for Zyprexa."
17 A. Yes.
18 Q. Are there any other goals
19 listed?
20 A. No. Those were the three
21 goals.
22 Q. The three goals -- all
23 right.
24 Now, I'm back to my
91: 1 question. When I looked at this
2 document, when the -- did you prepare
3 this document, by any chance?
4 A. I think I prepared a good
5 part of it, yes.
6 Q. That's what I figured,
7 because this is kind of your team, isn't

it?
A. Yes.

Denice M. Torres (December 15, 2006)

Q. Tell the jury what global marketing is.

A. Global marketing is a -- global marketing, a group of people that are responsible for overseeing the branding of -- the branding of certain elements of the strategy for a product. And so I would imagine you're going to ask me what are those elements.

What does a global marketing team do? Prior to launch, the global -- a global marketing team basically is in place to help prepare a product for launch, and that could happen three years prior to or four years prior to the actual launch of a product. And so that would be, you know, looking at things, identifying what are its customer needs, what's the size of the market, give input into what customers might want in clinical trials, would it be required in terms of getting reimbursement for the product, what are some new indications that we should take a look at that would be of good customer value and value to the company.

Other things we're looking at, the branding of the -- as you get closer to market, looking at the branding. So, what are the visual -- the marketing elements of the brand, and so it looks the same across the world. So, those are some of the key components.

After launch, the team -- the purpose of this initiative was really to look at what are the values of the team. And it actually became apparent over the years that the team should be disbanded, because a year or two years after launch, there really was not a huge need for a global marketing group.

Q. Okay.

Exhibit Number 1 concerning the "Restructuring of the Global Marketing for Zyprexa," this restructuring took place in what year, ma'am?

A. Like I said, I can't remember exactly when it was. We started working on it pretty quickly after I joined the team. And so I think -- I'm sure it happened within -- well, I'm not sure. But it seems to me like it happened within eight or nine months of me coming on the team.

Q. You came on the team when?

A. Again, I don't remember if it was 2000, 2001. I really don't remember.
Q. **Now, after this team was formed --**
A. It was 2001. My daughter was born in 2000. Okay.
Q. **After this team was formed, you still remained in charge of global marketing for Zyprexa until the time you left?**
A. Yes.

Denice M. Torres (December 15, 2006)

95:16 Ms. Torres, as the global marketing director for Zyprexa, what is the goal of marketing?

Denice M. Torres (December 15, 2006)

96:13 A. The goal of marketing is to understand customer needs, and a big basis of marketing is to understand what are needs, wants, concerns of a customer. And then you have a product or the hope of developing a product. The nirvana in marketing is being able to take a customer need and fill that need with a product of the company. And so that is -- you know, there's a whole process behind how that happens and ultimately how you reach customers and what are the 97: 1 messaging, but the epicenter, if you want to call it the engine room, begins with being able to identify customer needs and where is there an opportunity.
So, a product would have strengths and weaknesses, and from a customer standpoint, there's opportunities. What are those opportunities and how can we meet those needs? It doesn't matter what product is. That's pretty much the foundation.
Q. **It doesn't matter if it's a Ford truck --**
A. It doesn't matter.
Q. **-- or a drug, right?**
A. It doesn't.
Q. **So, your answer concerning marketing that you just gave this jury, as you clearly stated, it was your view, it didn't matter what the product was, that's how they go about it, right?**
A. In terms of a process. You know, for instance, if you were to go to 98: 1 business school, get your M.B.A., or pick up marketing textbooks, the process of understanding a customer is pretty much

the same. It's pretty much the same because they're underlying, you know -- they're underlying needs that people have. You could look at Maslow's Hierarchy of Needs. I mean, that's a lot of marketing is -- what are -- you know, any product that is born and is successful fills some kind of need for a person or for a group of people. And so the process, the process of understanding needs is very, very consistent because it's a human nature type of thing.

Denice M. Torres (December 15, 2006)

Let me just hand you Exhibit 5. Just for the record, we'll spend one second on it.

Denice M. Torres (December 15, 2006)

Q. Zyprexa marketing, August '02, Denice Torres, Director of Global Marketing. Does that reflect that?
A. Yes.
Q. All the individuals below that worked for you?
A. That's correct.
Q. Including, but not limited to Mr. Michael Bandick, director of marketplace management, right?
A. That's correct.
Q. Marketplace management is the same as issues management, is it not?
A. No.

Denice M. Torres (December 15, 2006)

THE WITNESS: Do you want me to explain marketplace management?
BY MR. ALLEN:

Denice M. Torres (December 15, 2006)

Q. Yes, ma'am, please, shortly, if you can.
A. Marketplace management entails all the groups that are listed here in terms of the reports, competition, issues management, access, thought leaders and -- access and basically, you know, thought leaders in the marketplace, meaning there are a number of different of these groups or categories that fit under one umbrella,

and that's marketplace management. So, issues management is one aspect of that.
Q. One other aspect is thought leaders?
A. Yes.
Q. And I see under there, there's -- in this graph -- Mr. Fibich wins the bet, it's going to be a little longer than we thought -- Mike Bandick goes down here, and underneath him, the position is open, but it says "Access, TL," that's thought leader?
A. Thought leader, yes.
Q. And "Customer Meetings"? Is that right?
A. Yes.
Q. The people under marketplace managers include Matt Pike, who is the manager of issues management; is that correct?
A. That's correct.
Q. "Issues management" is what, ma'am?
A. Issues management can -- it primarily focused in on issues that affected the affiliates and where there needed to be some type of an answer. It could be clinically oriented, it could be on the basis of, there were payor -- some payor things where there was information that was required, you know, certainly dealing with competitive challenges around data, et cetera. So, that was what that group did. It was a pretty -- it's whatever came up. And so, you know, you have a core amount of responsibilities, but with any drug, things come up that require some answer or solution.

Denice M. Torres (December 15, 2006)

Q. You were in senior management, though, at Eli Lilly in regard to Zyprexa, were you not?
A. With regard to Zyprexa, yes.

Denice M. Torres (December 15, 2006)

Now, as a sales representative, did you have an important job?
A. Yes.
Q. Why was your job important?
A. My job was important because of the responsibilities, and so responsibility from a company standpoint to share the information about a disease state and customers in a therapeutic

area, the responsibility to be well informed about customers, their challenges, about patient needs, et cetera, and ultimately to also share the role our drug would play in addressing some of those needs. And so that also was a very important aspect.

Q. Why does a company and why did Eli Lilly have sales representatives?

A. One of the -- you know, one big reason is that in many therapeutic areas, you know, whether Prozac or even Zyprexa, prescribers/physicians may not know about -- you know, they may not have learned as much in medical school about certain conditions, et cetera, because they can't be experts in everything. So, what a sales representative can do is to help bring information about a therapeutic area, about treating customers -- treating patients or an actual drug, bringing that information to those customers.

Q. Right. And I think you are hitting the nail right on the head. And let me just see if I can even define this better so the jury can better understand it and the people that will listen to your testimony when they evaluate their decision in this case. As a sales representative, you said doctors that you would go see can't know everything about drug products, right?

A. That's correct.

Q. And, in fact, you said, I think, and I'm paraphrasing your answer, that in their medical school training, there's no way they can learn about the drugs and the development of drugs and how drugs work and particularly about all the drugs that are on the market; is that correct?

Denice M. Torres (December 15, 2006)

THE WITNESS: I mean, there's certain things that they have a responsibility for, and there's certain things from a sales representative standpoint, say, they may not know the dose of a drug, they may not know interactions and ask an individual. And they get information from a lot of different sources, but the role of the sales force is to help them with that.

Denice M. Torres (December 15, 2006)

127: 6 Q. And the role of the sales
7 representative is to give doctors
8 truthful and accurate information about
9 the risk and benefits of the product; is
10 that true?
11 A. That's true.
12 Q. Is to give doctors truthful
13 and accurate information about the
14 indications for the product?
15 A. Absolutely.
16 Q. It is the role of the sales
17 representative not to promote a product
18 for off-label uses?
19 A. That's correct.
20 Q. To do so would be a
21 violation of law?
22 A. Yes.

Denice M. Torres (December 15, 2006)

130:15 Q. It's your job as a sales
16 representative to assist the doctor or
17 the physician who you are calling upon
18 with information that they need to know
19 that it's important for them to know with
20 their patients?
21 A. That's correct.
22 Q. And the reason you're going
23 to the doctors' offices on behalf of Eli
24 Lilly is to market and sell your product?
131: 1 A. To be of service to the
2 customer. And the reason that we go
3 there is to be of service, and the
4 outcome, to use the product for the
5 appropriate patient for the appropriate
6 reason, yes.

Denice M. Torres (December 15, 2006)

134:17 Q. Now, you said it would be
18 improper, illegal for the sales rep to
19 promote off-label use. Do you recall
20 that?
21 A. To promote for use, yes.
22 Q. Off-label use?
23 A. Yes.
24 Q. Tell the jury -- define what
135: 1 off-label use is.
2 A. Off-label use is if a
3 prescribing physician used a drug for
4 something other than it was indicated or
5 approved by the FDA, that would be
6 referred to as off-label use.
7 Q. Wasn't the majority of the
8 use of Zyprexa in the United States off
9 label?
10 A. I don't -- I don't know if
11 it was the majority, but a good portion

of use of all antipsychotics are used off label.

Denice M. Torres (December 15, 2006)

Q. Listen to my question. I'm not here to talk -- I'll let you know when I want to talk about Risperdal, Seroquel, Geodon, Abilify. I'll let you know that. You're here for Eli Lilly on behalf of the marketing of Zyprexa, right?

A. Yes.

Q. Okay.

So, I'm going to limit my questions to Zyprexa unless I tell you otherwise. All right?

A. Okay.

Q. Wasn't the majority of the use of Zyprexa in the United States off label?

A. There was a good portion. I don't -- I don't remember the exact numbers. I don't remember it being the majority.

Q. Can you give the jury your best estimate, please.

A. Maybe 30 to 40 percent.

Denice M. Torres (December 15, 2006)

As you became involved in global marketing for Zyprexa, you certainly knew that a substantial portion of Zyprexa sales both in the United States and around the world was related to off-label prescriptions?

A. When I joined the team? Yes.

Q. Yes, ma'am.

And, in fact, did you not and weren't you one of the individuals at Eli Lilly along with others that used different channels and methods to promote and facilitate off-label prescriptions of Zyprexa?

A. Absolutely not, no.

Q. You never would do that?

A. No.

Q. Didn't John Lechleiter do that?

A. I'm not familiar with John Lechleiter doing --

Q. How about Alan Breier, Dr. Breier?

A. I'm not familiar with --

Q. If they did that, it'd be wrong?

A. Yes, it would be wrong.

Q. It'd be illegal?
A. If they were advising physicians to use the drug for indications other than what was approved, it would be wrong, yes.
Q. It would be wrong for them to assist and train sales representatives to promote the use of Zyprexa off label, would it not?
A. Yes, for the purposes of getting prescribers to use a drug off label, that would be wrong.
Q. Right.
So, if they -- if Dr. Breier or Jack Jordan or John Lechleiter tried to train or inform sales representatives to assist them in getting doctors to use the drug off label, that would be wrong?
A. If the goal were to get physicians/prescribers to use the drug off label, that would be wrong. If the goal were to inform or educate about other uses of Zyprexa, that would not be wrong.

Denice M. Torres (December 15, 2006)

Q. So, when you told us earlier that there was no indication for Alzheimer's, Alzheimer's dementia or Alzheimer's psychosis, you would agree that there are no double blind, placebo-controlled clinical trials submitted to the FDA supporting the safety and efficacy of Zyprexa for those conditions; is that correct?
A. I can't remember what was submitted to the FDA, but what I can say is, no, there was no approved use for those indications.
Q. Similarly, there was no double blind, placebo-controlled trials submitted to the FDA supporting the safety and efficacy of Zyprexa for use in long-term nursing home or resident care, true?

Denice M. Torres (December 15, 2006)

THE WITNESS: I guess if you could preface or if you could restate your question, because in general, you know, writing a -- so no one would write a prescription for long-term nursing care. So, I'm not sure what you're referring to in terms of -- you know, could you have individuals with, you know, schizophrenia in a nursing

home? Absolutely. They're in every -- that's part of the population. For bipolar disorder, absolutely.

Denice M. Torres (December 15, 2006)

144:20 Q. Long-term care. I've seen
21 it summarized in your documents, LTC.
22 You've seen that in your marketing
23 documents, haven't you?
24 A. Yes.
145: 1 Q. Wasn't --
2 Just for the record, your
3 company and you in marketing concentrated
4 part of your efforts in marketing Zyprexa
5 for LTC, did you not?
6 A. The U.S. affiliate, yes.
7 Q. In fact, the U.S. affiliate
8 of Zyprexa had an LTC sales force, did
9 they not?
10 A. Yes, they did.

Denice M. Torres (December 15, 2006)

145:19 Q. You said they had a
20 long-term care sales force. What was
21 their job?
22 A. To promote an indication in
23 those settings.
24 Q. So, the long-term care sales
146: 1 force was only to promote Zyprexa for
2 indicated uses, and the only indicated
3 uses were what, ma'am?
4 A. Schizophrenia and bipolar
5 mania.

Denice M. Torres (December 15, 2006)

146:13 Just for the record, Zyprexa
14 never had an approved indication by the
15 FDA for bipolar depression, did it?
16 A. That's correct.
17 Q. Okay.
18 Zyprexa never, ever, not
19 ever as we sit here to this day, has ever
20 had an indication for depression at all,
21 has it?
22 A. That's correct.
23 Q. Bipolar or otherwise,
24 correct?
147: 1 A. Correct.
2 Q. Okay.
3 So, if anybody ever was
4 prescribing Zyprexa for depression or
5 bipolar depression, that was an off-label
6 prescription, wasn't it?

A. Yes.
Q. Okay.
Didn't Eli Lilly go out and try to get doctors to prescribe Zyprexa for depression and bipolar depression?
A. No.
Q. They never did that?
A. Not that I'm aware of.
Q. Let me get this clear on the record. Just so there's no doubt, Zyprexa never had an indication at any time for anxiety, did it?
A. No.
Q. So, it would be wrong to try to promote Zyprexa for anxiety?
A. Yes.
Q. It never had an indication for hallucinations, did it, unrelated to schizophrenia?
A. No. Unrelated to schizophrenia or bipolar.
Q. Right. Let me just get out the list here. I have a list.
Zyprexa never had an indication for complicated mood disorder, did it?
A. I don't think you can get an indication for complicated mood disorder.
Q. Therefore, you didn't have an indication for that, did you?
A. No.
Q. It didn't ever have an indication for attention deficit disorder, did it?
A. No.
Q. Therefore, it would be illegal to promote sales of and use of Zyprexa for attention deficit disorder, wouldn't it?
A. Correct.
Q. It never had an indication for hyperactivity disorder, did it?
A. No.

Denice M. Torres (December 15, 2006)

Q. Just for the record, it would have been illegal to promote Zyprexa for hyperactivity.
A. Hyperactivity associated with -- I mean, if it was part of a clustering of symptoms, if you're saying that the only thing that the person exhibited was hyperactivity, yes, that would be wrong.

Denice M. Torres (December 15, 2006)

Q. It would be wrong to suggest

in the sales and marketing of Zyprexa to physicians when you make sales calls to tell them Zyprexa is indicated for the cluster of symptoms of agitation and depression? That would be wrong, wouldn't it?

A. If those were the only two symptoms, yes.

Denice M. Torres (December 15, 2006)

Zyprexa had limited indications, did it not?

A. Zyprexa had an indication for schizophrenia and bipolar mania.

Q. That's it.

A. Yes.

Denice M. Torres (December 15, 2006)

Q. Ma'am, as you're looking through there, we're going to put Exhibit Number 2 up for the jury to see this document. "Zyprexa Product Team Off-Site, July 25, 2001." "Lilly. Answers that matter."

I will flip through the document along with you.

I feel relatively certain, ma'am, that you have read through this document now enough to tell the jury what this document is.

Denice M. Torres (December 15, 2006)

Q. Tell the jury what this document is, Exhibit Number 2, ma'am.

Denice M. Torres (December 15, 2006)

THE WITNESS: I'm finished looking at it. I don't remember this document.

Denice M. Torres (December 15, 2006)

This is a document that came from Lilly's files and has been produced in this case. And by the way, right down here, the jury will have seen this before by the time we go to trial, but there's a, what do we call that, a slogan at Eli Lilly, is there not?

A. "Answers that matter"?
Q. Yes.
A. Yes.
Q. What's that mean?
A. I can tell you what it means to me. It's providing people with information that in the customers, take holder, et cetera, that -- providing information that's pertinent to them, meaningful to them.
Q. It means that Lilly, when they give you the answer, they know the answers matter, that the answer is going to be truthful, it's going to be accurate, the information and data is not going to be spun, but it's going to be direct and to the point and truthful, right?

Denice M. Torres (December 15, 2006)

THE WITNESS: I think that's fair, right. Absolutely.

Denice M. Torres (December 15, 2006)

Q. What I said is fair, isn't it?
A. Absolutely.
Q. It's fair of doctors and patients to expect that when Lilly gives them answers about their product, the data is not going to be spun, and the answers are going to be accurate, right?

Denice M. Torres (December 15, 2006)

THE WITNESS: Yeah. I think it means that the company will be honest and --
BY MR. ALLEN:
Q. Truthful?
A. -- straightforward, truthful, thank you.

Denice M. Torres (December 15, 2006)

Design team on the Zyprexa product team under "Decision Makers," design team decision makers, team leaders, "Vin Rampey" and "Denice Torres." Did I read that correctly?
A. Yes.
Q. What is the design team?
A. I guess for this -- I

somewhat remember this. It definitely was a project. I don't remember this document or a meeting. Basically you can see the group on the bottom, what it looks like from going through this --

Q. This group on the bottom, the support group?

A. I'm sorry. The support group, yes. I'm thinking that maybe they put together a good portion of the document to lead the team through a discussion around the work of -- you know, the vision, developed the vision for the team and what's the culture, next steps. Basically, what does the brand represent. I don't know if -- what I don't know is, did the meeting happen? I don't know that.

Q. That's what the answer always is when we have PowerPoint presentations, but I'm just going to go with the document that I had.

Did y'all have meetings there at Eli Lilly?

A. Oh, we had a lot of meetings, yes.

Q. Did you have Zyprexa product team meetings?

A. Yes.

Q. Did you have Zyprexa product team meetings off site?

A. Yes. At times I'm sure we did.

Q. Yes.

Did you have PowerPoint presentations at the meetings?

A. Sure.

Q. And the PowerPoint presentations were prepared so the participants in the meeting could -- it would act as, I guess my word I'm choosing, as an anchor or focus on the next topic?

A. Yes. Or we're providing information, sure.

Denice M. Torres (December 15, 2006)

Q. Nevertheless, Exhibit Number 2 is a PowerPoint presentation of a Zyprexa product team off-site meeting July 25, 2001. You're listed as a member of the decision makers design team and a team leader; is that right?

A. Yes. The second one is right. The first one is -- I don't know if -- it looks like the document was prepared for that. I don't know if the meeting ever happened. I really don't remember the meeting.

Denice M. Torres (December 15, 2006)

169: 2 Q. Let me ask this. In global
3 marketing, you were the director of it,
4 we've seen that. We're going to see
5 where you were on some other teams. We
6 know you were on the Zyprexa product
7 team. Were you ever informed about any
8 of Patricia Cavazzoni's findings in
9 regard to blood sugar glucose levels and
10 Zyprexa?
11 A. Yes.
12 Q. Who told you about them?
13 A. I think I was -- I'm sure I
14 was in meetings where she made some
15 presentations in a group or, you know,
16 shared some of her findings. I wasn't on
17 the medical team, but, sure, she shared
18 some things broadly about the profile of
19 Zyprexa, yes.

Denice M. Torres (December 15, 2006)

170:14 Q. Everybody had a
15 responsibility to accurately and
16 truthfully market this product, right?
17 A. That's correct.
18 Q. Did Patricia Cavazzoni -- do
19 you recall being told about her data
20 concerning continuous analysis of blood
21 sugar glucose levels?
22 A. I don't specifically recall
23 that.
24
171: 1 Q. Do you recall being told
2 about her analysis that indicated Zyprexa
3 was statistically significantly related
4 to -- Zyprexa administration was
5 statistically significantly related to
6 increases in blood sugar glucose in
7 individuals who took Zyprexa?
8 A. I don't specifically
9 remember that.
10 Q. Do you recall being told --
11 any presentations by Dr. Charles Beasley.
12 A. I was only in one meeting
13 with Charles Beasley.
14 Q. Do you recall that meeting?
15 A. Only because he was
16 swearing, and someone said that was his
17 personality. But that's what I remember
18 about it.
19 Q. Tell me what year that
20 meeting took place.
21 A. It was right when -- pretty
22 early on when I joined the team.
23 Q. What were you all talking
24 about in that meeting?
172: 1 A. I don't know. I just
2 remember something he said. It was a
little bit, you know --

Q. Inappropriate?
A. I think he used a couple of swear words, which typically did not happen at a Lilly meeting.
Q. Somebody told you that was just his personality?
A. Yes.

Denice M. Torres (December 15, 2006)

173:18 Did Dr. Beasley ever come to you as director of global marketing and tell you Zyprexa was the worst offender in regard to weight gain among the second generation antipsychotics other than clozapine?
A. No. I really never had a one-on-one conversation with Charles Beasley.
Q. Did anybody at Eli Lilly ever tell you as director of global marketing that Zyprexa was the worst offender in regard to weight gain among the second generation antipsychotics except for clozapine?

Denice M. Torres (December 15, 2006)

173:18 Did Dr. Beasley ever come to you as director of global marketing and tell you Zyprexa was the worst offender in regard to weight gain among the second generation antipsychotics other than clozapine?
A. No. I really never had a one-on-one conversation with Charles Beasley.
Q. Did anybody at Eli Lilly ever tell you as director of global marketing that Zyprexa was the worst offender in regard to weight gain among the second generation antipsychotics except for clozapine?

Denice M. Torres (December 15, 2006)

174:15 A. I don't remember the terminology.
Q. Did anybody ever tell you at Eli Lilly that Zyprexa's weight gain profile, the average weight gain profile was double that of Risperdal?
A. I don't believe so.

Denice M. Torres (December 15, 2006)

175:19 Q. So, in order to be an
20 effective, truthful director of global
21 marketing and provide answers that
22 matter, you must be provided with the
23 accurate facts about the risk profile of
24 the drug?
176: 1 A. Yes.
2 Q. Assume with me that it was
3 known at Eli Lilly that the average
4 weight gain on Zyprexa was at least
5 double or approximately double that of
6 Risperdal. You should have been informed
7 of that?
8 A. With reference to Risperdal,
9 I knew about the weight gain. I mean,
10 with reference to Risperdal, I don't
11 specifically remember that. Maybe
12 someone said it, I don't remember. But
13 am I familiar with the weight gain
14 profile of Zyprexa, yes.
15 Q. That wasn't my question.
16 You know, you're talking about -- you
17 talked about, for example, that one of
18 the channels of the U.S. affiliate in
19 marketing was the sales department,
20 right?
21 A. Yes.
22 Q. You talked about the fact
23 that in the sales department, we know we
24 have sales representatives, you were one
177: 1 back in the early 1990s, right?
2 A. Yes.
3 Q. You talked about the fact
4 that you have to give accurate and
5 truthful and, as you said, direct
6 information, is that right?
7 A. That's correct.
8 Q. In order to give that type
9 of information to doctors, the sales
10 force must be told and the marketing
11 department must be told the accurate
12 information concerning the side effect
13 profile of the product, right?
14 A. Yes.
15 Q. Were you ever told that
16 there was animal model testing done on
17 Zyprexa in regard to weight gain?
18 A. Yes. I believe I was part
19 of conversations, yes.
20 Q. What were you told the
21 animal model testing showed, if you
22 recall?
23 A. I don't think I specifically
24 recall.
178: 1 Q. So, as you sit here today,
2 December of 2006, it's Friday, December
3 the 15th, I think we're in New Jersey,
4 Windsor Township, you cannot recall
5 anything you were told about animal
6 testing in regard to weight gain at Eli
7 Lilly on Zyprexa?
8 A. Not specific to animal
9 models. You know, in general what I was

told, I could tell you that. That's not to say it didn't happen. I just don't remember any specifics.

Q. Do you recall that Dr. --

Do you recall anybody from the medical or clinical department at Eli Lilly telling you that the animal model testing indicated that Zyprexa, when administered on diet-restricted rats, that is, in other words, food intake did not increase, that those animals still gained weight on Zyprexa? Were you ever told about that?

A. No. I don't remember that.

Denice M. Torres (December 15, 2006)

179:19 Q. As director of global marketing, were you ever told that there was statistically significant findings of elevated blood glucose levels in the HGAJ study for individuals who took Zyprexa?

180: 1 A. I don't remember the name of the study, so, I wouldn't remember the specifics.

Denice M. Torres (December 15, 2006)

180:17 Q. Were you ever told that Eli Lilly had in their review of their epidemiologic information determined that there was an association between second generation antipsychotics including Zyprexa and diabetes?

Denice M. Torres (December 15, 2006)

181: 1 THE WITNESS: No. There was a lot of discussion about weight and about diabetes, but an association directly with the antipsychotics? No. I mean, there were case reports, et cetera, but did they refer to it as, you know, a direct association? No.

Denice M. Torres (December 15, 2006)

181:11 Q. So, as director of global marketing, you were not told of any epidemiologic information or data supporting an association between second generation antipsychotics including Zyprexa and diabetes?

17 A. I'm sorry. I don't remember
18 that.

Denice M. Torres (December 15, 2006)

181:21 Let's go to Exhibit Number
22 2, the Zyprexa product team, "Answers
23 That Matter." I'm going to skip to the
24 page with the heading "The Chance to Make
182: 1 History." Do you see that? "The Chance
2 to Make History." All right? Are you
3 there?
4 A. Yes.
5 **Q. By the way, I think it would**
6 **help the jury to tell the jury in direct**
7 **language so they understand it because**
8 **when they look at your testimony, what is**
9 **the Zyprexa product team?**
10 A. When I joined the team, the
11 product team were a group of individuals
12 with different functions that were
13 responsible basically for clinical
14 studies. It was the medical portion of
15 the team, a regulatory portion of the
16 team, I believe reporting in to the
17 product team leader, which was Alan
18 Breier. So, medical, regulatory,
19 marketing and the whole clinical study
20 function.
21 **Q. Basically, as you said, I**
22 **think this is a term of art you used,**
23 **this was a cross-functional team?**
24 A. Yes.
183: 1 **Q. When you used that term, so**
2 **the jury understands it, you had**
3 **individuals at Eli Lilly from the medical**
4 **department, the regulatory department,**
5 **the clinical trials department, the**
6 **marketing department that all came**
7 **together who had as their responsibility**
8 **the successful marketing and sales of**
9 **Zyprexa on behalf of Eli Lilly?**
10 A. They had as their
11 responsibility -- it was much broader
12 than that.
13 **Q. Tell the jury.**
14 A. Their responsibility -- you
15 know, you used the words "safety" and
16 "efficacy." It was responsibility of the
17 product team to ensure both the safety
18 and understand the efficacy -- understand
19 the safety and the efficacy of the
20 product. And from a marketing
21 standpoint, yes, it was also important to
22 provide information to customers that,
23 you know, would help with the usage of
24 the product and, sure, the sales of the
184: 1 product.
2 **Q. Right.**
3 **That's what you said, and**
4 **it's back on that page, you don't need to**

turn to it, it's right there on the screen, the head of that whole team is Dr. Alan Breier? Do you see it?

A. Yes.

Q. The people on the team, as you said, included Dr. Breier, who's a medical doctor, medical department, but you also had marketing and marketing research individuals, scientific communications, right? Right?

A. Yes.

Q. And you, who were in global marketing and head of global marketing?

A. In -- marketing, yes.

Q. Let's go back to the page I was on on the Zyprexa product team, "The Chance to Make History." "Olanzapine," that's Zyprexa, "the first team to dramatically speed time to registration...making history and setting the new... registration standard." You got this drug through your efforts -- or through your team's efforts before you got there, took this drug to FDA and got it approved on a new speed system, right?

Denice M. Torres (December 15, 2006)

THE WITNESS: The -- what I remember from that time, I think there was some new way of submitting information to the FDA that would help facilitate them receiving the information.

Denice M. Torres (December 15, 2006)

Q. Now, this next -- this last one, I'm skipping down to number 3, it doesn't look like it's anything about science. It says, "Zyprexa: The first team with the opportunity to set the all industry commercialization standard for the most successful pharma brand in history." What does that mean?

A. The commercialization would be the product offering to the customer. So, in order to submit the -- in order to be a standard for commercialization, you'd have to be outstanding in understanding your customers, understanding your customer needs and delivering value to those customers. And doing all of those things right would be -- we would be incredibly successful financially, yes.

Q. Right. In fact, this commercialization and being successful financially was very important to Eli

Lilly because you were about to bet the farm on Zyprexa, right?

Denice M. Torres (December 15, 2006)

Q. Right?
A. You've asked me like two or three things in there. What's with the "bet the farm"?
Q. Well, let's go to the next page. Straight Talk - What's at Stake." Do you see that?
A. Yes, I do see that.
Q. Can you read that out loud for the jury, please.
A. "The company is betting the farm on Zyprexa...the ability of Eli Lilly to remain independent and emerge as the fastest growing pharma company of the decade depends solely on our ability to achieve world class commercialization of Zyprexa. If we succeed, Zyprexa will be the most successful product ever...we will have made history."
Q. Okay.
"Straight talk," that means no ambiguity, right? Correct?

Denice M. Torres (December 15, 2006)

Q. Correct?
A. Straight talk mean directly, yes.
Q. "What's at stake." What's that mean?
A. I don't know. Whoever wrote it, I don't know what they had in mind. "What's at stake" means here's the bottom line.
Q. Bottom line. "The company is betting the farm on Zyprexa." Did I read that right? Did I read that right?
A. That's what I see here.
Q. Does that offend you?
A. I wouldn't use those words.

Denice M. Torres (December 15, 2006)

Does it appear that the company, being Eli Lilly, in order to make history and to commercialize Zyprexa, under the direction of Dr. Alan Breier, was betting the farm on Zyprexa?

Denice M. Torres (December 15, 2006)

188:18 THE WITNESS: Was the
19 company betting the farm on
20 Zyprexa? I think I've answered
21 that before. In short term, it
22 was very successful, it was very
23 important to the company. But
24 betting the farm I don't think is
189: 1 accurate. It would mean that all
2 resources were going to Zyprexa,
3 and that was not the case.

Denice M. Torres (December 15, 2006)

189: 5 Q. "Straight talk," "Straight
6 talk." "The ability of Eli Lilly to
7 remain independent." What's that mean?
8 A. It means --
9 Q. To avoid a takeover?
10 A. Yes.
11 Q. "Straight talk - What's at
12 Stake. The company is betting the farm
13 on Zyprexa...the ability of Eli Lilly to
14 remain independent," i.e. avoid a
15 takeover, "and emerge as the fastest
16 growing pharma company of the decade
17 depends" -- what's that word "solely"?
18 A. That's what it says.
19 Q. "Solely," what's that mean?
20 A. Solely? It means primarily.
21 It means -- primarily.
22 Q. "Solely" actually means
23 only, doesn't it?
24 A. Yes.
190: 1 Q. The company's straight talk.
2 "What's a Stake, July 2001." Zyprexa
3 product team. "The company is betting
4 the farm on Zyprexa...the ability of Eli
5 Lilly to remain independent and emerge as
6 the fastest growing pharma company of the
7 decade depends solely on our ability to
8 achieve world class commercialization of
9 Zyprexa."

Denice M. Torres (December 15, 2006)

190:13 THE WITNESS: You read what
14 was on the page, yes.

Denice M. Torres (December 15, 2006)

192:10 And it would be
11 inappropriate if we found out later that
12 they hid information from doctors about
13 their product? That'd offend you,
14 wouldn't it?
15 A. Absolutely.
16 Q. It would be offensive if you

found out that some of the senior executives in the company were aware of off-label promotion activities and didn't stop it? That offend you?

Denice M. Torres (December 15, 2006)

193:
Q. It would be wrong if Dr. Lechleiter -- tell the jury who Dr. Lechleiter is.
A. Right now he's second in command at Lilly.
Q. Right. Sidney Taurel, who is he?
A. CEO.
Q. Sidney Taurel and John Lechleiter were fully familiar with the fact that off-label promotion of Zyprexa was taking place, weren't they?

Denice M. Torres (December 15, 2006)

193:
Q. If they were, what should they do?

Denice M. Torres (December 15, 2006)

193:
THE WITNESS: If they were aware that there was off-label promotion by the company?

Denice M. Torres (December 15, 2006)

194:
If they were aware of off-label promotion activities or attempts to get doctors to prescribe their product Zyprexa off label, what should those men do?
A. Anyone in the company would have responsibility to --
Q. To what?
A. It would be inappropriate. Inappropriate behavior, you know, would need to be addressed.
Q. Right. We're going on to your PowerPoint, "Describing our Culture, current and future" from a "consensus-driven" model to a "single point of accountability." What's that mean, if you know?
A. I believe what that would mean is that we spend a lot of time in meetings trying to gain consensus and move to a single point of accountability so we can make decisions and not spend as

195:

much time in meetings.
Q. Right. I think the last point I want to make is. I think the next to last page of this -- or three back, "deliverables." We see that all the time in your documents. The jury will see it when I try the case, "deliverables." Just tell the jury what deliverables are.
A. Deliverables would be outcomes.
Q. Outcomes?
A. (Witness nods.)

Denice M. Torres (December 15, 2006)

Q. Tell the jury. Your lawyer keeps on objecting. Tell the jury what it means, outcomes. What does it mean by that?
A. Responsibilities.

Denice M. Torres (December 15, 2006)

"Expected Deliverables," what's that mean?
A. It means outcomes that should happen as a result of this meeting, yes.
Q. Things that should happen, right?
A. Yes.
Q. And that's the responsibility of the members of the Zyprexa product team, correct?
A. Yes.
Q. Okay. And I'm going to get in here. We'll talk about one, "Regulatory and label reviews." Do you see that?
A. Yes.
Q. You were involved in label reviews, were you not, and voting on what you considered appropriate labels in marketing?

Denice M. Torres (December 15, 2006)

THE WITNESS: I don't remember any voting. I mean, we had a regulatory group. The regulatory and clinical group were very much -- worked together. Would they share information with me if they were going to propose verbiage to the FDA, et cetera or to other things? Yes, they would.

198: 1 BY MR. ALLEN:
2 Q. The reason you wanted to be
3 kept apprised -- in fact, you got to vote
4 in the key decision maker team on labels,
5 give your vote. The reason you did is
6 you knew labels could affect the sales of
7 the product, right?

Denice M. Torres (December 15, 2006)

198:10 THE WITNESS: I don't
11 remember any voting. I don't know
12 what form you're talking about.
13 BY MR. ALLEN:
14 Q. Then let me rephrase my
15 question. I will show you a document
16 clearly on that point, but let me
17 rephrase my question.
18 You knew in marketing that
19 what the label said on the product could
20 affect the sales of the product, right?
21 A. Sure. Could a label affect
22 the sales? Yes.
23 Q. Tell the jury how the labels
24 can affect the sales.
199: 1 A. Well, if the label said, do
2 not take with -- you know, while nursing,
3 okay, that would exclude anyone that's
4 nursing. If the label said don't -- I
5 mean, there's a whole do not, those
6 indications.
7 Q. Contraindications?
8 A. Absolutely.
9 Q. So, contraindications in the
10 label can affect the sales, right?
11 A. Yes.
12 Q. That's what you're trying to
13 say; is that right?
14 A. Basically anything that, you
15 know, would exclude a group of people
16 or -- yeah. I mean, that would
17 definitely affect the sales.
18 Q. How long have you known
19 that?
20 A. How long have I known the
21 label --
22 Q. Could affect the sales.
23 A. Gosh, 15 years.
24 Q. Ever since you were at Eli
200: 1 Lilly?
2 A. Yes.
3 Q. Is that just basic core
4 concept knowledge in the marketing
5 department of Eli Lilly?
6 A. Yes.
7 Q. Is it just basic core
8 concept knowledge on the Zyprexa product
9 team in this cross-functional team?
10 A. Yes.
11 Q. So there's no secret, so
12 there's no doubt, so there's no -- so you

can be clear and give this jury straight talk, what you say in a label can affect your product sales, right?

A. Yes.

Q. No doubt about it, right?

A. That's correct.

Q. In fact, you, personally, viewed potential label changes that would enhance the warning on Zyprexa as a threat to Zyprexa sales, did you not?

Denice M. Torres (December 15, 2006)

THE WITNESS: Were potential label changes a threat?

BY MR. ALLEN:

Q. Yes, ma'am. You personally know that?

A. Yes. Could they be a threat? Sure. But the point is, you do the right thing.

Q. Right.

You personally wrote down in memoranda that label changes on Zyprexa could threaten Zyprexa sales; is that right?

A. Yes.

Q. Now, you said -- one thing you indicated, if it says nursing mothers should not take the product, that, as you said, would exclude an entire segment or category, right?

A. Well, a physician may decide to -- well, from a company's standpoint, you know, I can give a lot of other examples, but from a company standpoint, we would not be able to promote for nursing mothers. Now, may a physician decide that the risk is worth it? Sure. But that would not be the company's responsibility.

Denice M. Torres (December 15, 2006)

Q. Thank you. Ma'am, I'm going to hand you what's been marked as Exhibit 7, and we're not going to read the whole thing. This is just -- I want to verify. This is a Zyprexa Global Brand Plan written or what you were responsible for for 2005 to 2007.

Denice M. Torres (December 15, 2006)

Q. You recognize this document, don't you, ma'am?

Yes.

Q. Back to the first page. Really, I'm going to focus on your title. It says, "Marketing Executive Director." Is that -- I think you tried to tell me this earlier when I didn't understand. That's just a title increase, I guess, over global marketing director?

A. Yes. Same job.

Q. Okay.

The executive, they add that on there. Did it come with a pay raise and a bigger office? I don't know.

A. Actually, we sat in cubicles regardless of what the level was, but was there a pay raise? Yes, there was.

Q. You have stock in Eli Lilly, do you not?

A. I have a small amount left, yes.

Q. You had stock options, did you not, in your role as --

A. Yes, I did.

Q. Let me finish.

In your goal -- in your role, excuse me.

In your role as global marketing director and marketing executive director, you received stock options in Eli Lilly, did you not?

A. Yes, I did.

Q. The better Eli Lilly did financially, the more money you made?

A. Well, I guess you could say that, yes.

Q. Also, you received substantial bonuses throughout the years that you were the global marketing director and marketing executive director for your work or due at least in major part due to your work on Zyprexa, correct?

A. Well, you'd have to determine -- you know, in terms of substantial, I would say, no, I did not find them to be substantial.

Q. Okay.

What did you --

When you left in December of 2004, what was your annual salary as global marketing director, executive director?

A. It was just about 200,000.

Q. And then your yearly bonus the proceeding year was what?

A. I don't remember. It might have been 40,000, 50,000.

Q. And in addition to $200,000 and $40,000 in bonus, you had stock options that you exercised?

A. I didn't have stock that was worth very much of anything. The stock had not increased over a number of years -- stock options, I should say.

Q. You had previously exercised stock options back in --

A. I --

Q. Let me finish my question. You had previously exercised stock options back in the late '90s, in 2000, 2001, 2002, in that time period, had you not?

A. I don't remember. I had a couple years where I exercised stock options, much of which I received when I was a manager with the company.

Q. What was the value of your stock and/or stock options as of, let's pick 2002, approximately? What was the value of your stock and your stock options?

A. Of my stock options? I don't think I had any value in stock options at that time.

Q. Your stock?

A. The stock I'd received from the time I started with the company? I guess from 1990 to -- are you including my 401K?

Q. It's a very simple question. What was your approximate value of your stock holdings in Eli Lilly, say, around December of 2002?

A. I could guess.

Q. Give us your best estimate. I usually know the value of what I own. What is your best estimate of the value of your stock around December of 2002?

A. I can't tell you for sure, because I ended up selling almost all my Lilly stock during that time period. So --

Q. Prior to the time of your sale, at the maximum --

A. What was the maximum?

Q. Prior to the time you started selling your stock which you remember, what was the maximum value of your Eli Lilly shareholdings?

A. Maybe 400,000.

Q. 400,000.

So, would you agree with me that you had both a career interest and a financial incentive to make sure that Zyprexa was as successful as possible?

A. I mean, I guess I didn't look at it that way. Did I want to do the best job possible? Yes. But was it to drive my Lilly stock up? No.

Q. And Lilly probably never tried to drive their stock up. They didn't do that either, did they?

A. Sure. I mean, it's a

for-profit organization. But I did not come to work every day thinking, boy, let's drive the stock up.

Denice M. Torres (December 15, 2006)

First thing that struck me is 2005/2007 you're gone, so obviously these plans were prepared well in advance of your leaving; is that correct?

Denice M. Torres (December 15, 2006)

Q. They had to be prepared before you left?

A. I believe that this was -- if it was done in 2004, this would have been called a longer range plan.

Q. Well, ma'am, I'm not -- I can only use the words y'all used. "Zyprexa Global Brand Plan." Right? What's that mean? What is that?

A. The brand plan would be a forward-looking outlook on the brand.

Q. And you were in charge of preparing this sometime in 2004?

A. Yeah. It would have been 2004.

Q. Before you left. So, you prepared these in advance, obviously, of the year indicated, right?

A. That's correct.

Q. Now, it says "Prelude to Zyprexa Marketing Plan." I'm not going to read the whole thing. I'd like to go to -- "Prelude to Zyprexa Marketing Plan. The atypical market is defined by product usage and not by indications." What does that mean? "The atypical market is defined by product usage and not by indications."

A. In terms of the atypical market, meaning antipsychotics, because there's so much grayness between -- the size of the market, I mean, basically what this is meaning is that the size of the market is the sum total of the sales for all antipsychotics.

Q. Well, it says "Prelude to Zyprexa Marketing Plan. The atypical market is defined by product usage and not by indications." Did I read that correctly?

A. You did read that correctly, yes.

Q. But isn't it true that the marketing of the product is supposed to be defined by the indications?

A. Sir, the word there is

"market" and not marketing in the atypical -- with atypicals. Basically what this is saying is that, as we talked about earlier, you could have 30 something percent off-label usage. That still is the atypical, the drug, the basket of uses for the drug. That all equates to a total number of sales. Nowhere does it say that that is -- that this plan is meant to capitalize on the sum total of what is used for the drug. All it is saying is that the market for or, excuse me, atypicals, if you took the basket of them, by and large is defined by the total usage of those drugs.

Q. You're not supposed to try to capitalize on the off-label uses, are you?

A. That's correct.

Q. It would be wrong for Eli Lilly to try to capitalize through their marketing on off-label usage. That would be wrong, right?

A. Yes, sir.

Q. It would be a violation of law?

A. Yes.

Q. Violation of regulations?

A. That's correct.

Denice M. Torres (December 15, 2006)

Q. Ma'am, my only question to you was, and the record will reflect it and I can almost do it verbatim, it would be wrong in the marketing of Zyprexa, in the marketing plan and activities for Eli Lilly to attempt to capitalize on the off-label usage?

A. That's correct.

Q. And just so -- you talked about --

You wanted to read the sentence, and you talked about diagnoses and medical diagnoses. This is under the heading of "Zyprexa Global Brand Plan." It's a marketing document. And it says, "Prelude to Zyprexa Marketing Plan." Isn't that what the heading is?

A. Yes. That's what the heading is.

Q. I was going to read the next sentence. "Off-label usage is commonplace with atypicals due to the medical necessity of addressing complicated symptomatology." Did I read that correctly?

A. Yes. And "It is important to note what while prescriptions are generated for these off-label uses, we have no intention or planned efforts to

influence off-label usage."
Q. Ma'am, my only question was, did I read that question -- read that sentence correctly?
A. I believe you did read the sentence correctly.
Q. And I'm going to go down. Does this discussion -- let me ask. Does this discussion of off-label marketing make you nervous?
A. Sir, it doesn't. It's a characterization of the market.
Q. Now, the second paragraph: "Zyprexa, like all medicines used to treat mental illness, is prescribed to address a host of symptoms and disorders. These uses extend beyond schizophrenia and bipolar disorder, into areas such as depression." Did I read that correctly?
A. Yes.
Q. First of all, was Zyprexa -- we've already established was not indicated for depression, right?
A. That's correct.
Q. It could not be marketed for depression?
A. That's correct.
Q. It could not be promoted for depression?
A. That's correct.
Q. It would be wrong for you to do so, you, at Eli Lilly?
A. That's correct.
Q. "Into areas such as depression, borderline personality." Did I read that correctly?
A. That's correct.
Q. Zyprexa was not indicated for borderline personality?
A. Correct.
Q. It could not be promoted for borderline personality?
A. Correct.
Q. It could not be marketed for borderline personality?
A. Correct.
Q. "Dementia," we've already established it's not indicated for dementia, right?
A. That's correct.
Q. It cannot be marketed for dementia?
A. That's correct.
Q. Cannot be promoted for dementia?
A. Correct.
Q. "Post traumatic stress disorder, stuttering and anxiety." Those last three, again, not in the indications for Zyprexa, right?
A. Correct.
Q. Could not be marketed for that purpose.

A. That's correct.
Q. Could not be promoted for that purpose?
A. Correct:
Q. "Consequently, a very large part of the market is not our target business given uses extend beyond our label." Did I read that correctly?
A. That's correct.

Denice M. Torres (December 15, 2006)

251: 9 Q. Yes. It would be wrong for Eli Lilly in their marketing plans or in their promotional activities to attempt to capitalize on these off-label uses?
A. That's correct.
Q. Now, in "The 'Something Special' about Zyprexa," I'm just going to the last sentence of the first paragraph. I think we kind of established this earlier, just to put this in context. "In 2003, Zyprexa was the Number Three selling brand in the world," and it says "(IMS)." Right?
A. Yes.
Q. IMS is a private company that keeps track of numbers of prescriptions that are written on various pharmaceutical products?
252: 1 A. Basically they're a very large data collection group, and so that would be --
Q. They can tell you --
A. -- one aspect of data about the marketplace.

Denice M. Torres (December 15, 2006)

253:10 Let me give you some of your competitors, and tell me if you agree. We're talking about the sentence "Like any market leader, we are the focus of every competitor." Did those competitors include Risperdal, Seroquel, Abilify, Geodon?
A. Yes.

Denice M. Torres (December 15, 2006)

254:16 Let me go on here to what I want to read. "Additionally, we face other marketplace pressures such as new competitive entrants, access challenges, litigation, increasing concerns around the impact of weight, and difficulties in maintaining premier share of voice."

Share of voice, it's often seen in the documents as SOV, right?
A. That's correct.
Q. Share of voice means are you getting what you consider at Eli Lilly your fair share of talk in the marketplace, right?

Denice M. Torres (December 15, 2006)

THE WITNESS: No. Share of voice is basically the amount of presence in a marketplace.

Denice M. Torres (December 15, 2006)

Q. Thank you.
And you at Eli Lilly and Zyprexa had the premier share of the voice, and that's what you wanted to maintain, right?
A. Yes.
Q. Thank you.
"Another factor that may heavily influence the marketplace is the results of the United States NIMH," that's the National Institutes of Mental Health, "CATIE Trial," CATIE is an acronym for Clinical Antipsychotic Trials of Intervention Effectiveness, "a research project to evaluate the clinical effectiveness of atypical antipsychotics in the treatment of schizophrenia. The results represent a significant upside or downside for Zyprexa, depending on the outcome."
Did I read that correctly?
A. Yes, you did.
Q. Now, tell the jury why -- what is the CATIE study?
A. The CATIE study was the -- you know, one of the largest studies that was initiated and I believe sponsored by all the different pharmaceutical companies to look at efficacy rates of new -- the newer antipsychotics and I think versus the older antipsychotics.
Q. And you said, and I'm paraphrasing, it was up on the board a minute ago, we're going to go to another page in a second.
The CATIE study results could affect Zyprexa sales either positively or negatively, right?

Denice M. Torres (December 15, 2006)

257: 3 THE WITNESS: That's
4 correct.

Denice M. Torres (December 15, 2006)

357:23 Q. Didn't you at Eli Lilly know
24 if you truly warned about diabetes and
358: 1 hyperglycemia, it would affect your
2 sales? Didn't you know that?
3 A. Did we know that if there
4 was a warning for diabetes that that
5 could impact sales? Is that the
6 question?
7 Q. Yes, ma'am.
8 A. Sure, yes.
9 Q. Why would a warning about
10 diabetes impact sales?
11 A. A warning about anything
12 could impact sales because, again,
13 looking at the patients and the
14 characteristics of those patients,
15 everyone comes with their own set of
16 medical considerations that a warning can
17 have implications for certain individuals
18 with those medical conditions.

Denice M. Torres (December 15, 2006)

359:15 Q. You at Eli Lilly, you said
16 you knew -- you said in one of your
17 answers that Eli Lilly knew a warning
18 about diabetes would affect sales. When
19 did you learn that?
20 A. When did I learn that a
21 warning about diabetes could impact
22 sales? When did I learn that?
23 Q. Yes, ma'am.
24 A. Boy, it's something that I
360: 1 don't think anyone had to tell me that.
2 One could surmise a warning about
3 anything could impact sales. You
4 wouldn't even have to be an expert in the
5 area to know. If you know anything about
6 pharmaceuticals, a warning, information
7 in the warning could impact sales just
8 like information on efficacy would be a
9 positive -- it could be a positive
10 impact.
11 Q. So, what you're saying is
12 you wouldn't even have to be in the
13 industry, it was just good old common
14 sense that if there was a warning in the
15 package insert, you knew from your
16 experience and common sense that it would
17 impact sales? Is that what you're
18 telling me?

Denice M. Torres (December 15, 2006)

360:20 THE WITNESS: I said in
21 general terms that information in
22 a warning could have the potential
23 to impact sales and, again, a
24 number of factors would have to be
361: 1 taken into consideration.

Denice M. Torres (December 15, 2006)

361: 3 Q. Can you remember or tell
4 this jury when you knew that a warning
5 about diabetes or hyperglycemia, when you
6 knew that warning would impact sales in
7 regard to Zyprexa. Can you tell us an
8 approximate date or year?
9 A. I think as I mentioned
10 earlier, I -- no. A date or year?
11 Absolutely not. I could have said that
12 the first day I started work that, you
13 know, again, something in the warning has
14 the potential to impact sales.

Denice M. Torres (December 15, 2006)

361:24 Q. Yes, ma'am. Let me hand you
362: 1 Exhibit Number 11. A copy for your
2 lawyer. This is a document Mr. Fibich
3 provided me today. Is this 11? Is that
4 right?
5 A. It says 11, yes.

Denice M. Torres (December 15, 2006)

362: 8 "Scenario and Contingency
9 Planning Session, US Zyprexa Brand Team."
10 Were you on the U.S. Zyprexa
11 Brand Team?
12 A. No, I was not.
13 Q. You were on the global brand
14 team, right?
15 A. Global product team.
16 Q. I'm sorry. You know these
17 members, you dealt with these members all
18 the time?

Denice M. Torres (December 15, 2006)

362:21 Q. You know Jack Jordan, right?
22 A. Yes.
23 Q. You worked with him on a
24 weekly basis, did you not?
363: 1 A. No, I didn't, sir.
2 Q. Mike Bandick, we saw the
3 organizational chart, he was right

underneath you, right in issues management? He was the director, correct?

A. He -- I'd have to go back and look at this data. At one point he was -- he reported to me, and he also had a portion of his job where he reported to Jack Jordan, that I was not involved with.

Q. Well, I guess my point is, you knew Mr. Bandick and he -- you worked with him and at times he reported to you, and at times he reported to other people, right?

A. Yes.

Denice M. Torres (December 15, 2006)

364:

Q. I just want to go to this "Metabolic Side Effects," number 1, here on this document. "Scenario Clarification and Probabilities." "A 'Black Box' label for Zyprexa appears to be a very low probability. However, a differential label warning of metabolic side effects for either Zyprexa only or a subset of the atypical antipsychotics is a very real possibility."

Did I read that correctly?

A. Yes, you did.

Q. Were you aware in 2003 that a change of the label concerning a warning about metabolic side effects was a very real possibility?

A. I can't say yes.

Q. If you can't say yes --

When did you become aware that it was a possibility? If you don't know, just tell me you don't know.

A. Well, a lot of information was submitted to the FDA in ongoing discussions with the FDA. So, was it a

365:

possibility that with the data that Lilly submitted and the other companies with atypical antipsychotics, that that could result in a label change, I can't tell you exactly when I would have become aware of that.

Q. You knew what the consequences would be if there was a label change, though, didn't you?

A. The consequences to whom?

Q. To the sales.

A. To the sales of atypical antipsychotics?

Q. Yes, in general, and Zyprexa in particular.

A. Well, if it were a class effect, there would be potentially no impact whatsoever. You're talking about a group of individuals that are very,

very ill. And, again, the risk/benefit would have to be taken into consideration. So, if this were a class effect like with increased suicidality for antidepressants, then all those things are taken into consideration when treating a patient. But I'm sure there's instances, you know, there have been label changes and no impact on prescribing because there's such an unmet patient need.

Denice M. Torres (December 15, 2006)

Q. We're back to the issue of how a label affects sales. You said you knew that from the day you started. We're on Exhibit 11, "Scenario Clarification and Probabilities." "A 'Black Box' label for Zyprexa appears to be a very low probability. However, a differential label warning of metabolic side effects for either Zyprexa only or a subset of the atypical antipsychotics is a very real possibility." You were aware of that at some point, correct?

A. Yes.

Q. You just don't remember when you were aware of it; is that right?

A. That would be fair.

Q. Bullet point number two, says "There would be little practical difference between these two scenarios, because Zyprexa would still lose access" -- and access to what, ma'am?

A. It would be basically reimbursement, certain reimbursement levels.

Q. Right. If you had a warning concerning Zyprexa, it may affect your access to formularies; is that correct?

A. Reimbursement likely.

Q. Right. "There would be little practical difference between these two scenarios, because Zyprexa would still lose access and become primarily a 2nd or 3rd line treatment." Did I read that correctly?

A. You read that correctly.

Denice M. Torres (December 15, 2006)

A. He's an individual that was on the global marketing team.

Q. Right.

A. For a couple of years.

Denice M. Torres (December 15, 2006)

394:20 Q. Let me hand you what's been
21 marked as Exhibit Number 14. This is
22 Anthony Fiola from global marketing,
23 3/30/01. This is over a year prior to
24 April of 2002, is it not? Just simple
395: 1 math. March --
2 A. Simple calendaring, yes.
3 Q. That's all I'm asking. "Dear
4 Affiliates." You said that your role in
5 global marketing was to work with the
6 affiliates, right?
7 A. Yes, I did say that.
8 Q. You said your role in global
9 marketing was to implement global
10 marketing plans that the affiliates could
11 utilize, right?
12 A. Yes.
13 Q. This says, "Dear Affiliates,
14 This hyperglycemia/diabetes document
15 contains new information on: Diabetes
16 Speaker Slides." Did I read that right?
17 A. Yes, you did.
18 Q. Eli Lilly hired speakers,
19 physicians to go out, and they provided
20 them with slide shows so they could go
21 out and talk to doctors, didn't they?

Denice M. Torres (December 15, 2006)

395:24 Q. Didn't they?
396: 1 A. I'm sorry. Repeat your
2 question.
3 Q. Eli Lilly provided doctors,
4 speakers, with slide shows to go and talk
5 to other doctors?
6 A. If those individuals chose
7 to talk to other doctors, they could use
8 the side kit.
9 Q. Let me just use the term.
10 Ma'am, I'm not trying to be difficult.
11 Let me see the word you used, "speaker."
12 What did you think the word "Speaker"
13 meant?
14 A. Speaker?
15 Q. Yes, ma'am.
16 A. It would be either someone
17 from the company or an opinion leader or
18 a prescriber that would give a talk, and
19 it could be a whole variety of settings.
20 Q. Right. This is somebody Eli
21 Lilly hoped got out their message, right?
22 A. The message? Would get out
23 information.
24
397: 1 Q. Yes.
2 A. Share information, sure.
3 Q. And Eli Lilly made their own
4 slides for these speakers, right?
5 A. As it pertained to Zyprexa,
yes.

Denice M. Torres (December 15, 2006)

398: 1 My question was, you in
2 global research, global marketing, in
3 your job, while you were on the global
4 marketing team, conducted market research
5 on hyperglycemia, your department, did it
6 not?
7 A. I would imagine that
8 questions were answered certainly in our
9 brand equity in terms of associations
10 with what was associated with Zyprexa.
11 We could determine things, especially
12 weight, with something that was
13 associated with Zyprexa. So, in terms of
14 overarching research, characteristics of
15 the profile would come up.
16 Q. Ma'am, just so the record is
17 clear, I didn't prepare this document.
18 People at Eli Lilly did. This isn't
19 talking about weight. It's talking about
20 hyperglycemia and diabetes, isn't it?
21 Hyperglycemia and diabetes, correct?
22 A. That is what it says.
23 Q. And it goes on to say after
24 it gives a list, "To maximize Zyprexa's
399: 1 success in the market, it is critical
2 that we actively address the issue." Did
3 I read that correctly?
4 A. You did read it correctly,
5 yes.

Denice M. Torres (December 15, 2006)

399:24 Q. It's been represented to me,
400: 1 ma'am, this came from your files. Do you
2 recognize this document?
3 A. No.
4 Q. Okay.
5 But you would agree that you
6 were on this global marketing team at or
7 near this time of this report of March
8 30, 2001, right?

Denice M. Torres (December 15, 2006)

400:10 THE WITNESS: Sure.

Denice M. Torres (December 15, 2006)

400:13 So, the goals, unless they
14 change in a day, the overall goals of the
15 team were as follows:
16 What's the number one goal
17 of the global marketing team? Let's read
18 it together. "Stop

hyperglycemia/diabetes from becoming a Top 10 Attribute influencing prescribing." Did I read that correctly?
A. You did, sir.
Q. Right.
Now, the number one goal was not to warn physicians about the potential of weight gain, hyperglycemia and diabetes, was it?
A. Number one goal?
Q. Yes, ma'am. Was it to warn physicians about diabetes? Yes or no?
A. No.

Denice M. Torres (December 15, 2006)

Q. You said "Stop hyperglycemia" and "diabetes from becoming a top 10 attribute influencing prescribing." Correct?
A. I think the key words are "influencing prescribing," which means influencing the choice.
Q. And you wanted to stop diabetes and hyperglycemia from influencing that choice, correct?
A. From being the overarching things that they considered.
Q. It doesn't say overarching. It's from being even in the top ten things they consider, correct?
A. Sir, I can't tell you what the person meant. But I could tell you, you're asking my opinion, you've given me a document, I have stated my opinion. Why did he choose top 10 and not top 5? How about top 20? I think with the sentiment of the sentences, we need to make Zyprexa seen in the sum total of its attributes. Are some of those attributes negative? Yes. Are there a lot of attributes positive? Yes. But in the sum total, what are the top attributes physicians associate with Zyprexa, the goal was to ensure that those positive things about Zyprexa were known and communicated.

Denice M. Torres (December 15, 2006)

Q. Ma'am, I'm going to hand you Exhibit 15, which is an e-mail you sent. Look at the very top. You sent this e-mail from Denice Torres. Do you see, Denice Torres sent this e-mail? That's you, right? Ma'am?
A. Did I send the -- it looks like I forwarded an e-mail.
Q. Yes, ma'am.

In September of 2002 from Denice Torres, you sent it to people in global marketing and people in U.S. marketing at the other affiliates, did you not?

A. Yes.

Q. You also sent it to Dr. Alan Breier, the head of the Zyprexa product team, right?

A. Yes.

Q. And we won't read the entire e-mail. You were forwarding an e-mail from Anthony Fiola, which is who you told me worked in global marketing under you, correct?

A. Yes, he did work on my team.

Q. And the subject matter is "Issues Update." And you talked about issues today, right?

A. Yes.

Q. In fact, you had a whole department that worked underneath you, as we saw in the organizational chart, on issues management, right?

A. It was called marketplace management.

Q. Right.

And then underneath that we have issues management. Do you recall that?

A. Yes.

Denice M. Torres (December 15, 2006)

Mr. Fiola is writing the affiliates, right?

A. Yes.

Q. And you, of course, take Mr. Fiola's e-mail, and you forward it along to people who were involved in Zyprexa sales and marketing, as well as the medicine side of the company, right?

A. Correct.

Q. Okay.

Including Mr. Pike, also, right here, who is involved in, as you said, issues management, right?

A. Yes.

Q. Okay.

Now, the subject line is "Issues Update." And I want to read this.

"I wanted to take this opportunity to give you a brief update on the current state of affairs with regards to the issues facing Zyprexa, focusing mainly on diabetes."

Did I read that correctly?

A. You did, sir.

Q. "There is increased intensity regarding Zyprexa and alleged

links to diabetes and serious metabolic concerns. During the past six weeks." Did I read that correctly?

A. Yes.

Q. And one of the things that happened during the last six weeks among others was, "Zyprexa-associated Diabetes Mellitus," an article by Dr. Koller was published in Pharmacotherapy in July; is that correct?

A. You read that correctly.

Q. And Dr. Koller had published an article in Pharmacotherapy looking at the FDA adverse events reporting database. Had she -- is it a she, I think?

A. I don't remember that.

Q. Well, Dr. Koller had published that article dealing with the FDA database, right?

A. I'd have to see the publication. I don't remember the specifics.

Q. And Dr. Koller's article had suggested that the incidence of diabetes associated with Zyprexa as a second generation antipsychotic, there was a statistical association, correct?

A. Again, sir, if you gave me the article, I could reference it, but I don't remember --

Q. You don't recall --

A. -- the specifics of it.

Q. You don't recall it now?

A. I don't.

Q. Another thing. Y'all had gotten legal correspondence from Johnson & Johnson who makes Risperdal, right?

A. Yes.

Q. "Regarding use of 'comparable rates,'" right?

A. That's what it says, yes.

I very much apologize.

You said that "comparable rates" is what you were telling doctors; is that right?

A. I told you it was one aspect of a communication.

Q. And what was the aspect? Just say it out loud for the jury so we can all hear it.

A. What was the aspect?

Q. Yes. This comparable rates in regard to diabetes, remember, we're talking about the subject of diabetes, and what did this "comparable rates" message to doctors, what was that?

A. If I remember correctly, it

was that atypicals in general had comparable rates as it pertained to the incidence of diabetes, and that in accordance with good medical practice, prescribers should evaluate every patient for their risks and take appropriate actions as they deem appropriate.

Denice M. Torres (December 15, 2006)

Q. Weren't you telling doctors in this "comparable rates" message that the rates of or incidence of diabetes associated with Zyprexa was no different from that of other second generation antipsychotics?

Denice M. Torres (December 15, 2006)

THE WITNESS: I think the word was "comparable." Comparable doesn't say no difference.

Denice M. Torres (December 15, 2006)

By the way, when you use "comparable," what does comparable mean to you?

A. By and large in the same category.

Q. That's the message you were giving doctors?

A. Comparable rates.

Q. Right.

In fact, if you look at Page 2, do you remember the tag line? I didn't come up with that myself. This is Mr. Fiola who worked in marketing. He says, "On the commercial front, our tag line has been 'comparable rates.'" Right? "Tag line." Is that the word he uses?

A. It's an inappropriate use of the word, but it is the word he used.

Q. Okay.

Well, you forwarded this e-mail along to Alan Breier, Jack Jordan, Matthew Pike and others, didn't you?

A. I would not have a memo rewritten on the basis of one word.

Q. Ma'am, that wasn't my question. You're anticipating another question.

My question to you is, you forwarded this e-mail of Mr. Fiola in which he says, "On the commercial front, our tag line has been 'comparable

rates.'"? You forwarded this very e-mail along, did you not?
A. Yes, I did.
Q. I assume before you forwarded it along, you read it?
A. I would not assume that.
Q. You wouldn't?
A. No.
Q. Okay. Well, let me ask this.

Since you brought it up, I don't see anywhere in this e-mail when you sent it out to Michael Bandick, who is in charge of marketplace management, to Alan Breier, who is head of the Zyprexa product team, to Matthew Pike, who is head of issues management, and to Jack Jordan, who is head of the U.S. affiliate marketing, that you made any corrections or criticisms of the e-mail, did you?
A. I wouldn't see that as material. It's just a person with one year marketing using a statement. I wouldn't see that as material. The use of the term "comparable rates" was used in the broader context.
Q. Right.

And so you also, obviously, didn't disagree with what was known in global marking as of the time this e-mail was sent that "Zyprexa does lead to increases in appetite, which can contribute to obesity, a major risk factor in developing diabetes"? Is that correct?
A. Yes.
Q. So, it was known that Zyprexa could lead to weight gain, which was a major risk factor in developing diabetes, correct?
A. Weight gain is a major risk factor in developing diabetes, yes.
Q. Let's read it together again.

"Zyprexa does lead to increase in appetite, which can contribute to obesity, a major risk factor in developing diabetes," correct?
A. That's correct.
Q. Right.

And that was known -- well, let's say at least at by -- we'll go back to some other ones even earlier.

But by September of 2002, in global marketing, Mr. Fiola and to all the affiliates to whom he sent it, and to all the people whom you sent it, including Dr. Breier, it was known that Zyprexa does lead to increase in appetite, it does contribute to obesity, and it is a major risk factor in developing diabetes, correct?

Denice M. Torres (December 15, 2006)

423:24 THE WITNESS: There was a
424: 1 whole chain there.

Denice M. Torres (December 15, 2006)

424: 3 Q. Yes, ma'am, there certainly
4 is.
5 A. Yes. Zyprexa can
6 potentially lead to weight gain, yes. Is
7 weight gain a major risk factor for
8 diabetes? Yes.

Denice M. Torres (December 15, 2006)

432:11 Q. Would it be wrong in
12 marketing for Eli Lilly to attempt to
13 minimize and eliminate weight gain and
14 diabetes from a doctor's risk/benefit
15 equation?

Denice M. Torres (December 15, 2006)

432:18 Q. Would it be wrong?
19 A. To minimize and eliminate
20 weight gain?
21 Q. And diabetes. That's
22 exactly what I said.
23 A. I do not know what you're --
24 I don't know what you're saying.
433: 1 Q. Maybe your own documents in
2 your company will help you realize what
3 I'm saying.

Denice M. Torres (December 15, 2006)

433:13 Q. "Issues Management
14 Planning," Exhibit 16.

Denice M. Torres (December 15, 2006)

433:20 Diabetes." We know from the
21 organizational chart and from your
22 testimony that this was part of the
23 marketing effort surrounding Zyprexa,
24 correct?

Denice M. Torres (December 15, 2006)

434: 2 THE WITNESS: What was part
3 of the marketing effort?
4 BY MR. ALLEN:
5 Q. Issues management.
6 A. Yes.

Denice M. Torres (December 15, 2006)

434: 8 Issues management. We also
9 saw that the tag line, or as you term or
10 the term you use for doctors was
11 "comparable rates," right?

Denice M. Torres (December 15, 2006)

434:14 Q. Comparable rates. Remember
15 that, your position?
16 A. I said it was one aspect of
17 the message.
18 Q. Right.

Denice M. Torres (December 15, 2006)

434:19 Now, Exhibit 16, "Issues
20 Management Planning, Diabetes," tells us,
21 and will tell the jury, what your
22 position was in regard to diabetes.
23 "Our Position. Diabetes"
24 and "hyperglycemia may occur in patients
435: 1 taking antipsychotics and/or mood
2 stabilizers, including Zyprexa, at
3 comparable rates, with the possible
4 exception of Clozapine."
5 Did I read that correctly
6 under "Our Position"?

Denice M. Torres (December 15, 2006)

468:11 Q. Exhibit Number 19. Ma'am,
12 let's get something straight on the
13 record. You don't have to be present to
14 understand something took place, do you?
15 A. Unless I knew -- got it from
16 some other way.
17 Q. Right.
18 And you knew there was a
19 primary care physician launch of Zyprexa
20 in the United States, did you not?
21 A. Yes.
22 Q. Okay.
23 That's no mystery to you,
24 was it?
469: 1 A. Mystery, no.
2 Q. Right.

And you knew that in June of 2002 and in all the years that the company prepared primary care sales force resource guides to assist the sales representatives when they went out to detail the product, right?

A. No. I was not -- whatever they developed for the sales force, the vast, vast majority of times I would not see the content.

Q. But you know this: You know as a former sales representative, as somebody in global marketing, that the sales force is trained concerning the detailing they will do on the product? You know that?

A. Yes, I do.

Q. You know this. You know that the sales force is part of the marketing efforts of the product, right? You told us that?

A. I did.

Q. Now, ma'am, I don't have much time, so, I'm just going to skip back to Page 7 of this document on patient profiles. Does this help you determine who Donna is? Have you ever heard or does this bring it back or tell you who Donna is?

A. No, sir. I was not involved with the U.S. promotional materials.

Denice M. Torres (December 15, 2006)

Q. You know who Mr. Glyn Parkin is?

A. Yes. Vice president of sales and marketing for the U.S. affiliate, Zyprexa.

Q. In fact, Exhibit Number 1, "Restructuring of the Marketing Component for Zyprexa Product Team," he was the one -- he wrote this document, he's one of the men that you thanked for his "significant leadership," along with Jack Jordan, right?

Denice M. Torres (December 15, 2006)

Q. "The U.S. Affiliate -- with significant leadership from Glyn Parkin and Jack Jordan -- were instrumental in the development of the new team," right?

A. Yes.

Q. Okay.

Now, in 2003, when did Mr. Parkin tell you that the engine of the company, Zyprexa, the heart and soul of the corporation, was slowing and

17 faltering?

Denice M. Torres (December 15, 2006)

475:20 THE WITNESS: I don't
21 remember that conversation.

Denice M. Torres (December 15, 2006)

476: 7 Ma'am, I'll hand you what's
8 been marked as Exhibit Number 20. It is
9 a "Neuro Sales Operations Neuroscience
10 Retail Action Plan." This one came from
11 Mr. Jordan's files. Glyn Parkin, who you
12 thank, says, "The Challenge. I need your
13 leadership, the corporation needs your
14 leadership, at this time your leadership
15 is needed in a massive way and in a way
16 that you will look back on as a defining
17 moment in your leadership careers. All
18 of you."
19
20 Going to the next page.
21 "The challenge. Our
22 business with Zyprexa, the heart and soul
23 of this corporation, the engine room, the
24 best mental health product on this
477: 1 planet, is faltering, slowing, and the
2 slowdown has been a sudden one."
3 Do you recall that occurring
4 in 2003, ma'am?
5 A. Do I recall --
6 Q. **Zyprexa sales suddenly began**
7 **to slow and falter in 2003?**
8 A. I don't recall the specifics
9 of the sales curve. There was a decline.
10 I don't remember when they started, what
11 the abruptness was.
12 Q. **Well, you were involved in**
13 **efforts to correct that, weren't you?**
14 A. Sales decline?
15 Q. **Yes.**
16 A. Or slowing?
17 Q. **In 2003, you were**
18 **specifically involved in efforts to**
19 **correct this sudden sales decline?**
20 A. I don't remember the date,
21 but sales decline in general, yes.
22 Q. **What caused the sales**
23 **decline, ma'am?**
24 A. New competition and concerns
478: 1 about weight gain.
2 Q. **What about concerns about**
3 **diabetes?**
4 A. Actually, I think it was
5 more -- I think there were three things.
6 The company launched our product for ADD,
7 Strattera, so, sales representatives were
8 taking off to promote for Strattera. And
another reason was, I believe,

competition. And this, it was concerns about weight.

Q. Do you remember the SWAT team being created, Zyprexa SWAT team? You remember that, don't you? You were at those meetings, weren't you?

Denice M. Torres (December 15, 2006)

478:17 THE WITNESS: I remember the term. I don't remember what the focus was.

Denice M. Torres (December 15, 2006)

479:13 Q. Ma'am, I'm putting up before the jury Exhibit 21. It's an e-mail correspondence from Mike Magdycz. You know who Mike Magdycz is, don't you?

A. Yes, I know Mike.

Q. Tell the jury who Mike Magdycz is.

A. Mike is an individual that worked in the U.S. affiliate and, at one point, came to the Zyprexa global marketing team.

Q. This was also sent to you, 480: 1 was it not?

A. Yes. I'm on the cc list.

Q. Mr. Magdycz at this point was working both for the U.S. affiliate and the global marketing team, was he not?

A. I don't know if it was during this time period.

Q. Well, it looks like in June of 2003 the subject matter of his e-mail is "Zyprexa Issues SWAT Team Urgent Action Required Privileged and Confidential."

Do you recall that?

A. No, I don't, sir. I could read the document and talk to you about it.

Q. Don't you recall being at the SWAT team meetings?

A. If you let me take a look at this, I'll take a look and see what it is, but --

Q. Your name is on this document, and both on the e-mail -- 481: 1

A. Sir, I'm not denying that. I really do not recall specifics of 2003 or '2 or '1. Depending on the topic. You've shown me a lot of different documents. I'm doing my best to answer the question. And if you want me to go through this document, I'll do that.

Q. Well, just go to the page as

"Who is going to deliver?" It's right over your right shoulder. You don't have to look in the dark, you can look over your right shoulder and you can see where we are.

A. I'd rather read on the paper.

Q. I know, ma'am. You can read on the paper, but I'm trying to help you. Right there. Look over your shoulder. "Who is going to deliver? The issues SWAT team."

A. (Reviewing document.)

Q. Are you on the page, ma'am? I'm on the page. "Who is going to deliver?" Are you there?

A. Yes, I am.

Q. It says at the top, "The issues SWAT team." It gives the members, including Dr. Richard Petty. You remember Dr. Petty, don't you?

A. No, I didn't know Dr. Petty. I've heard his name, but I didn't personally know him.

Q. It says we are going to "Need protection from outside influence while we get this done." The people assigned to that are Jordan, that's Jack Jordan, Denice Torres and Mike Bandick." Do you recall this now?

A. Do I recall the specifics? No.

Q. Tell us what you do recall about this issue.

A. Well, the team was put together. It looks like all individuals from the U.S. affiliate, Tom Hardy, U.S. affiliate, U.S. brand manager; U.S. affiliate, Vince Truax; Mike Yost, U.S. affiliate; Kelly Copes-Anderson, U.S. affiliate; Mike Magdycz, I don't know if he was U.S. or global at the time. Joe Welch was U.S. McKinsey was --

Q. Why was this team created is what I'm asking?

A. If I can go back to the document. Let me take a look at it and see.

Q. Well, there's a page called "What is the problem?" Do you see in this document, "What is the problem?" You were copied on this document. You were sent this e-mail. You were listed as somebody involved. Do you see where it says, "Sales" are "below" the "plan?"

A. If you're going to ask me questions, I would like to look at the document, please.

Q. I'm asking you about the page "What is the problem?" Do you see that? "What is the problem?" Right over your shoulder. You got it? Do you recall that in 2003 sales were below the

plan?
A. Again, I told you from a year's standpoint, I don't remember when they declined, but at some point, sales were below plan.
Q. It says, "Equity indicators." Equity means what people were thinking about the product, right, brand equity?
A. Yes.
Q. Okay.
So, when we talk about equity and we look at the documents concerning Zyprexa and it says "equity" or "brand equity," it means people's perception of our product, correct?
A. Actually, it can mean one of two things. It could mean the perception or the relevance of that attribute to prescribers. So, you could have weight gain that was always associated, but the relevance -- in the case of Zyprexa, my recollection is the relevance to prescribers changed.
Q. Right.

Denice M. Torres (December 15, 2006)

Q. Straightforward and honest and direct to a jury.
The problem in 2003 that was causing the dropoff in sales is physicians started to suspect and believe that Zyprexa caused more weight gain and was causing diabetes, correct?

Denice M. Torres (December 15, 2006)

THE WITNESS: Again, they were the three things. You asked me this question before, and the three things that we looked at in terms of decline in sales, new competition, the launch of Strattera, and the third were concerns about Zyprexa and weight gain.
BY MR. ALLEN:
Q. And you were on the issues focus team, weren't you?
A. Issues focus team. I'm not familiar with that.
Q. You are not familiar with that?
A. Issues focus team? No.
Q. Well, how about the Zyprexa focus team, you were on that, weren't you, in the summer of 2003?
A. Zyprexa focus team?

Q. Yes, ma'am. You don't remember that now?
A. Zyprexa focus team? No, I don't.
Q. Okay, sorry.
Well, you were. Let me show you that document.

Denice M. Torres (December 15, 2006)

Q. Exhibit 22. Do you recall being an author of a report to Zyprexa U.S. and global marketing, "Subject: Diabetes update" in the summer of 2003? "Diabetes Update," to the "Policy Committee," from, among others, Denice Torres in global marketing.
A. (Reviewing document.)
Q. Do you recall that?
A. Just give me a moment, please.
Q. There's only a question on the table.
A. Do I recall the focus team?
Q. You being on the Zyprexa focus team.
A. I remember this memo. I'm not sure of the term "focus." There were other teams, but I'm not sure that, you know, it was a branded focus team and people referred to a focus team.
Q. The only reason I said it is because it says it right on --
A. It says it on the document.
Q. It says on the document you wrote, "New Zyprexa 'Focus' Team." Did I read that correctly?
A. It does say that, yes.
Q. Right.
Do you recall that the focus team was created in the summer of 2003 to create new messages to surround Zyprexa? Do you recall that? Do you recall that?
A. If you're going to ask me questions, I need to read the document. So, if you can just give me a moment, let me look through it, and then I can answer your questions.
Q. Ma'am, my only question is, regardless of the document, do you recall that a new Zyprexa focus team was created in the summer of 2003 to create new messages surrounding diabetes and Zyprexa? Yes, no, or you do not recall?
A. I vaguely recall. There were so many teams created, I'd have to go through and say specifically what was this team.

But do you recall, without review of the document, just in honest and direct fashion to the jury that new messages were created surrounding diabetes and weight gain in the summer of 2003?

A. I don't know that -- no, I don't recall new messages being created. That doesn't mean they weren't created. I just don't recall new messages being created.

Q. Do you recall new stories being created?

Denice M. Torres (December 15, 2006)

THE WITNESS: No.
BY MR. ALLEN:

Denice M. Torres (December 15, 2006)

Q. There was a Dr. Rosenhac. Do you know Dr. Rosenhac or who he is?

A. No.

Q. Were you on the weight task force in January of 2004? Were you on the weight task force?

A. I don't believe so.

Q. Did you know a weight task force was created in January of 2004?

A. Do I remember?

Q. Yes, ma'am. That's all I asked.

A. No, no, I don't remember that. There were several -- as you can see from these documents, there were multiple task forces being formed. It doesn't surprise me. But I don't remember specifics of a weight task force being formed.

Q. The reason multiple task forces were being formed in 2003 and 2004 is because Zyprexa was losing sales all of a sudden due to the concerns about diabetes, correct?

Denice M. Torres (December 15, 2006)

Q. Ma'am?

A. The reason task forces were being created was that Zyprexa was losing sales. And you asked me why were they losing sales. And I gave you the three factors: One, new competitive entries; two, taking an eye off implementation with the Strattera launch; and three,

concerns about Zyprexa and weight. And I'm sure there were other concerns around that.

Denice M. Torres (December 15, 2006)

Q. Ma'am, you actually prepared, as marketing director, the Zyprexa global brand plan for 2004 and 2005, did you not, Exhibit 23?
A. Yes.
Q. And I'm going to skip back to Page 19, "World Wide Zyprexa Brand Equity - 2002." You told us what brand equity is, right?
A. Yes.
Q. This was a document you were in charge of preparing, right?
A. Yes. My team, yes.
Q. And your team was looking at global plan on marketing Zyprexa for 2004 to 2005, right?
A. Yes.
Q. And you have a chart or graph or table -- what did you call it, lines and graphs?

Denice M. Torres (December 15, 2006)

Q. What is this? Is this a table on Page 19?
A. Yes.
Q. Okay.
And it's on brand equity; is that correct?
A. Yes.
Q. And what you -- and the brand equity, the brand is Zyprexa, right?
A. (Witness reviewing document.)
Q. Zyprexa is the brand we're talking about, correct?
A. We are talking about Zyprexa.
Q. All right.
This is hard to read, the best copy they gave me. Under "Concerned will increase." Let me go to the second page, on Page 20. Do you see this? "When prescribed - worry patients will develop hyperglycemia" and "diabetes." It is a "weakness-linked to overall metabolic side effect concerns."
Did I read that correctly?
A. (Reviewing document.)
Q. Ma'am, I'll tell you, you understand this chart. You created it?
A. No, I do. I'm sorry. Did

you say "when prescr d - worry patients will develop diabetic ketoacidosis"? Is that what you asked me?

Q. Ma'am, I'm under "Worry patients will develop hyperglycemia" and "diabetes."

A. Yes, I do see that.

Q. Under the association, "Z" stands for Zyprexa, right? "Z" stands for Zyprexa?

A. Yes, it does.

Q. Okay.

Under the category of "Worry patients will develop hyperglycemia" and "diabetes," that's Zyprexa; is that correct?

A. Yes.

Q. "Worry patients will gain too much weight." That's Zyprexa, am I correct about that?

A. As a high association, and then you have other associations, yes.

Q. Yes.

Another high association is worry they "will develop hyperglycemia" and "diabetes," correct?

A. Yes.

Q. Okay.

So, just for the record, you keep on telling us the concerns around Zyprexa in the summer of 2003 were weight gain, but the fact of the matter is, in a very document you created, the concerns surrounding Zyprexa in the summer of 2003, a high concern was diabetes, correct?

Denice M. Torres (December 15, 2006)

THE WITNESS: The concern was, as I said, was weight gain, you know, concerns with weight gain and the implications of weight gain with other things, yes. It's not inconsistent.

BY MR. ALLEN:

Q. Ma'am, I didn't ask you about weight gain. So, you changed my question in your answer.

As reflected in the table in Exhibit 23, which you were in charge of preparing, another high concern, high concern was "hyperglycemia" and "diabetes," Zyprexa, correct?

Denice M. Torres (December 15, 2006)

A. You asked me about what is in the chart, and the chart said -- you

asked me about "worry patients will develop hyperglycemia/diabetes," and you asked me about "worry patients will gain too much weight," and you said are these under the category of "High Association," and I said yes.

Denice M. Torres (December 15, 2006)

Did you know --

Denice M. Torres (December 15, 2006)

Q. -- that as early as February of 2000, and even predating that date, that the U.S. marketing department was "driving the depression story" on Zyprexa to potential consumers? Did you know that?

A. No.

Q. It'd be wrong if they did that, wouldn't it?

Denice M. Torres (December 15, 2006)

A. Depression on its own? Yes. Depressive symptoms associated with schizophrenia? No.

Q. Just for the record, ma'am, you testified I think within the first hour this morning that Zyprexa was not indicated for depression, right?

A. I did.

Q. It was not indicated for bipolar depression, right?

A. That's correct.

Q. And has never been indicated for depression?

A. Correct.

Q. And to suggest that in any form, shape or manner that somehow Eli Lilly was entitled to promote or market Zyprexa for depression would be wrong? You're not entitled to do that, are you?

A. I did say that, yes, that is correct.

Denice M. Torres (December 15, 2006)

Q. Did you know that Eli Lilly was out promoting Zyprexa for depression?

A. Who said they were out promoting for depression?

Q. This document. Let's read it together. It is from John Richards.

Who is John Richards
A. He was on the U.S. brand team.
Q. Okay.
Then the answer to your question is, Mr. John Richards is the one that says you're out promoting Zyprexa for depression --

Denice M. Torres (December 15, 2006)

Q. -- and he was writing to Jack Jordan. You know who Jack Jordan is, don't you?
A. Yes. Head of the brand team.
Q. You were on the key decision team with him. Do you recall that?
A. Key decision team? No. You keep throwing these terms out of --
Q. All these terms came from your documents. You were on the --
A. They may be. What I'm saying is there was a lot of teams being formed. Did I work with Jack Jordan? Yes, absolutely.
Q. Who is Eric Prouty?
A. Eric Prouty was on Jack Jordan's team.
Q. Okay.
And Jack Jordan is one of the affiliates who you were responsible in global marketing as working with to help market Zyprexa, right?
A. Jack Jordan?
Q. Yes.
A. Yes.
Q. Okay.
E-mail from Mr. Richards. "Jack, attached as we discussed. As you can see, we have been driving the depression story with Zyprexa in our DTP" --
What's that, "DTP"?
A. Direct to physician.
Q. -- "in our direct to physician program since Q3 1998. We were ahead to the curve in recognizing communicating the importance of this attribute and how we can utilize it to differentiate ourselves in the marketplace. Please let me know if you have questions or comments. Thanks, JR."
Did I read that correctly?
A. Yes, you read it correctly.
Q. Was Eli Lilly out driving the depression story?
A. I don't have knowledge of Lilly -- what this said here, "communicating the importance of this attribute." So, I don't know in what

context, you know, it was promotion of depression, I'm not familiar with it.

Q. One thing you do know if you were driving a depression story to prescribe to doctors in direct to physician campaigns -- DTP is direct to physicians, right?

A. That's correct.

Q. If you were driving the depression story and trying to get a doctor to prescribe Zyprexa for depression, that would be promoting it for an off-label use, correct?

Denice M. Torres (December 15, 2006)

THE WITNESS: If the activity was around asking physicians or insinuating to physicians that Zyprexa should be used exclusively for the treatment of depression, that would be wrong.

Denice M. Torres (December 15, 2006)

Ma'am, you knew or did you know that when Zyprexa was launched to the primary care, this Viva Zyprexa market, you knew that there was not a specific indication for Lilly representatives to promote in the primary care physician market? You knew that, didn't you?

Denice M. Torres (December 15, 2006)

THE WITNESS: I don't know when the primary care group was launched.

BY MR. ALLEN:

Q. Well, assuming it was October of 2000, you said you didn't have to be there to remember if it was launched.

A. My dear sir, I was dealing with life and death with my daughter. I don't remember too much about that time period. I was not even at work in that time period, so, I'm sorry.

Q. Okay.

So, you weren't even at work in the fall of 2000?

A. No. I took an extended leave.

Q. Okay.

Whoever was at work in the

fall of 2000, in the primary care, strategy and implementation overview, you've been involved in drafting strategy documents, have you not?

Denice M. Torres (December 15, 2006)

THE WITNESS: Yes.
BY MR. ALLEN:
Q. A challenge, what's a challenge, ma'am?
A. A challenge is something that you have to deal with.
Q. Right.
Do you see the language here, "Zyprexa's primary indications - schizophrenia and bipolar." Let me stop here. Those are the only two indications, not the primary ones. They're the only indications, right? Schizophrenia and bipolar mania, correct?
A. Yes.
Q. "Zyprexa's primary indications - schizophrenia and bipolar - are not viewed as PCP," primary care physician "treated conditions, so, there's not a specific indication for Lilly representatives to promote in the primary care physician" market.
Did I read that correctly?
A. You read it correctly.
Q. Nevertheless, that didn't stop Eli Lilly, did it? They went ahead and marketed off label anyway, didn't they?

Denice M. Torres (December 15, 2006)

Q. Didn't they?
A. What was the question?
Q. The fact that there's no indication in the label didn't stop Eli Lilly, they went ahead and promoted off label anyway, didn't they?
MR. WASSON: Objection.
THE WITNESS: Off label for what?

Denice M. Torres (December 15, 2006)

Q. Off label for Zyprexa.
The fact that -- let me rephrase the question.
The fact that something is off label, the condition is off label from Zyprexa didn't stop Eli Lilly. They would still promote the product for an

508: 1 off-label use, would [illegible] they?

Denice M. Torres (December 15, 2006)

508: 4 THE WITNESS: No, sir. I
5 mean, I would compare this to when
6 Lilly launched Prozac, primary
7 care physicians did not treat a
8 lot of patients with depression.
9 And it was because of Lilly's
10 efforts and then Pfizer's efforts
11 and then other company's efforts
12 in terms of education that today
13 depression is readily treated by
14 primary care physicians.
15 So, at the time, was there a
16 lot of treatment of bipolar mania
17 patients? No. But,
18 unfortunately, these patients go
19 seven years before diagnosis is
20 made. So, I would consider
21 efforts to educate primary care
22 physicians about bipolar a good
23 thing for everyone.

Denice M. Torres (December 15, 2006)

509: 5 Q. My question to you simply
6 was, it didn't stop Eli Lilly from
7 promoting if a use was off label, did it?
8 MR. WASSON: Object to form.
9 THE WITNESS: I'm not aware
10 of an off-label promotion.

Denice M. Torres (December 15, 2006)

510: 5 Q. Did Eli Lilly have an
6 off-label strategy workshop to promote
7 the product to elderly people with
8 psychosis? This is Exhibit Number 27.

Denice M. Torres (December 15, 2006)

510:13 Q. And you knew about the
14 off-label workshop because you're on the
15 e-mail?

Denice M. Torres (December 15, 2006)

510:18 Q. "Subject:
19 Off-Label...Workshop," "Strategy
20 Workshop." October 2002. Do you recall
21 that?

A. I actually do recall this, yes.
Q. Okay.
Now, you've told us already, there's no indication for dementia, is there?
A. That's correct.
Q. There's no indication for Alzheimer's, is there?
A. That's correct.
Q. There's no indication for Alzheimer's or dementia-related symptoms or side effects, is there?
A. That's correct.
Q. And this is an "Off-Label Strategy Workshop"?
A. Actually, the person that sent this out, there was quite a hullalabu about this, because Jill Welch said, I don't like the off-label term. And that would have been --
Q. She was Jill Welch?
A. She was head of strategy and working for Jack Jordan.
Q. Yeah, she says that. She says, I do not like the 'off-label' term" and let's change to "'Elderly and new domains' maybe."
A. Actually, I think several people responded to this e-mail, because of the off label --
Q. Hey, ma'am. She says -- I'll read it to you. "I do not like the 'off-label' term - 'Elderly and new domains' maybe," correct?
A. That's what she said, yes.
Q. Okay.
We won't call it off-label workshop. We should call it an elderly and new domains maybe workshop; is that right?

Denice M. Torres (December 15, 2006)

THE WITNESS: That's not what she's saying. She's saying off label, and everyone knows off label, bad connotations. What he's talking about is work in the elderly. This was during a time period when -- 2002, you know, the studies, we're still looking at the studies around Alzheimer's dementia.
BY MR. ALLEN:
Q. Ma'am, in 2002, Zyprexa was not indicated --
A. It was not indicated.
Q. -- for Alzheimer's and Alzheimer's dementia?
A. That's correct.

Q. Never h[illegible] been.
A. That's correct.
Q. Shouldn't be promoted for it?
A. Shouldn't be promoted for it.
Q. Right.
Here it says in the e-mail, "A couple weeks ago when we stopped the borderline registration program." What was the borderline registration program?
A. It was a -- there were studies, if I remember correctly, studies that we were proposing, I don't remember if they started, to get an indication in borderline.
514: Q. "It was clear that the domain" -- what's a domain? The term is used here. "It was clear that the domain." What's that?
A. I don't know what that refers to.
Q. "It was clear that the domain was too important to be dropped completely. Furthermore, it is important that any activity on off-label use in general gets incorporated in the organization and planning of the global Zyprexa team."
Did I read that correctly?
A. You did.

Denice M. Torres (December 15, 2006)

527: Exhibit 26 is an e-mail chain from Dr. Lechleiter. He's the number two man in charge at Eli Lilly, is he not?
A. Yes.
Q. He writes this e-mail to many people, and then there's some other chains, but he writes it's to Sidney
528: Taurel. Who is Sidney Taurel?
A. The CEO of Lilly.
Q. He's the head man at Eli Lilly, right?
A. Yes.
Q. Okay.
And he's actually forwarding an e-mail that he received from Alan Breier, right, in November of 2001, correct?
A. Yes.
Q. Okay.
And in this e-mail, which you were a recipient of, right?
A. From Alan, yes.
Q. It says, "Update on Zyprexa Dementia Program." Do you see that, "Dementia Program"?
A. Yes.

Q. Did y'all have a program to promote Zyprexa to dementia patients?
A. We had studies ongoing in the area of dementia.
Q. The studies didn't turn out so well, did they?
A. No, they didn't.
Q. The studies determined that there was no proven safety or efficacy for the use of Zyprexa in the elderly patients with either Alzheimer's, psychosis or dementia; isn't that true?
A. It says there were "mixed results."
Q. Well, let's see what it says. It says, "John, Following is an update on our Alzheimer's psychosis program."
Did I read that correctly?
A. Yes.
Q. "Zyprexa Product Team" -- you were on that, weren't you?
A. Yes, I was.
Q. -- "conducted 4 clinical trials with mixed results to support an indication for Alzheimer's psychosis," right? Right?
A. Yes.
Q. Now, ma'am, we don't have time, but the end result of the studies that were done did not support an indication for Alzheimer's psychosis, did it?

Denice M. Torres (December 15, 2006)

THE WITNESS: I mean, it says that on the second page. I mean, Dr. Breier summarizes his points here. "We recommend not pursuing a formal indication for Alzheimer's psychosis because of the mixed clinical results, the need to initiate another global trial, the high FDA threshold, concerning safety risks, and strategic focus on high dose segments. The recommended approach is to support this segment with a publication strategy."

Denice M. Torres (December 15, 2006)

Your testing showed that there was not a proven indication on the testing, right? You could not support an indication on the testing?
A. With the clinical studies?

Q. Yes, ma'am.
A. Correct. Correct.
Q. Right.
Nevertheless, Dr. Breier says, "Lilly's current business in the elderly segment is about $500 million," right? Right?
A. I don't see that in here.
Q. Second page. It's right on the screen.
A. Okay, yes, uh-huh.
Q. As you just -- so, you sped read there. The bottom line is, he says, after "Lilly's current business in the elderly segment is about $500 million," he says, "We recommend not pursuing a formal indication for Alzheimer's psychosis because of the mixed clinical results, the need to initiate another global trial, the high FDA threshold, concerning safety risks, and strategic
532: 1 focus on high dose segments. The recommended approach is to support this segment with a publication strategy."
Did I read that correctly?
A. You did, sir.
Q. So, you couldn't get an indication from the FDA, but Dr. Breier says, we're not going to give up on promoting Zyprexa to the elderly, our approach will be to get publications out supporting the promotion to the elderly, correct?

Denice M. Torres (December 15, 2006)

532:15 THE WITNESS: There's two ways to read this. One is to "support this segment." Okay. Support this segment. There's $500 million, there's use in there. So, support this segment is one thing. That would be entirely correct.
If what he was saying here
533: 1 was to support the promotion of Alzheimer's dementia with a publication strategy, that would be wrong. I don't know exactly what he meant by that. There's two interpretations. But I couldn't tell you what Dr. Breier meant.
BY MR. ALLEN:
Q. At least we know he says we're doing $500 million in the elderly worth of business, right?
A. He did say that.
Q. And he's also saying we can't support an indication in the elderly because the studies are mixed in

that regard, right?
A. He did say that.
Q. And he's saying here's what we're going to do. Our approach will be to support the elderly through the publication plan, right?

Denice M. Torres (December 15, 2006)

534: 8 A. That's what he said.

Denice M. Torres (December 15, 2006)

534:12 Q. All of this is not only reported by Dr. Breier, the head of the Zyprexa product team, it's reported up to John Lechleiter, the second in command of your company, who reports it to the CEO of the entire company, Sidney Taurel, right?
A. That's what the e-mail said, yes.

Denice M. Torres (December 15, 2006)

535:17 Q. Ma'am, is this Exhibit 29? I apologize.
A. Yes, it is, sir.
Q. This is an e-mail chain.
A. I remember this e-mail.
Q. How do you remember this e-mail?
A. I remember because when it
536: 1 came across my desk, there was a reference on Page 3 or 4 of --
Q. Of what?
A. It's bolded. "It appears to me that the fact we are now talking to child psychs and peds" -- I'm sorry. The bolded section. The fact about seizing "the opportunity to expand our work with Zyprexa in the same child-adolescent population" was a statement that was not supported by regulatory, promotional law and is an inappropriate statement.
Q. Well, that's where we're heading. But this e-mail chain, you received this e-mail, right?
A. Absolutely. And took action on it. I had a discussion with Dr. Breier. Dr. Breier, I believe, sent an e-mail, but also had a discussion with John Lechleiter.
Q. And just for the record, John Lechleiter is the one that wrote this e-mail chain, right?
A. Yes, he did, sir.

537: 1 Q. And Dr. [redacted] is it Dr.
2 Lechleiter?
3 A. Yes, it is.
4 Q. He's second in command at
5 your entire company; isn't that right?
6 A. That's correct.
7 Q. And what he says in this
8 e-mail is, "Attached are my notes from a
9 recent visit to Cincinnati in late
10 February, where I met with a group of our
11 Neuroscience sales representatives and
12 spent part of the next day in the field
13 calling on psychiatrists. I have
14 highlighted" -- this is what he says.
15 "I have highlighted in bold
16 the inputs that I consider to be most
17 significant or that came up most often,
18 and would appreciate if the global" --
19 that's you, right -- "and U.S. teams
20 would follow up as appropriate," correct?
21 A. Yes.
22 Q. Now, Dr. Lechleiter is going
23 in the field with the sales
24 representatives, is what he's doing on
538: 1 this trip, right?
2 A. Yes.
3 Q. He says in bold that I want
4 you, the global and U.S. teams, to follow
5 up on what I found in out in the field,
6 right?
7 A. Yes.
8 Q. Now, some of this is
9 redacted. I'm going under Zyprexa on the
10 next page. You said you remember this
11 e-mail, right?
12 A. I do.
13 Q. This e-mail concerns
14 off-label marketing and promotion,
15 doesn't it?

Denice M. Torres (December 15, 2006)

538:19 A. The -- John's note was
20 inappropriate.

Denice M. Torres (December 15, 2006)

538:22 My question to you was,
23 John, which is Dr. Lechleiter, second in
24 command at Eli Lilly in 2003, is writing
539: 1 a memo concerning off-label promotion of
2 Zyprexa to pediatric and adolescent
3 patients, right?

Denice M. Torres (December 15, 2006)

539: 5 THE WITNESS: He doesn't say

that. He says, "we must seize the opportunity to expand our work with Zyprexa" --

Denice M. Torres (December 15, 2006)

THE WITNESS: He says, "we must seize the opportunity to expand our work with Zyprexa in this same child-adolescent population."

That's what he says. He doesn't go on to talk about off label. The fact is, John was new, and when he went out to the field, he was new in this marketing capacity. Following this memo, Dr. Breier talked to him and said let's talk about, you know, promotional regulation.

BY MR. ALLEN:

Q. How do you know? Were you privy to the conversation between Dr. Breier and Dr. Lechleiter?

A. No. Dr. Breier told me he had that conversation with him, and I believed him.

Q. When did Dr. Breier tell you this?

A. Well, the day the e-mail came out, I went and talked to Alan and said that's inappropriate.

Q. Why didn't you write an e-mail back and say this was inappropriate?

A. I thought Alan would address it with his boss. I can't remember. I may have written an e-mail to Alan. He was down the hall from me. I thought it was inappropriate.

Q. I don't see any e-mails from either you or Dr. Breier telling Dr. Lechleiter that his conduct was inappropriate. Are you familiar with such e-mails?

Denice M. Torres (December 15, 2006)

THE WITNESS: I don't -- I had the conversation. Dr. Breier said he had talked -- was going to and had talked to Dr. Lechleiter.

Denice M. Torres (December 15, 2006)

My question to you was, are you familiar with any e-mails being

written by yourself, Dr. Breier or anybody else saying Dr. Lechleiter's conduct in regard to exhibit -- what's the number -- 29 is inappropriate?

A. I thought I wrote an e-mail. I honestly don't remember. I do remember having a conversation.

Q. Dr. Lechleiter says, "we need to seize the opportunity." Doesn't he say that?

Denice M. Torres (December 15, 2006)

542: A. I think you've read that twice already, yes.

Denice M. Torres (December 15, 2006)

544:20 Ms. Torres, we're on Exhibit 29, Dr. Lechleiter's e-mail concerning off-label promotion. Do you follow me?

Denice M. Torres (December 15, 2006)

545: THE WITNESS: Nowhere does it here say anything about off-label promotion. It wasn't an e-mail about off-label promotion. It was an e-mail about his notes from a day in the field with neuroscience reps.

Denice M. Torres (December 15, 2006)

545:15 Q. Did it concern you?

A. This statement, I've said it several times, did concern me, but I also knew --

Q. What's the statement? Read it out loud and slowly for the jury, please.

A. "It appears to me that the fact we are now talking to child psychs and peds and others about Strattera means that we must seize the opportunity to expand our work with Zyprexa in this same child-adolescent population."

Q. That would be off-label promotion, wouldn't it?

Denice M. Torres (December 15, 2006)

546: THE WITNESS: If we were

talking to physicians about an indication for child-adolescent with Zyprexa, that would be off-label promotion.

BY MR. ALLEN:

Q. Now, Dr. Lechleiter, when he writes this e-mail and he says under "Physician comments," "Comment made that we are losing scripts to Risperdal for treatment of disruptive kids because J & J has the data and we don't." Did I read that correctly?

A. Yes, you did.

Q. Was Zyprexa indicated for disruptive kids?

A. No.

Denice M. Torres (December 15, 2006)

Q. Was it indicated for children with attention deficit or hyperactivity disorder?

A. No.

Q. Was it indicated for any pediatric patients?

A. No.

Q. Was it indicated for any pediatric patients for anything?

A. No.

Q. It would be wrong to even consider having your sales reps seize the opportunity and try to market Zyprexa to pediatric patients, wouldn't it?

Denice M. Torres (December 15, 2006)

THE WITNESS: Under the guise of an indication, yes, it would.

Denice M. Torres (December 15, 2006)

Remember he said whatever is in bold is the most important thing. Remember that? He said what I put in bold is the most important or words to that effect. "I have highlighted in bold, the inputs that I consider to be most significant." Right? Right?

A. That's what it says, yes.

Q. The next thing is in bold, "With child psychs, Zyprexa is a distant third across a range of disorders."

Did I read that correctly?

A. Yes.

Denice M. Torres (December 15, 2006)

549: 8 First of all, there was not
9 a range of disorders for which Zyprexa
10 was indicated, was it?
11 A. No. Just schizophrenia and
12 bipolar mania.

Denice M. Torres (December 15, 2006)

550:19 Q. So, when he says "Zyprexa is
20 a distant third across a range of
21 disorders" for pediatric patients, the
22 fact of the matter is, even in adult
23 patients there wasn't a range of
24 disorders other than bipolar mania,
551: 1 schizophrenia, and later bipolar
2 maintenance that could even be used in
3 adults; is that right?

Denice M. Torres (December 15, 2006)

551: 5 THE WITNESS: Yes. There
6 were three indications. I don't
7 know what he meant by this. I
8 don't know what he meant by this
9 statement. I could tell you there
10 were two indications and then
11 three -- how many indications are
12 there now? I don't know. I don't
13 know what he meant by this.
14 BY MR. ALLEN:
15 Q. He then has an "editorial
16 note." This is his words. "Editorial
17 Note: It appears to me" -- now, "me" is
18 the second highest person in the company,
19 right?

Denice M. Torres (December 15, 2006)

552: 1 A. Yes.
2 Q. What was his position back
3 at the time this was written?
4 A. He had just -- I remember
5 when he went out in the field, he was --
6 his doctor is a Ph.D. and he had just
7 been, I guess, promoted and assigned a
8 responsibility to take over marketing.
9 So, I mean, I looked at this and said, I
10 know John. John would not intentionally
11 do something that was illegal. And I
12 looked at this and said, you know what, I
13 don't think he knows some of the
14 promotional laws. That was the
15 discussion I had with Alan.
16 Q. You have no notes about that
17 discussion, you have no e-mails about

that discussion, you've no documents about this alleged discussion, do you?

Denice M. Torres (December 15, 2006)

THE WITNESS: Why don't you ask Dr. Breier.

Denice M. Torres (December 15, 2006)

A. I thought I wrote an e-mail to Alan. I don't remember for sure. I remember seeing the e-mail. I remember having a discussion with Alan. I don't remember other specifics.

Q. But all you know --

A. That's all I remember.

Q. All you know is Dr. Lechleiter took over, was in charge of marketing at the time he wrote this e-mail?

A. No. He was in charge of U.S. affiliate.

Q. I got you.

A. So, U.S. affiliate having all the different elements to it.

Q. Dr. Lechleiter, at the time he wrote this e-mail, was in charge of the U.S. affiliate marketing, was he not?

A. He was in charge of the U.S. affiliate, marketing being part of that.

Q. Right.

So, when we have this e-mail, Exhibit 29, written by Dr. Lechleiter, it's written by the person at the entire drug company who is in charge of marketing in the U.S. affiliate, right?

Denice M. Torres (December 15, 2006)

THE WITNESS: He had just taken over the job. Did anyone look at this and go, oh, gosh, look what John is asking us to do? No, that did not happen.

BY MR. ALLEN:

Q. "Editorial note: It appears to me that the fact we are now talking to child psychiatrists." Now, why would you want to even go detail a child psychiatrist on Zyprexa?

Denice M. Torres (December 15, 2006)

554:23 Q. See, if [redacted]'s not indicated,
24 why are you going to detail the child
555: 1 psychiatrist about Zyprexa when it's not
2 indicated?
3 A. I don't know why he was. He
4 was there for Strattera.
5 Q. And peds, P-E-D-S that's
6 pediatricians, right?
7 A. He says, "It appears to
8 me... talking to child psychs...and
9 others about Strattera."
10 Q. "About Strattera" means?
11 A. Strattera is indicated for
12 attention deficit disorder. They would
13 be talking to psychs and peds.
14 Q. "Means we must seize the
15 opportunity to expand our work with
16 Zyprexa in this same child-adolescent
17 population." Correct? Isn't that what
18 he wrote?
19 A. That's what he wrote.
20 Q. So, he's -- in his role, he
21 is advocating that we market off label,
22 correct?

Denice M. Torres (December 15, 2006)

556: 1 THE WITNESS: No. He wrote
2 a comment. Nobody took it
3 seriously. They thought, John is
4 coming in, he doesn't know all the
5 promotional regulations. That's
6 what we thought.

Denice M. Torres (December 15, 2006)

556:16 Q. You are a recipient of this
17 e-mail, are you not?
18 A. I am. I'm telling you what
19 I -- I read it, I read it back to you.
20 This is what I thought about it. I don't
21 know what John thought. I had a
22 conversation with Alan. That's all I
23 know.
24 Q. Well, Eli Lilly had
557: 1 supported through educational grants the
2 use of Zyprexa in antipsychotic therapy
3 in children and adolescents, hadn't it?
4 A. I have no idea.

Denice M. Torres (December 15, 2006)

557:13 Q. Let me ask you this. Have
14 you ever seen Exhibit 30?
15 A. No.
16 Q. "Antipsychotic Therapy in
17 Children and Adolescents."

A. No, I h[illegible]n't.
Q. Let me go to the third page. "We wish to acknowledge that the continuing education materials were made possible by an unrestricted educational grant from Eli Lilly & Company of Indianapolis, Indiana.
"The presenter of this activity has indicated that there is a relationship which, in the context of this presentation, could be perceived as a real or apparent conflict of interest," for example, "(...honoraria), but does not consider that it will influence the presentation of this continuing education activity." Did I read that correctly?
A. I'm sorry. What page is that?

Denice M. Torres (December 15, 2006)

THE WITNESS: Yes. You read that paragraph correctly.

Denice M. Torres (December 15, 2006)

Eli Lilly, if you look on the very last page of this document entitled "Antipsychotic Therapy in Children and Adolescents," was supported by a educational grant from Eli Lilly & Company, right? Very last page?
A. "Made possible by an unrestricted educational grant."
Q. Here's what it says. I'll read it slowly. "The continuing educational materials" contained in this activity" were made possible by an unrestricted educational grant from Eli Lilly & Company." Did I read that right?
A. Yes, you did, sir.

Denice M. Torres (December 15, 2006)

Q. Ma'am, we were almost through, but we'll read exactly what it says. First it was supported by an "educational grant from Eli Lilly," right? On page 3, right?
A. Yes.
Q. Under there it says, "By completing this activity, participants will be able to: Discuss the prevalence and epidemiology of childhood onset schizophrenia." Does it say that?
A. Yes.
Q. And then it goes on,

"Identify childhood psychiatric disorders that are effectively treated with antipsychotics." Do you see that?

A. I do see that.

Q. Now, this Zyprexa was not indicated for any childhood psychiatric disorder, was it?

A. Zyprexa? No.

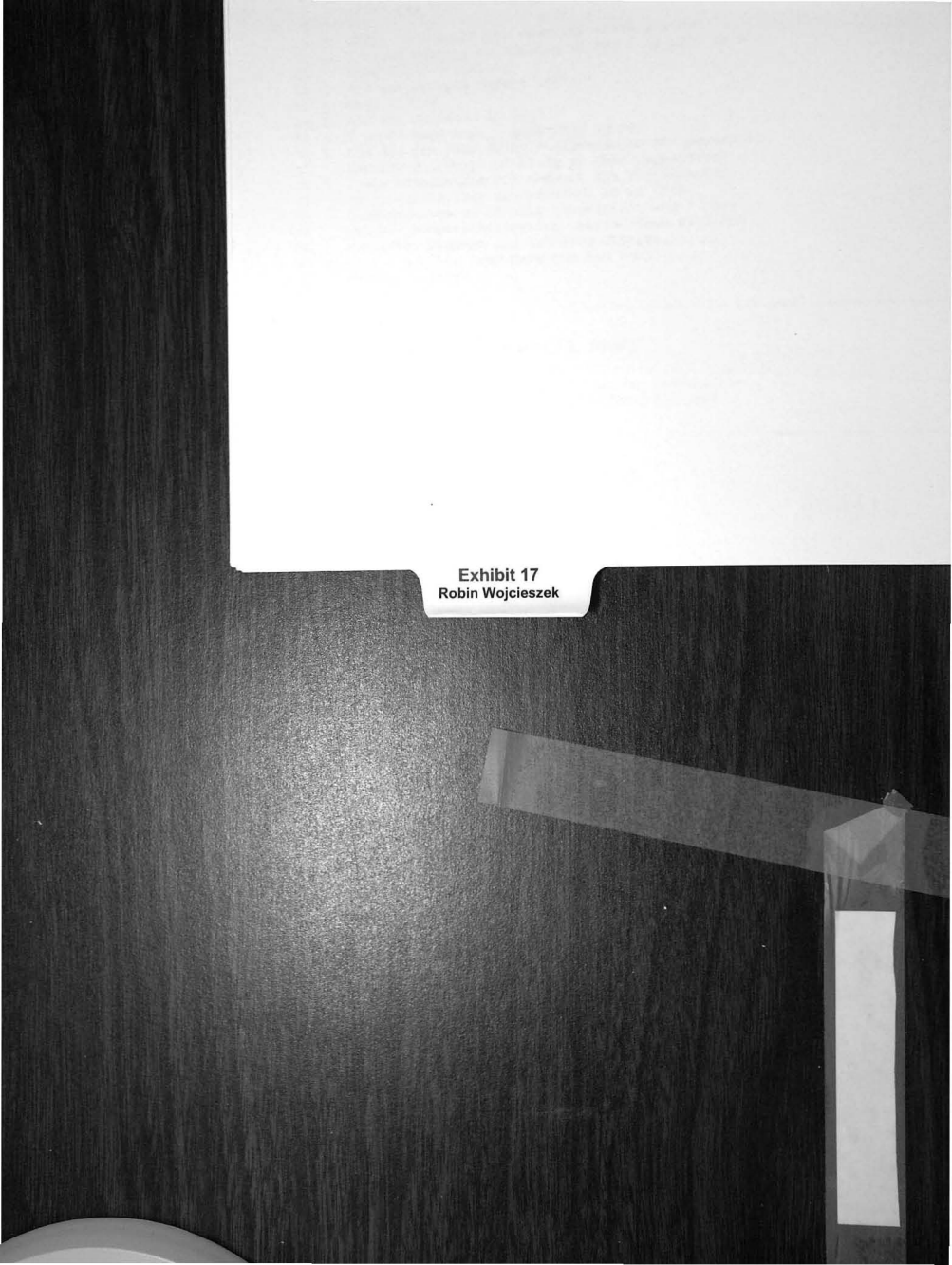


Exhibit 17
Robin Wojcieszek

Robin Pitts Wojcieszek (December 11, 2007)

6:10 Q Would you state your full name for the record,
11 please.
12 A Robin Pitts Wojcieszek.

Robin Pitts Wojcieszek (December 11, 2007)

6:15 Q And what's your occupation?

Robin Pitts Wojcieszek (December 11, 2007)

6:16 A I am a pharmacist, and I work at Eli Lilly &
17 Company in regulatory affairs.

Robin Pitts Wojcieszek (December 11, 2007)

10: 2 Q Okay. And when did you begin working for Eli
3 Lilly?
4 A I began working for Lilly in August of 2002.

Robin Pitts Wojcieszek (December 11, 2007)

11: 6 Q Did you have any job responsibilities with Zyprexa
7 after you came to Lilly?
8 A Yes.
9 Q Okay. And could you describe those for me?
10 A I began working on Zyprexa in April of 2003 as a
11 regulatory scientist.
12 Q And who did you report to?
13 A Greg Brophy.
14 Q And who reported to you?
15 A I don't have anyone reporting to me.
16 Q How did you come to be designated as the person to
17 testify on behalf of Lilly in this deposition?
18 A I was responsible for some of the supplemental
19 applications that are referred to in this
20 communication or in this deposition, and I have
21 primary responsibility for interactions with FDA
22 regarding Zyprexa and labeling changes.
23 Q Okay. And how long have you had that
24 responsibility?
25 A Since 2003.

Robin Pitts Wojcieszek (December 11, 2007)

12:15 Q Okay. Are you also the prime person responsible
16 for communicating with FDA regarding Symbyax?
17 A Yes, I am.

Robin Pitts Wojcieszek (December 11, 2007)

14: 2 Q Okay. Let's first talk about the first item in the
3 notice of deposition, which is regarding Lilly's
4 responses to a letter from FDA in March of 2007,
5 which was the subject of Plaintiff's Second Set of
6 Interrogatories and Document Requests to Defendants
7 in the Alaskan litigation. And I'm going to hand
8 you -- I'll hand you what we'll have marked as
9 Plaintiff's Exhibit 2.
10 (Plaintiff's Exhibit 2 was marked for
11 identification.)
12 Q And this appears to be a copy of a fax of a letter.
13 It bears several dates on the front page, the
14 earliest in time of which was March 28, 2007, and I
15 noticed that on the very last page there is an
16 electronic signature of Thomas Laughren at FDA
17 that's dated March 28, 2007. Do you see that?
18 A Yes, I do.
19 Q Was this letter faxed to you on March 28, 2007?
20 A Yes, it was.

Robin Pitts Wojcieszek (December 11, 2007)

15:20 Q Now, the letter from FDA makes reference to a
21 number of regulatory filings with FDA by Lilly
22 regarding Symbyax; correct?
23 A Correct.
24 Q And Symbyax is a combination drug containing both
25 Zyprexa and Prozac; correct?

Robin Pitts Wojcieszek (December 11, 2007)

16: 1 A That's correct.
2 Q Or, I guess, the generic terms would be containing
3 both olanzapine and fluoxetine; correct?
4 A That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

16: 7 Q Okay. And in those regulatory submissions, Lilly
8 was seeking approval from FDA to market the
9 combination drug Symbyax for use in treatment
10 resistant depression or TRD; is that correct?
11 A That's correct.
12 Q Okay. And it indicates that these prior
13 submissions had occurred in September of 2006, in
14 November of 2006, December of 2006, and February of
15 2007; correct?
16 A That's correct.
17 Q Okay. And am I correct that those submissions made
18 by Lilly to FDA included information from clinical
19 studies of the combination drug?
20 A That's correct.
21 Q Okay. And among other things, that clinical data
22 included information regarding changes in the blood
23 glucose of patients who were exposed to the
24 combination drug as compared to people who were

25 just receiving placebo; is that correct?
17: 1 A That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

17:23 Q Okay. I want to make sure I understand. So that
24 the submissions that occurred in the fall of 2006
25 to support the additional indication for
18: 1 treatment resistant depression included data from
2 studies that had been conducted in support of the
3 original Symbyax submission in 2002 as well as
4 other studies after that point, the last of which
5 had been completed by the fall of 2005. Is that a
6 fair statement?
7 A That's a fair statement, yes.
8 Q Okay. And the earliest of those studies that had
9 been done in support of the 2002 submission, I
10 presume, would have been completed sometime before
11 2002; is that correct?
12 A That's correct.
13 Q Do you know when it was that they would have been
14 completed?
15 A I don't know the exact dates, but, typically,
16 they're done about six months prior to a
17 submission.
18 Q So probably 2001 sometime?
19 A Some of them were, yes.

Robin Pitts Wojcieszek (December 11, 2007)

19: 1 Q Okay. So it'd be fair to say that the data that's
2 being referenced here in this letter is the data
3 that was generated between, say, early 2002 and
4 2005 in that time frame; correct?
5 A Majority of the data, yes.
6 Q Okay. Now, in order to approve Symbyax for use in
7 treatment resistant depression, FDA needed to
8 approve the labeling for the drug; correct?
9 A Correct.
10 Q Okay. And on the first page of the letter in --
11 there's a bolded heading that states "Updated
12 Information on Risks of Weight Gain, Hyperglycemia,
13 and Hyperlipidemia." Do you see that?
14 A Yes, I do.
15 Q In the first paragraph right after that heading, it
16 states "A primary concern with this application and
17 the primary basis for our not taking a final action
18 is our view that we lack important safety
19 information needed to adequately update the
20 labeling with all relevant risk information.
21 In particular, we are concerned that the
22 labeling is deficient with regard to information
23 about weight gain, hyperglycemia, and hyperlipidemia
24 that is associated with olanzapine use, whether
25 taken alone or in combination with fluoxetine. You

Robin Pitts Wojcieszek (December 11, 2007)

taken alone or in combination with fluoxetine. You must fully address these concerns before we will be able to take a final action on this application." Do you see that language that I read?

A Yes.

Q And I read it correctly; correct?

A Yes, you did.

Q And it was clear, was it not, that the concerns about weight gain, hyperglycemia, and hyperlipidemia that it's referring to in connection with Symbyax had to deal with the Zyprexa portion of the drug and not the Prozac portion; correct?

A That's correct.

Q Okay. And, in fact, FDA has not requested any change in the labeling of Prozac regarding weight gain, hyperglycemia, and hyperlipidemia recently, have they?

A No, they have not.

Q Okay. Now, if I could direct your attention to the following page, in the first full paragraph on that page, FDA is talking about the data that they would like to see presented in the labeling; correct?

MR. KANTRA: Objection to the form.

A What they're asking for is regarding -- if you look at the previous paragraph, it's an extension of what type of information that they would like to see prior to making any labeling change.

Q Ah, okay. Good point. So the FDA is telling you before they can approve a labeling change to allow for a further indication of treatment resistant depression they wanted to see the type of data that they're referring to in the first full paragraph on page 2; correct? Is that a fair statement?

A That's -- that's a fair statement.

Q Okay.

A Yes.

Q And what they said in that paragraph was "Regarding data displays, an overall strategy will be to subgroup patients on the basis of their status at baseline so that clinicians can better understand the risks associated with treatment of patients falling into different risk categories. For example, we note that your proposed Symbyax label includes information only on proportions of patients who are relatively normal at baseline with regard to random blood glucose (less than 140 milligrams per deciliter); i.e, 2.9 percent of such patients receiving OFC had on-treatment levels greater than or equal to 200 milligrams per deciliter compared to .3 percent of placebo-treated patients." Do you see that language?

A Yes, I do.

Q Now, when they talk about OFC, that's another way of talking about Symbyax or the combination of olanzapine and fluoxetine; is that correct?

A That's correct.

Q Okay. And was it your understanding that blood glucose levels greater than or equal to 200 milligrams per deciliter was regarded as diagnostic for diabetes by the American Diabetes

Association?
A Yes. Based on the -- kind of the ADA guidelines, that's correct.
Q So what the FDA was saying here was that the data that you had presented to them already indicated that 2.9 percent of the patients who had rand- -- who had baseline random blood glucose of less than 140 wound up having on-treatment levels greater than or equal to 200 compared to .3 percent of placebo-treated patients; correct?

Robin Pitts Wojcieszek (December 11, 2007)

A That -- that was an analysis included in the application.
Q Okay. And was that an analysis that had been done by Lilly or by FDA?
A By Lilly.

Robin Pitts Wojcieszek (December 11, 2007)

Q This particular analysis, however, showed essentially a tenfold higher rate of patients going from nondiabetic levels of blood glucose to blood glucose levels over 200; correct?
A For this particular analysis?
Q Yes.
A Yes.
Q Okay. And do you know who within Lilly did that analysis, finding that tenfold difference?
A That would have been done with our statistical group, with the medical group doing an evaluation of the results.
Q Okay. And I'm presuming that at some point they provided you in regulatory affairs with that data or write-up of the data, which you then submitted to FDA; correct?
A That's correct.
Q Okay. They then go on to say in their letter, FDA does, "However, we note that 46 percent of patients who were borderline to high at baseline (140 to 200) had such on-treatment levels compared to only 5 percent of placebo-treated patients." Do you see that?
A Yes.
Q Okay. And it was your understanding that they were saying there that when you looked at the data that Lilly had generated, it showed that those folks who had somewhat elevated levels of blood glucose in the 140 to 200 range that when you looked at those folks, about 46 percent of those people who were exposed to the combination drug went over 200 as compared to only 5 percent of the placebo-treated patients; correct?
A That's correct.
Q Okay. And that, again, would -- presuming would have been another analysis done by Lilly itself; correct?
A That's correct.

Q Okay. So in both of these statements here about what that data showed, FDA was really talking about what Lilly's own analysis had shown. And this was not some separate analysis that FDA had done. Is that a fair statement?
A That's a fair statement.
Q Okay. Continuing down in the letter a couple of lines, the FDA said, I believe, making reference to that latter analysis where the 46 percent of patients had blood levels over 200 after treatment, they go on to say "In addition, we were troubled that this important finding was not included in your proposed label." Do you see that?
A Yes.
Q Okay. And do you know who it was that made the decision not to include that information in the proposed label?
A That's a decision that's made -- it's actually a very cross-functional group of individuals within medical, regulatory, and global patient safety.

Robin Pitts Wojcieszek (December 11, 2007)

Q Ah, okay. Okay. So this analysis was done, you believe, probably in the summer of 2006?
A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

that was in that 2002 to -- strike that. The analysis that was done in the summer of 2006, as referred to in this first full paragraph on page 2, was an analysis of data that had been actually generated sometime between 2002 and 2005. Fair statement?
A That's correct.
Q Okay. I'd like to direct your attention to the third full paragraph on the second page of the FDA's letter, the one that starts off "Our overall goal..." Do you see that?
A Yes, I do.
Q It states "Our overall goal is to improve labeling with regard to these findings so that clinicians will be better informed on what the risks are for their patients. They cannot make reasonable treatment decisions until they have such information.
We do not feel that current labeling for either Symbyax or Zyprexa provides sufficient information on these risks, and we fully intend to insure that these labels are enhanced with the best available information to characterize these risks."
Do you see that language?
A Yes, I do.
Q Now, are you aware that in the Zyprexa litigation, not only in this case in Alaska, but in thousands of other cases around the country, Lilly has been asserting that its Zyprexa label was already sufficient and adequate?

22 A Yes.
23 Q But at least the -- and Lilly has never, to your
24 knowledge, admitted that its labeling was
25 inadequate, has it?
30: 1 A Yes, that's correct.
2 Q Okay. But in this March 2007 letter, FDA told the
3 company that it felt the Zyprexa labeling was not
4 adequate; correct?
5 A That's correct.
6 Q Okay. Now, after receiving this communication from
7 FDA in March of 2007 that it did not believe that
8 the Zyprexa label was adequate, the company did not
9 change the label in April, did it?
10 A No, we did not.
11 Q Or May?
12 A No.
13 Q Or June?
14 A No.
15 Q Or July?
16 A No.
17 Q Or August?
18 A No.
19 Q Or September?
20 A No.
21 Q There was, finally, a label change in October of
22 2007; correct?
23 A That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

31:20 Q Okay. The second full paragraph on page 2 of the
21 FDA letter makes reference to a New York Times
22 article. Do you see that?
23 A Yes, I do.

Robin Pitts Wojcieszek (December 11, 2007)

31:25 February 20, 2007 -- strike that. That paragraph
32: 1 also makes reference to a January 12, 2007, letter
2 from FDA to Lilly regarding the New York Times
3 article; correct?
4 A That's correct.
5 Q And it also makes reference to a February 20, 2000,
6 response from Lilly to FDA regarding that letter;
7 correct?
8 A Correct.
9 (Plaintiff's Exhibit 3 was marked for
10 identification.)
11 Q I'm going to hand you what I'll have marked as
12 Plaintiff's Exhibit 3, which is a copy of a New
13 York Times online article dated December 17, 2006,
14 with the headline "Eli Lilly Said to Play Down Risk
15 of Top Pill." Is that the New York Times article
16 that was being referred to there in the letter from
17 FDA?

Robin Pitts Wojcieszek (December 11, 2007)

32:22 Q Okay. And in this article it starts off after the
23 headline by saying "The drug maker Eli Lilly has
24 engaged in a decade-long effort to play down the
25 health risks of Zyprexa, its best-selling
33: 1 medication for schizophrenia, according to hundreds
2 of internal Lilly documents and e-mail messages
3 among top company managers.
4 "The documents given to The Times by a lawyer
5 representing mentally ill patients, show that
6 Lilly executives kept important information from
7 doctors about Zyprexa's links to obesity and its
8 tendency to raise blood sugar - both known risk
9 factors for diabetes." Did I read that correctly?
10 A Yes, you did.
11 Q And did you read that article when it first
12 appeared?
13 A Yes.
14 Q If you could drop down to the fifth paragraph in
15 that article, it starts off by saying "Critics,
16 including the American Diabetes Association, have
17 argued that Zyprexa, introduced in 1996, is more
18 likely to cause diabetes than other widely used
19 schizophrenia drugs. Lilly has consistently denied
20 such a link, and did so again on Friday in a written
21 response to questions about the documents." Do you
22 see that language?
23 A Yes.
24 Q And I gather that FDA was -- was wanting to know
25 Lilly's response to the information that was
34: 1 presented in this article; is that correct?
2 A That's correct.
3 (Plaintiff's Exhibit 4 was marked for
4 identification.)
5 Q I'm going to hand you what we'll have marked as
6 Plaintiff's Exhibit 4. Before I do that, am I
7 correct that there were essentially three parts to
8 Lilly's response to FDA regarding the New York
9 Times article?
10 A Yes.
11 Q Okay. One was -- Part 1 was submitted in February
12 of 2007, Part 2 was submitted in May of 2007, and
13 Part 3 in June of 2007; correct?
14 A Part 3 was in July.
15 Q I'm sorry. July 29 of 2007; correct?
16 A No. If I recall, it was July 2.
17 Q Okay. Okay. I'm going to hand you what I've
18 marked as Plaintiff's Exhibit 4, and I realize this
19 is Part 2. But at least in the way the documents
20 were presented to me, this is -- I have to refer to
21 parts in here to try to track through the sequence.
22 A Okay.
23 Q And for the record, Part 2 is a 77-page document
24 produced to the state bearing the title "Regulatory
25 Response, Response to the FDA Query Regarding the
35: 1 New York Times Articles, Part 2" and bears the date
2 May 10, 2007. Did I describe that accurately?
3 A Yes, you did.
4 Q And were you involved in preparing this response
5 and then submitting it to FDA?
6 A Yes.
7 Q Okay. If I could direct your attention to page 41,
8 they're numbered in the upper right-hand corner,
9 there is on that page a copy of a letter from FDA

to Lilly to the attention of your boss, Gregory Brophy, that is dated January 12, 2007. Do you see that?
A Yes.
Q And is that the January 12 letter that was referred to in the FDA's March 27 -- or March 28 letter?
A Yes, it is.
Q Did we mark that as 2, Exhibit 2?
A It's 2.
Q And in the second paragraph of FDA's January 12 letter, they state "Recent articles in the New York Times reported on clinical trial data from 70 clinical trials on Zyprexa that showed patients taking Zyprexa experienced high blood sugar levels and weight gain that may have differed from information Eli Lilly revealed publicly and to the FDA." Did I read that correctly?
A Yes.
Q And then if you can drop down to the last paragraph on the page, the FDA says "By this letter, we are asking you to ensure that you are in compliance with all applicable statutes and regulations, and we further request that you submit to the agency all data and information, including but not limited to those referenced in the recent New York Times articles that bear on the safety of Zyprexa. In particular, we are interested in receiving data and analyses bearing on these concerns about weight gain and hyperglycemia that have not already been submitted to the agency. Additionally, if you are in possession of other information not specifically required to be submitted by statute or regulation, but that would nevertheless be useful to FDA in evaluating the safety of Zyprexa regarding these concerns of weight gain and hyperglycemia, we request that you please submit this information to us as well." Do you see that language?
A Yes.
Q So, basically, what they were -- they were asking for was for Lilly to submit data and analyses about weight gain and hyperglycemia that had not already been submitted, and they were telling you to submit any other information that would be useful to FDA in analyzing the safety of Zyprexa regardless of whether such information was specifically required to be submitted by statute or regulation; is that correct?
A That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

that. At any time after receiving this letter in January of 2007, did Lilly tell FDA, no, we are not going to comply with your request to submit information bearing on this issue even if it's not called for by statute or regulation?
A What we did is we -- with receipt of this letter in January of this year, shortly after receipt, we had a teleconference with FDA to get a better understanding and clarity of what they would

like us to submit that we are not required to submit under the regulations, so getting clarity around that.

Q. Okay. But it's fair to say that Lilly never told the FDA, no, if it's not called for by statute or regulation, we're not giving it to you?

A. Right. No.

Q. FDA -- pardon me. Lilly never said that; correct?

A. No.

Q. Okay. So FDA would have been under the impression that if you had information that bore on the safety of Zyprexa, you were going to provide it to them even if it wasn't specifically called for by regulation or statute; correct?

Robin Pitts Wojcieszek (December 11, 2007)

A. Post -- post this letter we did commit and responded to this request.

Robin Pitts Wojcieszek (December 11, 2007)

Suppose that there was a particular document that was found. It was come across. It tended to indicate that Zyprexa was probably causally related to higher blood sugars.

Who within the team that was working on responding to FDA's request here, who on the team would have decided whether that was something to be included or not in what was submitted to FDA?

A. We had -- ultimately, Dr. Charles Beasley was involved in determining what was deemed as potentially discrepant.

Q. You said he was involved. Was he the play caller on that?

MR. KANTRA: Objection to the form.

A. He was -- there were some additional physicians that were involved in the review, but he made -- had the oversight of kind of those definitions.

Q. He would have been the most senior person involved in making that decision as to what was discrepant and should be submitted versus what was not?

A. That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

Q. Okay. Let me hand you what I will mark as Plaintiff's Exhibit 6. And for the record, Plaintiff's Exhibit 6 is a 26-page document, which is entitled "Regulatory Response, Response to Query About New York Times Articles," and is dated February 20, 2007. Is that a fair statement?

A. Yes.

Q. And although it doesn't say it on the front, am I correct that this would have, in fact, been Part 1 of the response to FDA?

A That's correct.
Q Okay. And this was the response that FDA referred to in its March 2007 letter; correct?
A Yes.
Q Okay. And am I correct that the general format of this response was for Lilly to lay out a number of what it characterized as allegations from the New York Times and to then provide a Lilly interpretation of the allegation and to then lay out their response to that?
A Yes.
52: Q Okay.
A That's correct.
Q And who was it that was involved in the actual responses? Let me rephrase the question. Who was it that was involved in drafting the actual responses that are laid out here?
A It was dependent on the particular allegation. We set up subgroups of individuals who were -- who may have been involved in the specifics.
Q Okay.
A So --
Q Was Dr. Beasley involved in responding to any or all of these?
A Majority them.

Robin Pitts Wojcieszek (December 11, 2007)

54: Q Sure. Would you agree with me that the New York Times article refers to a number of acts or conduct of Lilly before 2002?

Robin Pitts Wojcieszek (December 11, 2007)

54:11 A It -- yes, that's my recollection.
Q Okay. And, in fact, would you agree that most of the conduct that was referred to in the New York Times article had to do with conduct before 2002?

Robin Pitts Wojcieszek (December 11, 2007)

54:22 A Before 2002, that's correct.

Robin Pitts Wojcieszek (December 11, 2007)

54:24 response to the New York Times -- strike that. Of the people who were involved in the response
55: regarding the New York Times article, which of them, if any, besides Dr. Beasley, were involved with Zyprexa in 2002 and before?
A From a medical perspective, that would be Dr. -- Dr. Beasley and Dr. Cavazzoni.

Robin Pitts Wojcieszek (December 11, 2007)

55:24 Q Now I'm going to hand you what's been previously
25 marked as Plaintiff's Exhibit 5565. For the
56: 1 record, this is an e-mail chain. The most recent
2 of which in time was dated February 22, 2001, from
3 Jared Kerr to Mark Millikan, but I'm particularly
4 interested in the e-mail right below that, which is
5 from Charles Beasley to Ralf Dittman with copies to
6 Alan Breier, Patrizia Cavazzoni, Mark Millikan,
7 Anna Thornton, and Gary Tollefson regarding
8 olanzapine and hyperglycemia. Have you ever seen
9 this document?
10 MR. KANTRA: Wait. Hang on. Go ahead.
11 Q Have you ever seen this document before?
12 A No.

Robin Pitts Wojcieszek (December 11, 2007)

56:16 Q Is the Charles M. Beasley, Jr., that is there
17 listed there as the author of the -- the e-mail on
18 the middle of the first page, is that the same
19 Charles Beasley that was on the -- responding to
20 the FDA's request for information?
21 A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

56:23 I take it back. The third sentence states "Our
24 continuous analyses show that olanzapine does
25 result in statistically significant mean increases
57: 1 in random glucose relative to placebo and
2 haloperidol." Do you see that language?
3 A Yes.
4 Q It also goes on to say about three lines up from
5 the bottom over on the far right-hand side, the
6 sentence starts off by saying "These changes are
7 accounted for in part but not entirely by weight
8 increase." Do you see that language?
9 A Yes.
10 Q This document was not included as part of any
11 response to the FDA, was it?
12 A No.
13 Q Were you --
14 A It doesn't look familiar.
15 Q Were you aware that this document even existed
16 before I showed it to you today?
17 A No.
18 Q Okay. I'm going to hand you what's been previously
19 marked as Plaintiff's Exhibit 6128, and this is
20 another e-mail chain. And I'm particularly
21 concerned with the e-mail that is on the second
22 page.

Robin Pitts Wojcieszek (December 11, 2007)

58: 1 Q Directing your attention in particular to the
2 e-mail on the second page, which is an e-mail from

Charles M. Beasley on March 15, 2001, to Andrea Smith, Ernie Anand, Patricia Cavazzoni, Margaret Sowell, and Anna Thornton, the subject being "Olanzapine and Cardiovascular Risk."

If I could direct your attention to the third line down in that e-mail that states "One thing that we can say definitively is that olanzapine causes weight gain, and for approximately 50 percent of patients in trials who remained on the drug for more than six months, the amount of gain was greater than 10 pounds.

"Some patients in clinical trials gained as much as 80-plus pounds. Lacking empirical data to the contrary, it would be ludicrous to state that such a patient does not at long-term increased cardiac risk relative to prior to gaining that weight, especially, if in temporal association with that weight gain the patient developed an increase in fasting glucose and lipid levels." Do you see that language?

A Yes.

Q That e-mail was not submitted to FDA as part of the response, was it?

59: A No, it was not.

Q Okay. And have you ever seen this e-mail before I showed it to you today?

A No.

Q Okay. By the way, the Zyprexa labeling, even today, does not state that olanzapine causes weight gain, does it?

A No.

Q Dr. Beasley said he could say that definitively back on March of 2001; correct?

A Not understanding the overall context of what data he's referring to or the situation, I don't feel comfortable answering that question.

Q Okay. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 7802. For the record, this is a one-page document that appears to be a chart. I'll represent to you that the database that was provided to us by Eli Lilly says that this document is dated June 24, 2002.

And I'll also represent to you that the database provided to us by Lilly says that it came from the files of Michelle Sharp, and I believe that Michelle Sharp was at least once a colleague of yours in regulatory affairs; correct?

A That's correct.

60: Q And back in 2002 she had regulatory responsibility for Zyprexa, did she not?

A Yes.

Q Okay. And the title of this document is "Listing of Treatment-Emergent Abnormal Lab Findings in Olanzapine-Treated Patients, Placebo-Controlled F1D-MC-HGFU, Studies 1 and 2 Combined." Do you see that?

A Yes.

Q And then there is a listing of various laboratory findings, abnormal laboratory findings, and do you see that there's a listing for glucose, nonfasting, high?

A Yes.

Q And do you see that it indicates that the

percentage of olanzapine patients who had high glucose was 2.2 percent, and that the percentage for placebo patients was 0 percent?
A Yes, I do.
Q And do you see that there are, to the right of that, several -- several As, the letter As?
A Yes.
Q Okay. And if you look down at the bottom, there's a little legend as to what the letters mean.
A Uh-huh.
Q And it says, according to this, that the letter A means "Event probably causally related." Do you see that?
A Yes.
Q And this document was not submitted to FDA as part of the response in 2007, was it?
A No. I'm not -- no, it was not.
Q In fact, have you ever seen this document before I showed it to you this morning?
A No, I have not.
Q Okay. I'm going to hand you what's been previously marked as Plaintiff's Exhibit 8666, which is another e-mail chain. I'm concerned really only with the -- the one on the first page, which is the last one.
It is dated June 27, 2002. It is from Dr. Simeon Israel Taylor to a number of individuals, and if I could direct your attention to the last two sentences in the first paragraph over towards the right, do you see where the sentence starts off "however"? It's about two lines from the bottom.
A Yes.
Q Okay. It states "However, I feel that we need to deal with the scientific facts, whatever they are. Ultimately, I expect that a fair-minded scholarly evaluation of the available data is likely to support several conclusions.
"No. 1, Zyprexa, like other members of the class, causes weight gain.
"Two, like other causes of weight gain, Zyprexa-induced weight gain probably increases the risk of diabetes." Do you see that language?
A Yes.
Q And this was not provided to FDA in the response in 2007, was it?
A I'm taking a minute to --
Q Sure.
A -- look through it. No.
Q Okay. And, in fact, had you ever seen this document before I showed it to you this morning?
A No.
Q Okay. If I could get you to refer back to the March 28 letter from FDA, which we marked as Exhibit 2. This letter was, obviously, after -- this March 28, 2007, letter was, obviously, after your February 20 submission to FDA; correct?
A Correct.
Q Okay. And on the second page of the FDA letter in the second full paragraph on that page, the last sentence states "Your recent February 20, 2007, response to our January 12, 2007 -- 2007 letter regarding the New York Times has not been

particularly helpful in addressing these concerns." Do you see that language?
A Yes.
Q And they said in this letter in several places that they were concerned that the Zyprexa labeling did not provide sufficient information regarding the risks of weight gain, hyperglycemia, and diabetes; correct?
A Could you repeat the question?
MR. SUGGS: Could you read it back, please.
(The requested material was read back by the reporter.)
A I think it's related to information on the risks of weight gain, hyperglycemia, and hyperlipidemia.
Q On the first page they state in that first paragraph under the heading, under the bolded heading, about four lines up from the bottom in that paragraph "In particular, we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine"; correct?
A Correct.
Q And then on the second page on the third full paragraph they say, quote -- in about the middle of the paragraph. "We do not feel the current labeling for either Symbyax or Zyprexa provides sufficient information on these risks, and we fully intend to ensure that these labels are enhanced with the best available information to characterize these risks"; correct?
A Correct.
Q And the risks that they were talking about were the risks of weight gain, hyperglycemia, and hyperlipidemia; correct?
A That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

Q Okay. If I could get you to refer back to Part 2 of your response to FDA, which was what we previously marked as Exhibit 4.

Robin Pitts Wojcieszek (December 11, 2007)

Q Okay. And am I correct that basically what this portion of your response was was Lilly's analysis of about 100 published medical articles or abstracts that had not previously been submitted to FDA and which were regarded or characterized as being discrepant from Lilly's position?
A That's correct.
Q Okay. And in this response, Lilly took the position in several places that even considering all these materials that it's describing in here, these published articles that were discrepant with Lilly's conclusion, Lilly told FDA "Lilly does not believe there is a need to change the information

provided in olanzapine labeling regarding weight gain or the waring regarding hyperglycemia/ diabetes"; correct?

MR. KANTRA: Where are you?

MR. SUGGS: Page 7.

A That's correct.

Q Okay.

A That's what it states.

Q That's what it states on page 37, and, essentially, the same statement is made on page 38 under the overall conclusion; correct?

A That's correct.

(Plaintiff's Exhibit 7 was marked for identification.)

Q Okay. Next, I'm going to hand you what we will have marked as Plaintiff's Exhibit 7. And for the record, Exhibit 7 is a 52-page document entitled "Regulatory Response, Response to the FDA Query Regarding the New York Times articles, Part 3" and bears the date on the front page of June 29, 2007; correct?

A Correct.

Robin Pitts Wojcieszek (December 11, 2007)

well, Lilly described this submission as being its internal work product; correct?

A Yes.

Q And what this consists of was various analyses of data that had been performed by Lilly at various points in time; correct?

A Correct.

Q Okay. And Lilly took the position in this submission in June -- on June 29 that it was not necessary to change the labeling; correct?

A That's my recollection. I'm sure --

Q If you look at page --

A -- that's what we did.

Q Page 6, for example --

A Six, yes.

Q -- the first sentence there says "After careful review of the materials being submitted, Lilly continues to believe the information provided in olanzapine labeling regarding weight gain and hyperglycemia/diabetes is accurate"; correct?

A That's correct.

Q Okay. So FDA had taken the position back in March that they thought the labeling was not adequate regarding weight gain, hyperglycemia, and hyperlipidemia, and in several submissions thereafter from Lilly to FDA, Lilly took the position that the labeling was adequate and did not need to be changed. And those submissions were in May and in June; correct?

A Right. Based on, again, a small subset of information that we were submitting of data analyses. It does not reflect the ongoing discussions that we were having at the time with FDA in response to the approvable letters where we were analyzing various subsets in response to that approvable letter.

Robin Pitts Wojcieszek (December 11, 2007)

73: 1 Q Do you recall that about two months after receiving
2 Part 3 of your submission --
3 A Okay.
4 Q -- and after having reviewed that and all the prior
5 submissions that Lilly made to the agency, the
6 agency wrote to Lilly on August 28, 2007,
7 requesting that Lilly make substantial changes to
8 the Zyprexa labeling to protect the public health?
9 MR. KANTRA: Objection, foundation.
10 A They sent us a communication on that date
11 requesting labeling changes.
12 Q And they did that because they thought it was in
13 the best interest of the public health; correct?
14 A That was a statement made in that particular
15 letter.
16 (Plaintiff's Exhibit 8 was marked for
17 identification.)
18 Q Let me hand you what we'll have marked as
19 Plaintiff's Exhibit No. 8. For the record,
20 Exhibit 8 is a letter dated August 28, 2007, from
21 Thomas Laughren to Ms. Wojcieszek. Did I pronounce

Robin Pitts Wojcieszek (December 11, 2007)

74: 1 Q And is this, in fact, a true and accurate copy of
2 the letter you received from FDA on that date?
3 A Yes, it is.
4 Q Okay. At the top there's a reference to
5 NDA 21-520, which is to Symbyax, the
6 olanzapine/fluoxetine combination, and also to
7 several other NDAs, all of which are various forms
8 of Zyprexa; correct?
9 A Correct.
10 Q And those are the only three forms of Zyprexa that
11 are marketed in the U.S.; correct?
12 A Correct.
13 Q Okay. I suppose I should have said all of the
14 forms of Zyprexa that are marketed in the U.S.;
15 correct?
16 A Right.
17 Q So this letter was applicable to all forms of
18 Zyprexa marketed in the U.S.; correct?
19 A Correct.
20 Q As well as the Symbyax product?
21 A That's correct.
22 Q Okay. And in the letter to you on that date, the
23 FDA first asked you to refer to your new drug
24 applications that we've referred to up there.
25 And in the third paragraph they said "We have
75: 1 reviewed the data that you have submitted thus far
2 as well as the available literature, and we would
3 like to request that you make the labeling changes
4 listed below pertaining to the effect of olanzapine
5 and Symbyax on body weight, lipids, and glucose."
6 Do you see that language?
7 A Yes.
8 Q Okay. So notwithstanding the fact that Lilly had

taken the position that the labeling did not need to be changed and the FDA, after reviewing all of the material that you had submitted thus far by August 28, was of the view that, indeed, the labeling did need to be changed; correct?

A That's correct. The one point that we were also trying to get clarity is what data they were referring that they had reviewed thus far.

Q Okay. They go on to say "We anticipate that additional labeling changes will be necessary when we have reviewed the results of the additional analyses that we have requested." Do you see that language?

A Yes.

Q And do you know what analyses those were?

A Those were the analyses in response to the approvable letter for TRD.

Q Okay. With respect to Symbyax?

A With respect to Symbyax, but it also -- their request was also for olanzapine.

Q Analyses?

A Correct.

Q Okay. And were those analyses ultimately submitted to FDA?

A We had agreement that it was various analyses and a series of submissions --

Q Okay.

A -- that we would do. So at the time of this particular letter, it was actually two days prior to us submitting our first --

Q Okay.

A -- series of submissions.

Q And at this point in time, December 12 -- or 11 rather --

A Eleventh.

Q -- have all of the analyses been submitted to FDA yet?

A No, they have not.

Q Okay. What additional analyses have yet to be submitted?

A We are currently working on analyses related to these three metabolic measures on longer term data and also in special populations, such as antipsychotic naive --

Q Okay.

A -- patients.

Q And the data that's being analyzed, is it data that goes back in time?

A Yes.

Q Okay. When was the data generated?

A As early as -- some of the studies are -- were included in the original submission.

Q 1996?

A Correct.

Q Okay.

A Up until this year.

Q Okay. So spanning -- the data that's currently being analyzed spans the time frame from 1996 up through 2007; correct?

A Correct.

78:25 Q Okay. Referring back to the FDA's letter in that
79: 1 same paragraph, FDA goes on to say "Given that
2 you're completing these analyses and our review of
3 them will take some time, we believe that it is in
4 the best interest of the public health to make
5 interim labeling changes now based on the data that
6 we already have available." Do you see that
7 language?
8 A Yes.
9 Q Okay. And then FDA proceeds to lay out the
10 language that they were suggesting with respect to
11 changes to the wording section; correct?
12 A Correct.
13 Q Okay. But with the full contemplation that these
14 changes might well only be interim and that there
15 may be additional changes that may or may not come
16 into play after you submit all of your other data;
17 correct?
18 A That's correct.
19 Q Okay. And the first section that they have changes
20 that they request have to do with the hyperglycemia
21 and diabetes mellitus section of the warnings of
22 Zyprexa; correct?
23 A Correct.
24 Q Okay. And what they show there is by strike outs
25 and underlining the language that they want
80: 1 eliminated and the language they want to replace
2 it; correct?
3 A Correct.

Robin Pitts Wojcieszek (December 11, 2007)

80:23 well, on the second page of this letter, they show
24 under the heading "Hyperglycemia" what they are
25 propose -- what they, the FDA, are proposing;
81: 1 correct?
2 A Uh-huh, correct.
3 Q Okay. And in the -- at the end of the first
4 paragraph it states "Olanzapine and clozapine
5 treatments have been associated with a greater
6 potential to induce hyperglycemia than other
7 atypical antipsychotics." Do you see that?
8 A Yes.
9 Q And what does the word "induce" mean?
10 A It means that there's some sort of a kind of
11 relationship of olanzapine and hyperglycemia.
12 Q Well, in fact, the word induce indicates that it's
13 a causal relationship, does it not?
14 A It could mean that.
15 Q In fact, the ordinary definition -- the ordinary
16 dictionary definition of the word induce definitely
17 indicates that it's a causal relationship. If I
18 induce something, that means that I have brought --
19 brought about that result; correct?
20 MR. KANTRA: Asked and answered.
21 Q You may answer.
22 A Again, it could be defined that way.
23 Q And then they make reference in the third paragraph
24 in that section to the analyses that we have looked
25 at previously in the March 2007 letter. Is that a

fair statement?
A That's -- that's correct.
Q Okay. That's the analyses done by Lilly, which showed that the -- there was a tenfold increase in the number of patients who went from nonhyperglycemic to the state of being hyperglycemic; correct?
A That's looking at patients who were normal at baseline and went to a blood glucose of greater than 200.
Q The difference being between the olanzapine patient 2.4 percent of the patients became hyperglycemic compared to .3 percent. And that's about a threefold difference; correct? Pardon me. About a tenfold difference. I take it back. It's about an eightfold difference; correct?
A Yes. But it relates, again, to a categorical change of greater than 200.
Q And it notes that -- also that approximately one-third of patients on olanzapine, 33.3 percent, who had borderline increase serum blood glucose progressed to high blood glucose at some time during the 6 to 12 weeks of olanzapine treatment; correct?
A That's correct.
Q Okay. And these analyses that were done by Lilly were statistically significant, were they not?
MR. KANTRA: Objection, beyond the scope.
A Yeah. I don't recall if they were statistically significant.
Q Okay. And then FDA also proposed that on the following page a completely new section in the warnings section regarding weight gain; correct?
A Correct.
Q Up until this point in time, Lilly had never discussed weight gain in the warning section of the Zyprexa labeling; correct?
A At this time it was not in our current label; however, it was being proposed in the supplemental applications for TRD in adolescents --
Q When --
A -- submission.
Q When was that proposed?
A That was in 2000 -- late 2006.
Q Okay. And then also in this letter the FDA was requesting a completely new section on -- in the warning section for Zyprexa regarding hyperlipidemia; correct?
A That's correct.
Q Now, hyperlipidemia refers to fats in the blood; correct?
MR. KANTRA: Objection, beyond the scope.
A It -- it refers to, yes, things such as triglycerides, cholesterol, lipids, that's correct.
Q That's what hyperlipidemia means is elevated levels of triglycerides and cholesterol; correct?
A Correct.
Q Okay. And after receiving this letter in which FDA laid out the language it wanted to see in the labeling, Lilly did not accept the language requested by FDA and instead sought to change the language; correct?
MR. KANTRA: Objection to the form.

A In response to this -- this communication, we initiated discussions and proposals with FDA shortly after receipt.
Q Lilly did not accept the language that was laid out by FDA in their August 28, 2007, letter; correct?
MR. KANTRA: Objection to the form.
A We provided our proposal in response to their request based on data that we had available short -- you know, during this time frame.
Q Your response to FDA was not, okay, we'll make the -- we'll make the label change that you've suggested; correct?
A Correct.

Robin Pitts Wojcieszek (December 11, 2007)

Q Okay. If I could, I'll mark -- strike that. I'll mark as the next exhibit Plaintiff's Exhibit 9. I stuck it on my copy. And for the record, Exhibit 9 is a document entitled "FDA Briefing Document." In the upper left-hand corner it says "Revised September 12, 2007."
A That's correct.
Q And was this actually submitted to FDA?
A It was -- the information included in this was e-mailed to FDA --
Q Okay.
A -- in preparation for our meeting on September 17.

Robin Pitts Wojcieszek (December 11, 2007)

Q And I'm going to hand you what I've marked as Exhibit No. 10, but keep Exhibit 9 handy.
A Okay.
Q A document which purports to be meeting minutes of a meeting between FDA and Lilly on September 17, 2007?
A That's correct.
Q And did you prepare the minutes that are in Exhibit 10?
A Yes. In addition to my colleague, Catherine Melfi, from regulatory who was also in attendance.

Robin Pitts Wojcieszek (December 11, 2007)

Q And then in about the middle of the page there's a bold heading entitled "Meeting Objectives."
A Uh-huh.
Q And then there are a couple of numbered items below that; correct?
A Correct.
Q And on the second numbered item it states "Obtain clarification on the impact of FDA's requested changes on other parts of labeling; e.g., adverse reactions." Do you see that?
A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

89: 5 It states "Lilly agrees with the FDA on the
6 inclusion of certain significant glucose, lipid,
7 and weight changes in the warning section, but
8 suggests that some analyses should more
9 appropriately remain in the adverse reactions
10 section.
11 "For example, the weight gain with olanzapine
12 use and the specific data from clinical trials
13 should be in the adverse reactions section of the
14 labeling with appropriate cross reference in the
15 warning section." Do you see that language?
16 A Yes.
17 Q So the analyses that we referred to earlier in
18 Exhibit 8 on hyperglycemia and which were also
19 included in FDA's discussion in their March 2007
20 letter, Lilly wanted those not to be in the warning
21 section but to have them be in the adverse
22 reactions section; is that correct?

Robin Pitts Wojcieszek (December 11, 2007)

90: 4 A Our -- our proposal to FDA was to include the very
5 specific clinical trial data within the laboratory
6 section, which was kind of, in our experience and
7 interpretation of FDA's labeling guidance, was to
8 put that particular information in the adverse
9 reactions section.
10 Q And not in the warning section?
11 A Not in the warning, but keep the warning to very

Robin Pitts Wojcieszek (December 11, 2007)

94: 4 Q If I could direct your attention to the last two
5 sentences of the warning language that Lilly had
6 proposed after FDA's request, they start at the
7 very, very bottom of the page, the last three words
8 on the page "in contrast."
9 A Yeah.
10 Q Okay. They say "In contrast, the association
11 between atypical antipsychotics and glycemic
12 control appears to fall along a continuum, although
13 relevant risk estimates have been inconsistent.
14 Clozapine appears to have the greatest association
15 while olanzapine may have a slightly greater
16 association than quetiapine and risperidone and
17 greater association than ziprasidone." Did I read
18 that correctly?
19 A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

95:18 Q But you took about -- you took out any reference to
19 language that indicates a causal relationship?

Robin Pitts Wojcieszek (December 11, 2007)

95:25 A We -- we did not include that in our proposal.
96: 1 Q Okay. And, in fact, to this day, Lilly denies that
2 olanzapine can induce or cause hyperglycemia;
3 correct?
4 A We don't feel that the -- that we have data to
5 support that particular statement FDA included.

Robin Pitts Wojcieszek (December 11, 2007)

96:22 Q If I could have you look at Exhibit 10, please,
23 which is the minutes of the September 17, 2007,
24 meeting Lilly had with FDA. And was this meeting
25 at the FDA headquarters?
97: 1 A Yes, it was.
2 Q Would Dr. Thomas Laughren have been the leader of
3 the FDA side?
4 A Yes.
5 Q Okay. And within the Lilly participants, was there
6 one leader?
7 A I facilitated the meeting, and Dr. Corya was the
8 medical lead. So the two of us co-facilitated the
9 discussion.
10 Q Okay. And the purpose of this meeting was to
11 discuss Lilly's response to FDA's August 28, 2007,
12 letter. And just so, I guess, the record is clear,
13 the response that you're referring to there would
14 have been what we had marked as Exhibit 9; is that
15 correct?
16 A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

98:19 Q Point 2 was "FDA's requested labeling recommends
20 that all patients on olanzapine should be monitored
21 regularly for worsening of glucose control." And
22 that was different from what had been before;
23 correct?
24 A That's correct.
25 Q There had been -- the labeling change that was made
99: 1 in 2003 had suggested that there be monitoring of
2 glucose for patients who had diabetes or risk
3 factors for diabetes; correct?
4 A Correct.
5 Q And here FDA was -- was recommending that -- that
6 all patients on olanzapine should be monitored
7 regularly for worsening of glucose control
8 regardless of whether they had diabetes or risk
9 factors for diabetes; correct?
10 A That's correct.
11 Q Okay. And in the minutes here, it indicates that
12 "Lilly accepts the recommended monitoring; however,
13 Lilly believes that the recommendation should cover
14 the class of atypical antipsychotics"; correct?
15 A That's correct.
16 Q Okay. And as far as you know sitting here today,
17 you're not aware of any such change to the other

labeling of atypical antipsychotics saying there should be a monitoring of every patient; correct?
A That's correct.
Q Okay. And then in italics at the bottom of that section you note what FDA's response was; correct?
A Right.
Q And that was that FDA is not convinced that all patients on atypical antipsychotics require the same level of monitoring, but does agree with Lilly's assertion that all patients should get baseline glucose measurements; correct?
A Correct.
Q Okay. And then Point 3 stated that "FDA's requested labeling places olanzapine and clozapine in the same category in terms of association with glucose dysregulation; however, Lilly asserted that available data, including both Lilly clinical trial data and the available literature, support a differential association between clozapine and olanzapine and reiterated the belief that the association between antipsychotics and glucose dysregulation appears to fall on a continuum." Did I read that correctly?
A Yes, you did.
Q And then you note there that FDA agreed there was a continuum on which the atypicals fall in terms of association with -- with glucose dysregulation; correct?
A Correct.
Q By the way, with respect to the monitoring of all patients that FDA was insisting on here in 2007, that had been required by the Japanese label in -- as of April of 2002; correct?
MR. KANTRA: Objection, beyond the scope.
A It was -- that's my understanding based on, you know, the history. I was not involved in that particular issue.

Robin Pitts Wojcieszek (December 11, 2007)

Q Well, it was your understanding, I think you've already testified, that the label change that went into effect in Japan in April 2002 required glucose monitoring of all patients on Zyprexa regardless of whether they had diabetes or risk factors for diabetes; correct?
A That's correct.
Q And we know that the FDA did not require Lilly to do that until 2007; correct?
A Correct.
Q Which is more than five years after the Japanese regulatory authorities had required Lilly to do that; correct?
MR. KANTRA: Objection, beyond the scope.
A That is -- that is correct.

Robin Pitts Wojcieszek (December 11, 2007)

Exhibit 10 indicates that by September of 2007

Lilly was taking the position that the association between atypical antipsychotics and glucose dysregulation falls on a continuum; correct?
A We're saying as it appears to fall on a continuum.

Robin Pitts Wojcieszek (December 11, 2007)

That conclusion that you stated in September of 2007 is the same position that the consensus statement was taking back in January of 2004, almost four years earlier; correct?
MR. KANTRA: Objection, foundation, mischaracterizing the consensus statement.
A No, I don't believe that that was the overall conclusion of the consensus statement.
Q When I use the term consensus statement, you know what I'm referring to, don't you?
A The ADA consensus statement, yes.
Q Yes. And in January of 2004 there was a consensus statement published by the American Diabetes Association, American Psychiatric Association, The American Association of Clinical Endocrinologist, and the North American Association for the Study of Obesity; correct?
A That's correct.
Q You would have reviewed that at the time it came out in 2004; correct?
A Correct.
Q Okay. And that statement I will hand to you has been previously marked as Plaintiff's Exhibit 2368. If I could direct your attention to page 598 of the article, the page number of the article is on the lower left-hand corner.
By the way, the -- for the record, this article was published in "Diabetes Care," Volume 27, No. 2, in February of 2004. And if I could direct your attention to the middle column of page 598, about ten lines down, there's a sentence that starts off "Despite limitations..." Do you see that?
A Yes.
Q It says "Despite limitations in study design, the data consistently showed increased risk for diabetes in patients treated with clozapine or olanzapine compared with patients not receiving treatment with first generation antipsychotics, FGAs, or with other SGAs" -- standing for second generation antipsychotics -- "The risk in patients taking risperidone and quetiapine is less clear. Some studies show an increased risk for diabetes while others do not.
"The two most recently approved SGAs, aripiprazole and ziprasidone, have relatively limited epidemiological data but available clinical trial experience with these drugs has not shown an increased risk for diabetes." Do you see that language?
A Yes, I do.
Q And that indicates that, in fact, the risk was on a continuum; correct?
MR. KANTRA: Objection to the form.

A What we're reflecting in the meeting minutes and the data -- data and labeling proposal to FDA was not with regard to diabetes but rather an appearance of the continuum around glucose elevations.

Q Well, certainly, the consensus statement in that portion of the language that I just read indicated that there is a continuum of risk for diabetes amongst the second generation antipsychotics; correct?

A That is the opinion of this ADA consensus statement.

Q And if I could direct your attention to page 600 in the summary section in the second full paragraph in the summary section in the right-hand column, it says "These three adverse conditions are closely linked and their prevalence appears to differ depending on the SGA used.

"Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate affects. Aripiprazole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as the other agents." Do you see that language?

A Uh-huh.

Q And, again, that reflects a continuum of the risks for weight gain, diabetes, and dyslipidemia, at least as reflected in this consensus statement in 2004; correct?

A That's -- that's what's reflected in this particular document, yes.

Robin Pitts Wojcieszek (December 11, 2007)

Q Okay. And then I'm going to hand you what we'll have marked as Plaintiff's Exhibit 12, which I will represent to you is a "Dear Health Care Professional" letter that I copied off of the Lilly web site. And does this appear to be a full, complete, and accurate copy of the "Dear Health Care Professional" letter that was distributed by Lilly regarding the new warnings on October 5, 2007?

A Yes, it is.

Robin Pitts Wojcieszek (December 11, 2007)

Q And who would this letter have gone to? How widely distributed would it have been?

A It was -- I apologize. I'm drawing a blank on the exact number, but the approach that we took was looking at those health care professionals that had prescribed antipsychotics within the last 12 months would have received this letter in addition to posting it. We also posted it on our web site immediately.

Robin Pitts Wojcieszek (December 11, 2007)

115: 2 Q And do you have just sort of a ballpark as to
3 whether we're talking, you know, 10,000, 5,000,
4 20,000 physicians?
5 A If -- it was over hundreds of thousands.
6 Q Over hundreds of thousands?
7 A Yes.
8 Q And the first two sentences of the letter state
9 "Eli Lilly & Company would like to inform you of
10 the important information being added to the
11 Zyprexa (olanzapine) and Symbyax (olanzapine and
12 fluoxetine) labels. These labeling updates include
13 new warnings for weight gain and hyperlipidemia and
14 updated information in the warning for
15 hyperglycemia"; correct?
16 A Correct.
17 Q And then there is laid out in the roughly page and
18 a half after that sort of a summary of what the
19 changes were followed by the actual language in the
20 labeling per se; correct?
21 A Correct.
22 Q That was changed?
23 A Yes.

Robin Pitts Wojcieszek (December 11, 2007)

117: 3 Q And we talked earlier about some back and forth
4 that there was between Lilly and the FDA as to the
5 content of the language and the warning section
6 regarding hyperglycemia. But this that we have
7 before us in Exhibit 12 is, in fact, the final,
8 final -- this is what it turned out to be; correct?
9 A Correct.
10 Q Okay. If you could turn to page 3, the last part
11 of the first sentence, the last part of the first
12 paragraph that we talked about before with respect
13 to there being a continuum of -- with respect to
14 the relationship between antipsychotics and
15 hyperglycemia or glucose levels now reads in the
16 final version "The association between atypical
17 antipsychotics and increases in glucose levels
18 appears to fall on a continuum, and olanzapine
19 appears to have a greater association than some
20 other atypical antipsychotics." Did I read that
21 correctly?
22 A Yes, you did.
23 Q And who was it that made the decision that that is
24 what the final language would be?
25 A Very -- the very similar group that was involved --
118: 1 was involved in the proposal that was sent to FDA.
2 This reflects our kind of post-FDA discussion, what
3 we felt would be more appropriate for labeling,
4 kind of based on that discussion, kind of further
5 reflection of our data.

Robin Pitts Wojcieszek (December 11, 2007)

olanzapine following -- strike that. The language there about the association between atypical antipsychotics and increases in glucose levels falling on a continuum and the fact olanzapine appears to have a greater association than some other atypical antipsychotics is different from and contrary to what Lilly had been telling doctors for years; isn't that correct?

MR. KANTRA: Object to the form and foundation.

A. What it's -- what it's stating is our current evaluation and medical opinion of the data that we had available to us at the time of this particular submission, what we discussed with FDA, and taking into consideration previous reviews that we have done in the past.

Q. Were you aware that since at least 2000 Lilly had been claiming that rates of diabetes were comparable between the various antipsychotics?

MR. KANTRA: Objection, beyond the scope.

A. Yes, I am aware of it.

Q. And you were aware that that claim was made beginning in 2000; correct?

A. That's correct.

Robin Pitts Wojcieszek (December 11, 2007)

thereafter -- strike that. Were you aware that after 2000 and for years thereafter Lilly trained its sales force to assert that the rates of hyperglycemia and diabetes were comparable between the various atypical antipsychotics?

Robin Pitts Wojcieszek (December 11, 2007)

A. I'm aware that it was included in -- in materials, but the specifics I was not involved in.

Q. Okay. And when you say "It was included in materials," you're referring to the "it" being an assertion of comparable rates; correct?

A. That particular statement that you had mentioned before, yes.

Q. Okay. And when you referred to materials, you're referring to materials that were used by sales representatives?

A. That's correct.

Q. And distributing to physicians to influence their prescribing practices; correct?

MR. KANTRA: Objection to the form.

A. It was included in various materials. I don't know the specifics of how they were distributed.

Q. And to this day, has Lilly instructed its sales force to stop saying that rates of hyperglycemia or diabetes are comparable amongst various atypical antipsychotics?

MR. KANTRA: Objection to the form, also beyond the scope.

A. I'm not aware of a specific communication related

17 to that.

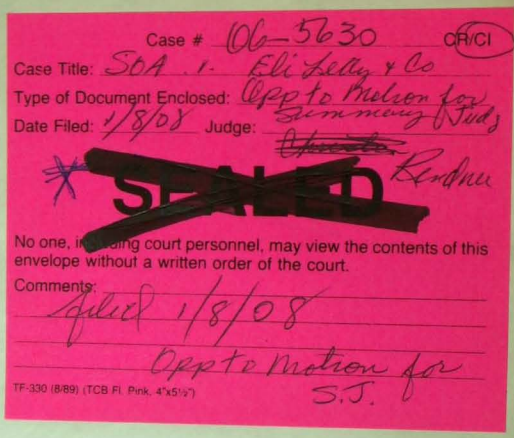
Robin Pitts Wojcieszek (December 11, 2007)

125:21 Q Okay. Now, we've talked about the -- the consensus
22 statement before, which was Exhibit 2368, I
23 believe, and I believe we established that, at
24 least in the language of the consensus statement,
25 there was the assertion by that statement that
126: 1 there was a continuum of rates of diabetes and
2 weight gain between the various atypical
3 antipsychotics; correct?
4 A They didn't use the specific word of -- of
5 continuum. What they're outlining is, you know,
6 based on their consensus of all the data evaluated
7 some specifics around risk factors between the
8 atypical antipsychotics.

Robin Pitts Wojcieszek (December 11, 2007)

128: 5 Q After -- after the consensus statement was
6 published in 2004, Lilly continued to assert that
7 the rates of diabetes were comparable between the
8 various atypical antipsychotics; correct?
9 A That's correct.
10 Q Okay. And, in fact, as you sit -- as you testified
11 before, as you sit here today right now, you're not
12 aware of any communications of the sales force to
13 stop saying that rates are comparable; correct?
14 A I am not aware of anything specific.

06-5630 CA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Pages 8145-8300

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

Filed in the Trial Courts
STATE OF ALASKA, THIRD DISTRICT
JAN 08 2008
Clerk of the Trial Courts
By _____ Deputy

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Case No. 3AN-06-05630 CI
	)	
ELI LILLY AND COMPANY,	)	
	)	
Defendant.	)	
	)	

NOTICE OF FILING PLEADINGS UNDER SEAL

The State of Alaska's Opposition to Lilly's Motion for Summary Judgment and the exhibits attached thereto, filed on January 8, 2008, contain CONFIDENTIAL information. Thus, the parties request that the pleading be filed under seal in the attached envelope.

RESPECTFULLY SUBMITTED this 8 day of January, 2008.

FELDMAN, ORLANSKY & SANDERS
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BY Susan Orlansky
Susan Orlansky
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Eric T. Sanders
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See Judge Rindner's 6/13/08 order, page 26, #2
Documents unsealed
lwade 8/11/08

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Pages 8145-8300

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Pages 8145-8300

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
vs.	)	
	)	
ELI LILLY AND COMPANY,	)	
	)	Case No. 3AN-06-5630 CIV
Defendant.	)	
	)	

STATE OF ALASKA'S OPPOSITION TO LILLY'S MOTION FOR SUMMARY JUDGMENT

INTRODUCTION

Eli Lilly's motion for summary judgment should be denied. Lilly advances three distinct arguments. None supports granting summary judgment to Lilly.

Lilly devotes the major part of its memorandum to arguing for dismissal of the State's strict liability design defect claim. The State has voluntarily dismissed that claim, so Lilly's arguments are now moot.

Second, Lilly contends that the State's strict liability failure to warn claim and the State's Unfair Trade Practices Act ("UTPA") claim should be dismissed because both rely on a fraud-on-the-market theory and most courts refuse to recognize the fraud-on-the-market theory in prescription drug cases. Lilly's motion fails because the State is not relying on a fraud-on-the-market theory. That theory was developed by plaintiffs seeking

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to recover for having paid drug prices that were inflated due to the manufacturer's misconduct. In this suit, the State does not seek that category of damages. Lilly also argues, citing the same recent federal district court decision, that the State may not rely on aggregate, statistical proof, but must show that individual Alaska doctors relied on Lilly's misrepresentations. To a large extent, this argument is intertwined with the argument that fraud-on-the-market is a rejected theory, and because the State does not rely on a fraud-on-the-market theory, Lilly's motion again misses the mark. To the extent that Lilly makes an independent argument about the nature of proof required to state a viable cause of action under Alaska's strict products liability and UTPA case law, Lilly is wrong as a matter of law. Aggregate, statistical proof is a viable way to prove that the defendant's misconduct caused the State's damages.

The third section of Lilly's motion addresses only the State's UTPA claims. It seeks dismissal as a sanction for alleged failure to provide discovery, but Lilly's one-paragraph argument does not establish any ground for summary judgment.

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ARGUMENTS

LILLY'S SUMMARY JUDGMENT MOTION SHOULD BE DENIED.

A. The State Has Dismissed Its Design Defect Claim.

The major part of Lilly's memorandum addresses the State's design defect claim.[1] The State will dismiss this claim. Therefore, this court need not resolve any of the issues in Part II.A of Lilly's memorandum.

B. The *Rezulin* Decision Provides No Basis For Granting Summary Judgment.

1. Introduction.

Lilly argues that a recent federal district court decision, *In re Rezulin Products Liability Litigation*,[2] requires dismissal of the State's strict liability failure to warn and UTPA claims, because the *Rezulin* case rejects the fraud-on-the-market theory of causation in litigation involving prescription drugs.[3] As discussed below, Lilly's argument fails because the State does not rely on a fraud-on-the-market theory. However, before describing what the State's case does not involve, it may be helpful to outline briefly what the State's case does involve, and how the State easily meets the

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1 *See* Defendant Eli Lilly and Company's Motion for Summary Judgment and Memorandum in Support [hereafter "Lilly Summary Judgment Memo."] at 3-9.

2 *In re Rezulin Products Liability Litigation*, __ F. Supp. 2d __, 2007 WL 4165703 (S.D.N.Y. Nov. 26, 2007).

3 *See* Lilly Summary Judgment Memo. at 10-12.

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standard for avoiding summary dismissal of its claims. Alaska law delineating the elements of these claims is the obvious starting point.[4]

2. The State has evidence to prove both its strict liability failure to warn claim and its UTPA claims.

(i) Strict liability failure to warn

The Alaska Supreme Court identified the key elements of a strict liability failure to warn claim in *Shanks v. Upjohn Co.*[5] A plaintiff must prove, first, that the product posed a risk of injury to one who used the product in a reasonably foreseeable manner and was marketed without adequate warnings of the risk; and, second, that this failure to warn of risks was the proximate cause of the plaintiff's injuries.[6] The defendant may avoid liability if it proves that the risk was scientifically unknowable at the time the product was distributed to the plaintiff.[7]

Lilly's summary judgment motion does not appear to challenge the State's ability to prove the first element -- and the State in fact has already demonstrated to this court that it has substantial evidence that Zyprexa poses risks of serious injuries (including

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4 Lilly's memorandum completely fails to analyze the elements of either a strict liability failure to warn claim or a UTPA claim under Alaska law.

5 835 P.2d 1189 (Alaska 1992).

6 *See id.* at 1199-1200.

7 *See id.* at 1200.

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weight gain and the development of diabetes) and that Lilly marketed Zyprexa without warning of these risks.[8]

The State's prima facie case can be summarized very briefly. The State will show first that Zyprexa posed (and still poses) a risk of injury to those to whom the drug is prescribed. The State will rely on documents and expert testimony establishing that, when used as directed, Zyprexa presents risks of significant weight gain, hyperglycemia, and hyperlipedemia, and does so to a greater extent than other drugs approved for the treatment of schizophrenia and bipolar disorder.[9] The State will use essentially the same evidence outlined by Judge Weinstein in his decision in one of his Zyprexa cases, in which he denied summary judgment to Lilly.[10] Second, the State will show that Lilly did not adequately warn of the risks. That point is easily proved through the FDA's letter that states explicitly that Lilly did not provide sufficient information for doctors to

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[8] *See* Plaintiff's Memorandum Describing Its Claims and Proofs, including its attached exhibits and other cited studies; *see also* Exhibit 1 (excerpts of recently-conducted deposition of Eli Lilly pharmacist Robin Wojcieszek); Exhibit 2 (March 28, 2007 letter from FDA to Lilly stating that the Zyprexa labeling did not contain sufficient information about the risks of weight gain, hyperglycemia, and hyperlipedemia to permit physicians to make reasonable treatment decisions); Exhibit 3 (October 5, 2007 "Dear Health Care Professional" letter distributed by Lilly at the insistence of the FDA, providing warnings of the risks of weight gain, hyperglycemia, and hyperlipedemia); Exhibit 4 at 8-36, 48-49 (Expert Witness Report and Declaration of William Wirshing, M.D.).

[9] *See, e.g.,* Exhibit 4 at 8-36, 48-49; Exhibit 5 (February 2004 article from DIABETES CARE, *Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes*).

[10] *See In re Zyprexa Products Liability Litigation,* 489 F. Supp. 2d 230, 248-50 (E.D.N.Y. 2007).

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evaluate the risks.[11] Third, the State will prove that failure to warn of the side effects was a proximate cause of the State's injuries.[12] It is not necessary for the State to establish that the defective labeling was the sole proximate cause of the State's injuries.[13] The State's evidence shows that in places where adequate warnings were provided, Zyprexa use declined.[14] These statistics provide a solid evidentiary basis for concluding that

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[11] *See* Exhibit 2 at 1 ("we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipedemia that is associated with olanzapine use"). *See generally Shanks,* 835 P.2d at 1200 (an adequate warning should: "1) clearly indicate the scope of the risk or danger posed by the product; 2) reasonably communicate the extent or seriousness of harm that could result from the risk or danger; and 3) be conveyed in such a manner as to alert the reasonably prudent person"); *see also In re Zyprexa Products Liability Litigation,* 489 F. Supp. 2d at 280 (holding that Lilly was not entitled to summary judgment on the adequacy of warnings after April 2003, even if it met the FDA's warning requirements: "The adequacy of the Zyprexa warning label approved by the FDA in April of 2003 is a question of fact for the jury.").

[12] There should be no dispute that Zyprexa contributes to weight gain, hyperglycemia, and hyperlipedemia. Lilly's label and Dear Health Care Professional letter acknowledge this fact. *See* Exhibit 3 at 1 ("[T]he association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics."; "Significantly greater mean increases in total cholesterol, LDL cholesterol, and triglycerides were observed in Zyprexa-treated patients compared with placebo-treated patients both with and without evidence of dyslipedemia at baseline."); *see also* Exhibit 4 at 8-36, 48-49.

[13] *See Prince v. Parachutes, Inc.,* 685 P.2d 83, 89 (Alaska 1984).

[14] *See* Exhibit 6 (July 1, 2002 Lilly Memorandum noting that prescriptions of Zyprexa dropped precipitously in 2002 after the Japanese regulatory authority required a stringent warning on the risk of diabetes, contradindicated the use of Zyprexa for patients with diabetes, and mandated blood glucose monitoring for all patients started on the drug (previously marked as Exhibit 5 to Breier Deposition)).

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physicians in Alaska would not have prescribed Zyprexa as frequently if they had been adequately warned of the risks.[15]

Lilly has never contended that it can satisfy the affirmative defense that the undisclosed risks were unknown and scientifically unknowable. Substantial evidence indicates that Lilly actually knew of the risks and concealed them. Certainly, the risks were knowable through the use of a scale to measure weight gain and simple blood tests to check glucose and cholesterol levels.

Because Lilly has not demonstrated the absence of dispute over material facts, Lilly's motion for summary judgment on the strict liability failure to warn claim should be denied.

(ii) Unfair Trade Practices Act Claims

To establish a claim under the Alaska UTPA, a plaintiff needs to prove, first, that the defendant is engaged in trade or commerce, and, second, that the defendant committed an unfair or deceptive act or practice in the conduct of trade or commerce.[16]

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[15] One of the State's expert witnesses has opined, and will testify, that "had Lilly provided full disclosure to the treating physicians of the actual potential consequences to their patients of the use of olanzapine over other atypical antipsychotic medications, and of olanzapine's lack of enhanced efficacy to justify the increased serious risk, a reasonably prudent doctor would not, given the fact that there are choices of typical antipsychotics and other atypical antipsychotics available to treat the same illness for which olanzapine is used, choose olanzapine as the drug of first choice for treatment of any of the illness[es] for which the drug has been marketed." Exhibit 4 at 49-50.

[16] *See* AS 45.50.471(a); *State v. O'Neill Investigations, Inc.*, 609 P.2d 520, 534 (Alaska 1980).

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The statute lists 51 specific (but non-exclusive) examples of acts that are unfair or deceptive, including "using or employing deception, fraud, false pretense, false promise, misrepresentation, or knowingly concealing, suppressing, or omitting a material fact with intent that others rely upon the concealment, suppression, or omission in connection with the sale or advertisement of goods or services whether or not a person has in fact been misled, deceived or damaged."[17]

The State's UTPA claims will focus on the ways that Lilly aggressively promoted Zyprexa for unapproved, off-label uses, such as to treat depression and sleep disorders. Promoting a drug for a usage for which the drug has not been demonstrated to be efficacious is in itself a UTPA violation.[18] Misleading promotion and failure to disclose known defects in the product are also clear violations.[19]

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[17] AS 45.50.471(b)(12). The State's complaint also cites to and alleges that Lilly violated subsections (b)(4) ("representing that goods . . . have . . . characteristics, . . . uses, [and/or] benefits . . . that they do not have"); (b)(6) ("representing that goods . . . are of a particular standard, quality, or grade . . . if they are of another"); (b)(8) ("advertising goods . . . with intent not to sell them as advertised"); (b)(11) ("engaging in any other conduct creating a likelihood of confusion or of misunderstanding and which misleads, deceives or damages a buyer . . . in connection with the sale or advertisement of goods"); and (b)(48) ("violating a labeling or advertising provision of AS 17.20 (Alaska Food, Drug, and Cosmetic Act)").

[18] *See* AS 45.50.471(b)(4), (48); AS 17.20.110.

[19] *See* AS 45.50.471(b)(4), (6), (11), (48).

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Under AS 45.50.551, the State may sue for civil penalties even without proof that anyone relied on the misleading promotions or was damaged.[20] Since the State plainly has evidence to satisfy the basic elements of a UTPA violation, Lilly's motion for summary judgment on the UTPA claim must fail.

Under AS 45.50.531(a), a private plaintiff, after proving the defendant committed an unfair or deceptive act, may recover damages if he also proves he "suffer[ed] an ascertainable loss of money or property as a result of [defendant's] act or practice declared unlawful by AS 45.50.471."[21] In the second trial, the State will seek damages under AS 45.50.531(a), in addition to its claims under AS 45.50.551, because the State can prove it suffered ascertainable losses as a result of Lilly's unfair and deceptive acts. The State's ascertainable losses include the costs it paid for prescriptions for off-label uses that were written as a result of Lilly's deceptive promotions and the costs the State paid to treat Zyprexa's side-effects that Lilly failed to disclose to physicians.[22] The State will use its Medicaid records to prove these losses occurred as a result of Lilly's unfair

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[20] This portion of the UTPA expressly permits the State to seek civil penalties before anyone is hurt by an unfair or deceptive act.

[21] AS 45.50.531(a).

[22] A Massachusetts court has held that the purchase of an intentionally falsely represented product may be, in itself, an "ascertainable loss" for purposes of establishing an entitlement to damages under that state's consumer protection law. *See Aspinall v. Phillip Morris Cos.*, 813 N.E.2d 476, 486 (Mass. 2004) ("We reject the proposition that the purchase of an intentionally falsely represented product cannot be, by itself, an ascertainable injury under our consumer protection statute.").

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and deceptive acts.[23] For off-label uses, such as the treatment of depression and sleep disorders, where no body of scientific literature establishes that Zyprexa is an efficacious treatment, the State's damages include the entire cost of the Zyprexa prescriptions written to treat these conditions. If those patients then developed diabetes or other side-effects due to their use of Zyprexa, the State's damages include the cost of treating those side-effects.

Because the State has evidence to prove each element of its UTPA claims, Lilly's motion for summary judgment on these claims must be denied.

3. The State does not rely on a fraud-on-the-market theory.

Lilly devotes the bulk of its argument for summary judgment on the failure to warn and UTPA claims to a discussion of the *Rezulin* decision.[24] The *Rezulin* court granted summary judgment to the drug manufacturer in that case, because the court believed the plaintiffs relied on the fraud-on-the-market theory, and the court determined that this theory is not viable in prescription drug cases.[25] *Rezulin* is a poorly reasoned decision, but, more important, it is largely irrelevant to the State's claims. The State in this case does not rely on the fraud-on-the-market theory.

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[23] This proximate cause requirement is different from a requirement to prove that plaintiff relied on the defendant's unfair or deceptive marketing. *See Aspinall,* 813 N.E.2d at 486*; see also* AS 45. 50.471(b)(12) (providing explicitly that proof of reliance is not required when the plaintiff proves that the defendant intended that consumers rely on its deceptive marketing).

[24] *See* Lilly Summary Judgment Memo. at 10-12.

[25] *See* 2007 WL 4165703 at *2-4.

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To understand the *Rezulin* decision, and why it does not support Lilly's position in the current case, it is useful to take a step back to examine the cases on which the *Rezulin* court relied. The *Rezulin* court accurately noted that the fraud-on-the-market theory is a creature of federal securities laws.[26] In securities fraud cases, purchasers of stocks have been permitted to sue to recover for excessive prices they paid for the stocks, when the defendant's fraud inflated the stock price.[27] Under that theory, plaintiffs do not need to prove that they personally relied on the defendant's fraudulent assertions, since all purchasers of the stock were harmed by the inflated price.[28]

In suits against prescription drug manufacturers, some plaintiffs seeking to recover for having paid artificially high prices due to the manufacturer's deceptive marketing practices attempted to import the fraud-on-the-market theory into their products liability cases.[29] The courts generally rejected the fraud-on-the-market theory as inapplicable to

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[26] *See id.* at *3.

[27] *See, e.g., Finkel v. Docutel/Olivetti Corp.*, 817 F.2d 356, 361 (5th Cir. 1987) ("The fraud on the market theory is premised on the hypothesis that the market price of a security, in an open market environment as opposed to a private transaction between seller and buyer, accurately reflects the value of that security if all relevant information has been disclosed to the marketplace. When one fails to disclose or misrepresents material information about a security, the market's efficient pricing mechanism is skewed and the price of the security is distorted. A purchaser or seller who relies on the market to accurately value the security suffers damages if the market does not have all the information.").

[28] *See id.*

[29] *See, e.g., Heindel v. Pfizer, Inc.*, 381 F. Supp. 2d 364, 379-80 (D.N.J. 2004); *International Union of Operating Engineers Local No. 68 Welfare Fund v. Merck & Co.*, 929 A.2d 1076, 1087-88 (N.J. 2007).

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prescription drug cases, because there is no "market" for prescription drugs in the same sense that there is a market for federal securities.[30] Most people purchase securities for investment purposes, and their purchases are extremely price-sensitive. By contrast, people purchase prescription drugs for medical reasons, and the decision has little to do with price.[31] Accordingly, these courts held that the fraud-on-the-market theory cannot be used to establish that plaintiffs paid more for a prescription drug than they would have paid absent the defendant's deceptive marketing tactics that inflated the price.

The fraud-on-the-market theory has no bearing on this case, since the State is not contending that Lilly's misrepresentations and concealments artificially inflated the price of Zyprexa. The State's damages claims do not include claims that it overpaid for each Zyprexa prescription that it purchased. Rather, the State seeks to recover the cost of Zyprexa prescriptions in instances where physicians prescribed Zyprexa for the off-label conditions for which Lilly promoted its use, such as depression and sleep disorders, although Zyprexa is not an efficacious treatment for these conditions. The State is not claiming, and will not attempt to prove, that the drug was overpriced as a result of fraudulent promotions. Instead, the State contends that, even if the price was fair, the entire prescription cost was a wasted expense, because the State was paying for a "treatment" that was not efficacious. The State also seeks to recover the cost of treating

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[30] *See Heindel,* 381 F. Supp. 2d at 380; *International Union of Operating Engineers Local No. 68 Welfare Fund,* 929 A.2d at 1088.

[31] *See Heindel,* 381 F. Supp. 2d at 380.

the side-effects suffered by patients who were not adequately warned, as well as statutory penalties for Lilly's violations of the Alaska UTPA. None of these damage claims depends on proving that the price of Zyprexa was inflated due to Lilly's misconduct. None depends on a fraud-on-the-market theory.

In short, contrary to Lilly's assertions, the State does not rely on a fraud-on-the-market theory. The recent *Rezulin* decision therefore does not support granting summary judgment to Lilly.

4. The State does not need to prove specific individual physicians relied on Lilly's misrepresentations, or that the State itself was misled.

Lilly makes two other arguments based on the *Rezulin* opinion. It argues that *Rezulin* requires proof that individual physicians relied on Lilly's misrepresentations when they prescribed Zyprexa, and it argues that *Rezulin* precludes a state, such as Alaska, from recovering damages without proving that it relied on Lilly's misconduct.[32] Neither argument has merit.

As to the strict liability failure to warn claim, the adequacy of warnings is always measured by an objective standard,[33] so plainly evidence that particular physicians believe they were not adequately advised of the risks to their patients is not required. With regard to proving proximate cause, Lilly proffers no sensible argument why *Shanks*

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[32] *See* Lilly Summary Judgment Memo. at 9-10.

[33] *See Shanks,* 835 P.2d at 1200 (describing requirements of an adequate warning (quoted *supra* n.11)); *see also In re Zyprexa Products Liability Litigation,* 489 F. Supp. 2d at 280 (quoted *supra* n.11).

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or any other Alaska case requires proof based on individual doctors' testimony that they prescribed the drug because they were misled by Lilly's incomplete and deceptive promotions, as distinct from statistical evidence from which a jury may infer that individual doctors prescribed the drug because they were misled. Alaska law does not distinguish between direct and circumstantial evidence.[34] Lilly is free to attempt to show that something other than the nondisclosure of side-effects caused doctors to prescribe Zyprexa, with its side-effects, instead of other drugs approved for treatment of schizophrenia and bipolar disorder. At the summary judgment stage, this court does not evaluate the credibility of competing evidence, only whether the non-moving party has presented some evidence in support of its legal theory.[35]

Lilly's arguments for requiring evidence of individual doctors' reliance are equally unpersuasive with regard to the State's UTPA claims. As discussed above, the State may

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[34] *See, e.g.,* Alaska Civil Pattern Jury Instruction No. 1.06 ("Facts may be proved by either direct or circumstantial evidence. The law accepts each as a reasonable method of proof.").

[35] *See Estate of Milos v. Quality Asphalt Paving, Inc.,* 145 P.3d 533, 537 (Alaska 2006) (noting that the standard for finding a genuine issue of fact is "lenient" and that the court may not weigh credibility but may determine only whether the nonmoving party has presented "some evidence in support of its legal theory"); *Meyer v. State, Dep't of Revenue,* 994 P.2d 365, 367-68 (Alaska 1999) (holding that summary judgment on a paternity claim was not properly granted even when defendant showed a 99.98% chance that plaintiff was the biological father, where plaintiff presented some evidence to refute that -- namely, his own affidavit that he did not have a sexual relationship with the mother around the time she most likely conceived).

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prevail on its claim for statutory penalties without proof of reliance by anyone.[36] For its claims under AS 45.50.531, the State also does not need to prove reliance, only damages as a result of the violation.[37] For the State's claims to recover the ascertainable damages caused to it as a result of Lilly's promotion of Zyprexa for off-label uses, neither *Rezulin* nor any Alaska case precludes Alaska from basing its proof on statistical models. Thoughtfully reasoned consumer protection cases, more directly on point than any cases cited by Lilly, have allowed the use of econometric models to prove that damages resulted from the defendant's misconduct.[38]

The State's plan to use statistical evidence to prove its claims is analogous to that approved by Judge Weinstein in *In re Zyprexa Products Liability Litigation.*[39] Plaintiffs in that case are insurers, who allege (like the State in this case) that Lilly engaged in a widespread effort to promote Zyprexa by intentionally misrepresenting its safety; they allege that, as a result of Lilly's marketing, doctors prescribed Zyprexa to patients for

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[36] *See* AS 45.50.551.

[37] *See, e.g.,* AS 45.50.471(b)(12); *see also Group Health Plan, Inc. v. Philip Morris Inc.,* 621 N.W.2d 2, 12 (Minn. 2001) (holding that a plaintiff under the Minnesota consumer protection statutes does not need to prove reliance, only damages as a result of the violation).

[38] *See, e.g., In re Neurontin Marketing & Sale Practices Litigation,* 244 F.R.D. 84, 112-15 (D. Mass. 2004) (denying certification of a class action but recognizing that statistical, econometric proof could suffice, particularly for a third-party payer seeking to recover a percentage of fees paid); *In re Zyprexa Products Liability Litigation,* 493 F. Supp. 2d 571, 578-79 (E.D.N.Y. 2007) (rejecting Lilly's argument that individualized, rather than aggregate, proof was required to establish causation for a RICO claim).

[39] 493 F. Supp. 2d 571 (E.D.N.Y. 2007).

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whom they would not have prescribed this drug but for Lilly's misrepresentations.[40] Judge Weinstein rejected Lilly's motion for summary judgment on this claim. He specifically rejected an argument that plaintiffs needed to prove reliance by individual physicians and expressly authorized plaintiffs to prove their claims in the aggregate, through economic analyses:

> Statistical proof of reliance is appropriate . . . where a sophisticated, broad-based scheme, by its very nature . . . likely to be designed to distort the entire body of public knowledge rather than to individually mislead millions of people, is alleged.[41]

Finally, this court should find no merit in Lilly's argument that the State cannot succeed on its products liability claim without proving that the State itself was misled. The State in fact is a proper plaintiff because it seeks to recover its own damages, and the State, as outlined above, is prepared to prove that its damages were the proximate result of Lilly's failure to warn of Zyprexa's risks.

Lilly's argument again relies entirely on the *Rezulin* decision.[42] A careful reading of the decision should convince this court not to follow it. First, that court applied

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[40] The plaintiffs there sought to recover the inflated price of Zyprexa. *See id.* at 576-78. As noted before, Alaska does not intend to seek damages for the inflated price of Zyprexa.

[41] *Id.* at 579 (internal quotes and brackets omitted). The Second Circuit similarly allowed plaintiff health insurers to seek the "excess" costs of paying for an expensive drug (there, Rezulin) because the drug manufacturer deceptively promoted it as safer than less expensive alternatives. *See DeSiano v. Warner-Lambert Co.*, 326 F.3d 339, 345-49 (2d Cir. 2003).

[42] *See* Lilly Summary Judgment Memo. at 9-12; *Rezulin*, 2007 WL 4165703 at *2-3.

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Louisiana law, not Alaska law. Second, that court went astray in characterizing Louisiana's claims as if they all depended on a fraud-on-the-market theory; it then rejected the claims because of the inapplicability of the fraud-on-the-market theory in prescription drug cases.[43] In fact, it appears that some of Louisiana's claims did not depend on a fraud-on-the-market theory. Louisiana claimed it paid inflated prices for Rezulin.[44] This claim apparently relied on a fraud-on-the-market theory, so the district court's rejection of that claim may have been correct. However, the holding is irrelevant to this case because the State of Alaska has expressly disavowed that category of damages in this litigation.

Louisiana also sought recovery for prescriptions that would not have been written but for the defendant's deceptive marketing.[45] That claim evidently did not rely on a fraud-on-the-market theory, but the federal district court did not separately analyze that claim. Claims for deceptively inducing physicians to write prescriptions are fundamentally different from claims for paying inflated prices. It does not follow logically that, because a plaintiff may not rely on a fraud-on-the-market theory to establish harm caused by inflated prices, the plaintiff therefore cannot rely on statistical proof that doctors were deceived -- yet that in essence is what the district court held

[43] *See* 2007 WL 4165703 at *2-3.

[44] *See id.* at *2 (noting that Louisiana sought to recover because it reimbursed for prescriptions "written at prices that otherwise could not have been charged").

[45] *See id.* (noting that Louisiana sought to recover for prescriptions "that otherwise would not have been written").

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without analysis. The grounds for rejecting the fraud-on-the-market theory as a way to prove inflated prices have nothing to do with whether a state, as distinct from an injured individual, may sue for the damages directly caused to it because a drug manufacturer failed to warn of the drug's side-effects. For that aspect of this case, this court should turn to Alaska law. Nothing in *Shanks* precludes the State from seeking to recover its own damages resulting from the marketing of a drug without adequate warnings.[46] *Rezulin* does not provide a well-reasoned basis for rejecting the State's ability to use statistical proof to establish that the State was damaged due to Lilly's failure to warn of Zyprexa's side-effects and by Lilly's promotion of the drug to treat conditions for which Zyprexa was not approved. This court therefore should deny Lilly's summary judgment motion based on *Rezulin*.

In short, Lilly's reliance on *Rezulin* is completely misplaced. The State does not rely on a fraud-on-the-market theory to prove either its strict liability failure to warn claim or its UTPA claim. The State has demonstrated that it has viable, well-recognized methods of proving the causal link between Lilly's misconduct and the State's damages. Therefore, Lilly's motion for summary judgment must be denied.

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[46] The Minnesota Supreme Court, in a thoughtful decision construing statutory language similar to that in the Alaska UTPA, specifically concluded that an HMO could sue for its own damages incurred as a result of a violation of a consumer protection law, noting the broad scope of the consumer protection laws and the fact that the statutes are not limited to those who are direct purchasers of a harmful product. *See Group Health Plan,* 621 N.W.2d at 8-11. That court also approved proof by statistics. *See id.* at 14-15.

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C. The State Has Not Failed To Explain To Lilly What Misconduct Lilly Committed.

The final section of Lilly's memorandum contends that Lilly should be granted summary judgment because the State, allegedly, has failed to provide Lilly with specific evidence of its misconduct.[47] Lilly's argument is a preview of a motion for discovery sanctions that it asserted it was planning to bring. Lilly did later file such a motion; the State responded.

As a basis for seeking summary judgment, Lilly's allegation of discovery violations fails (even if those allegations were accurate, which they are not). A defendant seeking summary judgment may not rely on the supposed absence of evidence presented by plaintiff. The defendant first must provide to the court admissible evidence that, if uncontradicted, would entitle the defendant to judgment in its favor.[48] Until the defendant provides that proof to the court, the plaintiff need not present the contradictory evidence.[49] Nonetheless, the State has provided this court with substantial evidence documenting Lilly's misconduct,[50] and Lilly's claim that it does not know what it

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47 Lilly Summary Judgment Memo. at 13.

48 *See Shade v. Co & Anglo Alaska Serv. Corp.*, 901 P.2d 434, 437 (Alaska 1995) ("[I]t is the moving party that bears the initial burden of proving, through admissible evidence, the absence of genuine factual disputes and its entitlement to judgment.").

49 *See id.* ("[A]lthough prudent counsel for the non-moving party will always attempt to demonstrate a genuine issue for trial, it is not obligated to do so until the moving party makes a prima facie showing of its entitlement to judgment on established facts.").

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supposedly did that violated the UTPA is baseless. Because Lilly has not demonstrated the absence of any material factual disputes or that it is entitled to prevail on any set of established facts, Lilly's motion for summary judgment must be denied.

CONCLUSION

This court should deny Lilly's motion for summary judgment.

DATED this 8 day of January, 2008.

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[50] *See, e.g.,* Exhibits 1-6; Plaintiff's Memorandum Describing Its Claims and Proofs, including its attached exhibits and other cited studies. In *Zok v. Collins,* 18 P.3d 39, 43 n.15 (Alaska 2001), the case cited by Lilly, which in fact does not support its position at all, the Supreme Court observed that, "[w]hen making a summary judgment determination, a court should examine the pleadings, affidavits, and discovery answers to ascertain whether any genuine issues of material fact exist."

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Certificate of Service

I hereby certify that a true and correct copy of the Foregoing **State of Alaska's Opposition to Lilly's Motion for Summary Judgment was** served by mail / messenger / facsimile on:

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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,)
)
Plaintiff,)
)
-v-) CAUSE NO.
) 3AN-06-5630 CIV
ELI LILLY & COMPANY,)
)
Defendant.)

The videotaped deposition upon oral examination of ROBIN PITTS WOJCIESZEK, a witness produced and sworn before me, Nancy M. Kottenstette, Notary Public in and for the County of Marion, State of Indiana, taken on behalf of the Plaintiff at the offices of Ice Miller, One American Square, Suite 3100, Indianapolis, Indiana, on December 11, 2007, at 9:37 a.m., pursuant to all applicable rules.

CONFIDENTIAL

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A Yes, I do.
Q Now, when they talk about OFC, that's another way of talking about Symbyax or the combination of olanzapine and fluoxetine; is that correct?
A That's correct.
Q Okay. And was it your understanding that blood glucose levels greater than or equal to 200 milligrams per deciliter was regarded as diagnostic for diabetes by the American Diabetes Association?
A Yes. Based on the -- kind of the ADA guidelines, that's correct.
Q So what the FDA was saying here was that the data that you had presented to them already indicated that 2.9 percent of the patients who had rand- -- who had baseline random blood glucose of less than 140 wound up having on-treatment levels greater than or equal to 200 compared to .3 percent of placebo-treated patients; correct?
A I'm sorry. Could you repeat the question again?
Q I know. It was kind of long.
A I'm sorry.

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MR. SUGGS: Could you read it back, please.
(The requested material was read back by the reporter.)
A That -- that was an analysis included in the application.
Q Okay. And was that an analysis that had been done by Lilly or by FDA?
A By Lilly.
Q Okay. So Lilly itself had concluded then that 2.9 percent of the patients receiving the combination drug who originally had nondiabetic levels of blood glucose went over the 200 mark, which is diagnostic for diabetes, as compared to only .3 percent of the placebo-treated patients; is that correct?
MR. KANTRA: I'm just -- I'm just going to object to the form of the question to the -- to the extent that it suggests that the ADA guidelines --
MR. SUGGS: Just say objection to form.
Q Do you recall the question?
A What this is saying is this is a particular analysis, categorical analysis or a shift analysis, that was done in the application. The overall conclusions would be something that our medical group would make. This is one of many analyses

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that we conducted.

Q This particular analysis, however, showed essentially a tenfold higher rate of patients going from nondiabetic levels of blood glucose to blood glucose levels over 200; correct?
A For this particular analysis?
Q Yes.
A Yes.
Q Okay. And do you know who within Lilly did that analysis, finding that tenfold difference?
A That would have been done with our statistical group, with the medical group doing an evaluation of the results.
Q Okay. And I'm presuming that at some point they provided you in regulatory affairs with that data or write-up of the data, which you then submitted to FDA; correct?
A That's correct.
Q Okay. They then go on to say in their letter, FDA does, "However, we note that 46 percent of patients who were borderline to high at baseline (140 to 200) had such on-treatment levels compared to only 5 percent of placebo-treated patients." Do you see that?
A Yes.

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Q Okay. And it was your understanding that they were saying there that when you looked at the data that Lilly had generated, it showed that those folks who had somewhat elevated levels of blood glucose in the 140 to 200 range that when you looked at those folks, about 46 percent of those people who were exposed to the combination drug went over 200 as compared to only 5 percent of the placebo-treated patients; correct?
A That's correct.
Q Okay. And that, again, would -- presuming would have been another analysis done by Lilly itself; correct?
A That's correct.
Q Okay. So in both of these statements here about what that data showed, FDA was really talking about what Lilly's own analysis had shown. And this was not some separate analysis that FDA had done. Is that a fair statement?
A That's a fair statement.
Q Okay. Continuing down in the letter a couple of lines, the FDA said, I believe, making reference to that latter analysis where the 46 percent of patients had blood levels over 200 after treatment, they go on to say "In addition, we were troubled

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that this important finding was not included in your proposed label." Do you see that?

A Yes.

Q Okay. And do you know who it was that made the decision not to include that information in the proposed label?

A That's a decision that's made -- it's actually a very cross-functional group of individuals within medical, regulatory, and global patient safety.

Q Was there a particular individual who would have been -- I'll use a football term -- the quarterback in terms of making that decision?

A No. A lot of our decisions are made -- we have a various -- a sign-off form. So it's definitely made within the consensus of the group.

Q Okay. Am I correct, though, that the proposed labeling that you had submitted did make reference to the first analysis that we talked about --

A That's correct.

Q -- showing 2.9 percent of the patients having blood glucose below 140 going over 200. That was, in fact, in the -- in the proposal that you guys had; correct?

A That's correct.

Q And I see you pawing through the document there.

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Are you going to --

MR. KANTRA: Object to the characterization of pawing.

MR. SUGGS: Well, I didn't -- I didn't mean it in a bad way. Let me restate the question.

THE WITNESS: Pawing.

Q Let me withdraw that. I see you paging through the document. Are you able to point to the section in the proposed labeling that does indicate where that was included?

A Yes.

Q And can you point that out to me, please?

A Sure. It is on page -- oh, my, with various page numbers on this fax, isn't it -- 20 of 38, top right-hand corner under laboratory changes.

Q Okay. In about the middle of the page. Actually, a little lower than that.

A Yes, uh-huh.

Q Okay. Okay. And this would have been the proposed labeling that Lilly had submitted to FDA; correct?

A That's correct.

Q Okay.

A My pawing's over.
Q I'm sorry. I don't know why -- I don't know why

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that word came to mind. Let's see here. Do you know when it would have been -- that particular data that we've been talking about on which those analyses were made, do you know when they would have been -- when that data would have been generated?
A That data would have been generated, you know, prior to our submissions, so the summer of 2006.
Q Okay. I thought you said that the -- that the data ranged from between 2002 and 2005?
A Correct. But this particular analysis is a pooling of studies.
Q Ah, okay. Okay. So this analysis was done, you believe, probably in the summer of 2006?
A Yes.
Q But it was done on data that was a pooling of data that was in that 2002 to -- strike that. The analysis that was done in the summer of 2006, as referred to in this first full paragraph on page 2, was an analysis of data that had been actually generated sometime between 2002 and 2005. Fair statement?
A That's correct.
Q Okay. I'd like to direct your attention to the third full paragraph on the second page of the

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FDA's letter, the one that starts off "Our overall goal..." Do you see that?
A Yes, I do.
Q It states "Our overall goal is to improve labeling with regard to these findings so that clinicians will be better informed on what the risks are for their patients. They cannot make reasonable treatment decisions until they have such information.
We do not feel that current labeling for either Symbyax or Zyprexa provides sufficient information on these risks, and we fully intend to insure that these labels are enhanced with the best available information to characterize these risks."
Do you see that language?
A Yes, I do.
Q Now, are you aware that in the Zyprexa litigation, not only in this case in Alaska, but in thousands of other cases around the country, Lilly has been asserting that its Zyprexa label was already sufficient and adequate?

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A Yes.
Q But at least the -- and Lilly has never, to your knowledge, admitted that its labeling was inadequate, has it?

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A Yes, that's correct.
Q Okay. But in this March 2007 letter, FDA told the company that it felt the Zyprexa labeling was not adequate; correct?
A That's correct.
Q Okay. Now, after receiving this communication from FDA in March of 2007 that it did not believe that the Zyprexa label was adequate, the company did not change the label in April, did it?
A No, we did not.
Q Or May?
A No.
Q Or June?
A No.
Q Or July?
A No.
Q Or August?
A No.
Q Or September?
A No.
Q There was, finally, a label change in October of 2007; correct?
A That's correct.
Q Do you have any idea how many new prescriptions there were of Zyprexa in the six-month time period

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between March to October 2007?
MR. KANTRA: Objection, beyond the scope. You may answer, if you know.
A No.
Q Were you aware that your annual sales of Zyprexa in 2006 were over $4 billion?
MR. KANTRA: Objection, beyond the scope.
A No.
Q You had no idea that Zyprexa sales were over $4 billion --
MR. KANTRA: Asked --
Q -- in 2006?
MR. KANTRA: Asked and answered.
Q You may answer.
A No.
MR. KANTRA: Objection, beyond the scope.
Q Were you aware that Zyprexa is the largest-selling drug in the company?
A Yes.

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Zyprexa; correct?
A Correct.
Q Okay. And what they show there is by strike outs and underlining the language that they want

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eliminated and the language they want to replace it; correct?
A Correct.
Q And the language that they strike out there was essentially the language that had been in the warning section of the Zyprexa labeling since 2003; correct?
MR. KANTRA: Objection to the form.
A Can you repeat the question?
MR. SUGGS: Can you read it back, please.
(The requested material was read back by the reporter.)
A There are certain components of that. I think the way they did the strike out and additions, it's difficult to track line by line what's kept but --
Q Okay.
A -- many of the elements that were in the 2003 warning are still included in the proposal.
Q Okay. Nevertheless, there's also some significant additions; correct?
A There were some additions that they included.
Q Okay. One of the additions that they requested -- well, on the second page of this letter, they show under the heading "Hyperglycemia" what they are propose -- what they, the FDA, are proposing;

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correct?
A Uh-huh, correct.
Q Okay. And in the -- at the end of the first paragraph it states "Olanzapine and clozapine treatments have been associated with a greater potential to induce hyperglycemia than other atypical antipsychotics." Do you see that?
A Yes.
Q And what does the word "induce" mean?
A It means that there's some sort of a kind of relationship of olanzapine and hyperglycemia.
Q Well, in fact, the word induce indicates that it's a causal relationship, does it not?
A It could mean that.
Q In fact, the ordinary definition -- the ordinary dictionary definition of the word induce definitely indicates that it's a causal relationship. If I induce something, that means that I have brought -- brought about that result; correct?

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MR. KANTRA: Asked and answered.
Q You may answer.
A Again, it could be defined that way.
Q And then they make reference in the third paragraph in that section to the analyses that we have looked at previously in the March 2007 letter. Is that a

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fair statement?
A That's -- that's correct.
Q Okay. That's the analyses done by Lilly, which showed that the -- there was a tenfold increase in the number of patients who went from nonhyperglycemic to the state of being hyperglycemic; correct?
A That's looking at patients who were normal at baseline and went to a blood glucose of greater than 200.
Q The difference being between the olanzapine patient 2.4 percent of the patients became hyperglycemic compared to .3 percent. And that's about a threefold difference; correct? Pardon me. About a tenfold difference. I take it back. It's about an eightfold difference; correct?
A Yes. But it relates, again, to a categorical change of greater than 200.
Q And it notes that -- also that approximately one-third of patients on olanzapine, 33.3 percent, who had borderline increase serum blood glucose progressed to high blood glucose at some time during the 6 to 12 weeks of olanzapine treatment; correct?
A That's correct.

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Q Okay. And these analyses that were done by Lilly were statistically significant, were they not?
MR. KANTRA: Objection, beyond the scope.
A Yeah. I don't recall if they were statistically significant.
Q Okay. And then FDA also proposed that on the following page a completely new section in the warnings section regarding weight gain; correct?
A Correct.
Q Up until this point in time, Lilly had never discussed weight gain in the warning section of the Zyprexa labeling; correct?
A At this time it was not in our current label; however, it was being proposed in the supplemental applications for TRD in adolescents --
Q When --
A -- submission.

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Q When was that proposed?
A That was in 2000 -- late 2006.
Q Okay. And then also in this letter the FDA was requesting a completely new section on -- in the warning section for Zyprexa regarding hyperlipidemia; correct?
A That's correct.
Q Now, hyperlipidemia refers to fats in the blood;

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correct?
MR. KANTRA: Objection, beyond the scope.
A It -- it refers to, yes, things such as triglycerides, cholesterol, lipids, that's correct.
Q That's what hyperlipidemia means is elevated levels of triglycerides and cholesterol; correct?
A Correct.
Q Okay. And after receiving this letter in which FDA laid out the language it wanted to see in the labeling, Lilly did not accept the language requested by FDA and instead sought to change the language; correct?
MR. KANTRA: Objection to the form.
A In response to this -- this communication, we initiated discussions and proposals with FDA shortly after receipt.
Q Lilly did not accept the language that was laid out by FDA in their August 28, 2007, letter; correct?
MR. KANTRA: Objection to the form.
A We provided our proposal in response to their request based on data that we had available short -- you know, during this time frame.
Q Your response to FDA was not, okay, we'll make the -- we'll make the label change that you've suggested; correct?

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A Correct.
Q Okay. Do you recall that Lilly wanted to require a change in the labeling of all antipsychotics?
MR. KANTRA: Objection. What time frame are we talking about?
MR. SUGGS: After the August 28, 2007, letter.
A Could you repeat the question?
Q Sure. Do you recall that -- that in your response to FDA's request, Lilly wanted there to be a change in the labeling of all atypical antipsychotics?
A In -- in part of our response to this request in initiating the discussion with them -- because the warning is a class labeling and that was our understanding based on their 2003 letter, that if initiations and discussions around changes to that

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changed label language in full size -- what I'll call full sized text; correct?
A Correct.
Q For both Zyprexa and Symbyax; correct?
A Correct.
Q And then following that are attachments showing the actual package insert sized font, and, I guess, that would be the full text of the full labeling for both products, correct, not just the warning section?
A Right. It's the full prescribing or the USPIs we refer to it.
Q The U.S. package insert?
A Correct.
Q And I guess we can see there the difference in the size of type between the -- what's in the package

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insert versus full size type; correct?
A Correct.
Q And we talked earlier about some back and forth that there was between Lilly and the FDA as to the content of the language and the warning section regarding hyperglycemia. But this that we have before us in Exhibit 12 is, in fact, the final, final -- this is what it turned out to be; correct?
A Correct.
Q Okay. If you could turn to page 3, the last part of the first sentence, the last part of the first paragraph that we talked about before with respect to there being a continuum of -- with respect to the relationship between antipsychotics and hyperglycemia or glucose levels now reads in the final version "The association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum, and olanzapine appears to have a greater association than some other atypical antipsychotics." Did I read that correctly?
A Yes, you did.
Q And who was it that made the decision that that is what the final language would be?
A Very -- the very similar group that was involved --

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was involved in the proposal that was sent to FDA. This reflects our kind of post-FDA discussion, what we felt would be more appropriate for labeling, kind of based on that discussion, kind of further reflection of our data.
Q Okay. And that language there talking about olanzapine following -- strike that. The language

there about the association between atypical antipsychotics and increases in glucose levels falling on a continuum and the fact olanzapine appears to have a greater association than some other atypical antipsychotics is different from and contrary to what Lilly had been telling doctors for years; isn't that correct?

MR. KANTRA: Object to the form and foundation.

A What it's -- what it's stating is our current evaluation and medical opinion of the data that we had available to us at the time of this particular submission, what we discussed with FDA, and taking into consideration previous reviews that we have done in the past.

Q Were you aware that since at least 2000 Lilly had been claiming that rates of diabetes were comparable between the various antipsychotics?

0119

MR. KANTRA: Objection, beyond the scope.

A Yes, I am aware of it.

Q And you were aware that that claim was made beginning in 2000; correct?

A That's correct.

Q Were you aware of or informed that the company had been warned in October of 2000 by outside consultants to the company that it should not make a claim that there were comparable rates of hyperglycemia or diabetes?

MR. KANTRA: Objection to the form, mischaracterization of the either document or the testimony you're referring to.

A Yeah. I'm not aware of that specific conversation.

Q Let me see if I can help refresh your recollection. I'm going to show you what's been previously marked as Plaintiff's Exhibit 1453, which is a series of e-mails. Can I see your exhibit?

A Oh, yes.

Q I think we have some extraneous pages on there. I think it does. I think it actually ends up being a four-page document. I think that's how it's been used before.

Directing your attention to the last page of this exhibit, there's an e-mail there from Thomas

0120

Brody to Robert Baker, and I believe you said that Dr. Baker was involved at some point in time with respect to the response to the FDA; am I correct?

A Can you clarify which response to the FDA?

Q Any of the three responses to the FDA.

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A So the ones --
MR. KANTRA: New York Times?
A New York Times? Is that --
Q Right.
A Yes, he was.
Q Okay. And in this last e-mail here on this page, it says "Robert," referring to Robert Baker, "clearly, this group of endocrinologists who spoke up, I would rate those who did speak up as the leaders of the pack, are very concerned with the approach Lilly is taking towards the issue that Zyprexa leads to diabetes.
"I can only hope that you and all of the team who attended the NADAB meeting are gaining the ear of senior leadership and articulating this finding. Although, the boards recommendation is not probably not the way typically -- Lilly typically does business, I do believe they made a very strong point that unless we come clean on this, it could get much more serious than we might anticipate."

0121

Do you see that language?
A Yes.
Q Had you ever seen this e-mail before I showed it to you this morning?
MR. KANTRA: Objection to the form and beyond the scope. This doesn't relate to what she's been designated for.
A This -- yes, I have seen this.
Q When did you see it?
A As part of my involvement in the New York Times piece.
Q Okay. And was this particular e-mail provided to FDA?
A If I recall, I do believe it was.
Q Okay. If I could direct your attention to the preceding page.
A Uh-huh.
Q There is an e-mail that ends in the middle of that page that actually starts on the second page from Charles Beasley to Alan Breier with copies to Dr. Baker and other folks as well. I presume you would have seen this e-mail as well; correct?
A Yes.
Q Okay. And the last paragraph of Dr. Beasley's e-mail states "With regard to the marketing side of

0122

this issue of impaired glucose tolerance/diabetes, the message was clear. Don't get too aggressive about denial, blaming it on schizophrenia, or

claiming no worse than other agents until we are sure of the facts and sure we can convince regulators and academicians." Do you see that language?
A Yes.
Q And when you saw this e-mail for -- in connection with responding to the New York Times articles, was that the first time that you were aware that outside consultants had warned about not claiming that Zyprexa was any worse than other agents?
MR. KANTRA: Objection to the form.
Q In 2000?
A As part of my involvement in the New York Times, I was aware of this particular e-mail. I was not briefed or discussed on the overall context of what it was referring to, other than the fact that this was one of the documents that was part of the allegations so...
Q And I take it you were not aware of the facts reflected in this e-mail before 2000?
MR. KANTRA: Objection. Objection to the form.

0123

Q I take it you were not aware of the facts related in this e-mail before your involvement in the response to the New York Times article; is that a fair statement?
A Could you repeat the question?
Q Sure. Were you aware of this e-mail or the contents of the e-mail before becoming involved in the response to the New York Times query from the FDA?
A No, I was not.
Q Okay. Were you aware that between 2000 and thereafter -- strike that. Were you aware that after 2000 and for years thereafter Lilly trained its sales force to assert that the rates of hyperglycemia and diabetes were comparable between the various atypical antipsychotics?
MR. KANTRA: Objection to the form, beyond the scope.
A I'm aware that it was included in -- in materials, but the specifics I was not involved in.
Q Okay. And when you say "It was included in materials," you're referring to the "it" being an assertion of comparable rates; correct?
A That particular statement that you had mentioned before, yes.

0124

Q Okay. And when you referred to materials, you're

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referring to materials that were used by sales representatives?
A That's correct.
Q And distributing to physicians to influence their prescribing practices; correct?
MR. KANTRA: Objection to the form.
A It was included in various materials. I don't know the specifics of how they were distributed.
Q And to this day, has Lilly instructed its sales force to stop saying that rates of hyperglycemia or diabetes are comparable amongst various atypical antipsychotics?
MR. KANTRA: Objection to the form, also beyond the scope.
A I'm not aware of a specific communication related to that.
Q So as you sit here today, you're not aware of any communication to the sales force telling them not to assert that there are comparable rates of diabetes and hyperglycemia between the various atypical antipsychotics?
MR. KANTRA: Objection to the form, beyond the scope.
Q Fair statement?

0125

MR. KANTRA: I'm sorry.
Q Fair statement?
MR. KANTRA: Objection to the form, beyond to scope.
A Could you repeat that again? I'm sorry. I just --
Q I know it's hard to keep track of the question and come up with an answer when there's an objection there.
A Yeah. Sorry.
Q As you sit here today in December of 2007 --
A Correct.
Q -- you are not aware of any communications to the sales force to stop claiming that there are comparable rates; correct?
MR. KANTRA: Beyond the scope.
A That's -- that's correct. What we involve is that the sales force should use the consistency of the label, which the labeling changes that occurred this year should be part of that -- that sales material.
Q Okay. Now, we've talked about the -- the consensus statement before, which was Exhibit 2368, I believe, and I believe we established that, at least in the language of the consensus statement, there was the assertion by that statement that

0126
there was a continuum of rates of diabetes and weight gain between the various atypical antipsychotics; correct?
A They didn't use the specific word of -- of continuum. What they're outlining is, you know, based on their consensus of all the data evaluated some specifics around risk factors between the atypical antipsychotics.
Q And what they said in their summary statement, which was on page 600 of that article in the right-hand column, was that clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia and that risperidone and quetiapine appear to have intermediate effects, and then two other drugs, aripiprazole and ziprasidone, are associated with little or no significant weight gain, diabetes, or dyslipidemia; correct?
MR. KANTRA: Were you going to finish the rest of the sentence?
MR. SUGGS: I wasn't quoting it, but I can.
Q They also pointed out that those drugs have not been used as extensively as the other agents; correct?
A That's correct. That's what it states.

0127
Q Okay. So, basically, they're talking about clozapine and olanzapine having the greatest weight gain in diabetes and then other drugs having an intermediate effect and then others appearing to have little or no effect; correct?
MR. KANTRA: Objection to the form.
A It states that, but it also states within the -- kind of the totality of the -- the paper that there are various caveats that need to be taken into consideration and what additional research needs to be done.
Q And am I correct that after publication of the consensus statement it was still the position of Lilly that rates were comparable between the various antipsychotic drugs with respect to weight gain, diabetes, and hyperglycemia?
MR. KANTRA: Compound question.
Q You may answer.
A Could you repeat the questions?
Q Sure. Even after the consensus statement was published in 2004, Lilly still took the position that the rates of weight gain, diabetes, and hyperlipidemia were comparable between the various

atypical antipsychotics; correct?
A You've included various different adverse events,
0128
adverse reactions within that particular question.
Q Does that raise a problem for you? Well, let me break it up.
A Yeah.
Q After -- after the consensus statement was published in 2004, Lilly continued to assert that the rates of diabetes were comparable between the various atypical antipsychotics; correct?
A That's correct.
Q Okay. And, in fact, as you sit -- as you testified before, as you sit here today right now, you're not aware of any communications of the sales force to stop saying that rates are comparable; correct?
A I am not aware of anything specific.
Q Okay. If I could direct your attention to -- back to Exhibit 12, in particular, the part on page 3 towards the bottom of the page, which talks about olanzapine monotherapy in adults.
A Okay. Which? Page 3?
Q Uh-huh.
A Yes.
Q And on this page, bottom of page 3 and -- and over on to page 4 is the detailed information or more detailed information about hyperglycemia that FDA wanted to have in the warning section and that
0129
Lilly wanted to have back in the adverse reactions section. Is that a fair statement?
A It is what we initially proposed to put in the adverse reactions, but based on the FDA feedback, incorporated it into the warning.
Q Okay. And it makes reference to five placebo-controlled adult olanzapine monotherapy studies?
A Yes.
Q Those would be studies where olanzapine alone was -- was used as opposed to any other drug; correct?
A That's correct.
Q Okay. So that would not have included Symbyax but just olanzapine alone; correct?
A That's correct.
Q Okay. And when were those studies done?
A These studies were done -- they actually collected fasting glucose levels, and they were completed any time between 2005 until 2007.
Q Okay. And was it only because -- was it -- strike

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-520/S-012

Eli Lilly & Company
Attention: Robin Pitts Wojcieszek, R.Ph.
Associate Director, U.S. Regulatory Affairs
Lilly Corporate Center
Indianapolis, IN 46285

Dear Ms. Wojcieszek:

Please refer to your supplemental new drug application dated September 28, 2006, received September 29, 2006 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Symbyax (olanzapine/fluoxetine) 3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, and 12 mg/50 mg (mg equivalent olanzapine/mg equivalent fluoxetine) capsules.

We acknowledge receipt of your amendments dated November 8, 28, 2006, December 11, 14, 2006, and February 5, 20, 2007.

This supplemental new drug application provides for the use of Symbyax (olanzapine/fluoxetine) capsules for Treatment Resistant Depression (TRD).

We completed our review of this application, and it is approvable. Before the application may be approved, however, you must address the following issues:

Updated Information on Risks of Weight Gain, Hyperglycemia, and Hyperlipidemia

A primary concern with this application and the primary basis for our not taking a final action is our view that we lack important safety information needed to adequately update the labeling with all relevant risk information. In particular, we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine. You must fully address these concerns before we will be able to take a final action on this application.

Defining what your response will need to be to fully address these concerns will likely involve an interactive process with us over a period of several weeks, because we, first of all, need to fully understand the universe of relevant olanzapine and olanzapine/fluoxetine combination (OFC) studies and their characteristics. Once we better understand this set of studies and what data pertinent to our concerns were collected, we will be in a better position to provide detailed advice on what studies to pool, what data to provide, and what additional analyses to conduct. In characterizing these trials, it will be important to provide details on what data were collected (e.g., plasma glucose, HbA1c, total cholesterol, HDL, LDL, triglyceride, and urine glucose), under what conditions (e.g., fasting vs non-

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fasting), the demographic characteristics of the subjects (e.g., pediatric vs adult), and at what intervals. Once we have this information, we will work with you to define what studies to pool, and what data to provide to us and in what format.

Regarding data displays, an overall strategy will be to subgroup patients on the basis of their status at baseline so that clinicians can better understand the risks associated with treatment of patients falling into different risk categories. For example, we note that your proposed Symbyax label includes information only on proportions of patients who are relatively normal at baseline with regard to random blood glucose (< 140 mg/dL), i.e., 2.9% of such patients receiving OFC had on-treatment levels ≥ 200 mg/dL compared to 0.3% of placebo-treated patients. However, we note that 46% of patients who were borderline to high at baseline (140 to 200) had such on-treatment levels compared to only 5% of placebo-treated patients. This latter finding was based on a small number of patients in the OFC program, and for this reason, we would like to see such data for the entire olanzapine program. In addition, we were troubled that this important finding was not included in your proposed label. We will want you to provide similar information based on subgroupings of patients on the basis of weight and BMI (for weight change), and lipid findings for the lipid data. We will want you to provide data both on proportions of patients meeting certain on-treatment criteria and also for mean change from baseline.

If you feel you have already aggregated and submitted data to address these concerns, then we ask that you direct us to precisely which submissions these are. If, on the other hand, you have aggregated the appropriate data for your own internal purposes but not submitted them, we ask you to submit them. Your recent February 20, 2007 response to our January 12, 2007 letter regarding the New York Times story has not been particularly helpful in addressing these concerns.

Our overall goal is to improve labeling with regard to these findings so that clinicians will be better informed on what the risks are for their patients. They cannot make reasonable treatment decisions until they have such information. We do not feel that current labeling for either Symbyax or Zyprexa, provides sufficient information on these risks, and we fully intend to insure that these labels are enhanced with the best available information to characterize these risks.

Post Marketing Commitments

Long-Term Efficacy Studies

Since TRD is a chronic illness, you are required to assess the longer-term effectiveness and safety of Symbyax in TRD. Accordingly, we ask for your commitment to submit, as a Postmarketing commitment, the results of this study to evaluate Symbyax's ability to reduce the risk of relapse in acutely remitted patients with TRD. We ask that you commit to submitting these results no later than 3 years after the date of approval of this supplemental application.

Labeling

Please submit revised draft labeling for the drug. The labeling should be identical in content to the enclosed labeling text for the package insert.

In addition, all previous revisions, as reflected in the most recently approved package insert, must be included. To facilitate review of your submission, provide a highlighted or marked-up copy that shows the changes.

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If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Foreign Regulatory Update/Labeling

We require a review of the status of all Symbyax actions taken or pending before foreign regulatory authorities. Approval actions can be noted, but we ask that you describe in detail any and all actions taken that have been negative, supplying a full explanation of the views of all parties and the resolution of the matter. If Symbyax has been approved by any non-US regulatory bodies, we ask that you provide us any approved labeling for Symbyax along with English translations when needed.

Request for Safety Update and World Literature Update

When you respond to the above deficiencies, include a safety update as described at 21 CFR 314.50(d)(5)(vi)(b). The safety update should include data from all non-clinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

1. Describe in detail any significant changes or findings in the safety profile.

2. When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
   - Present new safety data from the studies for the proposed indication using the same format as the original NDA submission.
   - Present tabulations of the new safety data combined with the original NDA data.
   - Include tables that compare frequencies of adverse events in the original NDA with the retabulated frequencies described in the bullet above.
   - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.

3. Present a retabulation of the reasons for premature study discontinuation by incorporating the drop-outs from the newly completed studies. Describe any new trends or patterns identified.

4. Provide case report forms and narrative summaries for each patient who died during a clinical study or who did not complete a study because of an adverse event. In addition, provide narrative summaries for serious adverse events.

5. Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original NDA data.

6. Prior to an approval action, we require an updated report on the world's archival literature pertaining to the safety of Symbyax. Please provide a summary of worldwide experience on the safety of this drug. Include an updated estimate of use for drug marketed in other countries. This report should include only literature not covered in your previous submissions. We will need your warrant that you have reviewed this literature systematically, and in detail, and that you have discovered no finding that would adversely affect conclusions about the safety of Symbyax. The report should also detail how the literature search was conducted, by whom (their credentials) and whether it relied on abstracts or full texts (including translations) of

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articles. The report should emphasize clinical data, but new findings in preclinical reports of potential significance should also be described. Should any report or finding be judged important, a copy (translated as required) should be submitted for our review.

Promotional Materials

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with the Division of Psychiatry Products to discuss what further steps need to be taken before the application may be approved.

If you have any questions, call LCDR Reuneet Grewal, Pharm.D., Regulatory Project Manager, at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

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This version of labeling is based up on the version submitted with the application. We have used track changes to indicate our additions and deletions. We have added bracketed comments to explain our actions where needed.]

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Symbyax safely and effectively. See full prescribing information for Symbyax.

SYMBYAX® (olanzapine and fluoxetine HCl capsules) for oral administration
Initial U.S. Approval: 2003

WARNING

See full prescribing information for complete boxed warning.

SUICIDALITY IN CHILDREN AND ADOLESCENTS:

- Increased risk of suicidal thinking and behavior in children and adolescents taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders. Not approved for use in children and adolescents.

INCREASED MORTALITY IN ELDERLY PATIENTS:

- Increased mortality in elderly patients with dementia-related psychosis compared to placebo. Not approved for the treatment of patients with dementia-related psychosis.

~~SUICIDALITY IN CHILDREN AND ADOLESCENTS:~~

- ~~Increased risk of suicidal thinking and behavior in children and adolescents taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders. Not approved for use in children and adolescents.~~

RECENT MAJOR CHANGES

~~Warnings and Precautions, Mortality in patients with dementia-related psychosis (5.3)~~	~~10/2005~~
Contraindications, Pimozide (4)	1/2006
Warnings and Precautions, Hepatobiliary events (5.14)	4/2006
Warnings and Precautions, Serotonin Syndrome (5.8)	8/2006

Warnings and Precautions, Weight Gain
Warnings and Precautions, Risk of Chronic Overmedication
Warnings and Precautions, Hyperlipidemia

INDICATIONS AND USAGE

SYMBYAX combines olanzapine, a psychotropic agent belonging to the thienobenzodiazepine class, and fluoxetine, a selective serotonin reuptake inhibitor, indicated for treatment of:

- Depressive episodes associated with bipolar disorder (1.1)
- Treatment Resistant Depression (major depressive disorder in patients who do not respond to 2 antidepressants of adequate dose and duration in the current episode) (1.2)

DOSAGE AND ADMINISTRATION

- Once daily in the evening, generally beginning with 6 mg/25 mg (2)
- Exercise dose cautiously in patients predisposed to hypotensive reactions, hepatic impairment, or with potential for slowed metabolism (2.3)
- Discontinue gradually (2.4)
- The safety of doses above 18 mg olanzapine with 75 mg fluoxetine had not been evaluated in clinical trials.

DOSAGE FORMS AND STRENGTHS

- Capsules: 3 mg/25 mg, 6 mg/25 mg, 6 mg/50 mg, 12 mg/25 mg, and 12 mg/50 mg (mg equivalent olanzapine/mg equivalent fluoxetine) (3)

CONTRAINDICATIONS

- Do not use with an MAOI or within 14 days of discontinuing an MAOI. At least 5 weeks should be allowed after stopping SYMBYAX before starting treatment with an MAOI (4, 7.13)
- Do not use with Pimozide (4, 7.15)
- Do not use with Thioridazine. Do not use Thioridazine within 5 weeks of discontinuing SYMBYAX (4, 7.18)

WARNINGS AND PRECAUTIONS

- Patients should be monitored for clinical worsening and suicidal thinking and behavior (5.2)
- Cerebrovascular adverse events including fatalities were reported more commonly with olanzapine than placebo in trials of elderly patients with dementia-related psychosis (5.3)
- Neuroleptic Malignant Syndrome has been reported with atypical antipsychotics (5.4)

[See Approvable Letter for information requested for hyperkinetic syntax.]

- Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients taking atypical antipsychotics, including olanzapine alone as well as olanzapine taken concomitantly with fluoxetine. Diabetic patients should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes should undergo fasting blood glucose testing at the beginning of and periodically during treatment. Monitor all patients for symptoms of hyperglycemia. (5.5)
- Hypertriglyceridemia (Insert empirewise warning here, per Approvable Letter.)

Clinically significant weight gain may occur.

- Serotonin Syndrome may occur with SYMBYAX (5.6)
- Discontinue upon appearance of rash or allergic phenomena (5.7)
- Screen for bipolar disorder and monitor for mania/hypomania (5.8)
- Screen for tardive dyskinesia and monitor for development (5.9)
- Tardive Dyskinesia may develop acutely or chronically (5.9)
- Orthostatic hypotension associated with dizziness, tachycardia, bradycardia, and in some patients, syncope may occur, especially during initial dose titration. Use caution in patients with cardiovascular disease, cerebrovascular disease, and those conditions that could affect hemodynamic responses (5.10)
- Use cautiously in patients at risk for aspiration pneumonia due to esophageal dysmotility (5.11)
- Use cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold (5.12)

Clinically significant weight gain may occur (5.13)

- Asymptomatic elevations of hepatic transaminases and alkaline phosphatase have been observed with olanzapine. Periodic assessment recommended in patients with hepatic disease (5.14)
- May increase the risk of bleeding. Use with NSAIDs or drugs that affect coagulation may potentiate the risk of gastrointestinal or other bleeding (5.15)
- Hyponatremia (some cases with serum sodium lower than 110 mmol/L) possibly associated with the syndrome of inappropriate antidiuretic hormone (SIADH) have been reported with fluoxetine (5.16)
- Has potential to impair judgment, thinking, and motor skills (5.17)
- May disrupt temperature regulation (5.18)
- Due to anticholinergic activity, use with caution in patients with clinically significant prostatic hypertrophy, narrow angle glaucoma, or a history of paralytic ileus or related conditions (5.19)
- Use a lower dose in patients with cirrhosis (5.19)
- May elevate prolactin levels (5.20)
- Use caution when prescribing with other products containing olanzapine, and/or fluoxetine as active ingredients (i.e., Zyprexa, Prozac, Sarafem) (5.21)
- Fluoxetine has a long elimination half-life (5.22)
- Monitor when discontinuing treatment since discontinuation symptoms may occur (5.23)

ADVERSE REACTIONS

Most common adverse events (≥5% and at least twice that for placebo) are disturbance in attention, dry mouth, fatigue, hypersomnia, increased appetite, peripheral edema, sedation, somnolence, tremor, vision blurred, and weight increased (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Lilly at 1-800-545-5979 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Antihypertensives – enhanced antihypertensive effect (7.1)
- Anti-Parkinsonian – may antagonize levodopa/dopamine agonists (7.2)

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- Benzodiazepines – may potentiate orthostatic hypotension and sedation (7.3)
- Carbamazepine – potential for elevated carbamazepine levels (7.5)
- Clozapine – may elevate Clozapine levels (7.6) .
- CNS Acting Drugs – caution should be used when taken in combination with other centrally acting drugs and alcohol (7.7)
- Ethanol – may potentiate sedation and orthostatic hypotension (7.9)
- Fluvoxamine – may double olanzapine levels (7.10)
- Haloperidol – elevated haloperidol levels have been observed (7.11)
- Lithium – monitor lithium levels (7.12)
- Phenytoin – potential for elevated phenytoin levels (7.14)
- Serotonergic drugs – potential for Serotonin Syndrome (5.6, 7.16, 7.20)
- Tricyclic antidepressants (TCAs) – monitor TCA levels (7.19)
- Warfarin – increase monitoring with SYMBYAX dose changes (7.23)
- Drugs that interfere with hemostasis (NSAIDs, aspirin, warfarin, etc.) may potentiate the risk of bleeding (7.24)
- Fluoxetine is an inhibitor of CYP450 2D6 enzyme pathway (7.25)
- Drugs tightly bound to plasma proteins, may cause shift in plasma concentrations (7.29)

USE IN SPECIFIC POPULATIONS

- Pregnancy: SYMBYAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (8.1)
- Nursing mothers, breast feeding is not recommended (8.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: [9/2006] (BNL5613AMP)

MAR 2 8 2007
G. Brophy

FULL PRESCRIBING INFORMATION: CONTENTS*

[Section references to be given must be re-entered to reflect changes, both here and in the body of the document.]

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FULL PRESCRIBING INFORMATION

WARNING

~~Suicidality in Children and Adolescents — Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of SYMBYAX or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. SYMBYAX is not approved for use in pediatric patients. *[See Warnings and Precautions (5.2) and Use in Specific Populations (8.4)].*~~

~~Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials. *[See Warnings and Precautions (5.2)].*~~

~~Increased Mortality in Elderly Patients — Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature. SYMBYAX (olanzapine and fluoxetine HCl) is not approved for the treatment of patients with dementia-related psychosis *[see Warnings and Precautions (5.1)]*.~~

~~Suicidality in Children and Adolescents — Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of SYMBYAX or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. SYMBYAX is not approved for use in pediatric patients. *[See Warnings and Precautions (5.2) and Use in Specific Populations (8.4)].*~~

~~Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. No suicides occurred in these trials. *[See Warnings and Precautions (5.2)].*~~

1 INDICATIONS AND USAGE

1.1 Bipolar Depression

SYMBYAX is indicated for the treatment of depressive episodes associated with bipolar disorder.

Unlike with unipolar depression, there are no established guidelines for the length of time patients with bipolar disorder experiencing a major depressive episode should be treated with agents containing antidepressant drugs.

The effectiveness of SYMBYAX for maintaining antidepressant response in this patient population beyond 8 weeks has not been established in controlled clinical studies. Physicians who elect to use SYMBYAX for extended periods should periodically reevaluate the benefits and long-term risks of the drug for the individual patient.

1.2 Treatment Resistant Depression

SYMBYAX is indicated for treatment resistant depression (major depressive disorder in patients who do not respond to 2 antidepressants of adequate dose and duration in the current episode) *[see Clinical Studies (14.2)]*.

The effectiveness of SYMBYAX for maintaining antidepressant response in this patient population beyond 8 weeks has not been established in controlled clinical studies. Physicians who elect to use SYMBYAX for extended periods should periodically reevaluate the benefits and long-term risks of the drug for the individual patient.

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2 DOSAGE AND ADMINISTRATION

2.1 Bipolar Depression

SYMBYAX should be administered once daily in the evening, generally beginning with the 6-mg/25-mg capsule. While food has no appreciable effect on the absorption of olanzapine and fluoxetine given individually, the effect of food on the absorption of SYMBYAX has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with SYMBYAX in a dose range of olanzapine 6 to 12 mg and fluoxetine 25 to 50 mg *[see Clinical Studies (14)]*.

The safety of doses above 18 mg/75 mg has not been evaluated in clinical studies.

2.2 Treatment Resistant Depression

SYMBYAX should be administered once daily in the evening, generally beginning with the 6-mg/25-mg capsule. While food has no appreciable effect on the absorption of olanzapine and fluoxetine given individually, the effect of food on the absorption of SYMBYAX has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with SYMBYAX in a dose range of olanzapine 6 to 18 mg and fluoxetine 25 to 50 mg *[see Clinical Studies (14)]*. The safety of doses above 18 mg/75 mg has not been evaluated in clinical studies.

2.3 Special Populations

The starting dose of SYMBYAX 3 mg/25 - 6 mg/25 mg should be used for patients with a predisposition to hypotensive reactions, patients with hepatic impairment, or patients who exhibit a combination of factors that may slow the metabolism of SYMBYAX (female gender, geriatric age, nonsmoking status) or those patients who may be pharmacodynamically sensitive to olanzapine. When indicated, dose escalation should be performed with caution in these patients. SYMBYAX has not been systematically studied in patients over 65 years of age or in patients <18 years of age *[see Warnings and Precautions (5.19), Use in Specific Populations (8.4 and 8.5), and Clinical Pharmacology (12.3)]*.

2.4 Discontinuation of Treatment with SYMBYAX

Symptoms associated with discontinuation of fluoxetine, a component of SYMBYAX, and other SSRIs and SNRIs, have been reported *[see Warnings and Precautions (5.23)]*.

3 DOSAGE FORM AND STRENGTHS

Capsules (mg equivalent olanzapine/mg equivalent fluoxetine):

- 3 mg/25 mg
- 6 mg/25 mg
- 6 mg/50 mg
- 12 mg/25 mg
- 12 mg/50 mg

4 CONTRAINDICATIONS

The use of SYMBYAX is contraindicated with the following:

- Monoamine Oxidase Inhibitors (MAOI) — *[see Drug Interactions (7.13)]*
- Pimozide — *[see Drug Interactions (7.15)]*
- Thioridazine — *[see Drug Interactions (7.18)]*

5 WARNINGS AND PRECAUTIONS

5.1 Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. SYMBYAX is not approved for the treatment of patients with dementia-related psychosis *(see Box Warning)*.

In olanzapine placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs 1.5%, respectively).

5.2 Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. There has been a long-standing concern that

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antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients.

Antidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders.

Pooled analyses of short-term placebo-controlled trials of 9 antidepressant drugs (SSRIs and others) in children and adolescents with MDD, OCD, or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal behavior or thinking (suicidality) during the first few months of treatment in those receiving antidepressants. The average risk of such events in patients receiving antidepressants was 4%, twice the placebo risk of 2%. There was considerable variation in risk among drugs, but a tendency toward an increase for almost all drugs studied. The risk of suicidality was most consistently observed in the MDD trials, but there were signals of risk arising from some trials in other psychiatric indications (obsessive compulsive disorder and social anxiety disorder) as well. No suicides occurred in any of these trials. It is unknown whether the suicidality risk in pediatric patients extends to longer-term use, i.e., beyond several months. It is also unknown whether the suicidality risk extends to adults.

All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. Such observation would generally include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks of treatment, then every other week visits for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks. Additional contact by telephone may be appropriate between face-to-face visits.

Adults with MDD or co-morbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed similarly for clinical worsening and suicidality, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms *(see Warnings and Precautions (5.2) and Dosage and Administration (2.4)*, for a description of the risks of discontinuation of SYMBYAX).

Families and caregivers of pediatric patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for SYMBYAX should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose. Families and caregivers of adults being treated for depression should be similarly advised.

It should be noted that SYMBYAX is not approved for use in treating any indications in the pediatric population.

5.3 Cerebrovascular Adverse Events (CVAE), Including Stroke, in Elderly Patients with Dementia-Related Psychosis

Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with olanzapine compared to patients treated with placebo. Olanzapine and SYMBYAX are not approved for the treatment of patients with dementia-related psychosis.

5.4 Neuroleptic Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as NMS has been reported in association with administration of antipsychotic drugs, including olanzapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or

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inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

If after recovering from NMS, a patient requires treatment with an antipsychotic, the patient should be carefully monitored, since recurrences of NMS have been reported.

[As noted above, we have requested additional information on treating patients with hyperglycemia in the Approvable Letter. Section 5.5 will be modified when we have reviewed the requested information. We have also grouped hyperglycemia, hyperlipidemia, and weight gain together (see Full Prescribing Contents section and order the appropriate sections below to correspond to these changes.)]

5.5 Hyperglycemia and Diabetes Mellitus

Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including olanzapine alone, as well as olanzapine taken concomitantly with fluoxetine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

5.6 Serotonin Syndrome

The development of a potentially life-threatening serotonin syndrome may occur with SYMBYAX, particularly with concomitant use of serotonergic drugs (including triptans) and with drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of SYMBYAX with MAOIs intended to treat depression is contraindicated *[see Contraindications (4) and Drug Interactions (7.13)]*.

If concomitant treatment of SYMBYAX with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases *[see Drug Interactions (7.19)]*.

The concomitant use of SYMBYAX with serotonin precursors (such as tryptophan) is not recommended *[see Drug Interactions (7.20)]*.

5.7 Allergic Events and Rash

In SYMBYAX premarketing controlled clinical studies, the overall incidence of rash or allergic events in SYMBYAX-treated patients [4.6% (26/571)] was similar to that of placebo [5.2% (25/477)]. The majority of the cases of rash and/or urticaria were mild; however, three patients discontinued (one due to rash, which was moderate in severity and two due to allergic events, one of which included face edema).

In fluoxetine US clinical studies, 7% of 10,782 fluoxetine-treated patients developed various types of rashes and/or urticaria. Among the cases of rash and/or urticaria reported in premarketing clinical studies, almost a third were withdrawn from treatment because of the rash and/or systemic signs or symptoms associated with the rash. Clinical findings reported in association with rash include fever, leukocytosis, arthralgias, edema, carpal tunnel syndrome, respiratory distress, lymphadenopathy, proteinuria, and mild transaminase elevation. Most patients improved promptly with discontinuation of fluoxetine and/or adjunctive treatment with antihistamines or steroids, and all patients experiencing these events were reported to recover completely.

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In fluoxetine premarketing clinical studies, 2 patients are known to have developed a serious cutaneous systemic illness. In neither patient was there an unequivocal diagnosis, but 1 was considered to have a leukocytoclastic vasculitis, and the other, a severe desquamating syndrome that was considered variously to be a vasculitis or erythema multiforme. Other patients have had systemic syndromes suggestive of serum sickness.

Since the introduction of fluoxetine, systemic events, possibly related to vasculitis, have developed in patients with rash. Although these events are rare, they may be serious, involving the lung, kidney, or liver. Death has been reported to occur in association with these systemic events.

Anaphylactoid events, including bronchospasm, angioedema, and urticaria alone and in combination, have been reported.

Pulmonary events, including inflammatory processes of varying histopathology and/or fibrosis, have been reported rarely. These events have occurred with dyspnea as the only preceding symptom.

Whether these systemic events and rash have a common underlying cause or are due to different etiologies or pathogenic processes is not known. Furthermore, a specific underlying immunologic basis for these events has not been identified. Upon the appearance of rash or of other possible allergic phenomena for which an alternative etiology cannot be identified, SYMBYAX should be discontinued.

5.8 **Screening Patients for Bipolar Disorder and Monitor for Mania/Hypomania**

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described for clinical worsening and suicide risk represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that SYMBYAX is approved for use in treating bipolar depression.

In the two controlled bipolar depression studies there was no statistically significant difference in the incidence of manic events (manic reaction or manic depressive reaction) between SYMBYAX- and placebo-treated patients. In one of the studies, the incidence of manic events was (7% [3/43]) in SYMBYAX-treated patients compared to (3% [5/184]) in placebo-treated patients. In the other study, the incidence of manic events was (2% [1/43]) in SYMBYAX-treated patients compared to (8% [15/193]) in placebo-treated patients. This limited controlled trial experience of SYMBYAX in the treatment of bipolar depression makes it difficult to interpret these findings until additional data is obtained. Because of this and the cyclical nature of bipolar disorder, patients should be monitored closely for the development of symptoms of mania/hypomania during treatment with SYMBYAX.

5.9 **Tardive Dyskinesia**

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses or may even arise after discontinuation of treatment.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

The incidence of dyskinetic movement in SYMBYAX-treated patients was infrequent. The mean score on the Abnormal Involuntary Movement Scale (AIMS) in the SYMBYAX-controlled database across clinical studies involving SYMBYAX-treated patients decreased from baseline. Nonetheless, SYMBYAX should be prescribed in a manner that is most likely to minimize the risk of tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear in a patient on SYMBYAX, drug discontinuation should be considered. However, some patients may require treatment with SYMBYAX despite the presence of the syndrome. The need for continued treatment should be reassessed periodically.

5.10 **Orthostatic Hypotension**

SYMBYAX may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia, and in some patients, syncope, especially during the initial dose-titration period.

In the SYMBYAX-controlled clinical trials across all indications, there were no significant differences between SYMBYAX-treated patients and olanzapine, fluoxetine or placebo-treated patients in exposure adjusted rates of orthostatic systolic blood pressure

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decreases of at least 30 mm Hg. Orthostatic syncope blood pressure decreases of at least 30 mm Hg occurred in 4.0% (28/705), 2.3% (19/831), 4.5% (18/399), and 1.8% (8/442) of the SYMBYAX, olanzapine, fluoxetine, and placebo groups, respectively. In this group of studies, the incidence of syncope-related adverse events (i.e., syncope and/or loss of consciousness) in SYMBYAX-treated patients was 0.4% (3/771) compared to placebo 0.2% (1/477).

In a clinical pharmacology study of SYMBYAX, three healthy subjects were discontinued from the trial after experiencing severe, but self-limited, hypotension and bradycardia that occurred 2 to 9 hours following a single 12-mg/50-mg dose of SYMBYAX. Reactions consisting of this combination of hypotension and bradycardia (and also accompanied by sinus pause) have been observed in at least three other healthy subjects treated with various formulations of olanzapine (one oral, two intramuscular). In controlled clinical studies, the incidence of patients with a ≥20 bpm decrease in orthostatic pulse concomitantly with a ≥20 mm Hg decrease in orthostatic systolic blood pressure was 0.3% (2/706) in the SYMBYAX group, 0.2% (1/445) in the placebo group, 0.7% (6/837) in the olanzapine group, and 0% (0/404) in the fluoxetine group.

SYMBYAX should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, or conditions that would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications).

5.11 Dysphagia

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's disease. Olanzapine and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

5.12 Seizures

Seizures occurred in 0.2% (4/2547) of SYMBYAX-treated patients during open-label clinical studies. No seizures occurred in the controlled SYMBYAX studies. Seizures have also been reported with both olanzapine and fluoxetine monotherapy. SYMBYAX should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold. Conditions that lower the seizure threshold may be more prevalent in a population of ≥65 years of age.

[As noted, we will want the Weight Section revised with new requested information and moved to be adjacent to the hyperglycemia and hyperlipidemia sections.]

5.13 Weight Gain

In clinical studies, the mean weight increase for SYMBYAX-treated patients after 8 weeks of treatment was statistically significantly greater than placebo-treated (4.3 kg vs -0.2 kg) and fluoxetine-treated (4.3 kg vs -0.2 kg) patients, but was not statistically significantly different from olanzapine-treated patients (4.3 kg vs 4.1 kg). Thirty-five percent of SYMBYAX-treated patients met criterion for having gained >7% of their baseline weight. This was statistically significantly greater than placebo-treated (3%) and fluoxetine-treated patients (3%) but was not statistically significantly different than olanzapine-treated patients (31%).

5.14 Transaminase Elevations

As with olanzapine, asymptomatic elevations of hepatic transaminases [ALT (SGPT), AST (SGOT), and GGT] and alkaline phosphatase have been observed with SYMBYAX. In the SYMBYAX-controlled database, ALT (SGPT) elevations (normal baseline and ≥3 times the upper limit of the normal range post-baseline) were observed in 3.4% (20/586) of patients exposed to SYMBYAX compared with none of the 342 placebo patients and 3.5% (23/665) of olanzapine-treated patients. The difference between SYMBYAX and placebo was statistically significant. Of the SYMBYAX patients who started normal at baseline and had increases in ALT ≥5 times the upper limit of normal range, none experienced jaundice and four had transient elevations >200 IU/L. ~~In the premarketing SYMBYAX controlled database, ALT (SGPT) elevations (≥3 times the upper limit of the normal range) were observed in 6.3% (31/495) of patients exposed to SYMBYAX compared with 0.5% (3/384) of the placebo patients and 1.5% (25/560) of olanzapine-treated patients [see Adverse Reactions (6.1)].~~

In olanzapine placebo-controlled studies, clinically significant ALT (SGPT) elevations (≥3 times the upper limit of the normal range) were observed in 2% (6/243) of patients exposed to olanzapine compared with 0% (0/115) of the placebo patients. None of these patients experienced jaundice. In 2 of these patients, liver enzymes decreased toward normal despite continued treatment, and in 2 others, enzymes decreased upon discontinuation of olanzapine. In the remaining 2 patients, 1, seropositive for hepatitis C, had persistent enzyme elevations for 4 months after discontinuation, and the other had insufficient follow-up to determine if enzymes normalized.

Within the larger olanzapine premarketing database of about 2400 patients with baseline SGPT ≤90 IU/L, the incidence of SGPT elevation to >200 IU/L was 2% (50/2381). Again, none of these patients experienced jaundice or other symptoms attributable to liver impairment and most had transient changes that tended to normalize while olanzapine treatment was continued. Among all 2500 patients in olanzapine clinical studies, approximately 1% (23/2500) discontinued treatment due to transaminase increases.

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Rare postmarketing reports of hepatitis have been received. Very rare cases of cholestatic or mixed liver injury have also been reported in the postmarketing period.

Caution should be exercised in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic drugs. Periodic assessment of transaminases is recommended in patients with significant hepatic disease *[see Warnings and Precautions (5.24)]*.

5.15 Abnormal Bleeding

Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two studies, concurrent use of a nonsteroidal anti-inflammatory drug (NSAID) or aspirin potentiated the risk of bleeding *[see Drug Interactions (7.23, 7.24)]*. Although these studies focused on upper gastrointestinal bleeding, there is reason to believe that bleeding at other sites may be similarly potentiated. Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of SYMBYAX with NSAIDs, aspirin, or other drugs that affect coagulation.

5.16 Hyponatremia

Hyponatremia has been observed in SYMBYAX premarketing clinical studies. In controlled trials, no SYMBYAX-treated patients had a treatment-emergent serum sodium below 129 mmol/L; however, a lowering of serum sodium below the reference range occurred at an incidence of 1.6% (11/693) of SYMBYAX-treated patients compared with 0.5% (2/380) of placebo patients. This difference was not statistically significant. In open label studies, 0.0% (1/2376) of these SYMBYAX-treated patients had a treatment-emergent serum sodium below 129 mmol/L.

Cases of hyponatremia (some with serum sodium lower than 110 mmol/L) have been reported with fluoxetine. The hyponatremia appeared to be reversible when fluoxetine was discontinued. Although these cases were complex with varying possible etiologies, some were possibly due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The majority of these occurrences have been in older patients and in patients taking diuretics or who were otherwise volume depleted. In two 6-week controlled studies in patients ≥60 years of age, 10 of 323 fluoxetine patients and 6 of 327 placebo recipients had a lowering of serum sodium below the reference range; this difference was not statistically significant. The lowest observed concentration was 129 mmol/L. The observed decreases were not clinically significant.

5.17 Cognitive and Motor Impairment

Sedation-related adverse events were commonly reported with SYMBYAX treatment occurring at an incidence of 26.6% in SYMBYAX-treated patients compared with 10.9% in placebo-treated patients. Sedation-related adverse events (sedation, somnolence, hypersomnia, and lethargy) led to discontinuation in 2% (15/771) of patients in the controlled clinical studies. As with any CNS-active drug, SYMBYAX has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that SYMBYAX therapy does not affect them adversely.

5.18 Body Temperature Regulation

Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic drugs. Appropriate care is advised when prescribing SYMBYAX for patients who will be experiencing conditions which may contribute to an elevation in core body temperature (e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration).

5.19 Use in Patients with Concomitant Illness

Clinical experience with SYMBYAX in patients with concomitant systemic illnesses is limited *[see Clinical Pharmacology (12.4)]*. The following precautions for the individual components may be applicable to SYMBYAX.

Olanzapine exhibits in vitro muscarinic receptor affinity. In premarketing clinical studies, SYMBYAX was associated with constipation, dry mouth, and tachycardia, all adverse events possibly related to cholinergic antagonism. Such adverse events were not often the basis for study discontinuations; SYMBYAX should be used with caution in patients with clinically significant prostatic hypertrophy, narrow angle glaucoma, a history of paralytic ileus, or related conditions.

In five placebo-controlled studies of olanzapine in elderly patients with dementia-related psychosis (n=1184), the following treatment-emergent adverse events were reported in olanzapine-treated patients at an incidence of at least 2% and significantly greater than placebo-treated patients: falls, somnolence, peripheral edema, abnormal gait, urinary incontinence, lethargy, increased weight, asthenia, pyrexia, pneumonia, dry mouth and visual hallucinations. The rate of discontinuation due to adverse events was significantly greater with olanzapine than placebo (13% vs 7%). Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

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If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised *[see Box Warning and Warnings and Precautions (5.1)]*.

As with other CNS-active drugs, SYMBYAX should be used with caution in elderly patients with dementia. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised *[see Box Warning and Warnings and Precautions (5.1)]*.

SYMBYAX has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from clinical studies during the premarket testing.

Caution is advised when using SYMBYAX in cardiac patients and in patients with diseases or conditions that could affect hemodynamic responses *[see Warnings and Precautions (5.10)]*.

In subjects with cirrhosis of the liver, the clearances of fluoxetine and its active metabolite, norfluoxetine, were decreased, thus increasing the elimination half-lives of these substances. A lower dose of the fluoxetine-component of SYMBYAX should be used in patients with cirrhosis. Caution is advised when using SYMBYAX in patients with diseases or conditions that could affect its metabolism *[see Clinical Pharmacology (12.4) and Dosage and Administration (2.3)]*.

Olanzapine and fluoxetine individual pharmacokinetics do not differ significantly in patients with renal impairment. SYMBYAX dosing adjustment based upon renal impairment is not routinely required *[see Clinical Pharmacology (12.4)]*.

5.20 Hyperprolactinemia

As with other drugs that antagonize dopamine D_2 receptors, SYMBYAX elevates prolactin levels, and a modest elevation persists during administration; however, possibly associated clinical manifestations (e.g., galactorrhea and breast enlargement) were infrequently observed.

Tissue culture experiments indicate that approximately one-third of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in a patient with previously detected breast cancer of this type. Although disturbances such as galactorrhea, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds, the clinical significance of elevated serum prolactin levels is unknown for most patients. As is common with compounds that increase prolactin release, an increase in mammary gland neoplasia was observed in the olanzapine carcinogenicity studies conducted in mice and rats *[see Nonclinical Toxicology (13.1)]*. However, neither clinical studies nor epidemiologic studies have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive.

5.21 Concomitant Use of Olanzapine and Fluoxetine Products

SYMBYAX contains the same active ingredients that are in Zyprexa and Zyprexa Zydis (olanzapine) and in Prozac, Prozac Weekly, and Sarafem (fluoxetine HCl). Caution should be exercised when prescribing these medications concomitantly with SYMBYAX *[see Overdosage (10)]*.

5.22 Long Half-Life of Fluoxetine

Because of the long elimination half-lives of fluoxetine and its major active metabolite, changes in dose will not be fully reflected in plasma for several weeks, affecting both strategies for titration to final dose and withdrawal from treatment *[see Clinical Pharmacology (12.3)]*.

5.23 Discontinuation of Treatment with SYMBYAX

During marketing of fluoxetine, a component of SYMBYAX, and other SSRIs and SNRIs (serotonin and norepinephrine reuptake inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional lability, insomnia, and hypomania. While these events are generally self-limiting, there have been reports of serious discontinuation symptoms. Patients should be monitored for these symptoms when discontinuing treatment with fluoxetine. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate. Plasma fluoxetine and norfluoxetine concentration decrease gradually at the conclusion of therapy, which may minimize the risk of discontinuation symptoms with this drug *[see Dosage and Administration (2.4)]*.

5.24 Laboratory Tests

Periodic assessment of transaminases is recommended in patients with significant hepatic disease *[see Warnings and Precautions, 5.14)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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The information below is derived from a clinical study database for SYMBYAX consisting of 2547 patients with treatment resistant depression, bipolar depression, major depressive disorder with psychosis, or sexual dysfunction with approximately 1085 patient-years of exposure. The conditions and duration of treatment with SYMBYAX varied greatly and included (in overlapping categories) open-label and double-blind phases of studies, inpatients and outpatients, fixed-dose and dose-titration studies, and short-term or long-term exposure.

Adverse events were recorded by clinical investigators using descriptive terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a limited (i.e., reduced) number of standardized event categories.

In the tables and tabulations that follow, MedDRA or COSTART Dictionary terminology has been used to classify reported adverse events. The data in the tables represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. It is possible that events reported during therapy were not necessarily related to drug exposure.

The prescriber should be aware that the figures in the tables and tabulations cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical studies. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing clinician with some basis for estimating the relative contribution of drug and non-drug factors to the side effect incidence rate in the population studied.

Incidence in Controlled Clinical Studies

The following findings are based on the short-term, controlled studies including bipolar depression and treatment resistant depression.

Adverse events associated with discontinuation of treatment — Overall, 11.3% of the 771 patients in the SYMBYAX group discontinued due to adverse events compared with 4.4% of the 477 patients for placebo. Adverse events leading to discontinuation associated with the use of SYMBYAX (incidence of at least 1% for SYMBYAX and greater than that for placebo) using MedDRA Dictionary coding were weight increased (2%) and sedation (1%) versus placebo patients which had 0% incidence of weight increased and sedation.

Commonly observed adverse events in controlled clinical studies — The most commonly observed adverse events associated with the use of SYMBYAX (incidence ≥5% and at least twice that for placebo in the SYMBYAX-controlled database) using MedDRA Dictionary coding were: disturbance in attention, dry mouth, fatigue, hypersomnia, increased appetite, peripheral edema, sedation, somnolence, tremor, vision blurred and weight increased. Adverse events reported in clinical trials of olanzapine/fluoxetine in combination are generally consistent with treatment-emergent adverse events during olanzapine or fluoxetine monotherapy.

Adverse events occurring at an incidence of 2% or more in short-term controlled clinical studies — Table 1 enumerates the treatment-emergent adverse events associated with the use of SYMBYAX (incidence of at least 2% for SYMBYAX and twice or more than for placebo). The SYMBYAX-controlled column includes patients with various diagnoses while the placebo column includes only patients with bipolar depression and major depression with psychotic features.

Table 1: Treatment-Emergent Adverse Events: Incidence in Controlled Clinical Studies

System Organ Class	Adverse Event	Percentage of Patients Reporting Event	
		SYMBYAX-Controlled (N=771)	Placebo (N=477)
Eye disorders	Vision blurred	5	2
Gastrointestinal disorders	Dry mouth	15	6
	Flatulence	3	1
	Abdominal distension	2	0
General disorders and administration site conditions	Fatigue	12	2
	Edema peripheral	9	0
	Edema	3	0
	Asthenia	3	1
	Pain	2	1

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	Pyrexia	2	1
Infections and infestations	Sinusitis	2	1
Investigations	Weight increased	25	3
Metabolism and nutrition disorders	Increased appetite	20	4
Musculoskeletal and connective tissue disorders	Arthralgia	4	1
	Pain in extremity	3	1
	Musculoskeletal stiffness	2	1
Nervous system disorders	Somnolence	14	6
	Tremor	9	3
	Sedation	8	4
	Hypersomnia	5	1
	Disturbance in attention	5	1
	Lethargy	3	1
Psychiatric disorders	Restlessness	4	1
	Thinking abnormal	2	1
	Nervousness	2	1
Reproductive system and breast disorders	Erectile dysfunction	2	1

Additional Findings Observed in Clinical Studies

Effect on cardiac repolarization — The mean increase in QT_c interval for SYMBYAX-treated patients (4.4 msec) in clinical studies was significantly greater than that for placebo-treated (-0.8 msec), olanzapine-treated (-0.3 msec) patients, and fluoxetine-treated (1.7 msec) patients. There were no significant differences between patients treated with SYMBYAX, placebo, olanzapine, or fluoxetine in the incidence of QT_c outliers (>500 msec).

[As discussed above, we intend to move and group together data relevant to treatment-emergent hyperglycemia, hyperlipidemia, and weight gain to Warnings/Precautions. In addition, the information in these sections will need to be revised to include new information based on requested new data searches and analyses.]

Laboratory changes — In SYMBYAX clinical studies, (including treatment resistant depression, bipolar depression, major depressive disorder with psychosis, or sexual dysfunction) SYMBYAX was associated with statistically significantly greater frequencies for the following treatment-emergent findings in laboratory analytes (normal at baseline to abnormal at any time during the trial) compared to placebo: elevated random blood glucose levels of ≥200 mg/dL in patients with levels of <140 mg/dL at baseline (2.9% vs. 0.3%); elevated random cholesterol ≥240 mg/dL in patients with levels of <200 mg/dL at baseline (9.7% vs. 1.9%); elevated prolactin (27.6% vs. 4.8%); elevated urea nitrogen (2.8% vs. 0.8%); elevated uric acid (2.9% vs. 0.3%); low albumin (2.7% vs. 0.3%); low bicarbonate (14.1% vs. 8.8%); low hemoglobin (2.6% vs. 0%); low inorganic phosphorus (1.9% vs. 0.3%); low lymphocytes (1.9% vs. 0%); and low total bilirubin (15.3% vs. 3.9%).

In olanzapine clinical studies among olanzapine-treated patients with random triglyceride levels of <150 mg/dL at baseline (N=659), 0.5% of patients experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean increase of 20 mg/dL in triglycerides from a mean baseline value of 175 mg/dL.

Sexual dysfunction — In the pool of controlled SYMBYAX studies in patients with bipolar depression, there were higher rates of the treatment-emergent adverse events decreased libido, anorgasmia, impotence and abnormal ejaculation in the SYMBYAX group than in the placebo group. One case of decreased libido led to discontinuation in the SYMBYAX group. In the controlled studies that contained a fluoxetine arm, the rates of decreased libido and abnormal ejaculation in the SYMBYAX group were less than the rates in the fluoxetine group. None of the differences were statistically significant.

Sexual dysfunction, including priapism, has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects.

Vital signs — Tachycardia, bradycardia, and orthostatic hypotension have occurred in SYMBYAX-treated patients *[see Warnings and Precautions (5.10)]*. The mean standing pulse rate of SYMBYAX-treated patients was reduced by 0.7 beats/min.

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Other Events Observed in Clinical Studies

Following is a list of treatment-emergent adverse events reported by patients treated with SYMBYAX in clinical trials. This listing is not intended to include events (1) already listed in previous tables or elsewhere in labeling, (2) for which a drug cause was remote, (3) which were so general as to be uninformative, (4) which were not considered to have significant clinical implications, or (5) which occurred at a rate equal to or less than placebo.

Events are classified by body system using the following definitions: frequent adverse events are those occurring in at least 1/100 patients; infrequent adverse events are those occurring in 1/100 to 1/1000 patients; and rare events are those occurring in fewer than 1/1000 patients.

[Provide your justification for modifying the listings of events below from currently approved labeling.]

Body as a Whole — *Frequent:* chills, neck rigidity, photosensitivity reaction.

Cardiovascular System — *Frequent:* vasodilatation; *Infrequent:* QT-interval prolonged.

Digestive System — *Frequent:* diarrhea; *Infrequent:* gastritis, gastroenteritis, nausea and vomiting, peptic ulcer; *Rare:* gastrointestinal hemorrhage, intestinal obstruction, liver fatty deposit, pancreatitis.

Hemic and Lymphatic System — *Frequent:* ecchymosis; *Infrequent:* anemia; *Rare:* leukopenia, purpura.

Metabolic and Nutritional — *Frequent:* generalized edema, weight loss; *Infrequent:* glycosuria, obesity; *Rare:* bilirubinemia, creatinine increased, gout.

Musculoskeletal System — *Rare:* osteoporosis.

Nervous System — *Frequent:* amnesia; *Infrequent:* ataxia, buccoglossal syndrome, cogwheel rigidity, dysarthria, emotional lability, euphoria, extrapyramidal syndrome, hypokinesia, movement disorder, myoclonus; *Rare:* dystonia, hyperkinesia, libido increased, withdrawal syndrome.

Respiratory System — *Infrequent:* epistaxis, yawn; *Rare:* laryngismus.

Skin and Appendages — *Infrequent:* alopecia, dry skin, pruritis; *Rare:* exfoliative dermatitis.

Special Senses — *Frequent:* taste perversion; *Infrequent:* abnormality of accommodation, dry eyes.

Urogenital System — *Frequent:* breast pain, menorrhagia[1], urinary frequency, urinary incontinence; *Infrequent:* amenorrhea[1], female lactation[1], hypomenorrhea[1], metrorrhagia[1], urinary retention, urinary urgency, urination impaired; *Rare:* breast engorgement[1].

[1] Adjusted for gender.

Other Events Observed with Olanzapine or Fluoxetine Monotherapy

The following adverse events were not observed in SYMBYAX-treated patients during premarketing clinical studies but have been reported with olanzapine or fluoxetine monotherapy: aplastic anemia, cholestatic jaundice, diabetic coma, dyskinesia, eosinophilic pneumonia, erythema multiforme, jaundice, rhabdomyolysis, serotonin syndrome, vasculitis, venous thromboembolic events (including pulmonary embolism and deep venous thrombosis), violent behaviors. Random triglyceride levels of ≥1000 mg/dL have been rarely reported.

7 DRUG INTERACTIONS

The risks of using SYMBYAX in combination with other drugs have not been extensively evaluated in systematic studies. The drug-drug interactions of the individual components are applicable to SYMBYAX. As with all drugs, the potential for interaction by a variety of mechanisms (e.g., pharmacodynamic, pharmacokinetic drug inhibition or enhancement, etc.) is a possibility. Caution is advised if the concomitant administration of SYMBYAX and other CNS-active drugs is required. In evaluating individual cases, consideration should be given to using lower initial doses of the concomitantly administered drugs, using conservative titration schedules, and monitoring of clinical status *[see Clinical Pharmacology (12.3)]*.

7.1 Antihypertensive agents

Because of the potential for olanzapine to induce hypotension, SYMBYAX may enhance the effects of certain antihypertensive agents *[see Warnings and Precautions (5.10)]*.

7.2 Anti-Parkinsonians

The olanzapine component of SYMBYAX may antagonize the effects of levodopa and dopamine agonists.

7.3 Benzodiazepines

Multiple doses of olanzapine did not influence the pharmacokinetics of diazepam and its active metabolite N-desmethyldiazepam. However, the coadministration of diazepam with olanzapine potentiated the orthostatic hypotension observed with olanzapine.

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15 When concurrently administered with fluoxetine, the half-life of diazepam may be prolonged in some patients *[see Clinical Pharmacology (7.29, 12.3)]*. Coadministration of alprazolam and fluoxetine has resulted in increased alprazolam plasma concentrations and in further psychomotor performance decrement due to increased alprazolam levels.

7.4 **Biperiden**

Multiple doses of olanzapine did not influence the pharmacokinetics of biperiden.

7.5 **Carbamazepine**

Carbamazepine therapy (200 mg BID) causes an approximate 50% increase in the clearance of olanzapine. This increase is likely due to the fact that carbamazepine is a potent inducer of CYP1A2 activity. Higher daily doses of carbamazepine may cause an even greater increase in olanzapine clearance.

Patients on stable doses of carbamazepine have developed elevated plasma anticonvulsant concentrations and clinical anticonvulsant toxicity following initiation of concomitant fluoxetine treatment.

7.6 **Clozapine**

Elevation of blood levels of clozapine has been observed in patients receiving concomitant fluoxetine.

7.7 **CNS Acting Drugs**

Given the primary CNS effects of olanzapine, caution should be used when olanzapine is taken in combination with other centrally acting drugs.

7.8 **Electroconvulsive therapy (ECT)**

There are no clinical studies establishing the benefit of the combined use of ECT and fluoxetine. There have been rare reports of prolonged seizures in patients on fluoxetine receiving ECT treatment *[see Warnings and Precautions (5.12)]*.

7.9 **Ethanol**

Ethanol (45 mg/70 kg single dose) did not have an effect on olanzapine pharmacokinetics. The coadministration of ethanol with SYMBYAX may potentiate sedation and orthostatic hypotension.

7.10 **Fluvoxamine**

Fluvoxamine, a CYP1A2 inhibitor, decreases the clearance of olanzapine. This results in a mean increase in olanzapine C_{max} following fluvoxamine administration of 54% in female nonsmokers and 77% in male smokers. The mean increase in olanzapine AUC is 52% and 108%, respectively. Lower doses of the olanzapine component of SYMBYAX should be considered in patients receiving concomitant treatment with fluvoxamine.

7.11 **Haloperidol**

Elevation of blood levels of haloperidol has been observed in patients receiving concomitant fluoxetine.

7.12 **Lithium**

Multiple doses of olanzapine did not influence the pharmacokinetics of lithium.

There have been reports of both increased and decreased lithium levels when lithium was used concomitantly with fluoxetine. Cases of lithium toxicity and increased serotonergic effects have been reported. Lithium levels should be monitored in patients taking SYMBYAX concomitantly with lithium.

7.13 **Monoamine oxidase inhibitors**

SYMBYAX should not be used in combination with an MAOI, or within a minimum of 14 days of discontinuing therapy with an MAOI. There have been reports of serious, sometimes fatal reactions (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma) in patients receiving fluoxetine in combination with an MAOI, and in patients who have recently discontinued fluoxetine and are then started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Since fluoxetine and its major metabolite have very long elimination half-lives, at least 5 weeks (perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses *[see Clinical Pharmacology (12.3)]* should be allowed after stopping SYMBYAX before starting an MAOI. *[See Contraindications (4)]*.

7.14 **Phenytoin**

Patients on stable doses of phenytoin have developed elevated plasma levels of phenytoin with clinical phenytoin toxicity following initiation of concomitant fluoxetine.

7.15 **Pimozide**

Concomitant use of fluoxetine and pimozide is contraindicated. Clinical studies of pimozide with other antidepressants demonstrate an increase in drug interaction or QT_c prolongation. While a specific study with pimozide and fluoxetine has not been conducted, the potential for drug interactions or QT_c prolongation warrants restricting the concurrent use of pimozide and fluoxetine. *[See Contraindications (4)]*.

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7.16 Serotonergic Drugs

Based on the mechanism of action of SYMBYAX and the potential for serotonin syndrome, caution is advised when SYMBYAX is coadministered with other drugs that may affect the serotonergic neurotransmitter systems, such as triptans, linezolid (an antibiotic which is a reversible non-selective MAOI), lithium, tramadol, or St. John's Wort *[see Warnings and Precautions (5.6)]*. The concomitant use of SYMBYAX with other SSRIs, SNRIs or tryptophan is not recommended *[see Drug Interactions (7.21)]*.

7.17 Theophylline

Multiple doses of olanzapine did not affect the pharmacokinetics of theophylline or its metabolites.

7.18 Thioridazine

Thioridazine should not be administered with SYMBYAX or administered within a minimum of 5 weeks after discontinuation of SYMBYAX.

In a study of 19 healthy male subjects, which included 6 slow and 13 rapid hydroxylators of debrisoquin, a single 25-mg oral dose of thioridazine produced a 2.4-fold higher C_{max} and a 4.5-fold higher AUC for thioridazine in the slow hydroxylators compared with the rapid hydroxylators. The rate of debrisoquin hydroxylation is felt to depend on the level of CYP2D6 isozyme activity. Thus, this study suggests that drugs that inhibit CYP2D6, such as certain SSRIs, including fluoxetine, will produce elevated plasma levels of thioridazine *[see Contraindications (4)]*.

Thioridazine administration produces a dose-related prolongation of the QT, interval, which is associated with serious ventricular arrhythmias, such as torsades de pointes-type arrhythmias and sudden death. This risk is expected to increase with fluoxetine-induced inhibition of thioridazine metabolism *[see Contraindications (4)]*.

7.19 Tricyclic antidepressants (TCAs)

Single doses of olanzapine did not affect the pharmacokinetics of imipramine or its active metabolite desipramine.

In two fluoxetine studies, previously stable plasma levels of imipramine and desipramine have increased >2- to 10-fold when fluoxetine has been administered in combination. This influence may persist for three weeks or longer after fluoxetine is discontinued. Thus, the dose of TCA may need to be reduced and plasma TCA concentrations may need to be monitored temporarily when SYMBYAX is coadministered or has been recently discontinued *[see Drug Interactions (7.23) and Clinical Pharmacology (12.3)]*.

7.20 Triptans

There have been rare postmarketing reports of serotonin syndrome with use of an SSRI and a triptan. If concomitant treatment of SYMBYAX with a triptan is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases *[see Warnings and Precautions (5.6)]*.

7.21 Tryptophan

Five patients receiving fluoxetine in combination with tryptophan experienced adverse reactions, including agitation, restlessness, and gastrointestinal distress. Concomitant use with tryptophan is not recommended.

7.22 Valproate

In vitro studies using human liver microsomes determined that olanzapine has little potential to inhibit the major metabolic pathway, glucuronidation, of valproate. Further, valproate has little effect on the metabolism of olanzapine in vitro. Thus, a clinically significant pharmacokinetic interaction between olanzapine and valproate is unlikely.

7.23 Warfarin

Warfarin (20-mg single dose) did not affect olanzapine pharmacokinetics. Single doses of olanzapine did not affect the pharmacokinetics of warfarin.

Altered anticoagulant effects, including increased bleeding, have been reported when fluoxetine is coadministered with warfarin *[see Warnings and Precautions (5.13)]*. Patients receiving warfarin therapy should receive careful coagulation monitoring when SYMBYAX is initiated or stopped.

7.24 Drugs that Interfere with Hemostasis (NSAIDs, aspirin, warfarin, etc.)

Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding *[see Warnings and Precautions (5.13)]*. Thus, patients should be cautioned about the use of such drugs concurrently with SYMBYAX.

7.25 Drugs metabolized by CYP2D6

In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP2D6. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by this enzyme.

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Approximately 7% of the normal population has a genetic variation that leads to reduced levels of activity of CYP2D6. Such individuals have been referred to as poor metabolizers of drugs such as debrisoquin, dextromethorphan, and TCAs. Many drugs, such as most antidepressants, including fluoxetine and other selective uptake inhibitors of serotonin, are metabolized by this isoenzyme; thus, both the pharmacokinetic properties and relative proportion of metabolites are altered in poor metabolizers. However, for fluoxetine and its metabolite, the sum of the plasma concentrations of the 4 enantiomers is comparable between poor and extensive metabolizers *[see Clinical Pharmacology (12.3)]*.

Fluoxetine, like other agents that are metabolized by CYP2D6, inhibits the activity of this isoenzyme, and thus may make normal metabolizers resemble poor metabolizers. Therapy with medications that are predominantly metabolized by the CYP2D6 system and that have a relatively narrow therapeutic index should be initiated at the low end of the dose range if a patient is receiving fluoxetine concurrently or has taken it in the previous five weeks. If fluoxetine is added to the treatment regimen of a patient already receiving a drug metabolized by CYP2D6, the need for a decreased dose of the original medication should be considered. Drugs with a narrow therapeutic index represent the greatest concern (including but not limited to, flecainide, vinblastine, and TCAs). Due to the risk of serious ventricular arrhythmias and sudden death potentially associated with elevated thioridazine plasma levels, thioridazine should not be administered with fluoxetine or within a minimum of five weeks after fluoxetine has been discontinued *[see Contraindications, (4) and Drug Interactions (7.18)]*.

7.26 Drugs metabolized by CYP3A

In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP3A. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by these enzymes.

In an in vivo interaction study involving the coadministration of fluoxetine with single doses of terfenadine (a CYP3A substrate), no increase in plasma terfenadine concentrations occurred with concomitant fluoxetine. In addition, in vitro studies have shown ketoconazole, a potent inhibitor of CYP3A activity, to be at least 100 times more potent than fluoxetine or norfluoxetine as an inhibitor of the metabolism of several substrates for this enzyme, including astemizole, cisapride, and midazolam. These data indicate that fluoxetine's extent of inhibition of CYP3A activity is not likely to be of clinical significance.

7.27 Effect of olanzapine on drugs metabolized by other CYP enzymes

In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP1A2, CYP2C9, and CYP2C19. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by these enzymes.

7.28 The effect of other drugs on olanzapine

Fluoxetine, an inhibitor of CYP2D6, decreases olanzapine clearance a small amount *[see Clinical Pharmacology (12.3)]*.. Agents that induce CYP1A2 or glucuronyl transferase enzymes, such as omeprazole and rifampin, may cause an increase in olanzapine clearance. Fluvoxamine, an inhibitor of CYP1A2, decreases olanzapine clearance *[see Drug Interactions (7.10)]*. The effect of CYP1A2 inhibitors, such as fluvoxamine and some fluoroquinolone antibiotics, on SYMBYAX has not been evaluated. Although olanzapine is metabolized by multiple enzyme systems, induction or inhibition of a single enzyme may appreciably alter olanzapine clearance. Therefore, a dosage increase (for induction) or a dosage decrease (for inhibition) may need to be considered with specific drugs.

7.29 Drugs tightly bound to plasma protein

The in vitro binding of SYMBYAX to human plasma proteins is similar to the individual components. The interaction between SYMBYAX and other highly protein-bound drugs has not been fully evaluated. Because fluoxetine is tightly bound to plasma protein, the administration of fluoxetine to a patient taking another drug that is tightly bound to protein (e.g., Coumadin, digitoxin) may cause a shift in plasma concentrations potentially resulting in an adverse effect. Conversely, adverse effects may result from displacement of protein-bound fluoxetine by other tightly bound drugs *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects — Pregnancy Category C

[We have removed inaccurate and redundant information in the following section.]

~~SYMBYAX — SYMBYAX has been shown to be teratogenic (as to have an embryocidal effect or other adverse effect) in rats when given in doses of olanzapine and fluoxetine in combination at 2 and 1 times the human dose, respectively. There are no adequate and well-controlled studies in pregnant women. SYMBYAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.~~ Embryo fetal development studies were conducted in rats and rabbits with olanzapine and fluoxetine in low-dose and high-dose combinations. In rats, the doses were 2 and 4 mg/kg/day (low-dose) [1 and 0.5 times the MRHD on a mg/m^2 basis, respectively], and 4 and 8 mg/kg/day (high-dose) [2 and 1 times the MRHD on a mg/m^2 basis, respectively]. In rabbits, the doses were 4 and 4 mg/kg/day (low-dose) [4 and 1 times the MRHD on a mg/m^2 basis, respectively], and 8 and 8 mg/kg/day (high-dose) [9 and 2 times the MRHD on a mg/m^2 basis, respectively]. In these studies, olanzapine and fluoxetine were

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also administered alone at the high-doses (4 and 8 mg/kg/day, respectively, in the rat; 8 and 8 mg/kg/day, respectively, in the rabbit). In the rabbit, there was no evidence of teratogenicity; however, the high-dose combination produced decreases in fetal weight and retarded skeletal ossification in conjunction with maternal toxicity. Similarly, in the rat there was no evidence of teratogenicity; however, a decrease in fetal weight was observed with the high-dose combination.

In a pre- and postnatal study conducted in rats, olanzapine and fluoxetine were administered during pregnancy and throughout lactation in combination (low-dose: 2 and 4 mg/kg/day [1 and 0.5 times the MRHD on a mg/m^2 basis], respectively, high-dose: 4 and 8 mg/kg/day [2 and 1 times the MRHD on a mg/m^2 basis], respectively), and alone: 4 and 8 mg/kg/day [2 and 1 times the MRHD on a mg/m^2 basis], respectively). Administration of the high-dose combination resulted in a marked elevation in offspring mortality and growth retardation in comparison to the same doses of olanzapine and fluoxetine administered alone. These effects were not observed with the low-dose combination; however, there were a few cases of testicular degeneration and atrophy, depletion of epididymal sperm and infertility in the male progeny. The effects of the high-dose combination on postnatal endpoints could not be assessed due to high progeny mortality.

There are no adequate and well-controlled studies with SYMBYAX in pregnant women.

SYMBYAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Olanzapine — In reproduction studies in rats at doses up to 18 mg/kg/day and in rabbits at doses up to 30 mg/kg/day (9 and 30 times the MRHD on a mg/m^2 basis, respectively), no evidence of teratogenicity was observed. In a rat teratology study, early resorptions and increased numbers of nonviable fetuses were observed at a dose of 18 mg/kg/day (9 times the MRHD on a mg/m^2 basis). Gestation was prolonged at 10 mg/kg/day (5 times the MRHD on a mg/m^2 basis). In a rabbit teratology study, fetal toxicity (manifested as increased resorptions and decreased fetal weight) occurred at a maternally toxic dose of 30 mg/kg/day (30 times the MRHD on a mg/m^2 basis).

Placental transfer of olanzapine occurs in rat pups.

There are no adequate and well-controlled clinical studies with olanzapine in pregnant women. Seven pregnancies were observed during premarketing clinical studies with olanzapine, including two resulting in normal births, one resulting in neonatal death due to a cardiovascular defect, three therapeutic abortions, and one spontaneous abortion.

Fluoxetine — In embryo fetal development studies in rats and rabbits, there was no evidence of teratogenicity following administration of up to 12.5 and 15 mg/kg/day, respectively (1.5 and 3.6 times the MRHD on a mg/m^2 basis, respectively) throughout organogenesis. However, in rat reproduction studies, an increase in stillborn pups, a decrease in pup weight, and an increase in pup deaths during the first 7 days postpartum occurred following maternal exposure to 12 mg/kg/day (1.5 times the MRHD on a mg/m^2 basis) during gestation or 7.5 mg/kg/day (0.9 times the MRHD on a mg/m^2 basis) during gestation and lactation. There was no evidence of developmental neurotoxicity in the surviving offspring of rats treated with 12 mg/kg/day during gestation. The no-effect dose for rat pup mortality was 5 mg/kg/day (0.6 times the MRHD on a mg/m^2 basis).

Treatment of Pregnant Women During the Third Trimester — Neonates exposed to fluoxetine, a component of ~~SYMBYAX~~SYMBYAX, and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome *[see Contraindications (4) and Drug Interactions (7.16)]*. When treating pregnant women with fluoxetine during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider tapering fluoxetine in the third trimester.

8.2 Labor and Delivery

SYMBYAX — The effect of SYMBYAX on labor and delivery in humans is unknown. Parturition in rats was not affected by SYMBYAX. SYMBYAX should be used during labor and delivery only if the potential benefit justifies the potential risk.

Olanzapine — The effect of olanzapine on labor and delivery in humans is unknown. Parturition in rats was not affected by olanzapine.

Fluoxetine — The effect of fluoxetine on labor and delivery in humans is unknown. Fluoxetine crosses the placenta; therefore, there is a possibility that fluoxetine may have adverse effects on the newborn.

8.3 Nursing Mothers

SYMBYAX — There are no adequate and well-controlled studies with SYMBYAX in nursing mothers or infants. Studies evaluating the individual components of SYMBYAX (olanzapine and fluoxetine) in nursing mothers are described below. It is not known whether SYMBYAX is excreted in human milk and because of the potential for serious adverse reactions in nursing infants

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from SYMBYAX, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. It is recommended that women not breast-feed when receiving SYMBYAX.

Olanzapine — In a study in lactating, healthy women, olanzapine was excreted in breast milk. Mean infant dose at steady state was estimated to be 1.8% of the maternal olanzapine dose. It is recommended that women receiving olanzapine should not breast-feed.

Fluoxetine — Fluoxetine is excreted in human breast milk. In one breast milk sample, the concentration of fluoxetine plus norfluoxetine was 70.4 ng/mL. The concentration in the mother's plasma was 295.0 ng/mL. No adverse effects on the infant were reported. In another case, an infant nursed by a mother on fluoxetine developed crying, sleep disturbance, vomiting, and watery stools. The infant's plasma drug levels were 340 ng/mL of fluoxetine and 208 ng/mL of norfluoxetine on the 2nd day of feeding.

8.4 Pediatric Use

SYMBYAX — Safety and effectiveness in the pediatric population have not been established *[see Box Warning and Warnings and Precautions (5.3)]*. Anyone considering the use of SYMBYAX in a child or adolescent must balance the potential risks with the clinical need.

Fluoxetine — Significant toxicity, including myotoxicity, long-term neurobehavioral and reproductive toxicity, and impaired bone development, has been observed following exposure of juvenile animals to fluoxetine. Some of these effects occurred at clinically relevant exposures.

In a study in which fluoxetine (3, 10, or 30 mg/kg) was orally administered to young rats from weaning (Postnatal Day 21) through adulthood (Day 90), male and female sexual development was delayed at all doses, and growth (body weight gain, femur length) was decreased during the dosing period in animals receiving the highest dose. At the end of the treatment period, serum levels of creatine kinase (marker of muscle damage) were increased at the intermediate and high doses, and abnormal muscle and reproductive organ histopathology (skeletal muscle degeneration and necrosis, testicular degeneration and necrosis, epididymal vacuolation and hypospermia) was observed at the high dose. When animals were evaluated after a recovery period (up to 11 weeks after cessation of dosing), neurobehavioral abnormalities (decreased reactivity at all doses and learning deficit at the high dose) and reproductive functional impairment (decreased mating at all doses and impaired fertility at the high dose) were seen; in addition, testicular and epididymal microscopic lesions and decreased sperm concentrations were found in the high dose group, indicating that the reproductive organ effects seen at the end of treatment were irreversible. The reversibility of fluoxetine-induced muscle damage was not assessed. Adverse effects similar to those observed in rats treated with fluoxetine during the juvenile period have not been reported after administration of fluoxetine to adult animals. Plasma exposures (AUC) to fluoxetine in juvenile rats receiving the low, intermediate, and high dose in this study were approximately 0.1-0.2, 1-2, and 5-10 times, respectively, the average exposure in pediatric patients receiving the maximum recommended dose (MRD) of 20 mg/day. Rat exposures to the major metabolite, norfluoxetine, were approximately 0.3-0.8, 1-8, and 3-20 times, respectively, pediatric exposure at the MRD.

A specific effect of fluoxetine on bone development has been reported in mice treated with fluoxetine during the juvenile period. When mice were treated with fluoxetine (5 or 20 mg/kg, intraperitoneal) for 4 weeks starting at 4 weeks of age, bone formation was reduced resulting in decreased bone mineral content and density. These doses did not affect overall growth (body weight gain or femoral length). The doses administered to juvenile mice in this study are approximately 0.5 and 2 times the MRD for pediatric patients on a body surface area (mg/m^2) basis.

In another mouse study, administration of fluoxetine (10 mg/kg intraperitoneal) during early postnatal development (Postnatal Days 4 to 21) produced abnormal emotional behaviors (decreased exploratory behavior in elevated plus-maze, increased shock avoidance latency) in adulthood (12 weeks of age). The dose used in this study is approximately equal to the pediatric MRD on a mg/m^2 basis. Because of the early dosing period in this study, the significance of these findings to the approved pediatric use in humans is uncertain.

8.5 Geriatric Use

SYMBYAX — Clinical studies of SYMBYAX did not include sufficient numbers of patients ≥65 years of age to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy *[see Dosage and Administration (2.1)]*.

Olanzapine — Of the 2500 patients in premarketing clinical studies with olanzapine, 11% (263 patients) were ≥65 years of age. In patients with schizophrenia, there was no indication of any different tolerability of olanzapine in the elderly compared with younger patients. Studies in patients with dementia-related psychosis have suggested that there may be a different tolerability profile in this population compared with younger patients with schizophrenia. In placebo-controlled studies of olanzapine in elderly patients with dementia-related psychosis, there was a significantly higher incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the

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treatment of patients with dementia-related psychosis. If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised [see *Box Warning, Warnings and Precautions* (5.19) and *Dosage and Administration* (2.3)].

As with other CNS-active drugs, olanzapine should be used with caution in elderly patients with dementia. Also, the presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine should lead to consideration of a lower starting dose for any geriatric patient.

Fluoxetine — US fluoxetine clinical studies (10,782 patients) included 687 patients ≥65 years of age and 93 patients ≥75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. As with other SSRIs, fluoxetine has been associated with cases of clinically significant hyponatremia in elderly patients.

9 DRUG ABUSE AND DEPENDENCE

9.3 Dependence

SYMBYAX, as with fluoxetine and olanzapine, has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. While the clinical studies did not reveal any tendency for any drug-seeking behavior, these observations were not systematic, and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, physicians should carefully evaluate patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of SYMBYAX (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

In studies in rats and rhesus monkeys designed to assess abuse and dependence potential, olanzapine alone was shown to have acute depressive CNS effects but little or no potential of abuse or physical dependence at oral doses up to 15 (rat) and 8 (monkey) times the MRHD (20 mg) on a mg/m^2 basis.

10 OVERDOSAGE

SYMBYAX — During premarketing clinical studies of the olanzapine/fluoxetine combination, overdose of both fluoxetine and olanzapine were reported in five study subjects. Four of the five subjects experienced loss of consciousness (3) or coma (1). No fatalities occurred.

Adverse events involving overdose of fluoxetine and olanzapine in combination, and SYMBYAX, have been reported spontaneously to Eli Lilly and Company. An overdose of combination therapy is defined as confirmed or suspected ingestion of a dose of >20 mg olanzapine in combination with a dose of >80 mg fluoxetine. Adverse events associated with these reports included somnolence (sedation), impaired consciousness (coma), impaired neurologic function (ataxia, confusion, convulsions, dysarthria), arrhythmias, lethargy, essential tremor, agitation, acute psychosis, hypotension, hypertension, and aggression. Fatalities have been confounded by exposure to additional substances including alcohol, thioridazine, oxycodone, and propoxyphene.

Olanzapine — In postmarketing reports of overdose with olanzapine alone, symptoms have been reported in the majority of cases. In symptomatic patients, symptoms with ≥10% incidence included agitation/aggressiveness, dysarthria, tachycardia, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Among less commonly reported symptoms were the following potentially medically serious events: aspiration, cardiopulmonary arrest, cardiac arrhythmias (such as supraventricular tachycardia as well as a patient that experienced sinus pause with spontaneous resumption of normal rhythm), delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypertension, and hypotension. Eli Lilly and Company has received reports of fatality in association with overdose of olanzapine alone. In 1 case of death, the amount of acutely ingested olanzapine was reported to be possibly as low as 450 mg; however, in another case, a patient was reported to survive an acute olanzapine ingestion of 1500 mg.

Fluoxetine — Worldwide exposure to fluoxetine is estimated to be over 38 million patients (circa 1999). Of the 1578 cases of overdose involving fluoxetine, alone or with other drugs, reported from this population, there were 195 deaths.

Among 633 adult patients who overdosed on fluoxetine alone, 34 resulted in a fatal outcome, 378 completely recovered, and 15 patients experienced sequelae after overdose, including abnormal accommodation, abnormal gait, confusion, unresponsiveness, nervousness, pulmonary dysfunction, vertigo, tremor, elevated blood pressure, impotence, movement disorder, and hypomania. The remaining 206 patients had an unknown outcome. The most common signs and symptoms associated with non-fatal overdose were seizures, somnolence, nausea, tachycardia, and vomiting. The largest known ingestion of fluoxetine in adult patients was 8 grams in a patient who took fluoxetine alone and who subsequently recovered. However, in an adult patient who took fluoxetine alone, an ingestion as low as 520 mg has been associated with lethal outcome, but causality has not been established.

Among pediatric patients (ages 3 months to 17 years), there were 156 cases of overdose involving fluoxetine alone or in combination with other drugs. Six patients died. 127 patients completely recovered, 1 patient experienced renal failure, and 22 patients

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had an unknown outcome. One of the 6 fatalities was a 9-year-old boy who had a history of OCD, Tourette's Syndrome with tics, attention deficit disorder, and fetal alcohol syndrome. He had been receiving 100 mg of fluoxetine daily for 6 months in addition to clonidine, methylphenidate, and promethazine. Mixed-drug ingestion or other methods of suicide complicated all 6 overdoses in children that resulted in fatalities. The largest ingestion in pediatric patients was 3 grams, which was non-lethal.

Other important adverse events reported with fluoxetine overdose (single or multiple drugs) included coma, delirium, ECG abnormalities (such as QT-interval prolongation and ventricular tachycardia, including torsades de pointes-type arrhythmias), hypotension, mania, neuroleptic malignant syndrome-like events, pyrexia, stupor, and syncope.

10.1 Management of Overdose

In managing overdose, the possibility of multiple drug involvement should be considered. In case of acute overdose, establish and maintain an airway and ensure adequate ventilation, which may include intubation. Induction of emesis is not recommended as the possibility of obtundation, seizures, or dystonic reactions of the head and neck following overdose may create a risk for aspiration. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

A specific precaution involves patients who are taking or have recently taken SYMBYAX and may have ingested excessive quantities of a TCA (tricyclic antidepressant). In such cases, accumulation of the parent TCA and/or an active metabolite may increase the possibility of serious sequelae and extend the time needed for close medical observation.

Due to the large volume of distribution of olanzapine and fluoxetine, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidote for either fluoxetine or olanzapine overdose is known. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. Do not use epinephrine, dopamine, or other sympathomimetics with β-agonist activity, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blockade.

The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*.

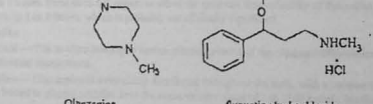
11 DESCRIPTION

SYMBYAX® (olanzapine and fluoxetine HCl capsules) combines 2 psychotropic agents, olanzapine (the active ingredient in Zyprexa®, and Zyprexa Zydis®) and fluoxetine hydrochloride (the active ingredient in Prozac®, Prozac Weekly™, and Sarafem®).

Olanzapine belongs to the thienobenzodiazepine class. The chemical designation is 2-methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*] [1,5]benzodiazepine. The molecular formula is $C_{17}H_{20}N_4S$, which corresponds to a molecular weight of 312.44.

Fluoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI). The chemical designation is (±)-N-methyl-3-phenyl-3-[(α,α,α-trifluoro-*p*-tolyl)oxy]propylamine hydrochloride. The molecular formula is $C_{17}H_{18}F_3NO{\cdot}HCl$, which corresponds to a molecular weight of 345.79.

The chemical structures are:



Olanzapine

fluoxetine hydrochloride

Olanzapine is a yellow crystalline solid, which is practically insoluble in water.

Fluoxetine hydrochloride is a white to off-white crystalline solid with a solubility of 14 mg/mL in water.

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Each capsule also contains pregelatinized starch, gelatin, dimethicone, titanium dioxide, sodium lauryl sulfate, edible black ink, red iron oxide, yellow iron oxide, and/or black iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Although the exact mechanism of SYMBYAX is unknown, it has been proposed that the activation of 5 monoaminergic neural systems (serotonin, norepinephrine, and dopamine) is responsible for its enhanced antidepressant effect. This is supported by animal studies in which the olanzapine/fluoxetine combination has been shown to produce synergistic increases in norepinephrine and dopamine release in the prefrontal cortex compared with either component alone, as well as increases in serotonin.

12.2 Pharmacodynamics

Olanzapine is a psychotropic agent with high affinity binding to the following receptors: serotonin $5HT_{2A/2C}$ (K_i=4 and 11 nM, respectively), dopamine D_{1-4} (K_i=11 to 31 nM), muscarinic M_{1-5} (K_i=1.9 to 25 nM), histamine H_1 (K_i=7 nM), and adrenergic α_1 receptors (K_i=19 nM). Olanzapine binds weakly to $GABA_A$, BZD, and β-adrenergic receptors (K_i>10 μM). Fluoxetine is an inhibitor of the serotonin transporter and is a weak inhibitor of the norepinephrine and dopamine transporters.

Antagonism at receptors other than dopamine and $5HT_2$ with similar receptor affinities may explain some of the other therapeutic and side effects of olanzapine. Olanzapine's antagonism of muscarinic M_{1-3} receptors may explain its anticholinergic effects. The antagonism of histamine H_1 receptors by olanzapine may explain the somnolence observed with this drug. The antagonism of α_1-adrenergic receptors by olanzapine may explain the orthostatic hypotension observed with this drug. Fluoxetine has relatively low affinity for muscarinic, α_1-adrenergic, and histamine H_1 receptors.

12.3 Pharmacokinetics

SYMBYAX — Fluoxetine (administered as a 60-mg single dose or 60 mg daily for 8 days) caused a small increase in the mean maximum concentration of olanzapine (16%) following a 5-mg dose, an increase in the mean area under the curve (17%) and a small decrease in mean apparent clearance of olanzapine (16%). In another study, a similar decrease in apparent clearance of olanzapine of 14% was observed following olanzapine doses of 6 or 12 mg with concomitant fluoxetine doses of 25 mg or more. The decrease in clearance reflects an increase in bioavailability. The terminal half-life is not affected, and therefore the time to reach steady state should not be altered. The overall steady-state plasma concentrations of olanzapine and fluoxetine when given as the combination in the therapeutic dose ranges were comparable with those typically attained with each of the monotherapies. The small change in olanzapine clearance, observed in both studies, likely reflects the inhibition of a minor metabolic pathway for olanzapine via CYP2D6 by fluoxetine, a potent CYP2D6 inhibitor, and was not deemed clinically significant. Therefore, the pharmacokinetics of the individual components is expected to reasonably characterize the overall pharmacokinetics of the combination.

Absorption and Bioavailability

SYMBYAX — Following a single oral 12-mg/50-mg dose of SYMBYAX, peak plasma concentrations of olanzapine and fluoxetine occur at approximately 4 and 6 hours, respectively. The effect of food on the absorption and bioavailability of SYMBYAX has not been evaluated. The bioavailability of olanzapine given as Zyprexa, and the bioavailability of fluoxetine given as Prozac were not affected by food. It is unlikely that there would be a significant food effect on the bioavailability of SYMBYAX.

Olanzapine — Olanzapine is well absorbed and reaches peak concentration approximately 6 hours following an oral dose. Food does not affect the rate or extent of olanzapine absorption when olanzapine is given as Zyprexa. It is eliminated extensively by first pass metabolism, with approximately 40% of the dose metabolized before reaching the systemic circulation.

Fluoxetine — Following a single oral 40-mg dose, peak plasma concentrations of fluoxetine from 15 to 55 ng/mL are observed after 6 to 8 hours. Food does not appear to affect the systemic bioavailability of fluoxetine given as Prozac, although it may delay its absorption by 1 to 2 hours, which is probably not clinically significant.

Distribution

SYMBYAX — The in vitro binding to human plasma proteins of the olanzapine/fluoxetine combination is similar to the binding of the individual components.

Olanzapine — Olanzapine is extensively distributed throughout the body, with a volume of distribution of approximately 1000 L. It is 93% bound to plasma proteins over the concentration range of 7 to 1100 ng/mL, binding primarily to albumin and α_1-acid glycoprotein.

Fluoxetine — Over the concentration range from 200 to 1000 ng/mL, approximately 94.5% of fluoxetine is bound in vitro to human serum proteins, including albumin and α_1-glycoprotein. The interaction between fluoxetine and other highly protein-bound drugs has not been fully evaluated *[see Drug Interactions (7.29)]*.

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Metabolism and Elimination

SYMBYAX — SYMBYAX therapy yielded steady-state concentrations of norfluoxetine similar to those seen with fluoxetine in the therapeutic dose range.

Olanzapine — Olanzapine displays linear pharmacokinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours (5th to 95th percentile; mean of 30 hr), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th percentile; mean of 25 L/hr). Administration of olanzapine once daily leads to steady-state concentrations in about 1 week that are approximately twice the concentrations after single doses. Plasma concentrations, half-life, and clearance of olanzapine may vary between individuals on the basis of smoking status, gender, and age *[see Dosage and Administration (2.3) and Clinical Pharmacology (12.4)]*.

Following a single oral dose of ^{14}C-labeled olanzapine, 7% of the dose of olanzapine was recovered in the urine as unchanged drug, indicating that olanzapine is highly metabolized. Approximately 57% and 30% of the dose was recovered in the urine and feces, respectively. In the plasma, olanzapine accounted for only 12% of the AUC for total radioactivity, indicating significant exposure to metabolites. After multiple dosing, the major circulating metabolites were the 10-N-glucuronide, present at steady state at 44% of the concentration of olanzapine, and 4'-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed.

Direct glucuronidation and CYP450-mediated oxidation are the primary metabolic pathways for olanzapine. In vitro studies suggest that CYP1A2, CYP2D6, and the flavin-containing monooxygenase system are involved in olanzapine oxidation. CYP2D6-mediated oxidation appears to be a minor metabolic pathway in vivo, because the clearance of olanzapine is not reduced in subjects who are deficient in this enzyme.

Fluoxetine — Fluoxetine is a racemic mixture (50/50) of *R*-fluoxetine and *S*-fluoxetine enantiomers. In animal models, both enantiomers are specific and potent serotonin uptake inhibitors with essentially equivalent pharmacologic activity. The *S*-fluoxetine enantiomer is eliminated more slowly and is the predominant enantiomer present in plasma at steady state.

Fluoxetine is extensively metabolized in the liver to its only identified active metabolite, norfluoxetine, via the CYP2D6 pathway. A number of unidentified metabolites exist.

In animal models, *S*-norfluoxetine is a potent and selective inhibitor of serotonin uptake and has activity essentially equivalent to *R*- or *S*-fluoxetine. *R*-norfluoxetine is significantly less potent than the parent drug in the inhibition of serotonin uptake. The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney.

Clinical Issues Related to Metabolism and Elimination

The complexity of the metabolism of fluoxetine has several consequences that may potentially affect the clinical use of SYMBYAX.

Variability in metabolism — A subset (about 7%) of the population has reduced activity of the drug metabolizing enzyme CYP2D6. Such individuals are referred to as "poor metabolizers" of drugs such as debrisoquin, dextromethorphan, and the tricyclic antidepressants (TCAs). In a study involving labeled and unlabeled enantiomers administered as a racemate, these individuals metabolized *S*-fluoxetine at a slower rate and thus achieved higher concentrations of *S*-fluoxetine. Consequently, concentrations of *S*-norfluoxetine at steady state were lower. The metabolism of *R*-fluoxetine in these poor metabolizers appears normal. When compared with normal metabolizers, the total sum at steady state of the plasma concentrations of the 4 enantiomers was not significantly greater among poor metabolizers. Thus, the net pharmacodynamic activities were essentially the same. Alternative nonsaturable pathways (non-CYP2D6) also contribute to the metabolism of fluoxetine. This explains how fluoxetine achieves a steady-state concentration rather than increasing without limit.

Because the metabolism of fluoxetine, like that of a number of other compounds including TCAs and other selective serotonin antidepressants, involves the CYP2D6 system, concomitant therapy with drugs also metabolized by this enzyme system (such as the TCAs) may lead to drug interactions *[see Drug Interactions (7.19 and 7.25)]*.

Accumulation and slow elimination — The relatively slow elimination of fluoxetine (elimination half-life of 1 to 3 days after acute administration and 4 to 6 days after chronic administration) and its active metabolite, norfluoxetine (elimination half-life of 4 to 16 days after acute and chronic administration), leads to significant accumulation of these active species in chronic use and delayed attainment of steady state, even when a fixed dose is used. After 30 days of dosing at 40 mg/day, plasma concentrations of fluoxetine in the range of 91 to 302 ng/mL and norfluoxetine in the range of 72 to 258 ng/mL have been observed. Plasma concentrations of fluoxetine were higher than those predicted by single-dose studies, because the metabolism of fluoxetine is not proportional to dose. However, norfluoxetine appears to have linear pharmacokinetics. Its mean terminal half-life after a single dose was 8.6 days and after multiple dosing was 9.3 days. Steady-state levels after prolonged dosing are similar to levels seen at 4 to 5 weeks.

The long elimination half-lives of fluoxetine and norfluoxetine assure that, even when dosing is stopped, active drug substance will persist in the body for weeks (primarily depending on individual patient characteristics, previous dosing regimen, and length of previous therapy at discontinuation). This is of potential consequence when drug discontinuation is required or when drugs are prescribed that might interact with fluoxetine and norfluoxetine following the discontinuation of fluoxetine.

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12.4 Special Populations

Geriatric — Based on the individual pharmacokinetic profiles of olanzapine and fluoxetine, the pharmacokinetics of SYMBYAX may be altered in geriatric patients. Caution should be used in dosing the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity.

In a study involving 24 healthy subjects, the mean elimination half-life of olanzapine was about 1.5 times greater in elderly subjects (≥65 years of age) than in non-elderly subjects (≤65 years of age).

The disposition of single doses of fluoxetine in healthy elderly subjects (≥65 years of age) did not differ significantly from that in younger normal subjects. However, given the long half-life and nonlinear disposition of the drug, a single-dose study is not adequate to rule out the possibility of altered pharmacokinetics in the elderly, particularly if they have systemic illness or are receiving multiple drugs for concomitant diseases. The effects of age upon the metabolism of fluoxetine have been investigated in 260 elderly but otherwise healthy depressed patients (≥60 years of age) who received 20 mg fluoxetine for 6 weeks. Combined fluoxetine plus norfluoxetine plasma concentrations were 209.3 ± 85.7 ng/mL at the end of 6 weeks. No unusual age-associated pattern of adverse events was observed in these elderly patients.

Renal Impairment — The pharmacokinetics of SYMBYAX has not been studied in patients with renal impairment. However, olanzapine and fluoxetine individual pharmacokinetics do not differ significantly in patients with renal impairment. SYMBYAX dosing adjustment based upon renal impairment is not routinely required.

Because olanzapine is highly metabolized before excretion and only 7% of the drug is excreted unchanged, renal dysfunction alone is unlikely to have a major impact on the pharmacokinetics of olanzapine. The pharmacokinetic characteristics of olanzapine were similar in patients with severe renal impairment and normal subjects, indicating that dosage adjustment based upon the degree of renal impairment is not required. In addition, olanzapine is not removed by dialysis. The effect of renal impairment on olanzapine metabolite elimination has not been studied.

In depressed patients on dialysis (N=12), fluoxetine administered as 20 mg once daily for 2 months produced steady-state fluoxetine and norfluoxetine plasma concentrations comparable with those seen in patients with normal renal function. While the possibility exists that renally excreted metabolites of fluoxetine may accumulate to higher levels in patients with severe renal dysfunction, use of a lower or less frequent dose is not routinely necessary in renally impaired patients.

Hepatic Impairment — Based on the individual pharmacokinetic profiles of olanzapine and fluoxetine, the pharmacokinetics of SYMBYAX may be altered in patients with hepatic impairment. The lowest starting dose should be considered for patients with hepatic impairment *[see Warnings and Precautions (5.19) and Dosage and Administration (2.3)]*.

Although the presence of hepatic impairment may be expected to reduce the clearance of olanzapine, a study of the effect of impaired liver function in subjects (N=6) with clinically significant cirrhosis (Childs-Pugh Classification A and B) revealed little effect on the pharmacokinetics of olanzapine.

As might be predicted from its primary site of metabolism, liver impairment can affect the elimination of fluoxetine. The elimination half-life of fluoxetine was prolonged in a study of cirrhotic patients, with a mean of 7.6 days compared with the range of 2 to 3 days seen in subjects without liver disease; norfluoxetine elimination was also delayed, with a mean duration of 12 days for cirrhotic patients compared with the range of 7 to 9 days in normal subjects.

Gender — Clearance of olanzapine is approximately 30% lower in women than in men. There were, however, no apparent differences between men and women in effectiveness or adverse effects. Dosage modifications based on gender should not be needed.

Smoking Status — Olanzapine clearance is about 40% higher in smokers than in nonsmokers, although dosage modifications are not routinely required.

Race — No SYMBYAX pharmacokinetic study was conducted to investigate the effects of race. Results from an olanzapine cross-study comparison between data obtained in Japan and data obtained in the US suggest that exposure to olanzapine may be about 2-fold greater in the Japanese when equivalent doses are administered. Olanzapine clinical study safety and efficacy data, however, did not suggest clinically significant differences among Caucasian patients, patients of African descent, and a 3rd pooled category including Asian and Hispanic patients. Dosage modifications for race, therefore, are not routinely required.

Combined Effects — The combined effects of age, smoking, and gender could lead to substantial pharmacokinetic differences in populations. The clearance of olanzapine in young smoking males, for example, may be 3 times higher than that in elderly nonsmoking females. SYMBYAX dosing modification may be necessary in patients who exhibit a combination of factors that may result in slower metabolism of the olanzapine component *[see Dosage and Administration (2.3)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity, mutagenicity, or fertility studies were conducted with SYMBYAX. The following data are based on findings in studies performed with the individual components.

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Carcinogenesis

Olanzapine — Oral carcinogenicity studies were conducted in mice and rats. Olanzapine was administered to mice in two 78-week studies at doses of 3, 10, and 30/20 mg/kg/day [equivalent to 0.8 to 5 times the maximum recommended human daily dose (MRHD) on a mg/m^2 basis] and 0.25, 2, and 8 mg/kg/day (equivalent to 0.06 to 2 times the MRHD on a mg/m^2 basis). Rats were dosed for 2 years at doses of 0.25, 1, 2.5, and 4 mg/kg/day (males) and 0.25, 1, 4, and 8 mg/kg/day (females) (equivalent to 0.1 to 2 and 0.1 to 4 times the MRHD on a mg/m^2 basis, respectively). The incidence of liver hemangiomas and hemangiosarcomas was significantly increased in one mouse study in females dosed at 8 mg/kg/day (2 times the MRHD on a mg/m^2 basis); these tumors were not increased in another mouse study in females dosed at 10 or 30/20 mg/kg/day (2 to 5 times the MRHD on a mg/m^2 basis); in this study, there was a high incidence of early mortalities in males of the 30/20 mg/kg/day group. The incidence of mammary gland adenomas and adenocarcinomas was significantly increased in female mice dosed at ≥2 mg/kg/day and in female rats dosed at ≥4 mg/kg/day (0.5 and 2 times the MRHD on a mg/m^2 basis, respectively). Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum prolactin levels were not measured during the olanzapine carcinogenicity studies; however, measurements during subchronic toxicity studies showed that olanzapine elevated serum prolactin levels up to 4-fold in rats at the same doses used in the carcinogenicity study. An increase in mammary gland neoplasms has been found in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin-mediated. The relevance for human risk of the finding of prolactin-mediated endocrine tumors in rodents is unknown *[see Warning and Precautions (5.20)]*.

Fluoxetine — The dietary administration of fluoxetine to rats and mice for two years at doses of up to 10 and 12 mg/kg/day, respectively (approximately 1.2 and 0.7 times, respectively, the MRHD on a mg/m^2 basis), produced no evidence of carcinogenicity.

Mutagenesis

Olanzapine — No evidence of mutagenic potential for olanzapine was found in the Ames reverse mutation test, in vivo micronucleus test in mice, the chromosomal aberration test in Chinese hamster ovary cells, unscheduled DNA synthesis test in rat hepatocytes, induction of forward mutation test in mouse lymphoma cells, or in vivo sister chromatid exchange test in bone marrow of Chinese hamsters.

Fluoxetine — Fluoxetine and norfluoxetine have been shown to have no genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow cells.

Impairment of Fertility

SYMBYAX — Fertility studies were not conducted with SYMBYAX. However, in a repeat-dose rat toxicology study of three months duration, ovary weight was decreased in females treated with the low-dose [2 and 4 mg/kg/day (1 and 0.5 times the MRHD on a mg/m^2 basis), respectively] and high-dose [4 and 8 mg/kg/day (2 and 1 times the MRHD on a mg/m^2 basis), respectively] combinations of olanzapine and fluoxetine. Decreased ovary weight, and corpora lutea depletion and uterine atrophy were observed to a greater extent in the females receiving the high-dose combination than in females receiving either olanzapine or fluoxetine alone. In a 3-month repeat-dose dog toxicology study, reduced epididymal sperm and reduced testicular and prostate weights were observed with the high-dose combination of olanzapine and fluoxetine [5 and 5 mg/kg/day (9 and 2 times the MRHD on a mg/m^2 basis), respectively] and with olanzapine alone (5 mg/kg/day or 9 times the MRHD on a mg/m^2 basis).

Olanzapine — In a fertility and reproductive performance study in rats, male mating performance, but not fertility, was impaired at a dose of 22.4 mg/kg/day and female fertility was decreased at a dose of 3 mg/kg/day (11 and 1.5 times the MRHD on a mg/m^2 basis, respectively). Discontinuance of olanzapine treatment reversed the effects on male-mating performance. In female rats, the precoital period was increased and the mating index reduced at 5 mg/kg/day (2.5 times the MRHD on a mg/m^2 basis). Diestrous was prolonged and estrous was delayed at 1.3 mg/kg/day (0.6 times the MRHD on a mg/m^2 basis); therefore, olanzapine may produce a delay in ovulation.

Fluoxetine — Two fertility studies conducted in adult rats at doses of up to 7.5 and 12.5 mg/kg/day (approximately 0.9 and 1.5 times the MRHD on a mg/m^2 basis) indicated that fluoxetine had no adverse effects on fertility *[see Use in Specific Populations (8.4)]*.

14 CLINICAL STUDIES

14.1 Bipolar Depression

The efficacy of SYMBYAX for the treatment of depressive episodes associated with bipolar disorder was established in 2 identically designed, 8-week, randomized, double-blind, controlled studies of patients who met Diagnostic and Statistical Manual 4th edition (DSM-IV) criteria for Bipolar I Disorder, Depressed utilizing flexible dosing of SYMBYAX (6/25, 6/50, or 12/50 mg/day), olanzapine (5 to 20 mg/day), and placebo. These studies included patients ≥18 years of age (n=788) with or without psychotic symptoms and with or without a rapid cycling course.

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The primary rating instrument used to assess depressive symptoms in these studies was the Montgomery-Asberg Depression Rating Scale (MADRS), a 10-item clinician-rated scale with total scores ranging from 0 to 60. The primary outcome measure of these studies was the change from baseline to endpoint in the MADRS total score. In both studies, SYMBYAX was statistically significantly superior to both olanzapine monotherapy and placebo in reduction of the MADRS total score. The results of the studies are summarized below (Table 3).

Table 3: MADRS Total Score
Mean Change from Baseline to Endpoint

	Treatment Group	Baseline Mean	Change to Endpoint Mean[1]
Study 1	SYMBYAX (N=40)	30	-16*
	Olanzapine (N=183)	33	-12
	Placebo (N=181)	31	-10
Study 3	SYMBYAX (N=42)	33	-18*
	Olanzapine (N=169)	33	-14
	Placebo (N=174)	31	-9

[1] Negative number denotes improvement from baseline.
*Statistically significant compared to both olanzapine and placebo

14.2 Treatment Resistant Depression

[We have revised the following section to more accurately reflect the data used to assess efficacy.]

The efficacy of SYMBYAX in treatment resistant depression was demonstrated with data from 5 3 clinical studies (n=579) (Table 3). Doses evaluated in these studies ranged from 6/5 -15 20 mg for olanzapine and 25/20 -50 60 mg for fluoxetine.

Two identically designed An 8-week randomized, double-blind controlled studyies (Study 1 and 5) w wasere conducted to evaluate the efficacy of SYMBYAX in patients (n = 300) who met DSM-IV criteria for major depressive disorder and did not respond to 2 antidepressants of adequate dose and duration in their current episode (N=605). Patients who were not responding to an antidepressant in their current episode entered an 8-week open-label fluoxetine lead-in; non-responders were randomized (1:1:1) to receive SYMBYAX, olanzapine, or fluoxetine, and were treated for 8 weeks. SYMBYAX was flexibly dosed between 6/50 mg, 12/50 mg, and 18/50 mg. Results from one (Study 1) of these 2 studiesthis study yielded statistically significant greater reduction (p<0.001) in mean total MADRS scores from baseline to endpoint for SYMBYAX (-14.6) versus fluoxetine (-9.0) and olanzapine (-7.7). A second study with the same treatment-resistant patient population (n=28), when analyzed with change in MADRS as the primary outcome measure, demonstrated statistically significantly greater reduction in MADRS scores for SYMBYAX versus fluoxetine and olanzapine. Additionally,A third study -3, similarly designed studies (Study 2, 3, and 4) of 8-13 weeks duration (n=28, 251, 369, respectively) demonstrated statistically significantly greater reduction in total MADRS scores for SYMBYAX versus fluoxetine (p=0.013, 0.021, 0.106) and or olanzapine alone (p=0.035, 0.003, 0.007) respectively, when analyzed for the same in a subpopulation of depressed patients (n=251) who met the definition of treatment resistance (patients who were had not responding responded to 2 antidepressants of adequate dose and duration, both, during in the current episode).

An integrated analysis of the 5 studies yielded statistically significant greater reduction in mean total MADRS scores from baseline to endpoint in the defined population (p=0.015, p=0.007 versus fluoxetine and olanzapine, respectively) for SYMBYAX (-12.3) versus fluoxetine (-8.5) and olanzapine (-7.7).

Table 3: MADRS Total Score
Mean Change from Baseline to Endpoint in
Treatment Resistant Depression

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	Treatment Group	Baseline Mean	Change to Endpoint Mean[1]
Study 1	SYMBYAX (N=97)	30.6	-14.6
	Fluoxetine (N=101)	30.1	-9.0**
	Olanzapine (N=102)	30.7	-7.7**
Study 3	SYMBYAX (N=10)	29.5	-13.6
	Fluoxetine (N=10)	33.8	-1.2*
	Olanzapine (N=8)	25.0	-2.8*
Study 3	SYMBYAX (N=163)	30.1	-12.3
	Fluoxetine (N=41)	31.1	-10.0*
	Olanzapine (N=47)	34.5	-8.8*
Study 4	SYMBYAX (N=51)	29.4	-9.0
	Fluoxetine (N=88)	28.9	-7.0**
	Olanzapine (N=90)	32.4	-5.1*
Study 5	SYMBYAX (N=101)	29.5	-10.8
	Fluoxetine (N=103)	29.7	-9.4**
	Olanzapine (N=95)	29.7	-10.1**
Integrated analysis of 5 studies	SYMBYAX (N=463)	29.9	-12.0
	Fluoxetine (N=342)	29.6	-8.5*
	Olanzapine (N=342)	29.6	-7.7*

[1] Negative number denotes improvement from baseline.
* SYMBYAX statistically significant ($p<0.05$) compared to fluoxetine and olanzapine.
** SYMBYAX demonstrated a greater reduction in total MADRS scores, however did not reach statistical significance ($p<0.05$)

16 HOW SUPPLIED/STORAGE AND HANDLING

SYMBYAX capsules are supplied in 3/25-, 6/25-, 6/50-, 12/25-, and 12/50-mg (mg equivalent olanzapine/mg equivalent fluoxetine*) strengths.

SYMBYAX	CAPSULE STRENGTH				
	3 mg/25 mg	6 mg/25 mg	6 mg/50 mg	12 mg/25 mg	12 mg/50 mg
Color	Peach & Light Yellow	Mustard Yellow & Light Yellow	Mustard Yellow & Light Grey	Red & Light Yellow	Red & Light Grey
Capsule No.	PU3230	PU3231	PU3233	PU3232	PU3234
Identification	Lilly 3230 3/25	Lilly 3231 6/25	Lilly 3233 6/50	Lilly 3232 12/25	Lilly 3234 12/50
NDC Codes					
Bottles 30	0002-3230-30	0002-3231-30	0002-3233-30	0002-3232-30	0002-3234-30
Bottles 100		0002-3231-02	0002-3233-02	0002-3232-02	0002-3234-02
Bottles 1000		0002-3231-04	0002-3233-04	0002-3232-04	0002-3234-04
Blisters ID[2] 100		0002-3231-33	0002-3233-33	0002-3232-33	0002-3234-33

* Fluoxetine base equivalent.
† IDENTI-DOSE®, Unit Dose Medication, Lilly.

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Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

Keep tightly closed and protect from moisture.

17 PATIENT COUNSELING INFORMATION

17.1 Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with SYMBYAX and should counsel them in its appropriate use. A patient Medication Guide About Using Antidepressants in Children and Teenagers is available for SYMBYAX. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking SYMBYAX.

Patients should be cautioned about the concomitant use of SYMBYAX and NSAIDs, aspirin, or other drugs that affect coagulation since the combined use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding *[see Warnings and Precautions (5.15)]*.

Patients should be advised to avoid alcohol while taking SYMBYAX.

As with any CNS-active drug, SYMBYAX has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that SYMBYAX therapy does not affect them adversely.

Patients should be advised to inform their physician if they are taking Prozac®, Prozac Weekly™, Sarafem®, fluoxetine, Zyprexa®, or Zyprexa Zydis®. Patients should be advised to inform their physicians if they are taking or plan to take any prescription or over-the-counter drugs, including herbal supplements, since there is a potential for interactions. Patients should also be advised to inform their physicians if they plan to discontinue any medications they are taking while taking SYMBYAX, as stopping a medication may also impact the overall blood level of SYMBYAX.

Patients should be advised regarding appropriate care in avoiding overheating and dehydration.

Patients, if taking SYMBYAX, should be advised not to breast-feed.

Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration and in association with the use of concomitant drugs that may potentiate the orthostatic effect of olanzapine, e.g., diazepam or alcohol *[see Warnings and Precautions (5.10) and Drug Interactions (7)]*.

Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during SYMBYAX therapy.

Patients should be advised to notify their physician if they develop a rash or hives while taking SYMBYAX.

Patients should be advised to take SYMBYAX exactly as prescribed, and to continue taking SYMBYAX as prescribed even after their mood symptoms improve. Patients should be advised that they should not alter their dosing regimen, or stop taking SYMBYAX, without consulting their physician.

Patient information is printed at the end of this insert. Physicians should discuss this information with their patients and instruct them to read the Medication Guide before starting therapy with SYMBYAX and each time their prescription is refilled.

17.2 Clinical Worsening and Suicide Risk

Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to observe for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

17.3 Serotonin Syndrome

Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of SYMBYAX and triptans, tramadol or other serotonergic agents.

17.4 FDA Approved Medication Guide

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Medication Guide

About Using Antidepressants in Children and Teenagers

What is the most important information I should know if my child is being prescribed an antidepressant?

Parents or guardians need to think about 4 important things when their child is prescribed an antidepressant:

1. There is a risk of suicidal thoughts or actions
2. How to try to prevent suicidal thoughts or actions in your child
3. You should watch for certain signs if your child is taking an antidepressant
4. There are benefits and risks when using antidepressants

1. There is a Risk of Suicidal Thoughts or Actions

Children and teenagers sometimes think about suicide, and many report trying to kill themselves.

Antidepressants increase suicidal thoughts and actions in some children and teenagers. But suicidal thoughts and actions can also be caused by depression, a serious medical condition that is commonly treated with antidepressants. Thinking about killing yourself or trying to kill yourself is called *suicidality* or *being suicidal*.

A large study combined the results of 24 different studies of children and teenagers with depression or other illnesses. In these studies, patients took either a placebo (sugar pill) or an antidepressant for 1 to 4 months. ***No one committed suicide in these studies***, but some patients became suicidal. On sugar pills, 2 out of every 100 became suicidal. On the antidepressants, 4 out of every 100 patients became suicidal.

For some children and teenagers, the risks of suicidal actions may be especially high. These include patients with

- Bipolar illness (sometimes called manic-depressive illness)
- A family history of bipolar illness
- A personal or family history of attempting suicide

If any of these are present, make sure you tell your health care provider before your child takes an antidepressant.

2. How to Try to Prevent Suicidal Thoughts and Actions

To try to prevent suicidal thoughts and actions in your child, pay close attention to changes in her or his moods or actions, especially if the changes occur suddenly. Other important people in your child's life can help by paying attention as well (e.g., your child, brothers and sisters, teachers, and other important people). The changes to look out for are listed in Section 3, on what to watch for.

Whenever an antidepressant is started or its dose is changed, pay close attention to your child.

After starting an antidepressant, your child should generally see his or her health care provider

- Once a week for the first 4 weeks
- Every 2 weeks for the next 4 weeks
- After taking the antidepressant for 12 weeks
- After 12 weeks, follow your health care provider's advice about how often to come back
- More often if problems or questions arise (see Section 3)

You should call your child's health care provider between visits if needed.

3. You Should Watch for Certain Signs if Your Child is Taking an Antidepressant

Contact your child's health care provider *right away* if your child exhibits any of the following signs for the first time, or if they seem worse, or worry you, your child, or your child's teacher:

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- Thoughts about suicide or dying
- Attempts to commit suicide
- New or worse depression
- New or worse anxiety
- Feeling very agitated or restless
- Panic attacks
- Difficulty sleeping (insomnia)
- New or worse irritability
- Acting aggressive, being angry, or violent
- Acting on dangerous impulses
- An extreme increase in activity and talking
- Other unusual changes in behavior or mood

Never let your child stop taking an antidepressant without first talking to his or her health care provider. Stopping an antidepressant suddenly can cause other symptoms.

4. There are Benefits and Risks When Using Antidepressants

Antidepressants are used to treat depression and other illnesses. Depression and other illnesses can lead to suicide. In some children and teenagers, treatment with an antidepressant increases suicidal thinking or actions. It is important to discuss all the risks of treating depression and also the risks of not treating it. You and your child should discuss all treatment choices with your health care provider, not just the use of antidepressants.

Other side effects can occur with antidepressants (see section below).

Of all the antidepressants, only fluoxetine (Prozac®) has been FDA approved to treat pediatric depression.

For obsessive compulsive disorder in children and teenagers, FDA has approved only fluoxetine (Prozac®), sertraline (Zoloft®), fluvoxamine, and clomipramine (Anafranil®).

Your health care provider may suggest other antidepressants based on the past experience of your child or other family members.

Is this all I need to know if my child is being prescribed an antidepressant?

No. This is a warning about the risk for suicidality. Other side effects can occur with antidepressants. Be sure to ask your health care provider to explain all the side effects of the particular drug he or she is prescribing. Also ask about drugs to avoid when taking an antidepressant. Ask your health care provider or pharmacist where to find more information.

Prozac® is a registered trademark of Eli Lilly and Company.
Zoloft® is a registered trademark of Pfizer Pharmaceuticals.
Anafranil® is a registered trademark of Mallinckrodt Inc.

This Medication Guide has been approved by the US Food and Drug Administration for all antidepressants.

Rx only

Literature revised September 8, 2006

Eli Lilly and Company
Indianapolis, IN 46285

www.SYMBYAX.com

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren
3/28/2007 02:51:39 PM

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Lilly

www.lilly.com

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285
U.S.A.

Phone 317 276 2000

October 5, 2007

Re: Safety data on Zyprexa® (olanzapine) and Symbyax® (olanzapine and fluoxetine HCl capsules) – Hyperglycemia, Weight Gain, and Hyperlipidemia

Dear Health Care Professional,

Eli Lilly and Company would like to inform you of important information being added to the Zyprexa® (olanzapine) and Symbyax® (olanzapine and fluoxetine HCl) labels. These labeling updates include new WARNINGS for Weight Gain and Hyperlipidemia and updated information in the WARNING for Hyperglycemia. These changes reflect results of recently completed pooled analyses of clinical trials in adults and adolescents as well as information from two published large studies of atypical antipsychotics, CATIE[1] and CAFE[2].

The new labeling language is detailed below. Monitoring of glucose, weight, and lipids is recommended during olanzapine and olanzapine/fluoxetine combination treatment. Guidelines published by the American Diabetes Association (ADA) following the consensus development conference[3] provide recommendations for the monitoring of blood glucose, weight, and lipid levels in those treated with atypical antipsychotics. Other highlights of the updated labeling include:

- Abnormal or borderline glucose levels at baseline are an important risk factor for further glucose increase.
- While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.
- Significantly greater mean increases in total cholesterol, LDL cholesterol, and triglycerides were observed in Zyprexa-treated patients compared with placebo-treated patients both with and without evidence of dyslipidemia at baseline.
- Labeling provides information on magnitude and distribution of weight gain over a two year period in Zyprexa-treated patients.
- Labeling also provides information on glucose, weight gain, and lipids from studies of Zyprexa for adolescent patients. Please note that Zyprexa and Symbyax are not approved currently for use in children and adolescents aged less than 18 years old.

Exhibit 3 Page 1 of 2
SOA Opposition to Lilly
Motion for Summary Judgment
Case No. 3AN-06-05630 CI

Answers That Matter.

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Eli Lilly and Company remains committed to providing you with the most current product information available for the management of your patients and we will continue our ongoing research and analyses in these areas.

Please refer to the full prescribing information for Zyprexa and Symbyax included with this letter.

Should you have any questions or would like additional information regarding this important safety information, please contact the Lilly medical department at 1-800-Lilly-Rx or your Eli Lilly and Company sales representative.

The Medical Community can further our understanding of adverse events by reporting all cases to the Agency via the MedWatch program by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, via the MedWatch website at www.fda.gov/medwatch or by mail:

MEDWATCH
Food and Drug Administration
5515 Security Lane
Suite 5100, HFD-001
Rockville, MD 20852

Sincerely,

Tim Garnett, M.D.
Vice President,
Global Patient Safety
Eli Lilly and Company

The following are the updated Hyperglycemia WARNINGS and the new Hyperlipidemia and Weight WARNINGS included in the Zyprexa label.

WARNINGS:

Zyprexa:
The following is updated language in the WARNINGS section of the Zyprexa package insert, and will be reflected in other materials.

Hyperglycemia — Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the two highest serum concentrations was 15.0 mg/dL.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled adult olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (2.76 mg/dL versus 0.17 mg/dL). The difference in mean changes between olanzapine and placebo was greater in patients with evidence of glucose dysregulation at baseline (patients diagnosed with diabetes mellitus or related adverse events, patients treated with antidiabetic agents, patients with a baseline random glucose level ≥200 mg/dL, and/or a baseline fasting glucose level ≥126 mg/dL). These patients had a statistically significantly greater mean increase in HbA_{1c} compared to placebo. In patients with baseline normal fasting glucose levels (<100 mg/dL), 2.2% (N= 543) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 3.4% (N= 293) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 17.4% (N=178) of those treated with

olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 11.5% (N=96) of those treated with placebo.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (2.68 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus or having borderline increased blood glucose level (fasting 100–126 mg/dL, non-fasting 140–200 mg/dL). Patients taking olanzapine should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hyperlipidemia — Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using olanzapine, is advised.

Significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had statistically significant increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.0 mg/dL, and 20.8 mg/dL respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL,

4.3 mg/dL, and 10.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse events, patients treated with lipid lowering agents, or patients with high baseline lipid levels. Table 1 shows categorical changes in fasting lipid values.

Table 1. Changes in Fasting Lipids Values from Adult Placebo-Controlled Olanzapine Monotherapy Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	745	39.6%*
		Placebo	402	26.1%
	Normal to High (<150 mg/dL to ≥200 mg/dL)	Olanzapine	457	9.2%*
		Placebo	251	4.4%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	135	39.3%*
		Placebo	65	20.0%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	745	21.6%*
		Placebo	402	9.5%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	Olanzapine	392	2.8%
		Placebo	207	2.4%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	Olanzapine	222	23.0%*
		Placebo	112	12.5%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	536	23.7%*
		Placebo	304	14.1%
	Normal to High (<100 mg/dL to ≥160 mg/dL)	Olanzapine	154	0%
		Placebo	82	1.2%
	Borderline to High (≥100 mg/dL and <160 mg/dL to ≥160 mg/dL)	Olanzapine	302	10.6%
		Placebo	173	8.1%

* Statistically significant compared to placebo.

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in triglycerides in patients taking olanzapine was 40.5 mg/dL. In phase 1 of CATIE, the mean increase in total cholesterol was 9.4 mg/dL.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), for fasting HDL cholesterol, no statistically significant

differences were observed between olanzapine-treated patients and placebo-treated patients. Table 2 shows categorical changes in fasting lipid values in adolescent patients.

Table 2. Changes in Fasting Lipids Values from Adolescent Placebo-Controlled Olanzapine Monotherapy Studies

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	138	37.0%[a]
		Placebo	66	15.2%
	Normal to High (<90 mg/dL to >130 mg/dL)	Olanzapine	67	26.9%
		Placebo	28	10.7%
	Borderline to High (≥90 mg/dL and ≥130 mg/dL to >130 mg/dL)	Olanzapine	37	59.5%
		Placebo	17	35.3%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	138	14.5%[a]
		Placebo	66	4.5%
	Normal to High (<170 mg/dL to ≥200 mg/dL)	Olanzapine	87	6.9%
		Placebo	43	2.3%
	Borderline to High (≥170 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	36	38.9%[a]
		Placebo	13	7.7%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	137	17.5%
		Placebo	63	11.1%
	Normal to High (<110 mg/dL to ≥130 mg/dL)	Olanzapine	98	5.1%
		Placebo	44	4.5%
	Borderline to High (≥110 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	29	48.3%[a]
		Placebo	9	0%

[a] Statistically significant compared to placebo.

Weight Gain — Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight.

Olanzapine Monotherapy in Adults — In an analysis of 13 placebo-controlled olanzapine monotherapy studies, olanzapine-treated patients gained an average of 2.6 kg, which was statistically significantly different compared to an average 0.3 kg weight loss in placebo-treated patients with a median exposure of 6 weeks; 22.2% of olanzapine-treated patients gained at least 7% of their baseline weight, which was statistically significantly different compared to 3% of placebo-treated patients, with a median exposure of 8 weeks; 4.2% of olanzapine-treated patients gained at least 15% of their baseline weight, which was statistically significantly different compared to 0.3% of placebo-treated patients, with a median exposure of 12 weeks. Clinically significant weight gain was observed across all baseline Body Mass

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Index (BMI) categories. Discontinuation due to weight gain occurred in 0.2% of olanzapine-treated patients and in zero placebo-treated patients.

During long-term continuation therapy with olanzapine (238 median days of exposure), 56% of olanzapine patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 5.4 kg.

Table 3 includes data on weight gain with olanzapine pooled from 68 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified.

Table 3. Weight Gain with Olanzapine Use

Amount Gained kg (lb)	6 Weeks (N=2976) (%)	6 Months (N=1536) (%)	12 Months (N=778) (%)	24 Months (N=422) (%)
≤0	27	21	20	22
0-5 (0-11 lb)	57	34	25	22
5-10 (11-22 lb)	15	26	25	22
10-15 (22-33 lb)	2	12	16	18
>15 (>33 lb)	0	6	14	16

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 4 placebo-controlled olanzapine monotherapy studies of adolescent patients (ages 13 to 17 years), including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine-treated patients gained an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.6% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 9.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 19 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

During long-term continuation therapy with olanzapine, 65% of olanzapine-treated patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 7.4 kg.

Information for Patients:

Hyperglycemia — Patients should be advised of the potential risk of hyperglycemia-related adverse events. Patients should be monitored regularly for worsening of glucose control.

Weight Gain — Patients should be counseled that olanzapine is associated with weight gain. Patients should have their weight monitored regularly.

The following are the updated Hyperglycemia WARNINGS and the new Hyperlipidemia and Weight WARNINGS included in the Symbyax label.

WARNINGS:

Symbyax:
The following is updated language in the WARNINGS section of the Symbyax package insert, and will be reflected in other materials.

Hyperglycemia -- Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including olanzapine alone, as well as olanzapine taken concomitantly with fluoxetine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase I of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the two highest serum concentrations was 15.0 mg/dL.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, with treatment duration up to 12 weeks, SYMBYAX was associated with a statistically significantly greater mean change in random glucose compared to placebo (8.65 mg/dL versus -3.86 mg/dL). In patients with baseline normal random glucose levels (<140 mg/dL), 2.3% of those treated with SYMBYAX were found to have high glucose levels (≥200 mg/dL) during SYMBYAX treatment and were statistically significantly different compared to 0.3% of those treated with placebo. In patients with baseline borderline random glucose levels (≥140 mg/dL and <200 mg/dL), 34.1% of those treated with SYMBYAX were found to have high glucose levels (≥200 mg/dL) during SYMBYAX treatment and were statistically significantly different compared to 3.6% of those treated with placebo. The difference in mean changes between SYMBYAX and placebo was greater in patients with evidence of glucose dysregulation at baseline (including those patients diagnosed with diabetes mellitus or related adverse events, patients treated with anti-diabetic agents,

patients with a baseline random glucose level ≥200 mg/dL, or a baseline fasting glucose level ≥126 mg/dL). These patients had a greater mean increase in HbA_{1c}.

Controlled fasting glucose data is limited for SYMBYAX; however, in an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (2.76 mg/dL vs 0.17 mg/dL).

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine and olanzapine and fluoxetine in combination have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (2.68 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing SYMBYAX to patients with an established diagnosis of diabetes mellitus or having borderline increased blood glucose level (fasting 100–126 mg/dL, nonfasting 140–200 mg/dL). Patients taking SYMBYAX should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hyperlipidemia — Undesirable alterations in lipids have been observed with SYMBYAX use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using SYMBYAX, is advised.

Significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with SYMBYAX use. Significant increases in total cholesterol have also been seen with SYMBYAX use.

Controlled fasting lipid data is limited for SYMBYAX.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, with treatment duration up to 12 weeks, SYMBYAX-treated patients had an increase from baseline in mean random total cholesterol of 12.1 mg/dL compared to a statistically significantly different increase from baseline in mean random total cholesterol of 4.8 mg/dL for olanzapine-treated patients and a decrease in mean random total cholesterol of 5.5 mg/dL for placebo-treated patients. Table 3 shows categorical changes in nonfasting lipid values.

Table 3. Changes in Nonfasting Lipids Values from Controlled Clinical Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients (%)
Nonfasting Triglycerides	Increase by ≥50 mg/dL	OFC	174	67.8%
		Olanzapine	172	72.7%
	Normal to High (<150 mg/dL to ≥500 mg/dL)	OFC	57	0%
		Olanzapine	58	0%
	Borderline to High (≥150 mg/dL and <500 mg/dL to ≥500 mg/dL)	OFC	106	15.1%
		Olanzapine	103	8.7%
Nonfasting Total Cholesterol	Increase by ≥40 mg/dL	OFC	685	35%[a,b]
		Olanzapine	749	22.7%
		Placebo	390	9%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	OFC	256	8.2%[a,b]
		Olanzapine	279	2.9%
		Placebo	175	1.7%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	OFC	213	36.2%[a,b]
		Olanzapine	261	27.6%
		Placebo	111	9.9%

[a] Statistically significant compared to olanzapine.
[b] Statistically significant compared to placebo.

Controlled fasting lipid data is limited for SYMBYAX; however, in an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had statistically significant increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.0 mg/dL, and 20.8 mg/dL respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL, 4.3 mg/dL, and 10.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in

patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse events, patients treated with lipid lowering agents, patients with high baseline lipid levels. Table 4 shows categorical changes in fasting lipid values.

Table 4. Changes in Fasting Lipids Values from Adult Placebo-Controlled Olanzapine Monotherapy Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	745	39.6%*
		Placebo	402	26.1%
	Normal to High (<150 mg/dL to ≥200 mg/dL)	Olanzapine	457	9.2%*
		Placebo	251	4.4%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	135	39.3%*
		Placebo	65	20.0%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	745	21.6%*
		Placebo	402	9.5%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	Olanzapine	392	2.8%
		Placebo	207	2.4%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	Olanzapine	222	23.0%*
		Placebo	112	12.5%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	536	23.7%*
		Placebo	304	14.1%
	Normal to High (<100 mg/dL to ≥160 mg/dL)	Olanzapine	154	0%
		Placebo	82	1.2%
	Borderline to High (≥100 mg/dL and <160 mg/dL to ≥160 mg/dL)	Olanzapine	302	10.6%
		Placebo	173	8.1%

* Statistically significant compared to placebo.

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in triglycerides in patients taking olanzapine was 40.5 mg/dL. In phase 1 of CATIE, the median increase in total cholesterol was 9.4 mg/dL.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine and olanzapine and fluoxetine in combination have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), for fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Table 5 shows categorical changes in fasting lipid values in adolescent patients.

Table 5. Changes in Fasting Lipids Values from Adolescent Placebo-Controlled Olanzapine Monotherapy Studies

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	138	37.0%[a]
		Placebo	66	15.2%
	Normal to High (<90 mg/dL to ≥130 mg/dL)	Olanzapine	67	26.9%
		Placebo	28	10.7%
	Borderline to High (≥90 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	37	59.5%
		Placebo	17	35.3%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	138	14.5%[a]
		Placebo	66	4.5%
	Normal to High (<170 mg/dL to ≥200 mg/dL)	Olanzapine	87	6.9%
		Placebo	43	2.3%
	Borderline to High (≥170 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	36	38.9%[a]
		Placebo	13	7.7%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	137	17.5%
		Placebo	63	11.1%
	Normal to High (<110 mg/dL to ≥130 mg/dL)	Olanzapine	98	5.1%
		Placebo	44	4.5%
	Borderline to High (≥110 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	29	48.3%[a]
		Placebo	9	0%

[a] Statistically significant compared to placebo.

Weight Gain — Potential consequences of weight gain should be considered prior to starting SYMBYAX. Patients receiving SYMBYAX should receive regular monitoring of weight.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, the mean weight increase for SYMBYAX-treated patients was statistically significantly greater than placebo-treated (4 kg vs -0.3 kg). Twenty-two percent of SYMBYAX-treated patients gained at least 7% of their baseline weight, with a median exposure of 6 weeks. This was statistically significantly greater than in placebo-treated patients (1.8%). Approximately 3% of SYMBYAX-treated patients gained at least 15% of their baseline weight, with a median exposure of 8 weeks. This was statistically significantly greater than in placebo-treated patients (0%). Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Discontinuation due to weight gain occurred in 2.5% of SYMBYAX-treated patients and zero placebo-treated patients.

Table 6 includes data on weight gain with olanzapine pooled from 68 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified.

Table 6. Weight Gain with Olanzapine Use

Amount Gained kg (lb)	6 Weeks (N=2976) (%)	6 Months (N=1536) (%)	12 Months (N=778) (%)	24 Months (N=422) (%)
≤0	27	21	20	22
0-5 (0-11 lb)	57	34	25	22
5-10 (11-22 lb)	15	26	25	22
10-15 (22-33 lb)	2	12	16	18
>15 (>33 lb)	0	6	14	16

During long-term continuation therapy with olanzapine monotherapy (238 median days of exposure), 56% of olanzapine patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 5.4 kg.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine and olanzapine and fluoxetine in combination have not been established in patients under the age of 18 years. In an analysis of 4 placebo-controlled olanzapine monotherapy studies of adolescent patients (ages 13 to 17 years), including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine-treated patients gained an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.6% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 9.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 19 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

During long-term continuation therapy with olanzapine, 65% of olanzapine-treated patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 7.4 kg.

Information for Patients:

Hyperglycemia — Patients should be advised of the potential risk of hyperglycemia-related adverse events. Patients should be monitored regularly for worsening of glucose control.

Weight Gain -- Patients should be counseled that SYMBYAX is associated with weight gain. Patients should have their weight monitored regularly.

References:

1. Lieberman, JA, Stroup, TS, McEvoy, JP, S. Swartz, MS, Rosenheck, RA, Perkins, DO, Keefe, RSE, Davis, SM, Davis, CE, Lebowitz, BD, Severe, J, Hsiao, JK. 2005. Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. New Engl J Med 353(12): 1209-1223.

2. McEvoy, JP, Lieberman,JA, Perkins, DO, Hamer, RM, Gu, H, Lazarus, A, Sweitzer, D, Olexy, C, Weiden, P, Strakowski, SD. 2007. Efficacy and Tolerability of Olanzapine, Quetiapine, and Risperidone in the Treatment of Early Psychosis: A Randomized, Double-Blind 52-Week Comparison. Am J Psychiatry 164:1050–1060.

3. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for Study of Obesity. 2004. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. Diabetes Care 27: 596-601. http://care.diabetesjournals.org/cgi/content/full/27/2/596

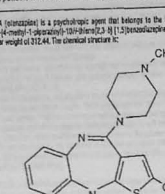
Zyprexa® (olanzapine) is indicated for the short-term and maintenance treatment of schizophrenia. Zyprexa is also indicated as monotherapy or in combination with lithium or valproate for the short-term treatment of acute mixed or manic episodes associated with Bipolar I Disorder and as maintenance treatment in bipolar disorder. Symbyax® (olanzapine and fluoxetine HCl capsules) is indicated for treatment of depressive episodes associated with bipolar disorder.

ZYPREXA® Olanzapine Tablets
ZYPREXA® ZYDIS® Olanzapine Orally Disintegrating Tablets
ZYPREXA® IntraMuscular Olanzapine for Injection

WARNING

Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. ZYPREXA (olanzapine) is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS).

DESCRIPTION: ZYPREXA (olanzapine) is a psychotropic agent that belongs to the thienobenzodiazepine class. The chemical designation is 2-methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno[2,3-*b*][1,5]benzodiazepine. The molecular formula is $C_{17}H_{20}N_4S$, which corresponds to a molecular weight of 312.44. The chemical structure is:



Olanzapine is a yellow crystalline solid, which is practically insoluble in water.

ZYPREXA tablets are intended for oral administration only.

Each tablet contains olanzapine equivalent to 2.5 mg (8 µmol), 5 mg (16 µmol), 7.5 mg (24 µmol), 10 mg (32 µmol), 15 mg (48 µmol), or 20 mg (64 µmol). Inactive ingredients are cornstarch, croscarmellose, hydroxypropyl cellulose, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, and other inactive ingredients. The color coating contains Titanium Dioxide (all strengths), FD&C Blue No. 2 Aluminum Lake (15 mg), or Synthetic Red Iron Oxide (20 mg). The 2.5, 5, 7.5, and 10 mg tablets are imprinted with edible ink which contains FD&C Blue No. 2 Aluminum Lake.

ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) is intended for oral administration only.

Each orally disintegrating tablet contains olanzapine equivalent to 5 mg (16 µmol), 10 mg (32 µmol), 15 mg (48 µmol) or 20 mg (64 µmol). It begins disintegrating in the mouth within seconds, allowing its contents to be subsequently swallowed with or without liquid. ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) also contains the following inactive ingredients: gelatin, mannitol, methacrylic acid copolymer, sodium methyl paraben and sodium propyl paraben.

ZYPREXA IntraMuscular (olanzapine for injection) is intended for intramuscular use only.

Each vial provides for the administration of 10 mg (32 µmol) olanzapine with inactive ingredients 50 mg lactose monohydrate and 13 mg lactic acid. Hydrochloric acid and/or sodium hydroxide may have been added during manufacture to adjust pH.

CLINICAL PHARMACOLOGY: Pharmacodynamics—Olanzapine is a selective monoaminergic antagonist with high affinity binding to the following receptors: serotonin $5HT_{2A/2C}$, $5HT_3$, (K_i=4, 11, and 5 nM, respectively), dopamine D_1, (K_i=11-31 nM), histamine H_1 (K_i=7 nM), and adrenergic α_1 receptors (K_i=19 nM). Olanzapine is an antagonist with moderate affinity binding for serotonin $5HT_6$ (K_i=51 nM) and muscarinic M_{1-5} (K_i=73, 96, 132, 37, and 45 nM, respectively). Olanzapine binds weakly to GABA$_A$, BZD, and β adrenergic receptors (K_i>10 µM).

The mechanism of action of olanzapine, as with other drugs having efficacy in schizophrenia, is unknown. However, it has been proposed that this drug's efficacy in schizophrenia is mediated through a combination of dopamine and serotonin type 2 ($5HT_2$) antagonism. The mechanism of action of olanzapine in the treatment of acute manic episodes associated with Bipolar I Disorder is unknown.

Antagonism at receptors other than dopamine and $5HT_2$ may explain some of the other therapeutic and side effects of olanzapine. Olanzapine's antagonism of muscarinic M_{1-5} receptors may explain its anticholinergic-like effects. Olanzapine's antagonism of histamine H_1 receptors may explain the somnolence observed with this drug. Olanzapine's antagonism of adrenergic α_1 receptors may explain the orthostatic hypotension observed with this drug.

Pharmacokinetics—*Oral Administration*—Olanzapine is well absorbed and reaches peak concentrations in approximately 6 hours following an oral dose. It is eliminated extensively by first pass metabolism, with approximately 40% of the dose metabolized before reaching the systemic circulation. Food does not affect the rate or extent of olanzapine absorption. Pharmacokinetic studies showed that ZYPREXA tablets and ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) dosage forms of olanzapine are bioequivalent.

Olanzapine displays linear kinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours (5th to 95th percentile; mean of 30 hr), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th percentile; mean of 25 L/hr).

Administration of olanzapine once daily leads to steady-state concentrations in about one week that are approximately twice the concentrations after single doses. Plasma concentrations, half-life, and clearance of olanzapine may vary between individuals on the basis of smoking status, gender, and age (see Special Populations).

Olanzapine is extensively distributed throughout the body, with a volume of distribution of approximately 1000 L. It is 93% bound to plasma proteins over the concentration range of 7 to 1000 ng/mL, binding primarily to albumin and α_1-acid glycoprotein.

Metabolism and Elimination—Following a single oral dose of ^{14}C-labeled olanzapine, 7% of the dose of olanzapine was recovered in the urine as unchanged drug, indicating that olanzapine is highly metabolized. Approximately 57% and 30% of the dose was recovered in the urine and feces, respectively, in the plasma, olanzapine accounted for only 12% of the AUC for total radioactivity, indicating significant exposure to metabolites. After multiple dosing, the major circulating metabolites were the 10-N-glucuronide, present at steady state at 44% of the concentration of olanzapine, and 4'-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed.

Direct glucuronidation and cytochrome P450 (CYP) mediated oxidation are the primary metabolic pathways for olanzapine. In vitro studies suggest that CYPs 1A2 and 2D6, and the flavin-containing monooxygenase system are involved in olanzapine oxidation. CYP2D6 mediated oxidation appears to be a minor metabolic pathway in vivo, because the clearance of olanzapine is not reduced in subjects who are deficient in this enzyme.

Intramuscular Administration—ZYPREXA IntraMuscular results in rapid absorption with peak plasma concentrations occurring within 15 to 45 minutes. Based upon a pharmacokinetic study in healthy volunteers, a 5 mg dose of intramuscular olanzapine for injection produces, on average, a maximum plasma concentration approximately 5 times higher than the maximum plasma concentration produced by a 5 mg dose of oral olanzapine. Area under the curve achieved after an intramuscular dose is similar to that achieved after oral administration of the same dose. The half-life observed after intramuscular administration is similar to that observed after oral dosing. The pharmacokinetics are linear over the clinical dosing range. Metabolic profiles after intramuscular administration are qualitatively similar to metabolic profiles after oral administration.

Special Populations—Renal Impairment—Because olanzapine is highly metabolized before excretion and only 7% of the drug is excreted unchanged, renal dysfunction alone is unlikely to have a major impact on the pharmacokinetics of olanzapine. The pharmacokinetic characteristics of olanzapine were similar in patients with severe renal impairment and normal subjects, indicating that dosage adjustment based upon the degree of renal impairment is not required. In addition, olanzapine is not removed by dialysis. The effect of renal impairment on metabolism of olanzapine has not been studied.

Hepatic Impairment—Although the presence of hepatic impairment may be expected to reduce the clearance of olanzapine, a study of the effect of impaired liver function in subjects (n=6) with clinically significant (Child's Pugh Classification A and B) cirrhosis revealed little effect on the pharmacokinetics of olanzapine.

Age—In a study involving 24 healthy subjects, the mean elimination half-life of olanzapine was about 1.5 times greater in elderly (>65 years) than in non-elderly subjects (≤65 years). Caution should be used in dosing the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity (see DOSAGE AND ADMINISTRATION).

Gender—Clearance of olanzapine is approximately 50% lower in women than in men. There was, however, no apparent differences between men and women in effectiveness or adverse effects. Dosage modifications based on gender should not be needed.

Smoking Status—Olanzapine clearance is about 40% higher in smokers than in nonsmokers, although dosage modifications are not routinely recommended.

Race—In vivo studies have shown that exposures are similar among Japanese, Chinese and Caucasians, especially after normalization for body weight differences. Dosage modifications for race are, therefore, not recommended.

Combined Effects—The combined effects of age, smoking, and gender could lead to substantial pharmacokinetic differences in populations. The clearance in young smoking males, for example, may be 3 times higher than that in elderly nonsmoking females. Dosing modifications may be necessary in patients who exhibit a combination of factors that may result in slower metabolism of olanzapine (see DOSAGE AND ADMINISTRATION).

For specific information about the pharmacology of lithium or valproate, refer to the CLINICAL PHARMACOLOGY section of the package inserts for these other products.

CLINICAL EFFICACY DATA: *Schizophrenia*—The efficacy of oral olanzapine in the treatment of schizophrenia was established in 2 short-term (6-week) controlled trials of inpatients who met DSM III-R criteria for schizophrenia. A single haloperidol dose was 2 short-term (6-week) controlled trials of inpatients who met DSM III-R criteria for schizophrenia. A single haloperidol dose was included as a comparative treatment in one of the two trials, but this trial did not compare these two drugs on the full range of clinically relevant doses for both.

Several instruments were used for assessing psychiatric signs and symptoms in these studies, among them the Brief Psychiatric Rating Scale (BPRS), a multi-item inventory of general psychopathology traditionally used to evaluate the effects of drug treatment in schizophrenia. The BPRS psychosis cluster (conceptual disorganization, hallucinatory behavior, suspiciousness, and unusual thought content) is considered a particularly useful subset for assessing actively psychotic schizophrenic patients. A second traditional assessment, the Clinical Global Impression (CGI), reflects the impression of a skilled observer, fully familiar with the manifestations of schizophrenia, about the overall clinical state of the patient. In addition, two more recently developed scales were employed; these schizophrenia, about the overall clinical state of the patient. In addition, two more recently developed scales were employed; these included the 30-item Positive and Negative Symptom Rating Scale (PANSS), in which are embedded the 18 items of the BPRS, and the Scale for Assessing Negative Symptoms (SANS). The trial summaries below focus on the following outcomes: PANSS total and/or BPRS total, BPRS psychosis cluster, PANSS negative subscale, or SANS and CGI Severity. The results of the trials follow:

(1) In a 6-week, placebo-controlled trial (n=149) involving two fixed olanzapine doses of 1 and 10 mg/day (once daily schedule), olanzapine, at 10 mg/day (but not at 1 mg/day), was superior to placebo on the PANSS total score (also on the extracted BPRS total), on the BPRS psychosis cluster, on the PANSS negative subscale, and on CGI Severity.

(2) In a 6-week, placebo-controlled trial (n=552) involving 3 fixed dose ranges of olanzapine (5 ± 2.5 mg/day, 10 ± 2.5 mg/day, and 15 ± 2.5 mg/day) on a once daily schedule, the two highest olanzapine dose groups (actual mean doses of 12 and 16 mg/day, respectively) were superior to placebo on BPRS total score, BPRS psychosis cluster, and CGI severity scores; the highest olanzapine dose group was superior to placebo on the SANS. There was no clear advantage for the high dose group over the medium dose group.

Examination of population subsets (race and gender) did not reveal any differential responsiveness on the basis of these subgroupings.

In a longer-term trial, adult outpatients (n=326) who predominately met DSM-IV criteria for schizophrenia and who remained stable on olanzapine during open label treatment for at least 8 weeks were randomized to continuation on their current olanzapine doses (ranging from 10 to 20 mg/day) or to placebo. The below-up period to observe patients for relapse, defined as a history of increases in BPRS positive symptoms or hospitalization, was planned for 12 months, however, criteria were met for stopping the trial early due to an excess of positive relapses compared to olanzapine relapses, and olanzapine was superior to placebo on time to relapse, the primary outcome for this study. Thus, olanzapine was more effective than placebo at maintaining efficacy in patients stabilized for approximately 8 weeks and followed for an observation period of up to 8 months.

Bipolar Disorder—Monotherapy—The efficacy of oral olanzapine in the treatment of acute manic or mixed episodes was established in 2 short-term (one 3-week and one 4-week) placebo-controlled trials in patients who met the DSM-IV criteria for Bipolar I Disorder with manic or mixed episodes. These trials included patients with or without psychotic features and with or without a rapid-cycling course.

The primary efficacy instrument used for assessing manic symptoms in these trials was the Young Mania Rating Scale (Y-MRS), an 11-item clinician-rated scale traditionally used to assess the degree of manic symptomatology (irritability, disruptive/aggressive behavior, elevated mood, speech, increased activity, sexual interest, language/thought disorder, thought content, appearance, and insight) in a range from 0 (no manic features) to 60 (maximum score). The primary outcome in these trials was change from baseline in the Y-MRS total score. The results of the trials follow:

(1) In one 3-week placebo-controlled trial (n=67) which involved a dose range of olanzapine (5-20 mg/day, once daily, starting at 10 mg/day), olanzapine was superior to placebo in the reduction of Y-MRS total score. In an identically designed and conducted simultaneously with the first trial, olanzapine demonstrated a similar treatment difference, but possibly due to sample size and site variability, was not shown to be superior to placebo on this outcome.

(2) In a 4-week placebo-controlled trial (n=115) which involved a dose range of olanzapine (5-20 mg/day, once daily, starting at 15 mg/day), olanzapine was superior to placebo in the reduction of Y-MRS total score.

(3) In another trial, 361 patients meeting DSM-IV criteria for a manic or mixed episode of bipolar disorder who had responded during an initial open-label treatment phase for about two weeks, on average, to olanzapine 5 to 20 mg/day were randomized to either continuation of olanzapine at their same dose (n=225) or to placebo (n=136), for observation of relapse. Approximately 50% of the patients had discontinued from the olanzapine group by day 56 and 50% of the placebo group had discontinued by day 23 of double-blind treatment. Response during the open-label phase was defined as having a decrease of the Y-MRS total score to ≤12 and HAM-D 21 to ≤8. Relapse during the double-blind phase was defined as an increase of the Y-MRS or HAM-D 21 total score to ≥15, or being hospitalized for either manic or depression. In the randomized phase, patients receiving continued olanzapine experienced a significantly longer time to relapse.

Combination Therapy—The efficacy of oral olanzapine with concomitant lithium or valproate in the treatment of acute manic episodes was established in two controlled trials in patients who met the DSM-IV criteria for Bipolar I Disorder with manic or mixed episodes. These trials included patients with or without psychotic features and with or without a rapid-cycling course. The results of the trials follow:

(1) In one 6-week placebo-controlled combination trial, 175 outpatients on lithium or valproate therapy with inadequately controlled manic or mixed symptoms (Y-MRS ≥16) were randomized to receive either olanzapine or placebo, in combination with their original therapy. Olanzapine (in a dose range of 5-20 mg/day, once daily, starting at 10 mg/day) combined with lithium or valproate (to a therapeutic range of 0.6 mEq/L to 1.2 mEq/L or 50 µg/mL to 125 µg/mL, respectively) was superior to lithium or valproate alone in the reduction of Y-MRS total score.

(2) In a second 6-week placebo-controlled combination trial, 169 outpatients on lithium or valproate therapy with inadequately controlled manic or mixed symptoms (Y-MRS ≥16) were randomized to receive either olanzapine or placebo, in combination with their original therapy. Olanzapine (in a dose range of 5-20 mg/day, once daily, starting at 10 mg/day) combined with lithium or valproate (to a therapeutic range of 0.6 mEq/L to 1.2 mEq/L or 50 µg/mL to 125 µg/mL, respectively) was superior to lithium or valproate alone in the reduction of Y-MRS total score.

Agitation Associated with Schizophrenia and Bipolar I Mania—The efficacy of intramuscular olanzapine for injection for the treatment of agitation was established in 2 short-term (24 hours of IM treatment) placebo-controlled trials in agitated inpatients from two diagnostic groups: schizophrenia and Bipolar I Disorder (manic or mixed episodes). Each of the trials included a single active comparator treatment arm of either haloperidol injection (schizophrenia study) or lorazepam injection (bipolar mania study). Patients enrolled in the trials needed to be: (1) judged by the clinical investigators as clinically agitated and clinically appropriate candidates for treatment with intramuscular medication, and (2) exhibiting a level of agitation that met or exceeded a threshold score of ≥14 on the hostility, uncooperativeness and excitement items) with at least one individual item score and using a 1-7 scoring system (1=absent, 4=moderate, 7=extreme). In the studies, the mean baseline PANSS Excited Component score was 18.4, with scores ranging from 13 to 32 (out of a maximum score of 35). Both supporting predominantly moderate levels of agitation with some patients experiencing mild or severe levels of agitation. The primary efficacy measure used for assessing agitation signs and symptoms in these trials was during the 24 hour IM treatment periods; however, patients could not receive the second injection until after the initial 2 hour period when the primary efficacy measure was assessed. The results of the trials follow:

(1) In a placebo-controlled trial in agitated inpatients meeting DSM-IV criteria for schizophrenia (n=270), four fixed intramuscular olanzapine for injection doses of 2.5 mg, 5 mg, 7.5 mg and 10 mg were evaluated. All doses were statistically superior to placebo on the PANSS Excited Component at 2 hours post-injection. However, the effect was larger and more consistent for the three higher doses. There were no significant pairwise differences for the 7.5 and 10 mg doses over the 5 mg dose.

(2) In a second placebo-controlled trial in agitated inpatients meeting DSM-IV criteria for schizophrenia (n=311), one fixed intramuscular olanzapine for injection dose of 10 mg was evaluated. Olanzapine for injection was statistically superior to placebo on the PANSS Excited Component at 2 hours post-injection.

(3) In a placebo-controlled trial in agitated inpatients meeting DSM-IV criteria for Bipolar I Disorder (and currently displaying an acute manic or mixed episode with or without psychotic features) (n=201), one fixed intramuscular olanzapine for injection dose of 10 mg was evaluated. Olanzapine for injection was statistically superior to placebo on the PANSS Excited Component at 2 hours post-injection.

Actuals Deposition
SOA Opposition to Lilly
Summary Judgment
ZYPREXA® (Olanzapine Tablets)
ZYPREXA® ZYDIS® (Olanzapine Orally Disintegrating Tablets)
ZYPREXA® IntraMuscular (Olanzapine for Injection)
Case No. 3:06-CV-00633-DRH-DGW
PV 5199 AMP
008232

Examination of population subsets (age, race, and gender) did not reveal any differential responsiveness on the basis of these subgroupings.

INDICATIONS AND USAGE: Schizophrenia—Oral ZYPREXA is indicated for the treatment of schizophrenia. [see CLINICAL EFFICACY DATA].

The efficacy of ZYPREXA was established in short-term (6-week) controlled trials of schizophrenic inpatients [see CLINICAL EFFICACY DATA].

The effectiveness of oral ZYPREXA at maintaining a treatment response in schizophrenic patients who had been stable on ZYPREXA for approximately 8 weeks and were then followed for a period of up to 8 months has been demonstrated in a placebo-controlled trial [see CLINICAL EFFICACY DATA]. Nevertheless, the physician who elects to use ZYPREXA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient [see DOSAGE AND ADMINISTRATION].

Bipolar Disorder—Acute Monotherapy—Oral ZYPREXA is indicated for the treatment of acute manic or mixed episodes associated with Bipolar I Disorder.

The efficacy of ZYPREXA was established in two placebo-controlled trials (one 3-week and one 4-week) with patients meeting DSM-IV criteria for Bipolar I Disorder who currently displayed an acute manic or mixed episode with or without psychotic features [see CLINICAL EFFICACY DATA].

Maintenance Monotherapy—The benefit of maintaining bipolar patients on monotherapy with oral ZYPREXA after achieving a response status for an average duration of two weeks was demonstrated in a controlled trial [see CLINICAL EFFICACY DATA]. The physician who elects to use ZYPREXA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient [see DOSAGE AND ADMINISTRATION].

Combination Therapy—The combination of oral ZYPREXA with lithium or valproate is indicated for the short-term treatment of acute manic or mixed episodes associated with Bipolar I Disorder.

The efficacy of ZYPREXA in combination with lithium or valproate was established in two placebo-controlled (6-week) trials with patients meeting DSM-IV criteria for Bipolar I Disorder who currently displayed an acute manic or mixed episode with or without psychotic features [see CLINICAL EFFICACY DATA].

Agitation Associated with Schizophrenia and Bipolar I Mania—ZYPREXA IntraMuscular is indicated for the treatment of agitation associated with schizophrenia and bipolar I mania. "Psychomotor agitation" is defined in DSM-IV as "excessive motor activity associated with a feeling of inner tension." Patients experiencing agitation often manifest behaviors that interfere with their diagnosis and care, e.g., threatening behavior, pacing, or urgently distressing behavior, or self exhausting behavior, leading clinicians to the use of intramuscular antipsychotic medications to achieve immediate control of the agitation.

The efficacy of ZYPREXA IntraMuscular for the treatment of agitation associated with schizophrenia and bipolar I mania was established in 3 short-term (24 hours) placebo-controlled trials in agitated inpatients with schizophrenia or Bipolar I Disorder (manic or mixed episodes) [see CLINICAL EFFICACY DATA].

CONTRAINDICATIONS: ZYPREXA is contraindicated in patients with a known hypersensitivity to the product.

For specific information about the contraindications of lithium or valproate, refer to the CONTRAINDICATIONS section of the package insert for these other products.

WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. ZYPREXA is not approved for the treatment of patients with dementia-related psychosis [see BOX WARNING].

In placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs 1.5%, respectively).

Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients with Dementia-Related Psychosis—Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dermentia-related psychosis.

Hyperglycemia—Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the two highest serum concentrations was 15.6 mg/dL.

Olanzapine Monotherapy in Adults—In an analysis of 5 placebo-controlled adult olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (3.76 mg/dL versus 0.17 mg/dL). The difference in mean changes between olanzapine and placebo was greater in patients with evidence of glucose dysregulation at baseline (patients diagnosed with diabetes mellitus or related adverse events, patients treated with anti-diabetic agents, patients with a baseline random glucose level ≥200 mg/dL, and/or a baseline fasting glucose level ≥126 mg/dL). These patients had a statistically significantly greater mean increase in HbA_{1c} compared to placebo. In patients with baseline normal fasting glucose levels (<100 mg/dL), 2.2% (N=543) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 0.4% (N=253) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 17.4% (N=178) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 11.5% (N=96) of those treated with placebo.

Olanzapine Monotherapy in Adolescents—The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (2.56 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus, or having borderline increased blood glucose level (fasting 100–126 mg/dL, non-fasting 140–200 mg/dL). Patients taking olanzapine should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hypercholesterolemia—Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients receiving olanzapine, is advised.

Significant, and sometimes very high (≥500 mg/dL), elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Olanzapine Monotherapy in Adults—In an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had statistically significant increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.5 mg/dL, and 20.6 mg/dL, respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL, 4.3 mg/dL, and 16.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse events, patients treated with lipid lowering agents, or patients with high baseline lipid levels. Table 1 shows categorical changes in fasting lipid values.

Table 1. Changes in Fasting Lipids Values from Adult Placebo-Controlled Olanzapine Monotherapy Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	745	30.6%*
		Placebo	402	26.1%
	Normal to High (<150 mg/dL to ≥200 mg/dL)	Olanzapine	457	9.2%*
		Placebo	251	4.4%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	135	39.3%*
		Placebo	65	20.0%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	745	21.8%*
		Placebo	402	9.5%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	Olanzapine	392	2.8%
		Placebo	207	2.4%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	Olanzapine	222	23.0%*
		Placebo	112	12.5%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	536	23.7%*
		Placebo	304	14.1%
	Normal to High (<100 mg/dL to ≥160 mg/dL)	Olanzapine	154	0%
		Placebo	82	1.2%
	Borderline to High (≥100 mg/dL and <160 mg/dL to ≥160 mg/dL)	Olanzapine	302	10.6%
		Placebo	173	8.1%

* Statistically significant compared to placebo.

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in triglycerides in patients taking olanzapine was 40.5 mg/dL. In phase 1 of CATIE, the mean increase in total cholesterol was 9.4 mg/dL.

Olanzapine Monotherapy in Adolescents—The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine-treated patients gained at least 7% of their baseline weight, which was statistically significantly different compared to an average 0.3 kg in placebo-treated patients, with an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.8% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 9.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 15 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

Table 2. Changes in Fasting Lipids Values from Adolescent Placebo-Controlled Olanzapine Monotherapy Studies

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	138	37.0%*
		Placebo	66	15.2%
	Normal to High (<90 mg/dL to >130 mg/dL)	Olanzapine	67	26.9%
		Placebo	28	10.7%
	Borderline to High (≥90 mg/dL and ≤130 mg/dL to >130 mg/dL)	Olanzapine	97	59.8%
		Placebo	17	35.3%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	138	14.5%*
		Placebo	66	4.5%
	Normal to High (<170 mg/dL to ≥200 mg/dL)	Olanzapine	87	6.9%
		Placebo	43	2.3%
	Borderline to High (≥170 mg/dL and <200 mg/dL to ≥240 mg/dL)	Olanzapine	36	38.9%*
		Placebo	13	7.7%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	137	17.5%
		Placebo	63	11.1%
	Normal to High (<110 mg/dL to ≥130 mg/dL)	Olanzapine	98	5.1%
		Placebo	44	4.5%
	Borderline to High (≥110 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	29	48.3%*
		Placebo	9	0%

* Statistically significant compared to placebo.

Weight Gain—Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight.

Olanzapine Monotherapy in Adults—In an analysis of 13 placebo-controlled olanzapine monotherapy studies, olanzapine-treated patients gained an average of 2.8 kg, which was statistically significantly different compared to an average 0.3 kg weight loss in placebo treated patients with a median exposure of 6 weeks; 22.2% of olanzapine-treated patients gained at least 7% of their baseline weight, which was statistically significantly different compared to 2% of placebo-treated patients, with a median exposure of 8 weeks; 4.2% of olanzapine-treated patients gained at least 15% of their baseline weight, which was statistically significantly different compared to 0.3% of placebo-treated patients, with a median exposure of 12 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Discontinuation due to weight gain occurred in 0.2% of olanzapine-treated patients and in zero placebo-treated patients.

During long-term continuation therapy with olanzapine (238 median days of exposure), 56% of olanzapine patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 5.4 kg.

Table 3 includes data on weight gain with olanzapine pooled from 88 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified.

Table 3. Weight Gain with Olanzapine Use

Amount Gained kg (%)	6 Weeks (N=2070) (%)	6 Months (N=1536) (%)	12 Months (N=778) (%)	24 Months (N=422) (%)
≥7	27	41	44	45
0-6 (0-11 lb)	57	34	25	22
5-10 (11-22 lb)	15	20	25	22
10-15 (22-33 lb)	2	12	16	18
>15 (>33 lb)	0	6	14	18

Olanzapine Monotherapy in Adolescents—The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 4 placebo-controlled olanzapine monotherapy studies of adolescent patients (ages 13 to 17 years), including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine-treated patients gained an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.8% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 9.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 15 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

During long-term continuation therapy with olanzapine, 65% of olanzapine-treated patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 7.4 kg.

Neuroleptic Malignant Syndrome (NMS)—A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including olanzapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

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The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be closely monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia—A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible, in the absence of prevalence estimates for people not receiving antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increases. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may possibly mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, clozapine should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients (1) who suffer from a chronic illness that is known to respond to antipsychotic drugs, and (2) for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on clozapine, drug discontinuation should be considered. However, some patients may require treatment with clozapine despite the presence of the syndrome.

For specific information about the warnings of Rilast or valproate, refer to the WARNINGS section of the package inserts for those other products.

PRECAUTIONS: General—Hypokinetic Effects—Clozapine may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period, probably reflecting its α_1-adrenergic antagonist properties. Hypotension, bradycardia with or without hypotension, tachycardia, and syncope were also reported during the clinical trials with intramuscular clozapine for injection. In an open-label clinical pharmacology study in non-agitated patients with schizophrenia in which the safety and tolerability of intramuscular clozapine were evaluated under a maximal dosing regimen (first two days dose administered 4 hours apart), approximately one-third of these patients experienced a significant orthostatic decrease in systolic blood pressure (i.e., decrease ≥30 mmHg) [see DOSAGE AND ADMINISTRATION]. Syncope was reported in 0.8% (15/2500) of clozapine-treated patients in phase 2/3 clozapine multicenter studies and in 0.2% (2/722) of clozapine-treated patients with agitation in the intramuscular clozapine for injection studies. Three normal volunteers in phase 1 studies with intramuscular clozapine experienced hypotensive, bradycardia, and silent pauses of up to 8 seconds that spontaneously resolved (in 2 cases the events occurred in subcutaneous clozapine, and in 1 case, as a result of an inadvertent intravascular administration). The risk for this sequence of hypotension, bradycardia, and silent pauses may be greater in nonpsychiatric patients compared to psychiatric patients who are possibly more adapted to certain effects of psychotropic drugs.

For oral clozapine therapy, the risk of orthostatic hypotension and syncope may be minimized by initiating therapy with 5 mg QD [see DOSAGE AND ADMINISTRATION]. A more gradual titration to the target dose should be considered if hypotension occurs.

For intramuscular clozapine for injection therapy, patients should remain recumbent if dizziness or dizzy after injection until examination has indicated that they are not experiencing postural hypotension, bradycardia, and/or hypoventilation.

Clozapine should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities [block, cardiomyopathy], and conditions which predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications) where the occurrence of syncope, hypotension and/or bradycardia might put the patient at increased medical risk.

Caution is necessary in patients who receive treatment with other drugs having effects that can induce hypotension, bradycardia, respiratory or central nervous system depression [see Drug Interactions]. Concomitant administration of intramuscular clozapine and parenteral benzodiazepines has not been studied and is therefore not recommended. If use of parenteral benzodiazepines in conjunction with parenteral benzodiazepines is considered, careful evaluation of clinical status for excessive sedation and cardiorespiratory depression is recommended.

Seizures—During premarketing testing, seizures occurred in 5.9% (202/5500) of clozapine-treated patients. There were confounding factors that may have contributed to the occurrence of seizures in many of these cases. Clozapine should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold, e.g., Alzheimer's dementia. Conditions that lower the seizure threshold may be more prevalent in a population of 65 years or older.

Discontinuation—As with other drugs that antagonize dopamine D$_2$ receptors, clozapine elevates prolactin levels, and a modest elevation persists during chronic administration. Tissue culture experiments indicate that approximately one-half of human breast cancers are prolactin dependent in vitro, a factor of potential importance if the prescription of these drugs is contemplated in patients with previously detected breast cancer. In a long-term, case-control study of tardive dyskinesia, amenorrhea, gynecomastia, and impotence have been reported with prolactin-elevating compounds, the clinical significance of elevated serum prolactin levels is unknown for most patients. As is common with compounds which increase prolactin release, an increase in mammary gland neoplasia was observed in the clozapine carcinogenicity studies performed in mice and rats [see Carcinogenesis]. However, neither clinical studies nor epidemiologic studies have shown an association between chronic administration of this class of drugs and tumorigenesis in humans; the available evidence is considered too limited to be conclusive.

Discontinuation Studies—In placebo-controlled studies, clinically significant ALT (SGPT) elevations [all times the upper limit of the normal range] were observed in 2% (6/242) of patients exposed to clozapine compared to none (0/153) of the placebo patients. None of these patients experienced jaundice, in two of these patients, liver enzymes decreased to normal despite continued treatment and in two others, enzymes decreased upon discontinuation of clozapine, in the remaining two patients, one, seropositive for hepatitis C, had persistent enzyme elevation for four months after discontinuation, and the other had insufficient follow-up to determine if enzymes normalized.

Within the large premarketing database of about 2400 patients with baseline SGPT ≤80 IU/L, the incidence of SGPT elevation to >200 IU/L was 2.3% (53/2341). Again, none of these patients experienced jaundice or other signs/symptoms attributable to liver impairment and most had transient changes that tended to normalize while clozapine treatment was continued.

Among 2500 patients in our clozapine clinical trials, about 1% (25/2500) discontinued treatment due to transaminase increases.

Rare postmarketing reports of hepatitis have been received. Very rare cases of cholestatic or mixed liver injury have also been reported during the postmarketing period.

Caution should be exercised in patients with signs and symptoms of hepatic impairment, in patients with pre-existing conditions associated with limited hepatic functional reserve, and in patients who are being treated with potentially hepatotoxic drugs. Periodic assessment of transaminases is recommended in patients with significant hepatic disease [see Laboratory Tests].

Interference with Cardiac and Pulmonary Function—Clozapine has a pronounced anticholinergic effect. Anticholinergic effects, including constipation, tachycardia, and sedation have been associated with clozapine treatment, occurring at an incidence of 31% in clozapine patients compared to 15% in placebo patients. This adverse event was dose related. Somnolence led to discontinuation in 0.4% (9/2500) of patients in the premarketing database.

Since clozapine has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that clozapine therapy does not affect them adversely.

Body Temperature Regulation—Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing clozapine for patients who will be experiencing conditions which may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Aspiration pneumonia is a common cause of morbidity and mortality in patients with advanced Alzheimer's disease. Clozapine and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

Suicide—The possibility of a suicide attempt is inherent in schizophrenia and in bipolar disorder, and close supervision of high-risk patients should accompany drug therapy. Prescriptions for clozapine should be written for the smallest quantity consistent with good patient management, in order to reduce the risk of overdose.

Use in Patients with Concomitant Illness—Clinical trials with clozapine in patients with certain concomitant systemic illnesses (see Renal Impairment and Hepatic Impairment under CLINICAL PHARMACOLOGY, Special Populations) is limited.

Clozapine exhibits in vitro muscarinic receptor affinity. In premarketing clinical trials with clozapine, constipation was associated with constipation, dry mouth, and tachycardia, all adverse events possibly related to cholinergic antagonism. Such adverse events were not taken the basis for discontinuations from clozapine, but clozapine should be used with caution in patients with clinically significant prostatic hypertrophy, narrow angle glaucoma, or a history of paralytic ileus.

In five placebo-controlled studies of clozapine in elderly patients with dementia-related psychosis (n=184), the incidence of cerebrovascular/cerebral ischemia events were reported in clozapine-treated patients at an incidence of at least 2% and significantly greater than placebo-treated patients: falls, somnolence, peripheral edema, abnormal gait, urinary incontinence, lethargy, increased weight, asthenic pyrexia, pneumonia, dry mouth and visual hallucinations. The rate of discontinuation due to adverse events was significantly greater with clozapine than placebo (12% vs 7%). Elderly patients with dementia-related psychosis treated with clozapine are at an increased risk of death compared to placebo. Clozapine is not approved for the treatment of patients with dementia-related psychosis. If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised [see BOX WARNING and WARNINGS].

Clozapine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from premarketing clinical studies. Because of the risk of orthostatic hypotension with clozapine, caution should be observed in cardiac patients [see Hemodynamic Effects].

For specific information about the precautions of Rilast or valproate, refer to the PRECAUTIONS section of the package inserts for those other products.

Information for Patients—Physicians are advised to discuss the following issues with patients for whom they prescribe clozapine:

Hypertension—Patients should be advised of the potential risk of hypoglycemia-related adverse events. Patients should be counseled regarding the monitoring of glucose control.

Weight Gain—Patients should be counseled that clozapine is associated with weight gain. Patients should have their weight monitored regularly.

Orthostatic Hypotension—Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration and in association with the use of concomitant drugs that may potentiate the orthostatic effect of clozapine, e.g., diazepam or alcohol [see Drug Interactions].

Interference with Cognitive and Motor Performance—Because clozapine has the potential to impair judgment, thinking, or motor skills, patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that clozapine therapy does not affect them adversely.

Pregnancy—Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during therapy with clozapine.

Nursing—Patients should be advised not to breast-feed an infant if they are taking clozapine.

Concomitant Medication—Patients should be advised to inform their physicians if they are taking, or plan to take, any prescription or over-the-counter drugs, since there is a potential for interactions.

Alcohol—Patients should be advised to avoid alcohol while taking clozapine.

Heat Exposure and Dehydration—Patients should be advised regarding appropriate care in avoiding overheating and dehydration.

Phenylketonurics—Orally disintegrating TABLETS (clozapine orally disintegrating tablets) contain phenylalanine (0.34 mg for 12.5 mg, 0.67 mg per 25 mg, 1.34 mg per 50 mg, 2.68 mg per 100 mg, and 5.36 mg per 200 mg tablet, respectively).

Laboratory Tests—Periodic assessment of transaminases is recommended in patients with significant hepatic disease [see Transaminase Elevations].

Drug Interactions—The risks of using clozapine in combination with other drugs have not been extensively evaluated in systematic studies. Given the primary CNS effects of clozapine, caution should be used when clozapine is taken in combination with other centrally acting drugs and alcohol.

Because of its potential for inducing hypotension, clozapine may enhance the effects of certain antihypertensive agents.

Clozapine has the potential to enhance the effects of levodopa and dopamine agonists.

The Effect of Other Drugs on Clozapine—Agents that induce CYP1A2 or glucuronyl transferase enzymes, such as omeprazole and rifampin, may cause an increase in clozapine clearance. Inhibitors of CYP1A2 could potentially increase clozapine plasma concentrations. Fluvoxamine is a potent CYP1A2 inhibitor and a moderate inhibitor of some cytochrome P450 enzymes, reduction or termination of fluvoxamine therapy may appreciably alter clozapine clearance. Therefore, a dosage increase (for induction) or a dosage decrease (for inhibition) may need to be considered with specific drugs.

Ciprofloxacin—The administration of ciprofloxacin 250 mg BID to 4 patients for 7 days increased the mean Cmax and AUC of oral clozapine by about 60%. As peak clozapine levels are not typically observed until about 6 hours after dosing, clinicians may be a useful treatment for clozapine overdose.

Clozapine and Antacids—Single doses of clozapine (600 mg) or aluminum- and magnesium-containing antacids did not affect the oral bioavailability of clozapine.

Carbamazepine—Carbamazepine therapy (200 mg bid) causes an approximately 50% increase in the clearance of clozapine. This increase is likely due to the fact that carbamazepine is a potent inducer of CYP1A2 activity. Higher daily doses of carbamazepine may cause an even greater increase in clozapine clearance.

Ethanol—Ethanol (45 mg/70 kg single dose) did not have an effect on clozapine pharmacokinetics.

Fluoxetine—Fluoxetine (60 mg single dose or 60 mg daily for 8 days) causes a small (mean 16%) increase in the maximum concentration of clozapine and a small (mean 16%) decrease in clozapine clearance. The magnitude of the impact of this factor is small in comparison to the overall variability between individuals, and therefore dose modification is not routinely recommended.

Fluvoxamine—Fluvoxamine, a CYP1A2 inhibitor, decreases the clearance of clozapine. This results in a mean increase in clozapine Cmax following fluvoxamine of 54% in female nonsmokers and 77% in male smokers. The mean increase in clozapine AUC is 52% and 108%, respectively. Lower doses of clozapine should be considered in patients receiving concomitant treatment with fluvoxamine.

Warfarin—Warfarin (20 mg single dose) did not affect clozapine pharmacokinetics.

Effect of Clozapine on Other Drugs—In vitro studies utilizing human liver microsomes suggest that clozapine has little potential to inhibit the cytochrome P450 isozymes CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. Thus, clozapine is unlikely to cause clinically important drug interactions mediated by these enzymes.

Lithium—Multiple doses of clozapine (10 mg for 8 days) did not influence the kinetics of lithium. Therefore, concomitant clozapine administration does not require dosage adjustment of lithium.

Valproate—Studies in vitro using human liver microsomes demonstrated that clozapine has little potential to inhibit the major metabolic pathways, glucuronidation, of valproate. Further, valproate has little effect on the metabolism of clozapine in vivo. In vivo administration of clozapine (10 mg daily for 2 weeks) did not affect the steady state plasma concentrations of valproate. Therefore, concomitant clozapine administration does not require dosage adjustment of valproate.

Single doses of clozapine did not affect the pharmacokinetics of imipramine or its active metabolite desipramine, and warfarin. Multiple doses of clozapine did not influence the kinetics of diazepam and its active metabolite N-desmethyldiazepam, ethanol, or ibuprofen. However, the co-administration of either diazepam or ethanol with clozapine potentiated the sedation and orthostasis observed with clozapine. Single doses of clozapine did not affect the pharmacokinetics of theophylline or its metabolites.

Lorazepam—Administration of intramuscular lorazepam (2 mg) 1 hour after intramuscular clozapine for injection (5 mg) did not significantly affect the pharmacokinetics of clozapine, unconjugated lorazepam, or total lorazepam. However, this co-administration of intramuscular lorazepam and intramuscular clozapine for injection added to the somnolence observed with either drug alone [see Hemodynamic Effects].

Carcinogenesis, Mutagenesis, Impairment of Fertility—Carcinogenesis—Oral carcinogenicity studies were conducted in mice and rats. Clozapine was administered to mice in two 78-week studies at doses of 3, 10, 30/20 mg/kg/day (equivalent to 0.8-5 times the maximum recommended human daily oral dose on a mg/m^2 basis) and 0.25, 2, 8 mg/kg/day (equivalent to 0.06-2 times the maximum recommended human daily oral dose on a mg/m^2 basis). Rats were dosed for 2 years at doses of 0.25, 1, 2.5, 4 mg/kg/day (males) and 0.25, 1, 4, 8 mg/kg/day (females) (equivalent to 0.13-2 and 0.13-4 times the maximum recommended human daily oral dose on a mg/m^2 basis, respectively). The incidence of liver hemangiomas and hemangiosarcomas was significantly increased in one mouse study in male mice treated with 8 mg/kg/day (2 times the maximum recommended human daily oral dose on a mg/m^2 basis). These tumors were not increased in another mouse study in females dosed at 10 or 30/20 mg/kg/day (2-5 times the maximum recommended human daily oral dose on a mg/m^2 basis) in the study, there was a high incidence of early mortalities in rodents of the breed of rat highly susceptible to the development of spontaneous and clozapine-induced mammary gland adenomas and adenocarcinomas. These tumors were significantly increased in female mice at 8 mg/kg/day and in female rats dosed at all mg/kg/day (0.5 and 2 times the maximum recommended human daily oral dose on a mg/m^2 basis, respectively). Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum prolactin levels were not measured during the clozapine carcinogenicity studies; however, measurements during subchronic toxicity studies showed that clozapine elevated serum prolactin levels up to 4-fold in rats at the same doses tested in the carcinogenicity study. An increase in mammary gland neoplasms has been found in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin mediated. The relevance for human risk of the finding of prolactin mediated endocrine tumors in rodents is unknown [see Hyperprolactinemia under PRECAUTIONS, General].

Mutagenesis—No evidence of mutagenic potential for clozapine was found in the Ames reverse mutation test, in vivo chromosomal aberration test in mouse bone marrow cells, unscheduled DNA synthesis test in rat hepatocytes, induction of forward mutation test in mouse lymphoma cells, or in vivo sister chromatid exchange test in bone marrow of Chinese hamsters.

Impairment of Fertility—In an oral fertility and reproductive performance study in rats, male mating performance, but not fertility, was impaired at a dose of 22.4 mg/kg/day and female fertility was decreased at a dose of 2 mg/kg/day (11 and 1.5 times the maximum recommended human daily oral dose on a mg/m^2 basis, respectively). Discontinuance of clozapine treatment reversed the effects on male mating performance. In female rats, the prestrital period was increased following administration of either subcutaneous or oral clozapine. Intramuscular recommended human daily oral dose on a mg/m^2 basis). Diestrous was prolonged and anovulatory estrous developed at 5 mg/kg/day (2.5 times 1.5 mg/kg/day (0.8 times the maximum recommended human daily oral dose on a mg/m^2 basis). Therefore clozapine may produce a delay in ovulation.

Teratogenic—Pregnancy Category C—In oral reproductive studies in rats at doses up to 18 mg/kg/day and in rabbits at doses up to 30 mg/kg/day (9 and 30 times the maximum recommended human daily oral dose on a mg/m^2 basis, respectively) no evidence of teratogenicity was observed. In an oral rat teratology study, early resorptions and increased stillbirths were observed at a dose of 18 mg/kg/day (9 times the maximum recommended human daily oral dose on a mg/m^2 basis). Stillbirths were increased at 10 mg/kg/day (5 times the maximum recommended human daily oral dose on a mg/m^2 basis). Gestation was prolonged at 10 mg/kg/day (5 times the maximum recommended human daily oral dose on a mg/m^2 basis). Gestation was prolonged at 10 mg/kg/day (5 times the maximum recommended human daily oral dose on a mg/m^2 basis). In an oral rabbit teratology study, fetal toxicity (manifested as increased resorptions and decreased fetal weight) occurred at a maternally toxic dose of 30 mg/kg/day (30 times the maximum recommended human daily oral dose on a mg/m^2 basis).

Placental transfer of clozapine occurs in rat pups.

There are no adequate and well-controlled trials with clozapine in pregnant females. Seven pregnancies were observed during clinical trials with clozapine, including 2 resulting in normal births, 1 resulting in neonatal death due to a cardiovascular defect, 3 therapeutic abortions, and 1 spontaneous abortion. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery—Parturition in rats was not affected by clozapine. The effect of clozapine on human parturition is unknown.

Exhibit 3, Page Index 2
Humans
SOA Opposition to Lilly
ZYPREXA® ZYDIS® (Olanzapine Orally Disintegrating Tablets) Preliminary Injunction Summary Judgment
ZYPREXA® IntraMuscular (Olanzapine for Injection)
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Nursing Mothers—It is likely that olanzapine will be excreted in breast milk. Mean infant dose at steady state was estimated to be 1.8% of the maternal olanzapine dose. It is recommended that women receiving olanzapine should not breast-feed.

Pediatric Use—Safety and effectiveness in pediatric patients have not been established.

Geriatric Use—Of the 2500 patients in premarketing clinical studies with oral olanzapine, 11% (263) were 65 years of age or over. In patients with schizophrenia, there was no indication of any different tolerability of olanzapine in the elderly compared to younger patients. Studies in elderly patients with dementia-related psychosis have suggested that there may be a different tolerability profile in this population compared to younger patients with schizophrenia. Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised. Also, the presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine should lead to consideration of a lower starting dose for any geriatric patient (see BOX WARNING, WARNINGS, PRECAUTIONS, and DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS: The information below is derived from a clinical trial database for olanzapine consisting of 8661 patients with approximately 4185 patient-years of exposure to oral olanzapine and 722 patients with exposure to intramuscular olanzapine for injection. This database includes: (1) 2500 patients who participated in multiple-dose oral olanzapine premarketing trials in schizophrenia and Alzheimer's disease representing approximately 1122 patient-years of exposure at or February 14, 1995; (2) 982 patients who participated in oral olanzapine premarketing bipolar mania trials representing approximately 65 patient-years of exposure; (3) 191 patients who participated in an oral olanzapine trial of patients having various psychiatric symptoms in association with Alzheimer's disease representing approximately 25 patient-years of exposure; (4) 5798 patients from 89 additional oral olanzapine clinical trials as of December 31, 2001; and (5) 722 patients who participated in intramuscular olanzapine for injection premarketing trials in agitated patients with schizophrenia, Bipolar I Disorder (manic or mixed episodes), or dementia. In addition, information from the premarketing 6-week clinical study database for olanzapine in combination with lithium or valproate, consisting of 224 patients who participated in bipolar mania trials with approximately 23 patient-years of exposure, is included below.

The conditions and duration of treatment with olanzapine varied greatly and included (in overlapping categories) open-label and double-blind phases of studies, inpatients and outpatients, fixed-dose and dose-titration studies, and short-term or longer-term exposures. Adverse reactions were assessed by collecting adverse events, results of physical examinations, vital signs, weights, laboratory analyses, ECGs, chest x-rays, and results of ophthalmologic examinations.

Certain portions of the discussion below relating to objective or numeric safety parameters, namely, dose-dependent adverse events, vital sign changes, weight gain, laboratory changes, and ECG changes are derived from studies in patients with schizophrenia and have not been duplicated for bipolar mania or agitation. However, this information is also generally applicable to bipolar mania and agitation.

Adverse events during exposure were obtained by spontaneous report and recorded by clinical investigators using terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a smaller number of standardized event categories. In the tables and tabulations that follow, standard COSTART dictionary terminology has been used initially to classify reported adverse events.

The listed frequencies of adverse events represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. The reported events do not include those events terms that were so general as to be uninformative. Events listed elsewhere in labeling may not be repeated below. It is important to emphasize that, although the events reported occurred during treatment with olanzapine, they were not necessarily caused by it. The entire label should be read to gain a complete understanding of the safety profile of olanzapine.

The prescriber should be aware that the figures in the tables and tabulations cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical trials. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing physician with some basis for estimating the relative contribution of drug and nondrug factors to the adverse event incidence in the population studied.

Incidence of Adverse Events in Short-Term, Placebo-Controlled and Combination Trials—The following findings are based on premarketing trials of (1) oral olanzapine for schizophrenia, bipolar mania, a subsequent trial of patients having various psychiatric symptoms in association with Alzheimer's disease, and premarketing combination trials; and (2) intramuscular olanzapine for injection in agitated patients with schizophrenia or bipolar mania.

Adverse Events Associated with Discontinuation of Treatment in Short-Term, Placebo-Controlled Trials—Schizophrenia—Overall, there was no difference in the incidence of discontinuation due to adverse events (5% for oral olanzapine vs 6% for placebo). However, discontinuations due to increases in SGPT were considered to be drug related (2% for oral olanzapine vs 0% for placebo) (see PRECAUTIONS).

Bipolar Mania Monotherapy—Overall, there was no difference in the incidence of discontinuation due to adverse events (2% for oral olanzapine vs 2% for placebo).

Agitation—Overall, there was no difference in the incidence of discontinuation due to adverse events (0.4% for intramuscular olanzapine for injection vs 0% for placebo).

Adverse Events Associated with Discontinuation of Treatment in Short-Term Combination Trials—Bipolar Mania Combination Therapy—In a study of patients who were already tolerating either lithium or valproate as monotherapy, discontinuation rates due to adverse events were 11% for the combination of oral olanzapine with lithium or valproate compared to 2% for patients who remained on lithium or valproate monotherapy. Discontinuations with the combination of oral olanzapine and lithium or valproate that occurred in more than 1 patient were: somnolence (2%), weight gain (1%), and peripheral edema (1%).

Commonly Observed Adverse Events in Short-Term, Placebo-Controlled Trials—The most commonly observed adverse events associated with the use of oral olanzapine (incidence of 5% or greater) and not observed at an equivalent incidence among placebo-treated patients (olanzapine incidence at least twice that for placebo) were:

Common Treatment-Emergent Adverse Events Associated with the Use of Oral Olanzapine in 6-Week Trials—SCHIZOPHRENIA

Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine (N=248)	Placebo (N=118)
Postural hypotension	5	2
Constipation	9	3
Weight gain	5	1
Dizziness	11	4
Personality disorder[1]	8	4
Akathisia	5	1

[1] Personality disorder is the COSTART term for designating non-aggressive objectionable behavior.

Common Treatment-Emergent Adverse Events Associated with the Use of Oral Olanzapine in 3-Week and 4-Week Trials—BIPOLAR MANIA

Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine (N=125)	Placebo (N=129)
Asthenia	15	6
Dry mouth	22	7
Constipation	11	5
Dyspepsia	11	5
Increased appetite	6	3
Somnolence	35	13
Dizziness	18	6
Tremor	6	3

There was one adverse event (somnolence) observed at an incidence of 5% or greater among intramuscular olanzapine for injection-treated patients and not observed at an equivalent incidence among placebo-treated patients (olanzapine incidence at least twice that for placebo) during the placebo-controlled premarketing studies. The incidence of somnolence during the 24 hour (4 treatment period) in clinical trials in agitated patients with schizophrenia or bipolar mania was 8% for intramuscular olanzapine for injection and 3% for placebo.

Adverse Events Occurring at an Incidence of 2% or More Among Oral Olanzapine-Treated Patients in Short-Term, Placebo-Controlled Trials—Table 4 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred in 2% or more of patients treated with oral olanzapine (doses ≥5 mg/day) and not observed at an equivalent incidence among placebo-treated patients who participated in the acute phase of placebo-controlled premarketing trials.

Table 4. Treatment-Emergent Adverse Events: Incidence in Short-Term, Placebo-Controlled Clinical Trials[1] with Oral Olanzapine

Body System/Adverse Event	Percentage of Patients Reporting Event		Body System/Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine (N=532)	Placebo (N=294)		Olanzapine (N=532)	Placebo (N=294)
Body as a Whole			**Musculoskeletal System**		
Accidental injury	12	8	Extremity pain	5	3
Asthenia	10	9	(other than joint)		
Fever	6	2	Joint pain	5	3
Chest pain	5	2	**Nervous System**		
Back pain	3	1	Somnolence	29	13
Cardiovascular System			Insomnia	12	11
Postural hypotension	3	1	Dizziness	11	4
Tachycardia	3	1	Abnormal gait	4	1
Hypertension	2	1	Tremor	4	3
Digestive System			Akathisia	3	2
Dry mouth	9	5	Hypertonia	3	2
Constipation	9	4	Articulation impairment	2	1
Dyspepsia	7	5	**Respiratory System**		
Vomiting	4	3	Rhinitis	7	6
Increased appetite	3	2	Cough increased	6	3
Hemic and Lymphatic System			Pharyngitis	4	3
			Special Senses		
Ecchymosis	5	3	Amblyopia	3	2
Metabolic and Nutritional Disorders			**Urogenital System**		
			Urinary incontinence	2	1
Weight gain	5	3	Urinary tract infection	2	1
Peripheral edema	3	1			

[1] Events reported by at least 2% of patients treated with olanzapine, except the following events which had an incidence equal to or less than placebo: abdominal pain, agitation, anorexia, anxiety, apathy, confusion, dyspepsia, diarrhea, dysmenorrhea (denominator used was for females only [olanzapine, N=201; placebo, N=114]), hallucinations, headache, hostility, hyperkinesia, myalgia, nausea, nervousness, paranoid reaction, personality disorder (COSTART term for designating non-aggressive objectionable behavior), rash, thinking abnormal, weight loss.

Commonly Observed Adverse Events in Short-Term Combination Trials—In the bipolar mania combination placebo-controlled trials, the most commonly observed adverse events associated with the combination of olanzapine and lithium or valproate (incidence of ≥5% and at least twice placebo) were:

Common Treatment-Emergent Adverse Events Associated with the Use of Oral Olanzapine in 6-Week Combination Trials—BIPOLAR MANIA

Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine with lithium or valproate (N=229)	Placebo with lithium or valproate (N=115)
Dry mouth	32	9
Weight gain	26	7
Increased appetite	24	8
Dizziness	14	7
Back pain	8	4
Constipation	8	4
Speech disorder	7	1
Increased salivation	6	2
Amnesia	5	2
Paresthesia	5	2

Adverse Events Occurring at an Incidence of 2% or More Among Oral Olanzapine-Treated Patients in Short-Term Combination Trials—Table 5 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred in 2% or more of patients treated with the combination of olanzapine (doses ≥5 mg/day) and lithium or valproate and with incidence greater than lithium or valproate alone who participated in the acute phase of placebo-controlled combination trials.

Table 5. Treatment-Emergent Adverse Events: Incidence in Short-Term, Placebo-Controlled Combination Clinical Trials[1] with Oral Olanzapine

Body System/Adverse Event	Percentage of Patients Reporting Event		Body System/Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine with lithium or valproate (N=229)	Placebo with lithium or valproate (N=115)		Olanzapine with lithium or valproate (N=229)	Placebo with lithium or valproate (N=115)
Body as a Whole			**Nervous System (cont.)**		
Asthenia	18	13	Speech disorder	7	1
Back pain	8	4	Amnesia	5	2
Accidental injury	4	2	Paresthesia	5	2
Chest pain	3	2	Apathy	4	3
Cardiovascular System			Confusion	4	1
Hypertension	2	1	Euphoria	3	2
Digestive System			Incoordination	2	0
Dry mouth	32	9	**Respiratory System**		
Increased appetite	24	8	Pharyngitis	4	1
Thirst	10	6	Dyspnea	3	1
Constipation	8	4	**Skin and Appendages**		
Increased salivation	6	2	Sweating	3	1
Metabolic and Nutritional Disorders			Acne	2	0
			Dry skin	2	0
Weight gain	26	7	**Special Senses**		
Peripheral edema	6	4	Amblyopia	6	5
Edema	2	1	Abnormal vision	2	0
Nervous System			**Urogenital System**		
Somnolence	52	27	Dysmenorrhea[2]	2	0
Tremor	23	13	Vaginitis[2]	2	0
Depression	18	17			
Dizziness	14	7			

[1] Events reported by at least 2% of patients treated with olanzapine, except the following events which had an incidence equal to or less than placebo: abdominal pain, abnormal dreams, abnormal ejaculation, agitation, anorexia, anxiety, arthralgia, cough increased, diarrhea, dyspepsia, emotional lability, fever, flatulence, flu syndrome, headache, hostility, hypertonia, libido decreased, libido increased, menstrual disorder (dysmenorrhea [used was for females only [olanzapine, N=128; placebo, N=58]]), myalgia, nausea, nervousness, paranoid reaction, personality disorder, rash, rhinitis, sinus dilatation, thinking abnormal, vomiting.

[2] Denominator used was for females only (olanzapine, N=128; placebo, N=58).

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For specific information about the adverse reactions observed with lithium or valproate, refer to the ADVERSE REACTIONS section of the package inserts for these other products.

Adverse Events Occurring at an Incidence of 1% or More Among Intramuscular Olanzapine for Injection-Treated Patients in Short-Term, Placebo-Controlled Trials—Table 6 enumerates the incidence, rounded to the nearest percent, of treatment-emergent adverse events that occurred in 1% or more of patients treated with intramuscular olanzapine for injection (dose range of 2.5-10 mg/injection) and with incidence greater than placebo who participated in the short-term, placebo-controlled trials in agitated patients with schizophrenia or bipolar mania.

Table 6. Treatment-Emergent Adverse Events: Incidence in Short-Term (24 Hour), Placebo-Controlled Clinical Trials with Intramuscular Olanzapine for Injection in Agitated Patients with Schizophrenia or Bipolar Mania[1]

Body System/Adverse Event	Percentage of Patients Reporting Event	
	Olanzapine (N=415)	Placebo (N=150)
Body as a Whole		
Asthenia	2	1
Cardiovascular System		
Hypotension	2	0
Postural hypotension	1	0
Nervous System		
Somnolence	6	3
Dizziness	4	2
Tremor	2	0

[1] Events reported by at least 1% of patients treated with olanzapine for injection, except the following events which had an incidence equal to or less than placebo: agitation, anxiety, dry mouth, headache, hypertension, insomnia, nervousness.

Dose Dependency of Adverse Events in Short-Term, Placebo-Controlled Trials—*Extrapyramidal Symptoms*—The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by categorical analyses of normal rating scales during acute therapy in a controlled clinical trial comparing oral olanzapine at 3 fixed doses with placebo in the treatment of schizophrenia.

Treatment-Emergent Extrapyramidal Symptoms Assessed by Rating Scales Incidence in a Fixed Dosage Range, Placebo-Controlled Clinical Trial of Oral Olanzapine in Schizophrenia—Acute Phase[a]

	Percentage of Patients Reporting Event			
	Placebo	Olanzapine 5 ± 2.5 mg/day	Olanzapine 10 ± 2.5 mg/day	Olanzapine 15 ± 2.5 mg/day
Parkinsonism[b]	15	14	12	14
Akathisia[c]	22	16	19	27

[a] No statistically significant differences.
[b] Percentage of patients with a Simpson-Angus Scale total score >3.
[c] Percentage of patients with a Barnes Akathisia Scale global score ≥2.

The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by spontaneously reported adverse events during acute therapy in the same controlled clinical trial comparing olanzapine at 3 fixed doses with placebo in the treatment of schizophrenia.

Treatment-Emergent Extrapyramidal Symptoms Assessed by Adverse Events Incidence in a Fixed Dosage Range, Placebo-Controlled Clinical Trial of Oral Olanzapine in Schizophrenia—Acute Phase

	Percentage of Patients Reporting Event			
	Placebo (N=66)	Olanzapine 5 ± 2.5 mg/day (N=65)	Olanzapine 10 ± 2.5 mg/day (N=64)	Olanzapine 15 ± 2.5 mg/day (N=69)
Dystonic events[1]	1	3	2	3
Parkinsonism events[2]	10	8	14	20
Akathisia events[3]	1	5	11*	10*
Dyskinetic events[4]	4	0	2	1
Medical events[5]	5	2	5	1
Any extrapyramidal event	16	13	23	32*

* Statistically significantly different from placebo.
[1] Patients with the following COSTART terms were counted in this category: dystonia, generalized spasm, neck rigidity, oculogyric crisis, opisthotonos, torticollis.
[2] Patients with the following COSTART terms were counted in this category: akinesia, cogwheel rigidity, extrapyramidal syndrome, hypertonia, hypokinesia, masked facies, tremor.
[3] Patients with the following COSTART terms were counted in this category: akathisia, hyperkinesia.
[4] Patients with the following COSTART terms were counted in this category: buccolingual syndrome, choreoathetosis, dyskinesia, tardive dyskinesia.
[5] Patients with the following COSTART terms were counted in this category: movement disorder, myoclonus, twitching.

The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by categorical analyses of normal rating scales during controlled clinical trials comparing fixed doses of intramuscular olanzapine for injection with placebo in agitated patients. Patients in each dose group could receive up to three injections during the trials (see CLINICAL EFFICACY DATA). Patient assessments were conducted during the 24 hours following the initial dose of intramuscular olanzapine for injection. There were no statistically significant differences from placebo.

Treatment-Emergent Extrapyramidal Symptoms Assessed by Rating Scales Incidence in a Fixed Dose, Placebo-Controlled Clinical Trial of Intramuscular Olanzapine for Injection in Agitated Patients with Schizophrenia[a]

	Percentage of Patients Reporting Event			
	Placebo	Olanzapine IM 2.5 mg	Olanzapine IM 5 mg	Olanzapine IM 7.5 mg	Olanzapine IM 10 mg
Akathisia[b]	0	0	0	0	3

[a] No statistically significant differences.
[b] Percentage of patients with a Barnes Akathisia Scale total score ≥3.

The following table enumerates the percentage of patients with treatment-emergent extrapyramidal symptoms as assessed by spontaneously reported adverse events in the same controlled clinical trial comparing fixed doses of intramuscular olanzapine for injection with placebo in agitated patients with schizophrenia. There were no statistically significant differences from placebo.

Treatment-Emergent Extrapyramidal Symptoms Assessed by Adverse Events Incidence in a Fixed Dose, Placebo-Controlled Clinical Trial of Intramuscular Olanzapine for Injection in Agitated Patients with Schizophrenia[a]

	Percentage of Patients Reporting Event				
	Placebo (N=48)	Olanzapine IM 2.5 mg (N=48)	Olanzapine IM 5 mg (N=45)	Olanzapine IM 7.5 mg (N=42)	Olanzapine IM 10 mg (N=46)
Dystonic events[1]	0	0	0	0	0
Parkinsonism events[2]	0	0	0	0	0
Akathisia events[3]	0	0	0	0	0
Dyskinetic events[4]	0	0	0	0	0
Medical events[5]	0	0	0	0	0
Any extrapyramidal event	0	0	0	0	0

[a] No statistically significant differences.
[1] Patients with the following COSTART terms were counted in this category: dystonia, generalized spasm, neck rigidity, oculogyric crisis, opisthotonos, torticollis.
[2] Patients with the following COSTART terms were counted in this category: akinesia, cogwheel rigidity, extrapyramidal syndrome, hypertonia, hypokinesia, masked facies, tremor.
[3] Patients with the following COSTART terms were counted in this category: akathisia, hyperkinesia.
[4] Patients with the following COSTART terms were counted in this category: buccolingual syndrome, choreoathetosis, dyskinesia, tardive dyskinesia.
[5] Patients with the following COSTART terms were counted in this category: movement disorder, myoclonus, twitching.

Other Adverse Events—The following table addresses dose relatedness for other adverse events using data from a schizophrenia trial involving fixed dosage ranges of oral olanzapine. It enumerates the percentage of patients with treatment-emergent adverse events for the three fixed-dose range groups and placebo. The data were analyzed using the Cochran-Armitage test, excluding the placebo group, and the table includes only those adverse events for which there was a statistically significant trend.

Adverse Event	Percentage of Patients Reporting Event			
	Placebo (N=68)	Olanzapine 5 ± 2.5 mg/day (N=65)	Olanzapine 10 ± 2.5 mg/day (N=64)	Olanzapine 15 ± 2.5 mg/day (N=69)
Asthenia	15	8	9	13
Dry mouth	4	5	5	9
Nausea	9	3	2	9
Somnolence	16	20	30	39
Tremor	3	6	2	9

Additional Findings—In a single 8-week randomized, double-blind, fixed-dose study comparing 10 (N=198), 20 (N=200) and 40 (N=200) mg/day of olanzapine in patients with schizophrenia or schizoaffective disorder, statistically significant differences among 3 dose groups were observed for the following safety outcomes: weight gain, prolactin elevation, fatigue and dizziness. Mean baseline to endpoint increase in weight (10 mg/day: 1.9 kg; 20 mg/day: 2.3 kg; 40 mg/day: 4 kg) was observed with significant differences between 10 vs 40 mg/day. Incidence of treatment-emergent prolactin elevation (>24.2 ng/mL (female) or >18.77 ng/mL (male)) at any time during the trial (10 mg/day: 31.2%; 20 mg/day: 42.7%; 40 mg/day: 61.1%) with significant differences between 10 vs 40 mg/day and 20 vs 40 mg/day; fatigue (10 mg/day: 1.5%; 20 mg/day: 2.1%; 40 mg/day: 6.6%) with statistical differences between 10 vs 40 and 20 vs 40 mg/day; and dizziness (10 mg/day: 2.6%; 20 mg/day: 1.6%; 40 mg/day: 6.5%) with significant differences between 20 vs 40 mg, was observed.

Additional Findings Observed in Clinical Trials—The following findings are based on clinical trials.

Vital Sign Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (see PRECAUTIONS).

Laboratory Changes—An assessment of the premarketing experience for olanzapine revealed an association with asymptomatic increases in SGPT, SGOT, and GGT (see PRECAUTIONS). Olanzapine administration was also associated with increases in serum prolactin (see PRECAUTIONS), with an asymptomatic elevation of the eosinophil count in 0.3% of patients, and with an increase in CPK.

Given the concerns about neutropenia associated with other psychotropic compounds and the finding of neutropenia associated with the administration of olanzapine in several animal models (see ANIMAL TOXICOLOGY), careful attention was given to examination of hematologic parameters in premarketing studies with olanzapine. There was no indication of a risk of clinically significant neutropenia associated with olanzapine treatment in the premarketing database for 4646 pts.

ECG Changes—Between-group comparisons for pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in the proportions of patients experiencing potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine oral was associated with a mean heart rate of 2.4 beats per minute compared to no change among placebo patients. This slight tendency in tachycardia may be related to olanzapine's potential for inducing orthostatic changes (see PRECAUTIONS).

Other Adverse Events Observed During the Clinical Trial Evaluation of Olanzapine—Following is a list of terms that reflect treatment-emergent adverse events reported by patients treated with oral olanzapine (at multiple doses ≥1 mg/day) in clinical trials (1951 patients, 4185 patient-years of exposure). This listing may not include those events already listed in previous tables or elsewhere in labeling, those events for which a drug cause was remote, those event terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1000 patients; rare events are those occurring in fewer than 1/1000 patients.

Body as a Whole—Frequent: dental pain and flu syndrome; *Infrequent:* abdomen enlarged, chills, face edema, intestinal injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, and suicide attempt; *Rare:* chills and fever, hangover effect, and suicide death.

Cardiovascular System—Frequent: hypotension; *Infrequent:* atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, and ventricular extrasystoles; *Rare:* afibrillation, heart failure, and pulmonary embolism.

Digestive System—Frequent: flatulence, increased salivation, and thirst; *Infrequent:* dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, and tooth caries; *Rare:* aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, and tongue discoloration.

Endocrine System—Infrequent: diabetes mellitus; *Rare:* diabetic acidosis and goiter.

Hemic and Lymphatic System—Infrequent: anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, and thrombocytopenia; *Rare:* normocytic anemia and thrombocythemia.

Metabolic and Nutritional Disorders—Infrequent: acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesterolemia, hyperglycemia, hyperlipemia, hypernatremia, hyperuricemia, hypocalcemia, hypokalemia, hypomagnesemia, lower extremity edema, and upper extremity edema; *Rare:* gout, hyperkalemia, hypermagnesemia, hyponatremia, hypovolemia, and water intoxication.

Musculoskeletal System—Frequent: joint stiffness and twitching; *Infrequent:* arthralgia, arthritis, bursitis, leg cramps, and myasthenia; *Rare:* bone pain, bursitis, myopathy, osteoporosis, and rheumatoid arthritis.

Nervous System—Frequent: abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, and schizophrenic reaction; *Infrequent:* ataxia, alcohol intoxication, antisocial reaction, ataxia, CNS stimulation, coma/near coma, dementia, depersonalization, dysarthria, facial paralysis, hyperkinesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant rebound, stupor, stuttering, tardive dyskinesia, vertigo, and withdrawal syndrome; *Rare:* abnormal paresthesia, coma, encephalopathy, neuralgia, nystagmus, paralysis, peripheral neuritis, subarachnoid hemorrhage, and tobacco amblyopia.

Respiratory System—Frequent: dyspnea; *Infrequent:* apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, hypoxydis, and voice alteration; *Rare:* atelectasis, hiccup, hypoventilation, lung edema, and stridor.

Skin and Appendages—Frequent: sweating; *Infrequent:* alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, and vesiculobullous rash; *Rare:* herpes simplex and pustular rash.

Special Senses—Frequent: conjunctivitis; *Infrequent:* abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, and tinnitus; *Rare:* corneal lesion, glaucoma, keratoconjunctivitis, macular pigmentation, mioses, mydriasis, and pigment deposits iuns.

Urogenital System—Frequent: vaginitis*; *Infrequent:* abnormal ejaculation*, amenorrhea*, breast pain, cystitis, decreased menstruation*, female lactation*, glycosuria, gynecomastia, hematuria, impotence*, increased menstruation*, menorrhagia*, metrorrhagia*, polyuria, premenstrual syndrome*, pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged*, and vaginal hemorrhage*; *Rare:* albuminuria, breast enlargement, mastitis, and oliguria.

* Adjusted for gender.

Following is a list of terms that reflect treatment-emergent adverse events reported by patients treated with intramuscular olanzapine for injection (at one or more doses ≥2.5 mg/injection) in clinical trials (722 patients). This listing may not include those events already listed in previous tables or elsewhere in labeling, those events for which a drug cause was remote, those event terms which were so general as to be uninformative, and those events reported only once which did not have a substantial probability of being acutely life-threatening.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions: frequent adverse events are those occurring in at least 1/100 patients (only those not already listed in the tabulated results from placebo-controlled trials appear in this listing); infrequent adverse events are those occurring in 1/100 to 1/1000 patients.

Body as a Whole—Frequent: injection site pain; *Infrequent:* abdominal pain and fever.

Cardiovascular System—Infrequent: AV block, heart block, and syncope.

Digestive System—Infrequent: diarrhea and nausea.

Hemic and Lymphatic System—Infrequent: anemia.

Metabolic and Nutritional Disorders—Infrequent: creatine phosphokinase increased, dehydration, and hyperkalemia.

Musculoskeletal System—Infrequent: twitching.

Nervous System—Infrequent: abnormal gait, akathisia, articulation impairment, confusion, and emotional lability.

Skin and Appendages—Infrequent: sweating.

Postmarketing Reports—Adverse events reported since market introduction that were temporally (but not necessarily causally) related to ZYPREXA therapy include the following: allergic reaction (e.g., anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, jaundice, neutropenia, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels ≥ 240 mg/dL, or large increases in triglyceride levels to ≥1000 mg/dL have been reported.

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DRUG ABUSE AND DEPENDENCE: Controlled Substance Class—Olanzapine is not a controlled substance.

Physical and Psychological Dependence—In studies prospectively designed to assess abuse and dependence potential, olanzapine was shown to have tests (oprioidlike CNS effects but little or no potential of abuse or physical dependence in rats administered oral doses up to 15 times the maximum recommended human daily oral dose (90 mg) and chronic monkeys administered oral doses up to 5 times the maximum recommended human daily oral dose on a mg/m² basis.

Olanzapine has not been systematically studied in humans for its potential for abuse, tolerance, or physical dependence. While the clinical trials did not reveal any tendency for any drug-seeking behavior, these observations were not systematic, and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, patients should be evaluated carefully for a history of drug abuse, and such patients should be observed closely for signs of misuse or abuse of olanzapine (e.g., development of tolerance, increases in dose, drug-seeking behavior).

OVERDOSAGE: Human Experience—In premarketing trials involving more than 3100 patients and/or normal subjects, accidental or intentional acute overdosage of olanzapine was identified in 67 patients. In the patient taking the largest identified amount, 300 mg, the only symptoms reported were drowsiness and slurred speech. In the limited number of patients who were evacuated to hospitals, including the patient taking 300 mg, there were no observations indicating an adverse change in laboratory analytes or ECG. Vital signs were usually within normal limits following overdoses.

In postmarketing reports of overdose with olanzapine alone, symptoms have been recorded in the majority of cases. In symptomatic patients, symptoms with ≥10% incidence included agitation/dysarthria/severe, dysarthria, tachycardia, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Among less commonly reported symptoms were the following potentially medically serious events: agitation, cardiorespiratory arrest, cardiac arrhythmias (such as supraventricular tachycardia and one patient experiencing stress paces with spontaneous resumption of normal rhythm), delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypotension, and hypotension. Eli Lilly and Company has received reports of fatality in association with overdose of olanzapine alone. In one case of death, the amount of acutely ingested olanzapine was reported to be possibly as low as 450 mg; however, in another case, a patient was reported to survive an acute olanzapine ingestion of 1500 mg.

Overdosage Management—The possibility of multiple drug involvement should be considered. In case of acute overdosage, establish and maintain an airway and ensure adequate oxygenation and ventilation, which may include intubation. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. The possibility of obtundation, seizures, or dystonic reaction of the head and neck following overdose may create a risk of aspiration with induced emesis. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

There is no specific antidote to olanzapine. Therefore, appropriate supportive measures should be initiated. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. (Do not use epinephrine, dopamine, or other sympathomimetics with beta-agonist activity, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blockade.) Close medical supervision and monitoring should continue until the patient recovers.

DOSAGE AND ADMINISTRATION: Schizophrenia—Usual Dose—Oral olanzapine should be administered on a once-a-day schedule without regard to meals, generally beginning with 5 to 10 mg initially, with a target dose of 10 mg/day within several days. Further dosage adjustments, if indicated, should generally occur at intervals of not less than 1 week, since steady state for olanzapine would not be achieved for approximately 1 week in the typical patient. When dosage adjustments are necessary, dose increments/decrements of 5 mg QD are recommended.

Efficacy in schizophrenia was demonstrated in a dose range of 10 to 15 mg/day in clinical trials; however, doses above 10 mg/day were not demonstrated to be more efficacious than the 10 mg/day dose. An increase to a dose greater than the target dose of 10 mg/day (i.e., to a dose of 15 mg/day or greater) is recommended only after clinical assessment. The safety of doses above 20 mg/day has not been evaluated in clinical trials.

Doses in Special Populations—The recommended starting dose is 5 mg in patients who are debilitated, who have a predisposition to hypotensive reactions, who otherwise exhibit a combination of factors that may result in slower metabolism of olanzapine (e.g., nonsmoking female patients ≥65 years of age), or who may be more pharmacodynamically sensitive to olanzapine (see CLINICAL PHARMACOLOGY, also see Use in Patients with Concomitant Illness and Drug Interactions under PRECAUTIONS). When indicated, dose escalation should be performed with caution in these patients.

Maintenance Treatment—While there is no body of evidence available to answer the question of how long the patient treated with olanzapine should remain on it, the effectiveness of oral olanzapine, 10 mg/day to 20 mg/day, in maintaining treatment response in schizophrenic patients who had been stable on ZYPREXA for approximately 6 weeks and were then followed for a period of up to 8 months has been demonstrated in a placebo-controlled trial (see CLINICAL EFFICACY DATA). Patients should be periodically reassessed to determine the need for maintenance treatment with appropriate dose.

Bipolar Disorder—Usual Monotherapy Dose—Oral olanzapine should be administered on a once-a-day schedule without regard to meals, generally beginning with 10 or 15 mg. Dosage adjustments, if indicated, should generally occur at intervals of not less than 24 hours, reflecting the precedures in the placebo-controlled trials. When dosage adjustments are necessary, dose increments/decrements of 5 mg QD are recommended.

Short-term (3-4 weeks) antimanic efficacy was demonstrated in a dose range of 5 mg to 20 mg/day in clinical trials. The safety of doses above 20 mg/day has not been evaluated in clinical trials.

Maintenance Monotherapy—The benefit of maintaining bipolar patients on monotherapy with oral ZYPREXA at a dose of 5 to 20 mg/day, after achieving a responder status for an average duration of two weeks, was demonstrated in a controlled trial (see CLINICAL EFFICACY DATA). The physician who elects to use ZYPREXA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Bipolar Mania Usual Dose in Combination with Lithium or Valproate—When administered in combination with lithium or valproate, oral olanzapine dosing should generally begin with 10 mg once-a-day without regard to meals.

Short-term (2 weeks) antimanic efficacy was demonstrated in a dose range of 5 mg to 20 mg/day in clinical trials. The safety of doses above 20 mg/day has not been evaluated in clinical trials.

Dosing in Special Populations—See Dosing in Special Populations under DOSAGE AND ADMINISTRATION, Schizophrenia.

Administration of ZYPREXA ZYDIS (olanzapine orally disintegrating tablets)—Peel open the blister. Do not push tablet through foil. Immediately upon opening the blister, using dry hands, remove tablet and place entire ZYPREXA ZYDIS in the mouth. Tablet disintegration occurs rapidly in saliva so it can be easily swallowed with or without liquid.

Agitation Associated with Schizophrenia and Bipolar I Mania—Usual Dose for Agitated Patients with Schizophrenia or Bipolar Mania—The efficacy of intramuscular olanzapine for injection in controlling agitation in these disorders was demonstrated in a dose range of 2.5 mg to 10 mg. The recommended dose in these patients is 10 mg. A lower dose of 5 or 7.5 mg may be considered when clinical factors warrant (see CLINICAL EFFICACY DATA). If agitation warranting additional intramuscular doses persists following the initial dose, subsequent doses up to 10 mg may be given. However, the efficacy of repeated doses of intramuscular olanzapine for injection in agitated patients has not been systematically evaluated in controlled clinical trials. Also, the safety of total daily doses greater than 20 mg, or 10 mg injections given more frequently than 2 hours after the initial dose, and 4 hours after the second dose have not been evaluated in clinical trials. Maximal dosing of intramuscular olanzapine (e.g., three doses of 10 mg administered 2-4 hours apart) may be associated with a substantial occurrence of significant orthostatic hypotension (see PRECAUTIONS, Hematologic Effects). Thus, it is recommended that patients requiring subsequent intramuscular injections be assessed for orthostatic hypotension prior to the administration of any subsequent doses of intramuscular olanzapine for injection. The administration of an additional dose to a patient with a clinically significant postural change in systolic blood pressure is not recommended.

If ongoing olanzapine therapy is clinically indicated, oral olanzapine may be initiated in a range of 5-20 mg/day as soon as clinically appropriate (see Schizophrenia or Bipolar Disorder under DOSAGE AND ADMINISTRATION).

Intramuscular Dosing in Special Populations—A dose of 5 mg per injection should be considered for geriatric patients or when other clinical factors warrant. A lower dose of 2.5 mg per injection should be considered for patients who otherwise might be debilitated, be predisposed to hypotensive reactions, or be more pharmacodynamically sensitive to olanzapine (see CLINICAL PHARMACOLOGY, also see Use in Patients with Concomitant Illness and Drug Interactions under PRECAUTIONS).

Administration of ZYPREXA IntraMuscular—ZYPREXA IntraMuscular is intended for intramuscular use only. Do not administer intravenously or subcutaneously. Inject slowly, deep into the muscle mass.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Directions for preparation of ZYPREXA IntraMuscular with Sterile Water for Injection—Dissolve the contents of the vial using 2.1 mL of Sterile Water for Injection to provide a solution containing approximately 5 mg/mL of olanzapine. The resulting solution should appear clear and yellow. ZYPREXA IntraMuscular reconstituted with Sterile Water for Injection should be used immediately (within 1 hour) after reconstitution. Discard any unused portion.

The following table provides injection volumes for delivering various doses of intramuscular olanzapine for injection reconstituted with Sterile Water for Injection.

Dose, mg Olanzapine	Volume at Injection, mL Withdraw total contents of vial
10	2.1
7.5	1
5	0.5
2.5	

Physical Incompatibility Information—ZYPREXA IntraMuscular should be reconstituted only with Sterile Water for Injection. ZYPREXA IntraMuscular should not be combined in a syringe with olanzapine injection because precipitation occurs when these products are mixed. Lorazepam injection should not be used to reconstitute ZYPREXA IntraMuscular as the combination results in a delayed reconstitution time. ZYPREXA IntraMuscular should not be combined in a syringe with haloperidol injection because the resulting low pH has been shown to degrade olanzapine over time.

HOW SUPPLIED: The ZYPREXA 2.5 mg, 5 mg, 7.5 mg, and 10 mg tablets are white, round, and imprinted in blue ink with LILLY and tablet number. The 15 mg tablets are elliptical, blue, and debossed with LILLY and tablet number. The 20 mg tablets are elliptical, pink, and debossed with LILLY and tablet number. The tablets are available as follows:

	TABLET STRENGTH					
	2.5 mg	5 mg	7.5 mg	10 mg	15 mg	20 mg
Tablet No. Identification	4112 LILLY 4112	4115 LILLY 4115	4116 LILLY 4116	4117 LILLY 4117	4415 LILLY 4415	4420 LILLY 4420
NDC Codes:						
Bottles 30	NDC 0002-4112-30	NDC 0002-4115-30	NDC 0002-4116-30	NDC 0002-4117-30	NDC 0002-4415-30	NDC 0002-4420-30
Blisters-ID* 100	NDC 0002-4112-33	NDC 0002-4115-33	NDC 0002-4116-33	NDC 0002-4117-33	NDC 0002-4415-33	NDC 0002-4420-33
Bottles 1000	NDC 0002-4112-04	NDC 0002-4115-04	NDC 0002-4116-04	NDC 0002-4117-04	NDC 0002-4415-04	NDC 0002-4420-04

* Identi-Dose® (unit dose medication, Lilly).

ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) are yellow, round, and debossed with the tablet strength. The tablets are available as follows:

	TABLET STRENGTH			
ZYPREXA ZYDIS Tablets	5 mg	10 mg	15 mg	20 mg
Tablet No. Debossed*	4453 5	4454 10	4455 15	4456 20
NDC Codes: Dose Pack 30 (CMS Restriction)	NDC 0002-4453-85	NDC 0002-4454-85	NDC 0002-4455-85	NDC 0002-4456-85

ZYPREXA is a registered trademark of Eli Lilly and Company.
ZYDIS is a registered trademark of Catalent Pharma Solutions.
ZYPREXA ZYDIS (olanzapine orally disintegrating tablets) is manufactured for Eli Lilly and Company by Catalent Pharma Solutions, United Kingdom, SAS S/N.

ZYPREXA IntraMuscular is available in:
NDC 0002-7697-01 (No. VL7597) – 10 mg vial (1s)

Store ZYPREXA tablets, ZYPREXA ZYDIS, and ZYPREXA IntraMuscular vials (before reconstitution) at controlled room temperature, 20° to 25°C (68° to 77°F) [see USP]. Reconstituted ZYPREXA IntraMuscular may be stored at controlled room temperature, 20° to 25°C (68° to 77°F) [see USP] for up to 1 hour if necessary. Discard any unused portion of reconstituted ZYPREXA IntraMuscular. The USP defines controlled room temperature as a temperature maintained thermostatically that encompasses the usual and customary working environment of 20° to 25°C (68° to 77°F); that results in a mean kinetic temperature calculated to be not more than 25°C; and that allows for excursions between 15° and 30°C (59° and 86°F) that are experienced in pharmacies, hospitals, and warehouses.

Protect ZYPREXA tablets and ZYPREXA ZYDIS from light and moisture. Protect ZYPREXA IntraMuscular from light, do not freeze.

ANIMAL TOXICOLOGY: In several studies with olanzapine, the principal hematologic findings were reversible peripheral cytopenias in individual dogs dosed at 10 mg/kg (17 times the maximum recommended human daily oral dose on a mg/m² basis). Dose-related decreases in lymphocytes and neutrophils in mice, and lymphopenia in rats. A few dogs treated with 10 mg/kg developed reversible neutropenia and/or reversible hemolytic anemia between 1 and 10 months of treatment. Dose-related decreases in lymphocytes and neutrophils were seen in mice given doses of 10 mg/kg (equal to 2 times the maximum recommended human daily oral dose on a mg/m² basis) in studies of 3 months' duration. Nonspecific lymphopenia, consistent with decreased body weight gain, occurred in rats receiving 22.5 mg/kg (11 times the maximum recommended human daily oral dose on a mg/m² basis) for 3 months or 16 mg/kg (8 times the maximum recommended human daily oral dose on a mg/m² basis) for 6 or 12 months. No evidence of bone marrow cytotoxicity was found in any of the species examined. Bone marrows were normocellular or hypercellular, indicating that the reductions in circulating blood cells were probably due to peripheral (non-marrow) factors.

Literature revised October 1, 2007

PV 5199 AMP

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Lilly Eli Lilly and Company
Indianapolis, IN 46285, USA

www.ZYPREXA.com

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ZYPREXA® (Olanzapine Tablets)
ZYPREXA® ZYDIS® (Olanzapine Orally Disintegrating Tablets)
ZYPREXA® IntraMuscular (Olanzapine for Injection) PV 5196 AMP

Exhibit 3, Page 21 of 27
SOA Opposition to Lilly
Summary Judgment
Case No. SAN-06-05630 CV

SYMBYAX® (olanzapine and fluoxetine HCl capsules)

WARNING

Suicidality and Antidepressant Drugs—Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of SYMBYAX or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other conditions are also associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. SYMBYAX is not approved for use in pediatric patients. (See WARNINGS, Clinical Worsening and Suicide Risk, PRECAUTIONS, Information for Patients, and PRECAUTIONS, Pediatric Use.)

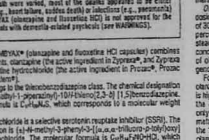
Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10-week controlled trial, the death rate in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infection (e.g., pneumonia) in nature. SYMBYAX (olanzapine and fluoxetine HCl) is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS).

DESCRIPTION: SYMBYAX® (olanzapine and fluoxetine HCl capsules) combines 2 psychotropic agents, olanzapine (the active ingredient in Zyprexa®, and Zyprexa Zydis®) and fluoxetine hydrochloride (the active drug product in Prozac®, Prozac Weekly™, and Sarafem®).

Olanzapine belongs to the thienobenzodiazepine class. The chemical designation is 2-methyl-4-(4-methyl-1 -piperazinyl)-10*H*-thieno[2,3-*b*] [1,5]benzodiazepine. The molecular formula is $C_{17}H_{20}N_4S$, which corresponds to a molecular weight of 312.44.

Fluoxetine hydrochloride is a selective serotonin reuptake inhibitor (SSRI). The chemical designation is (±)-*N*-methyl-γ-phenyl-[(α,α,α-trifluoro-*p*-tolyl)oxy] propylamine hydrochloride. The molecular formula is $C_{17}H_{18}F_3NO \cdot HCl$, which corresponds to a molecular weight of 345.79.

The chemical structures are:



olanzapine fluoxetine hydrochloride

Olanzapine is a yellow crystalline solid, which is practically insoluble in water. Fluoxetine hydrochloride is a white to off-white crystalline solid with a solubility of 14 mg/mL in water.

SYMBYAX capsules are available for oral administration in the following strength combinations:

	3 mg/ 25 mg	6 mg/ 25 mg	6 mg/ 50 mg	12 mg/ 25 mg	12 mg/ 50 mg
olanzapine equivalent	3	6	6	12	12
fluoxetine hydrochloride equivalent	25	25	50	25	50

Each capsule also contains pregelatinized starch, gelatin, dimethicone, titanium dioxide, sodium lauryl sulfate, edible black ink, red iron oxide, yellow iron oxide, and/or black iron oxide.

CLINICAL PHARMACOLOGY: Pharmacodynamics—Although the exact mechanism of SYMBYAX is unknown, it has been proposed that the activation of 5 monoaminergic neural systems (serotonin, norepinephrine, and dopamine) is responsible for its enhanced antidepressant effect. This is supported by animal studies in which the olanzapine/fluoxetine combination has been shown to produce synergistic increases in norepinephrine and dopamine release in the prefrontal cortex compared with either component alone, as well as increases in serotonin.

Olanzapine is a psychotropic agent with high affinity binding to the following receptors: serotonin 5HT$_{2A/2C}$, 5HT$_6$ (K$_i$=4, 11, and 5 nM, respectively), dopamine D$_{1-4}$ (K$_i$=11 to 31 nM), histamine H$_1$ (K$_i$=7 nM), and adrenergic α_1 receptors (K$_i$=19 nM). Olanzapine is an antagonist with moderate affinity binding for serotonin 5HT$_3$ (K$_i$=57 nM) and muscarinic M$_{1-5}$ (K$_i$=73, 96, 132, 32, and 48 nM, respectively). Olanzapine binds weakly to GABA$_A$, BZD, and β-adrenergic receptors (K$_i$>10 μM). Fluoxetine is an inhibitor of the serotonin transporter and is a weak inhibitor of the norepinephrine and dopamine transporters.

Antagonism at receptors other than dopamine and 5HT$_2$ may explain some of the other therapeutic and side effects of olanzapine. Olanzapine's antagonism of muscarinic M$_{1-5}$ receptors may explain its anticholinergic-like effects. The antagonism of histamine H$_1$ receptors by olanzapine may explain the somnolence observed with this drug. The antagonism of α_1-adrenergic receptors by olanzapine may explain the orthostatic hypotension observed with this drug. Fluoxetine has relatively low affinity for muscarinic receptors.

Pharmacokinetics—Fluoxetine (administered as a 60-mg single dose or 60 mg daily for 8 days) caused a small increase in the mean maximum concentration of olanzapine (16%) following a 5-mg dose, an increase in the mean area under the curve (17%) and a small decrease in mean apparent clearance of olanzapine (16%). In another study, a similar decrease in apparent clearance of olanzapine of 14% was observed following olanzapine doses of 6 or 12 mg with concomitant fluoxetine doses of 25 mg or more. The decrease in clearance reflects an increase in bioavailability. The terminal half-life is not affected, and it appears the dose to reach steady state should not be altered. The overall steady-state plasma concentrations of olanzapine and fluoxetine when given as the combination in the therapeutic dose ranges were comparable with those typically attained with each of the monotherapies. The small change in olanzapine clearance, observed in both studies, likely reflects the addition of a minor metabolic pathway for olanzapine via CYP2D6 by fluoxetine, a potent CYP2D6 inhibitor, and was not deemed clinically significant. Therefore, the pharmacokinetics of the individual components is expected to reasonably characterize the overall pharmacokinetics of the combination.

Absorption and Bioavailability—*SYMBYAX*—Following a single oral 12-mg/50-mg dose of SYMBYAX, peak plasma concentrations of olanzapine and fluoxetine occur at approximately 4 and 6 hours, respectively. The effect of food on the absorption and bioavailability of SYMBYAX has not been evaluated. The bioavailability of olanzapine given as Zyprexa, and the bioavailability of fluoxetine given as Prozac were not affected by food. It is unlikely that there would be a significant food effect on the bioavailability of SYMBYAX.

Olanzapine—Olanzapine is well absorbed and reaches peak concentration approximately 6 hours following an oral dose. Food does not affect the rate or extent of olanzapine absorption when olanzapine is given as Zyprexa. It is eliminated extensively by first pass metabolism, with approximately 40% of the dose metabolized before reaching the systemic circulation.

Fluoxetine—Following a single oral 40-mg dose, peak plasma concentrations of fluoxetine from 15 to 55 ng/mL are observed after 6 to 8 hours. Food does not appear to affect the systemic bioavailability of fluoxetine given as Prozac, although it may delay its absorption by 1 to 2 hours, which is probably not clinically significant.

Distribution—*SYMBYAX*—The in vitro binding to human plasma proteins of the olanzapine/fluoxetine combination is similar to the binding of the individual components.

Olanzapine—Olanzapine is extensively distributed throughout the body, with a volume of distribution of approximately 1000 L. It is 93% bound to plasma proteins over the concentration range of 7 to 1103 ng/mL, binding primarily to albumin and to α_1-acid glycoprotein.

Fluoxetine—Over the concentration range from 200 to 1000 ng/mL, approximately 94.5% of fluoxetine is bound in vitro to human serum proteins, including albumin and α_1-glycoprotein. The interaction between fluoxetine and other highly protein-bound drugs has not been fully evaluated (see PRECAUTIONS, Drugs highly bound to plasma proteins).

Metabolism and Elimination—*SYMBYAX*—SYMBYAX therapy yielded steady-state concentrations of norfluoxetine similar to those seen with fluoxetine in the therapeutic dose range.

Olanzapine—Olanzapine displays linear pharmacokinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours (5th to 95th percentile, mean dosing range, 33 hours), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th of 30 hr), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th percentile; mean of 25 L/hr). Administration of olanzapine once daily leads to steady-state concentrations in about 1 week and are approximately twice the concentrations after single doses. Plasma concentrations, half-life, and clearance of olanzapine may vary between individuals on the basis of smoking status, gender, and age (see Special Populations).

Following a single oral dose of ^{14}C-labeled olanzapine, 7% of the dose of olanzapine was recovered in the urine as unchanged drug, indicating that olanzapine is highly metabolized. Approximately 57% and 30% of the dose was recovered in the urine and feces, respectively. In the plasma, olanzapine accounted for only 12% of the total drug-related material, indicating significant exposure to metabolites. After multiple dosing, the major circulating metabolites were the 10-N-glucuronide, present at steady state at 44% of the concentration of olanzapine, and 4'-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed.

Direct glucuronidation and CYP450-mediated oxidation are the primary metabolic pathways for olanzapine. In vitro studies suggest that CYP1A2, CYP2D6, and the flavin-containing monooxygenase system are involved in olanzapine oxidation. CYP2D6-mediated oxidation appears to be a minor metabolic pathway in vivo, because the clearance of olanzapine is not reduced in subjects who are poor metabolizers.

Fluoxetine—Fluoxetine is a racemic mixture (50/50) of *R*-fluoxetine and *S*-fluoxetine enantiomers. Both optical isomers, both enantiomers are specific and potent serotonin uptake inhibitors with essentially equivalent pharmacologic activity. The *S*-fluoxetine enantiomer is eliminated more slowly and is the predominant enantiomer present in plasma at steady state.

Fluoxetine is extensively metabolized in the liver to its only identified active metabolite, norfluoxetine, via the CYP2D6 pathway. A number of unidentified metabolites exist.

In animal models, *S*-norfluoxetine is a potent and selective inhibitor of serotonin uptake and has been consistently equipotent to *R*- or *S*-fluoxetine. Plasma clearance is significantly less potent than the parent drug in the inhibition of serotonin uptake. The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney.

Clinical Issues Related to Metabolism and Elimination—The complexity of the metabolism of fluoxetine has several consequences that may potentially affect the clinical use of SYMBYAX.

Variability in metabolism—A subset (about 7%) of the population has reduced activity of the drug metabolizing enzyme CYP2D6. Such individuals are referred to as "poor metabolizers" of drugs such as debrisoquin, sparteine/nortropan, and the tricyclic antidepressants (TCAs). In a study involving labeled and unlabeled enantiomers administered as a racemate, these individuals metabolized *S*-fluoxetine at a slower rate and thus achieved higher concentrations of *S*-fluoxetine. Consequently, concentrations of *S*-norfluoxetine at steady state were lower. The metabolism of *R*-fluoxetine in these poor metabolizers appears normal. When compared with normal metabolizers, the total sum at steady state of the plasma concentrations of the 4 enantiomers was not significantly greater among poor metabolizers. Thus, the net pharmacodynamic activities were essentially the same.

Alternative substrate pathways (non-CYP2D6) also contribute to the metabolism of fluoxetine. This explains how fluoxetine achieves a steady-state concentration rather than increasing without limit.

Because the metabolism of fluoxetine, like that of a number of other compounds including TCAs and other selective serotonin antidepressants, involves the CYP2D6 system, concomitant therapy with drugs also metabolized by this enzyme system (such as the TCAs) may lead to drug interactions (see PRECAUTIONS, Drug Interactions).

Accumulation and slow elimination—The relatively slow elimination of fluoxetine (elimination half-life of 1 to 3 days after acute administration and 4 to 6 days after chronic administration) and its active metabolite, norfluoxetine (elimination half-life of 4 to 16 days after acute and chronic administration), leads to significant accumulation of these active species in chronic use and delayed attainment of steady state, even when a fixed dose is administered. After 30 days of dosing at 40 mg/day, plasma concentrations of fluoxetine in the range of 91 to 302 ng/mL and norfluoxetine in the range of 72 to 258 ng/mL have been observed. Plasma concentrations of fluoxetine were higher than those predicted by single-dose studies, because the metabolism of fluoxetine is not proportional to dose. However, norfluoxetine appears to have linear pharmacokinetics. Its mean terminal half-life after a single dose was 8.6 days but after multiple dosing was 9 days. Steady-state levels after prolonged dosing are similar to levels seen at 4 to 5 weeks.

The long elimination half-lives of fluoxetine and norfluoxetine assure that, even when dosing is discontinued, the drug substance will persist in the body for weeks (primarily depending on individual patient characteristics, previous dosing regimen, and length of previous therapy at discontinuation). This is of potential consequence if drug discontinuation is required or when drugs are prescribed that might interact with fluoxetine and norfluoxetine following the discontinuation of fluoxetine.

Special Populations—*Geriatric*—Based on the individual pharmacokinetic profiles of olanzapine and fluoxetine, the pharmacokinetics of SYMBYAX may be altered in geriatric patients. Caution should be used in dosing the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity.

In a study involving 24 healthy subjects, the mean elimination half-life of olanzapine was about 1.5 times greater in elderly subjects (>65 years of age) than in non-elderly subjects (≤65 years of age).

The disposition of single doses of fluoxetine in healthy elderly subjects (>65 years of age) did not differ significantly from that in younger normal subjects. However, advanced age can affect the disposition of the drug, a single-dose study given the long half-life and nonlinear disposition of the drug, a single-dose study is not adequate to rule out the possibility of altered pharmacokinetics in the elderly particularly if they have systemic illness or are receiving multiple drugs for concomitant diseases. The effects of age upon the metabolism of fluoxetine have been investigated in 260 elderly but otherwise healthy depressed patients (≥60 years of age) who received 20 mg fluoxetine for 6 weeks. Combined fluoxetine plus norfluoxetine plasma concentrations were 209.3 ± 85.7 ng/mL at the end of 6 weeks. No unusual age-associated patterns of adverse events was observed in these elderly patients.

Renal Impairment—The pharmacokinetics of SYMBYAX has not been studied in patients with renal impairment. However, olanzapine and fluoxetine individual pharmacokinetics do not differ significantly in patients with renal impairment. SYMBYAX dosing adjustment based upon renal impairment is not necessary.

Because olanzapine is highly metabolized before excretion and only 7% of the drug is excreted unchanged, renal dysfunction alone is unlikely to have a major impact on the pharmacokinetics of olanzapine. The pharmacokinetic characteristics of olanzapine were similar in patients with severe renal impairment and normal subjects, indicating that dosage adjustment based upon the degree of renal impairment is not required. In addition, olanzapine is not removed by dialysis. The impairment is not required. In addition, olanzapine is not removed by dialysis. The effect of renal impairment on olanzapine metabolite elimination has not been studied.

In depressed patients on dialysis (N=12), fluoxetine administered as 20 mg once daily for 2 months produced steady-state fluoxetine and norfluoxetine plasma concentrations comparable with those seen in patients with normal renal function. While the possibility exists that renally excreted metabolites of fluoxetine may accumulate to higher levels in patients with severe renal dysfunction, use of a lower or less frequent dose is not routinely necessary in renally impaired patients.

Hepatic Impairment—Based on the individual pharmacokinetic profiles of olanzapine and fluoxetine, the pharmacokinetics of SYMBYAX may be altered in patients with hepatic impairment. The lowest starting dose should be considered for patients with hepatic impairment (see PRECAUTIONS, Use in Patients with Concomitant Illness and DOSAGE AND ADMINISTRATION, Special Populations).

Although the presence of hepatic impairment may be expected to increase the clearance of olanzapine, a study of the effect of impaired liver function in subjects (N=5) with clinically significant cirrhosis (Childs-Pugh Classification A and B) revealed little effect on the pharmacokinetics of olanzapine.

As might be predicted from its primary site of metabolism, liver impairment can affect the elimination of fluoxetine. The elimination half-life of fluoxetine was prolonged in a study of cirrhotic patients, with a mean of 7.6 days compared with the range of 2 to 3 days seen in subjects without liver disease; norfluoxetine elimination was also delayed, with a mean duration of 12 days for cirrhotic patients compared with the range of 7 to 9 days in normal subjects.

Gender—Clearance of olanzapine is approximately 30% lower in women than in men. There were, however, no apparent differences between men and women in effectiveness or adverse event profiles; dosage modifications based on gender should not be needed.

Smoking Status—Olanzapine clearance is about 40% higher in smokers than in nonsmokers, although dosage modifications are not routinely required.

Race—No SYMBYAX pharmacokinetic study was conducted to investigate the effects of race. In vivo studies have shown that exposures to olanzapine are similar among Japanese, Chinese and Caucasians, especially after normalization for body weight differences. Dosage modifications for race, therefore, are not routinely required.

Combined Effects—The combined effects of age, smoking, and gender could lead to substantial pharmacokinetic differences in populations. The clearance of olanzapine in young smoking males, for example, may be 3 times higher than that in elderly nonsmoking females. SYMBYAX dosing modification may be necessary in patients who exhibit a combination of factors that may result in slower metabolism of the olanzapine component (see DOSAGE AND ADMINISTRATION, Special Populations).

CLINICAL STUDIES: The efficacy of SYMBYAX for the treatment of depressive episodes associated with bipolar disorder was established in 2 identically designed, 8-week, randomized, double-blind, controlled studies of patients who met Diagnostic and Statistical Manual 4th edition (DSM-IV) criteria for Bipolar I Disorder, Depressed utilizing flexible dosing of SYMBYAX (6/25, 9/50, or 12/50 mg/day), olanzapine (5 to 20 mg/day), and placebo. These studies included patients (≥18 years of age) with or without psychotic symptoms and with or without a rapid cycling course.

The primary rating instrument used to assess depressive symptoms in these studies was the Montgomery-Asberg Depression Rating Scale (MADRS), a 10-item clinician-rated scale with total scores ranging from 0 to 60. The primary outcome measure of these studies was the change from baseline to endpoint in the MADRS total score. In both studies, SYMBYAX was statistically significantly superior to both olanzapine monotherapy and placebo in reduction of the MADRS total score. The results of the studies are summarized below (Table 1).

Table 1: MADRS Total Score
Mean Change from Baseline to Endpoint

	Treatment Group	Baseline Mean	Change to Endpoint Mean[1]
Study 1	SYMBYAX (N=46)	30	-16[2]
	Olanzapine (N=182)	32	-12
	Placebo (N=181)	31	-10
Study 2	SYMBYAX (N=42)	32	-18[2]
	Olanzapine (N=189)	33	-14
	Placebo (N=189)	31	-9

[1] Negative number denotes improvement from baseline.
[2] Statistically significant compared to both olanzapine and placebo.

INDICATIONS AND USAGE: SYMBYAX is indicated for the treatment of depressive episodes associated with bipolar disorder. The efficacy of SYMBYAX was established in 2 identically designed, 8-week, randomized, double-blind clinical studies.

Unlike with unipolar depression, there are no established guidelines for the length of time patients with bipolar disorder experiencing a major depressive episode should be treated with agents containing antidepressant drugs.

The effectiveness of SYMBYAX for maintaining antidepressant response in this patient population beyond 8 weeks has not been established in controlled clinical studies. Physicians who elect to use SYMBYAX for extended periods should periodically reevaluate the benefits and long-term risks of the drug for the individual patient.

CONTRAINDICATIONS: *Hypersensitivity*—SYMBYAX is contraindicated in patients with a known hypersensitivity to the product or any component of the product.

Monoamine Oxidase Inhibitors (MAOIs)—There have been reports of serious, sometimes fatal reactions (including hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delirium and coma) in patients receiving fluoxetine in combination with a MAOI, and in patients who have recently discontinued fluoxetine and are then started on a MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Therefore,

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008238

SYMBYAX should not be used in combination with an MAOI, or within a minimum of 14 days of discontinuing therapy with an MAOI. Since olanzapine and its major metabolite have very long elimination half-lives, at least 5 weeks [perhaps longer, especially if fluoxetine has been prescribed chronically and/or at higher doses (see CLINICAL PHARMACOLOGY, Accumulation and slow elimination)] should be allowed after stopping SYMBYAX before starting an MAOI.

Pimozide—Concomitant use in patients taking pimozide is contraindicated (see PRECAUTIONS).

Thioridazine—Thioridazine should not be administered with SYMBYAX or administered within a minimum of 5 weeks after discontinuation of SYMBYAX (see WARNINGS, Thioridazine).

WARNINGS: Clinical Worsening and Suicide Risk—Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders, and these disorders themselves are the strongest predictors of suicide. There has been a long-standing concern, however, that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients during the early phases of treatment. Pooled analyses of short-term placebo-controlled trials of antidepressant drugs (SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18-24) with major depressive disorder (MDD) and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

The pooled analyses of placebo-controlled trials in children and adolescents with MDD, obsessive-compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4400 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over 77,000 patients. There was considerable variation in risk of suicidality among drugs, but a tendency toward an increase in the younger patients for almost all drugs studied. There were differences in absolute risk of suicidality across the different indications, with the highest incidence in MDD. The risk differences (drug versus placebo), however, were relatively stable within age strata and across indications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1000 patients treated) are provided in Table 2.

Table 2

Age Range	Drug–Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated
<18	Increases Compared to Placebo 14 additional cases
18-24	5 additional cases
25-64	Decreases Compared to Placebo 1 fewer case
≥65	6 fewer cases

No suicides occurred in any of the pediatric trials. There were suicides in the adult trials, but the number was not sufficient to reach any conclusion about drug effect on suicide.

It is unknown whether the suicidality risk extends to longer-term use, i.e., beyond several months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with depression that the use of antidepressants can delay the recurrence of depression.

All patients being treated with antidepressants for any indication should be monitored appropriately and observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases.

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, and mania, have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and nonpsychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, there is concern that such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients whose depression is persistently worse, or who are experiencing emergence of suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

If the decision has been made to discontinue treatment, medication should be tapered, as rapidly as is feasible, but with recognition that abrupt discontinuation can be associated with certain symptoms [see PRECAUTIONS and DOSAGE AND ADMINISTRATION, Discontinuation of Treatment with SYMBYAX, for a description of the risks of discontinuation of SYMBYAX].

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to health care providers. Such monitoring should include daily observation by families and caregivers. Prescriptions for SYMBYAX should be written for the smallest quantity of capsules consistent with good patient management, in order to reduce the risk of overdose.

It should be noted that SYMBYAX is not approved for use in treating any indications in the pediatric population.

Screening Patients for Bipolar Disorder—A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed (though not established in controlled trials) that treating such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described above represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. It should be noted that SYMBYAX is approved for use in treating bipolar depression.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis—Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. SYMBYAX (olanzapine and fluoxetine HCl) is not approved for the treatment of patients with dementia related psychosis [see BOX WARNING].

In olanzapine placebo-controlled clinical trials of elderly patients with dementia-related psychosis, the incidence of death in olanzapine-treated patients was significantly greater than placebo-treated patients (3.5% vs 1.5%, respectively). *Cerebrovascular Adverse Events (CVAE), Including Stroke, in Elderly Patients with Dementia-Related Psychosis*—Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients in trials of olanzapine in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia—Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including olanzapine alone, as well as olanzapine taken concomitantly with fluoxetine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the two highest serum concentrations was 15.0 mg/dL.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, with indirect duration up to 12 weeks, SYMBYAX was associated with a statistically significantly greater mean change in random glucose compared to placebo (15.65 mg/dL versus -3.86 mg/dL). In patients with baseline normal random glucose levels (<140 mg/dL), 2.3% of those treated with SYMBYAX were found to have high glucose levels (≥200 mg/dL) during SYMBYAX treatment and were statistically significantly different from those treated with placebo. In patients with baseline borderline random glucose levels (≥140 mg/dL and <200 mg/dL), 34.1% of those treated with SYMBYAX were found to have high glucose levels (≥200 mg/dL) during SYMBYAX treatment and were statistically significantly different compared to 9.6% of those treated with placebo. The difference in mean changes between SYMBYAX and placebo was greater in patients with evidence of glucose dysregulation at baseline (pooling these patients diagnosed with diabetes mellitus or related adverse events, patients treated with anti-diabetic agents, patients with a baseline random glucose level ≥200 mg/dL, or a baseline fasting glucose level ≥126 mg/dL). These patients had a greater mean increase in HbA_{1c}.

Controlled fasting glucose data is limited for SYMBYAX; however, in an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine was associated with a greater mean change in fasting glucose (mean increase of 5.3 mg/dL vs 0.17 mg/dL).

Dyslipidemia Monotherapy in Adolescents—The safety and efficacy of olanzapine and olanzapine and fluoxetine in combination have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (0.68 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing SYMBYAX to patients with an established diagnosis of diabetes mellitus, or those with other clinical risk factors for impaired glucose tolerance, such as obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hyperlipidemia—Undesirable alterations in lipids have been observed with SYMBYAX use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using SYMBYAX, is advised.

Significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with SYMBYAX use. Significant increases in total cholesterol have also been seen with SYMBYAX use.

Controlled fasting lipid data is limited for SYMBYAX.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, with treatment duration up to 12 weeks, SYMBYAX-treated patients had an increase from baseline in mean random total cholesterol of 12.1 mg/dL compared to a statistically significantly different increase from baseline in mean random total cholesterol of 4.8 mg/dL for olanzapine-treated patients and a decrease in mean random total cholesterol of 5.5 mg/dL for placebo-treated patients. Table 3 shows categorical changes in nonfasting lipid values.

Table 3: Changes in Nonfasting Lipids Values from Adult Placebo-Controlled Clinical Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Nonfasting Triglycerides	Increase by ≥50 mg/dL	OFC	174	67.8%
		Olanzapine	172	72.7%
		Placebo	57	47.4%
	Normal to High (<150 mg/dL to ≥500 mg/dL)	Olanzapine	58	5%
		OFC	105	15.1%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥500 mg/dL)	Olanzapine	103	8.7%
Nonfasting Total Cholesterol	Increase by ≥40 mg/dL	OFC	685	35%*
		Olanzapine	749	27.7%
		Placebo	360	9%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	OFC	256	8.2%*
		Olanzapine	279	2.9%
		Placebo	179	1.7%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	OFC	213	36.2%*
		Olanzapine	281	27.9%
		Placebo	111	5.9%

* Statistically significant compared to olanzapine.
† Statistically significant compared to placebo.

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Controlled fasting lipid data is limited for SYMBYAX; however, in an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had statistically significant increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.0 mg/dL, and 20.8 mg/dL respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL, 4.3 mg/dL, and 10.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse events, patients treated with lipid lowering agents, or patients with high baseline lipid levels. Table 4 shows categorical changes in fasting lipid values.

Table 4: Changes in Fasting Lipids Values from Adult Placebo-Controlled Olanzapine Monotherapy Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	745	39.6%*
		Placebo	402	26.1%
	Normal to High (<150 mg/dL to ≥200 mg/dL)	Olanzapine	457	9.9%*
		Placebo	251	4.4%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	155	39.3%*
		Placebo	85	20.0%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	745	21.6%*
		Placebo	402	9.5%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	Olanzapine	257	2.7%
		Placebo	237	2.4%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	Olanzapine	222	23.0%*
		Placebo	112	12.5%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	535	23.7%*
		Placebo	304	14.1%
	Normal to High (<130 mg/dL to ≥160 mg/dL)	Olanzapine	154	2%
		Placebo	82	1.2%
	Borderline to High (≥130 mg/dL and <160 mg/dL to ≥160 mg/dL)	Olanzapine	302	10.6%
		Placebo	173	8.1%

* Statistically significant compared to placebo

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in triglycerides in patients taking olanzapine was 40.5 mg/dL. In phase 1 of CATIE, the median increase in total cholesterol was 9.4 mg/dL.

Olanzapine Monotherapy in Adolescents—The safety and efficacy of olanzapine and olanzapine and fluoxetine in combination have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (0.68 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing SYMBYAX to patients with an established diagnosis of diabetes mellitus, or those with other clinical risk factors for impaired glucose tolerance, such as obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hyperlipidemia—Undesirable alterations in lipids have been observed with SYMBYAX use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using SYMBYAX, is advised.

Significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with SYMBYAX use. Significant increases in total cholesterol have also been seen with SYMBYAX use.

Controlled fasting lipid data is limited for SYMBYAX.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, with treatment duration up to 12 weeks, SYMBYAX-treated patients had an increase from baseline in mean random total cholesterol of 12.1 mg/dL compared to a statistically significantly different increase from baseline in mean random total cholesterol of 4.8 mg/dL for olanzapine-treated patients and a decrease in mean random total cholesterol of 5.5 mg/dL for placebo-treated patients. Table 3 shows categorical changes in nonfasting lipid values.

Table 3: Changes in Nonfasting Lipids Values from Adult Placebo-Controlled Clinical Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Nonfasting Triglycerides	Increase by ≥50 mg/dL	OFC	174	67.8%
		Olanzapine	172	72.7%
		Placebo	57	47.4%
	Normal to High (<150 mg/dL to ≥500 mg/dL)	Olanzapine	58	5%
		OFC	105	15.1%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥500 mg/dL)	Olanzapine	103	8.7%
Nonfasting Total Cholesterol	Increase by ≥40 mg/dL	OFC	685	35%*
		Olanzapine	749	27.7%
		Placebo	360	9%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	OFC	256	8.2%*
		Olanzapine	279	2.9%
		Placebo	179	1.7%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	OFC	213	36.2%*
		Olanzapine	281	27.9%
		Placebo	111	5.9%

* Statistically significant compared to olanzapine.
† Statistically significant compared to placebo.

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Table 5 shows categorical changes in fasting lipids values from 6 clinical trials. The olanzapine-treated patients had a greater increase in total cholesterol, LDL cholesterol, and triglycerides compared to placebo-treated patients who completed treatment periods of 6 or 8 weeks.

Table 5: Changes in Fasting Lipids Values from Adolescent Placebo-Controlled Olanzapine Monotherapy Studies

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	135	37.0%*
		Placebo	56	15.2%
	Normal to High (<90 mg/dL to ≥130 mg/dL)	Olanzapine	67	28.9%
		Placebo	28	10.7%
	Borderline to High (≥90 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	37	59.5%
		Placebo	17	35.3%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	138	14.5%*
		Placebo	66	4.5%
	Normal to High (<170 mg/dL to ≥200 mg/dL)	Olanzapine	67	6.9%
		Placebo	43	2.3%
	Borderline to High (≥170 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	36	38.9%*
		Placebo	13	7.7%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	137	17.5%
		Placebo	63	11.1%
	Normal to High (<110 mg/dL to ≥130 mg/dL)	Olanzapine	98	5.1%
		Placebo	44	4.5%
	Borderline to High (≥110 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	29	48.3%*
		Placebo	9	0%

* Statistically significant compared to placebo

Weight Gain—Potential consequences of weight gain should be considered prior to starting SYMBYAX. Patients receiving SYMBYAX should receive regular monitoring of weight.

In an analysis of 7 controlled clinical studies, 2 of which were placebo-controlled, the mean weight increase for SYMBYAX-treated patients was statistically significantly greater than placebo-treated patients (4 kg vs 0.3 kg). Twenty-two percent of SYMBYAX-treated patients gained at least 7% of their baseline weight, with a median exposure of 6 weeks. This was statistically significantly greater than in placebo-treated patients (1.8%). Approximately 3% of SYMBYAX-treated patients gained at least 15% of their baseline weight, with a median exposure of 8 weeks. This was statistically significantly greater than in placebo-treated patients (0%). Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories. Discontinuation due to weight gain occurred in 2.5% of SYMBYAX-treated patients and in 0.3% of placebo-treated patients.

Table 6 includes data on weight gain observed in 6 clinical trials of SYMBYAX-treated patients. The olanzapine-treated patients had a greater increase in weight compared to placebo-treated patients who completed treatment periods of 6 or 8 weeks.

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Table 6: Weight Gain with Olanzapine Use

Amount Gained kg (lb)	6 Weeks (N=2976) (%)	6 Months (N=1539) (%)	12 Months (N=778) (%)	24 Months (N=422) (%)
≤0	37	21	20	22
0-5 (0-11 lb)	57	34	25	22
5-10 (11-22 lb)	15	28	25	22
10-15 (22-33 lb)	2	12	16	18
>15 (>33 lb)	0	5	14	16

During long-term combination therapy with olanzapine monotherapy (238 median days of exposure), 56% of olanzapine patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 4.4 kg.

Olanzapine Monotherapy in Adolescents—The safety and efficacy of olanzapine and olanzapine and fluoxetine combination were not been established in adolescent patients under the age of 18 years. In an analysis of 4 placebo-controlled olanzapine monotherapy studies of adolescent patients (ages 13 to 17 years), including those with schizophrenia (5 weeks) or bipolar disorder (mania or mixed episodes) (3 weeks), olanzapine-treated patients gained an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.6% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 8.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 19 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

During long-term combination therapy with olanzapine, 65% of olanzapine-treated patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 7.4 kg.

Orthostatic Hypotension—SYMBYAX may induce orthostatic hypotension associated with dizziness, tachycardia, bradycardia, and in some patients, syncope, especially during the initial dose-titration period.

In the bipolar depression studies, statistically significantly more orthostatic changes occurred with the SYMBYAX group compared to placebo and olanzapine groups. Orthostatic systolic blood pressure decrease of at least 30 mm Hg occurred in 7.3% (6/82), 1.4% (5/346), and 1.4% (5/352) of the SYMBYAX, olanzapine and placebo groups, respectively. Among the group of controlled clinical studies with SYMBYAX, an orthostatic systolic blood pressure decrease of ≥30 mm Hg occurred in 4% (21/512) of SYMBYAX-treated patients, 5% (12/264) of fluoxetine-treated patients, 2% (16/644) of olanzapine-treated patients, and 2% (6/404) of placebo-treated patients. In the group of studies, the incidence of syncope in SYMBYAX-treated patients was 0.4% (2/512) compared to placebo 0.2% (1/477).

In a clinical pharmacology study of SYMBYAX, three healthy subjects were discontinued from the trial after experiencing severe, but self-limited, hypotension and bradycardia that occurred 2 to 8 hours following a single 12-mg/50-mg dose of SYMBYAX. Reactions consisting of this combination of hypotension and bradycardia (and also accompanied by sinus pause) have been observed in at least three other healthy subjects treated with various formulations of olanzapine (one oral, two intramuscular). In controlled clinical studies, the incidence of patients with a ≥20 bpm decrease in heart rate and pulse concomitantly with a ≥20 mm Hg decrease in orthostatic systolic blood pressure was 0.4% (2/512) in the SYMBYAX group, 0.2% (1/455) in the placebo group, 0.8% (5/659) in the olanzapine group, and 0% (0/241) in the fluoxetine group.

SYMBYAX should be used with particular caution in patients with known cardiovascular disease (history of myocardial infarction or ischemia, heart failure, or conduction abnormalities), cerebrovascular disease, or conditions that would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medications).

Allergic Events and Rash—In SYMBYAX premarketing controlled clinical studies, the overall incidence of rash or allergic events in SYMBYAX-treated patients (4.6% (56/751)) was similar to that of placebo (5.2% (25/477)). The majority of these cases of rash and/or urticaria were mild; however, three patients discontinued (one due to rash, which was moderate in severity, and two due to allergic events, one of which included face edema).

In fluoxetine US clinical studies, 7% of 10,782 fluoxetine-treated patients developed various types of rashes and/or urticaria. Among the cases of rash and/or urticaria reported in premarketing clinical studies, almost a third were withdrawn from treatment because of the rash and/or systemic signs or symptoms associated with the rash. Clinical findings reported in association with rash include fever, leukocytosis, arthralgia, edema, carpal tunnel syndrome, respiratory distress, lymphadenopathy, proteinuria, and mild transaminase elevation. Most patients improved promptly with discontinuation of fluoxetine and/or adjunctive treatment with antihistaminics or steroids, and all patients experiencing these events were reported to recover completely.

In fluoxetine premarketing clinical studies, 2 patients are known to have developed a serious cutaneous systemic illness. In neither patient were there any other obvious etiologies, but it was considered to have a leukocytoclastic vasculitis, and the other, a severe desquamating syndrome that was considered variously to be a severe rash or erythema multiforme. Other patients have had systemic syndromes suggestive of serum sickness.

Since the introduction of fluoxetine, systemic events, possibly related to vasculitis, have developed in patients with rash. Although these events are rare, they may be serious, involving the lung, kidney, or liver. Death has been reported to occur in association with these systemic events.

Anaphylactoid events, including bronchospasm, angioedema, and urticaria alone and in combination, have been reported.

Pulmonary events, including inflammatory processes of varying histopathology and/or fibrosis, have been reported rarely. These events have occurred with dyspnea as the only preceding symptom.

Whether these systemic events and such have a common underlying cause or are due to different etiologies or pathogenic processes is not known. Furthermore, a specific underlying pathophysiologic basis for these events has not been identified. Upon the appearance of rash or of other possible allergic phenomena for which an alternative etiology cannot be identified, SYMBYAX should be discontinued.

Serotonin Syndrome—The development of a potentially life-threatening serotonin syndrome may occur with SSRIs and SSRIs, including SYMBYAX treatment, particularly with concomitant use of serotonergic drugs (including triptans) and drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome symptoms may include mental status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular symptoms (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of SYMBYAX with MAOIs intended to treat depression is contraindicated (see CONTRAINDICATIONS, Monoamine Oxidase Inhibitors (MAOI) and PRECAUTIONS, Drug Interactions).

If concomitant treatment of SYMBYAX with a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see PRECAUTIONS, Drug Interactions).

The concomitant use of SYMBYAX with serotonin precursors (such as tryptophan) is not recommended (see PRECAUTIONS, Drug Interactions).

Neuroleptic Malignant Syndrome (NMS)—A potentially fatal symptom complex sometimes referred to as NMS has been reported in association with administration of antipsychotic drugs, including olanzapine. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure.

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system pathology.

The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about specific pharmacological treatment regimens for NMS.

If after recovering from NMS, a patient requires treatment with an antipsychotic, the patient should be carefully monitored, since recurrences of NMS have been reported.

Tardive Dyskinesia—A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, which patients are likely to develop the syndrome. Whether antipsychotic drug products differ in their potential to cause tardive dyskinesia is unknown.

The risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. It may even arise after discontinuation of treatment.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment itself, however, may suppress (or partially suppress) the sign and symptoms of tardive dyskinesia and thereby may mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

The likelihood that a seemingly indicated (i.e., SYMBYAX-treated patients was) will be present can be minimized by use of the smallest dose and the shortest duration of treatment producing a satisfactory clinical response. Periodic assessment for the presence of this disorder should be conducted, although each one commonly, after relatively brief treatment periods at low doses, may even arise after discontinuation of treatment.

There is no known treatment for established cases of tardive dyskinesia, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment itself, however, may suppress (or partially suppress) the sign and symptoms of tardive dyskinesia and thereby may mask the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown.

Given these considerations, SYMBYAX should be prescribed in a manner that is most likely to minimize the risk of tardive dyskinesia. If signs and symptoms of tardive dyskinesia appear in a patient on SYMBYAX, drug discontinuation should be considered. However, some patients may require treatment with SYMBYAX despite the presence of the syndrome. The need for continued treatment should be reassessed periodically.

Thioridazine—In a study of 19 healthy male subjects, which included 6 slow and 13 rapid hydroxylators of debrisoquin, a single 25-mg dose of oral thioridazine produced a 2.4-fold higher C_{max} and a 4.5-fold higher AUC for thioridazine in the slow hydroxylators compared with the rapid hydroxylators. The rate of debrisoquin hydroxylation is felt to depend on the level of CYP2D6 enzyme activity. This study suggests that drugs that inhibit CYP2D6, such as certain SSRIs, including fluoxetine, will produce elevated plasma levels of thioridazine (see PRECAUTIONS).

Thioridazine administration produces a dose-related prolongation of the QT_c interval, which is associated with serious ventricular arrhythmias and sudden death. This risk is expected to increase with fluoxetine-induced inhibition of thioridazine metabolism (see CONTRAINDICATIONS, Thioridazine).

PRECAUTIONS: General—*Concomitant Use of Olanzapine and Fluoxetine Products*—SYMBYAX contains the same active ingredients that are in Zyprexa and Zyprexa Zydis (olanzapine) and in Prozac, Prozac Pulvule, and Sarafem (fluoxetine HCl). Caution should be exercised when prescribing these medications concomitantly with SYMBYAX.

Abnormal Bleeding—Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies of case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding. In two of these studies, concurrent use of a nonsteroidal anti-inflammatory drug (NSAID) or aspirin potentiated the risk of bleeding (see DRUG INTERACTIONS). Although these studies focused on upper gastrointestinal bleeding, there is reason to believe that bleeding at other sites may be similarly potentiated. Patients should be cautioned regarding the risk of bleeding associated with the concomitant use of SYMBYAX and NSAIDs, aspirin, or other drugs that affect coagulation.

Mania/Hypomania—In the two controlled bipolar depression studies there was no statistically significant difference in the incidence of manic events (manic reaction or mania) between SYMBYAX and placebo-treated patients. In one of the studies, the incidence of manic events was (7% (34/512)) in SYMBYAX-treated patients compared to (3% (5/194)) in placebo-treated patients. In the other study, the incidence of manic events was (2% (1/43)) in SYMBYAX-treated patients compared to (6% (15/193)) in placebo-treated patients. The risk of precipitation of a manic episode in patients with bipolar disorder is believed to be increased by the use of antidepressant monotherapy. Whether this risk is increased by the use of antidepressants in combination with mood stabilizers is not known. As with all antidepressants, SYMBYAX should be used cautiously in patients with a history of mania.

Activation of Mania/Hypomania—Activation of mania or hypomania has been reported in a small proportion of patients with mood disorders who were treated with antidepressants. Activation of mania/hypomania has been reported in a small proportion of patients with mood disorders who were treated with olanzapine. Activation of mania/hypomania has been reported in a small proportion of patients with mood disorders who were treated with fluoxetine. Activation of mania/hypomania has been reported in a small proportion of patients with mood disorders who were treated with SYMBYAX. As with all antidepressants, SYMBYAX should be used cautiously in patients with a history of mania.

Hyperglycemia and Diabetes Mellitus—Hyperglycemia and exacerbation of diabetes mellitus, sometimes associated with ketoacidosis or hyperosmolar coma, including some fatal cases, have been reported in patients treated with olanzapine. Olanzapine is not approved for the treatment of patients with diabetes mellitus. Patients with an established diagnosis of diabetes mellitus who are started on olanzapine should be monitored regularly for worsening of glucose control. Those with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) should be observed during treatment with olanzapine. Patients who develop symptoms of hyperglycemia during treatment with olanzapine should undergo fasting blood glucose testing. In some of these cases, hyperglycemia resolved when olanzapine was discontinued; however, some patients required continuation of antidiabetic treatment despite discontinuation of olanzapine.

In placebo-controlled trials of olanzapine in elderly patients with dementia-related psychosis (n=1184), the following treatment-emergent adverse events were reported in olanzapine-treated patients at an incidence of at least 2% and significantly greater than placebo-treated patients: abnormal gait, somnolence, peripheral edema, abnormal gait, urinary incontinence, lethargy, increased salivation, dysphasia, pneumonia, dry mouth and visual hallucinations. The rate of discontinuation due to adverse events was similar for olanzapine and placebo-treated patients (13% vs 7%). Elderly patients with dementia-related psychosis treated with olanzapine are at an increased risk of death compared to placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. The prescriber should not treat elderly patients with dementia-related psychosis without vigilance should be exercised (see BOX WARNING and WARNINGS).

As with other CNS-active drugs, SYMBYAX should be used with caution in elderly patients with dementia. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. The prescriber should not treat elderly patients with dementia-related psychosis without vigilance should be exercised (see BOX WARNING and WARNINGS).

SYMBYAX should not be used routinely in combination with other drugs that prolong the QT interval in patients with congestive heart failure, bradyarrhythmias, or electrolyte disturbances. Patients with these diagnoses were excluded from the clinical studies of SYMBYAX.

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Caution is advised when using SYMBYAX in cardiac patients and in patients with diseases or conditions that could affect hemodynamic responses (see WARNINGS, Orthostatic Hypotension).

In subjects with cirrhosis of the liver, the clearances of fluoxetine and its active metabolite, norfluoxetine, were decreased, thus increasing the elimination half-lives of these substances. A lower dose of the fluoxetine-component of SYMBYAX should be used in patients with cirrhosis. Caution is advised when using SYMBYAX in patients with diseases or conditions that could affect its metabolism (see CLINICAL PHARMACOLOGY, Hepatic Impairment and DOSING AND ADMINISTRATION, Special Populations).

Olanzapine: Baseline olanzapine pharmacokinetics do not differ significantly in patients with renal impairment. SYMBYAX dosing adjustment based upon renal impairment is not routinely required (see CLINICAL PHARMACOLOGY, Renal Impairment).

Information for Patients—Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with SYMBYAX and should counsel them in its appropriate use. A patient Medication Guide about "Antidepressant Medicines, Depression and other Serious Mental Illness, and Suicidal Thoughts or Actions" is available for SYMBYAX. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Patients should be advised of the following issues and asked to alert their prescriber if these occur while taking SYMBYAX.

Clinical Worsening and Suicide Risk—Patients, their families, and their caregivers should be encouraged to be alert to the emergence of anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness, impulsivity, akathisia (psychomotor restlessness), hypomania, mania, other unusual changes in behavior, worsening of depression, and suicidal ideation, especially early during antidepressant treatment and when the dose is adjusted up or down. Families and caregivers of patients should be advised to look for the emergence of such symptoms on a day-to-day basis, since changes may be abrupt. Such symptoms should be reported to the patient's prescriber or health professional, especially if they are severe, abrupt in onset, or were not part of the patient's presenting symptoms. Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close monitoring and possibly changes in the medication.

Hyperglycemia—Patients should be advised of the potential risk of hyperglycemia-related adverse events. Patients should be monitored regularly for worsening of glucose control.

Weight Gain—Patients should be counseled that SYMBYAX may cause weight gain. Patients should have their weight monitored regularly.

Serotonin Syndrome—Patients should be cautioned about the risk of serotonin syndrome with the concomitant use of SYMBYAX and triptans, tramadol or other serotonergic agents.

Abnormal Bleeding—Patients should be cautioned about the concomitant use of SYMBYAX and NSAIDs, aspirin, or other drugs that affect coagulation since the combination use of psychotropic drugs that interfere with serotonin reuptake and these agents has been associated with an increased risk of bleeding (see PRECAUTIONS, Abnormal Bleeding).

Alcohol—Patients should be advised to avoid alcohol while taking SYMBYAX.

Cognitive and Motor Impairment—As with any CNS-active drug, SYMBYAX has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that SYMBYAX therapy does not affect them adversely.

Concomitant Medication—Patients should be advised to inform their physician if they are taking Prozac®, Prozac Weekly™, Sarafem®, fluoxetine, Zyprexa®, or Zyprexa Zydis®. Patients should also be advised to inform their physicians if they are taking or plan to take any prescription or over-the-counter drugs, including herbal supplements, since there is a potential for interactions.

Heat Exposure and Dehydration—Patients should be advised regarding appropriate care in avoiding overheating and dehydration.

Nursing—Patients, if taking SYMBYAX, should be advised not to breast-feed.

Orthostatic Hypotension—Patients should be advised of the risk of orthostatic hypotension, especially during the period of initial dose titration and in association with the use of concomitant drugs that may potentiate the orthostatic effect of olanzapine, e.g., diazepam or alcohol (see WARNINGS and Drug Interactions).

Pregnancy—Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during SYMBYAX therapy.

Rash—Patients should be advised to notify their physician if they develop a rash or hives while taking SYMBYAX.

Treatment Adherence—Patients should be advised to take SYMBYAX exactly as prescribed, and to continue taking SYMBYAX as prescribed even after their mood symptoms improve. Patients should be advised that they should not alter their dosing regimen, or stop taking SYMBYAX, without consulting their physician.

Patient information is printed at the end of this insert. Physicians should discuss this information with their patients and instruct them to read the Medication Guide before starting therapy with SYMBYAX and each time their prescription is refilled.

Laboratory Tests—Periodic assessment of transaminases is recommended in patients with significant hepatic disease (see Transaminase Elevations).

Drug Interactions—The ratio of using SYMBYAX in combination with other drugs have not been extensively evaluated in systematic studies. The drug-drug interactions of the individual components are applicable to SYMBYAX. As with all drugs, the potential for interaction by a variety of mechanisms (e.g., pharmacodynamic, pharmacokinetic drug inhibition or enhancement, etc.) is a possibility. Caution is advised if the concomitant administration of SYMBYAX and other CNS-active drugs is required. In evaluating individual cases, consideration should be given to using lower initial doses of the concomitantly administered drugs, using conservative titration schedules, and monitoring of clinical status (see CLINICAL PHARMACOLOGY, Accumulation and slow elimination).

Antihypertensive Agents—Because of the potential for olanzapine to induce hypotension, SYMBYAX may enhance the effects of certain antihypertensive agents (see WARNINGS, Orthostatic Hypotension).

ESS Fluoxetine—The olanzapine component of SYMBYAX may antagonize the effects of levodopa and dopamine agonists.

Benzodiazepines—Multiple doses of olanzapine did not influence the pharmacokinetics of diazepam and its active metabolite N-desmethyldiazepam. However, the coadministration of diazepam with olanzapine potentiated the orthostatic hypotension observed with olanzapine.

When concomitantly administered with fluoxetine, the half-life of diazepam may be prolonged in some patients (see CLINICAL PHARMACOLOGY, Accumulation and slow elimination). Coadministration of alprazolam and fluoxetine has resulted in increased alprazolam plasma concentrations and in further psychomotor performance decrement due to increased alprazolam levels.

Biperiden—Multiple doses of olanzapine did not influence the pharmacokinetics of biperiden.

Carbamazepine—Carbamazepine therapy (200 mg BID) causes an approximate 50% increase in the clearance of olanzapine. This increase is likely due to the fact that carbamazepine is a potent inducer of CYP1A2 activity. Higher daily doses of carbamazepine may cause an even greater increase in olanzapine clearance.

Patients on stable doses of carbamazepine have developed elevated plasma anticonvulsant concentrations and clinical anticonvulsant toxicity following initiation of concomitant fluoxetine treatment.

Clozapine—Elevation of blood levels of clozapine has been observed in patients receiving concomitant fluoxetine.

Electroconvulsive therapy (ECT)—There are no clinical studies establishing the benefit of the combined use of ECT and fluoxetine. There have been rare reports of prolonged seizures in patients on fluoxetine receiving ECT treatment (see Seizures).

Ethanol—Ethanol (45 mg/70 kg single dose) did not have an effect on olanzapine pharmacokinetics. The coadministration of ethanol with SYMBYAX may potentiate sedation and orthostasis.

Fluvoxamine—Fluvoxamine, a CYP1A2 inhibitor, decreases the clearance of olanzapine. This results in a mean increase in olanzapine C_{max} following fluvoxamine administration of 54% in female nonsmokers and 77% in male smokers. The mean increase in olanzapine AUC is 52% and 108%, respectively. Lower doses of the olanzapine component of SYMBYAX should be considered in patients receiving concomitant treatment with fluvoxamine.

Haloperidol—Elevation of blood levels of haloperidol has been observed in patients receiving concomitant fluoxetine.

Lithium—Multiple doses of olanzapine did not influence the pharmacokinetics of lithium.

There have been reports of both increased and decreased lithium levels when lithium was used concomitantly with fluoxetine. Cases of lithium toxicity and increased serotonergic effects have been reported. Lithium levels should be monitored in patients taking SYMBYAX concomitantly with lithium.

Monoamine oxidase inhibitors—See CONTRAINDICATIONS.

Phenytoin—Patients on stable doses of phenytoin have developed elevated plasma levels of phenytoin with clinical phenytoin toxicity following initiation of concomitant fluoxetine.

Pimozide—Clinical studies of pimozide with other antidepressants demonstrate an increase in the risk of QTc prolongation. While a specific study with pimozide and fluoxetine has not been conducted, the potential for drug interactions or QTc prolongation warrants restricting the concurrent use of pimozide and fluoxetine. Concomitant use of fluoxetine and pimozide is contraindicated (see CONTRAINDICATIONS).

Sertraline—See CONTRAINDICATIONS and WARNINGS, Thioridazine.

Thioridazine—(TCAs)—Single doses of olanzapine did not affect the pharmacokinetics of imipramine or its active metabolite desipramine.

In two fluoxetine studies, previously stable plasma levels of imipramine and desipramine have increased >2- to 10-fold when fluoxetine has been administered in combination. This interaction should be expected for three weeks or longer after fluoxetine is discontinued. Thus, the dose of TCA may need to be reduced and plasma TCA concentrations may need to be monitored temporarily when SYMBYAX is coadministered with a TCA. In patients receiving stable doses of nortriptyline, a single dose of olanzapine did not affect the pharmacokinetics of nortriptyline.

Alterid anticoagulant effects, including increased bleeding, have been reported when fluoxetine is coadministered with warfarin (see PRECAUTIONS, Abnormal Bleeding). Patients receiving warfarin therapy should receive careful coagulation monitoring when SYMBYAX is initiated or stopped.

Drugs that interfere with hemostasis (NSAIDs, aspirin, warfarin, etc.)—Serotonin release by platelets plays an important role in hemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding (see PRECAUTIONS, Abnormal Bleeding). Thus, patients should be cautioned about the use of such drugs concurrently with SYMBYAX.

Drugs metabolized by CYP2D6—In vitro studies utilizing human liver microsomes suggest that olanzapine has the potential to inhibit CYP2D6. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by this enzyme.

Fluoxetine inhibits the activity of a putative assay measuring CYP2D6 activity. In normal CYP2D6 metabolic activity volunteers, the dose metabolized. Coadministration of fluoxetine with other drugs that are metabolized by CYP2D6, including certain antidepressants (SSRIs, TCAs), antipsychotics (e.g., phenothiazines and most atypicals), and antiarrhythmics (e.g., propafenone, flecainide, and others) should be approached with caution. Therapy with medications that are predominantly metabolized by the CYP2D6 system and that have a relatively narrow therapeutic index should be initiated at the low end of the dose range if a concomitant fluoxetine regimen is or has been in the previous five weeks. If fluoxetine is added to the treatment regimen of a patient already receiving a drug metabolized by CYP2D6, the need for a decreased dose of the original medication should be considered. Particular caution and careful therapeutic index represent the greatest concern (including but not limited to, flecainide, propafenone, vinblastine, and TCAs). Due to the risk of serious ventricular arrhythmias and sudden death potentially associated with elevated plasma concentrations of certain tricyclic antidepressants, TCAs metabolized by CYP2D6 (e.g., protriptyline, nortriptyline, desipramine) should be avoided with fluoxetine or within a minimum of five weeks after Cordoxe inhibitors (MAOI) and WARNINGS, Thioridazine.

Drugs metabolized by CYP3A—In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP3A. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by this enzyme.

In an in vivo interaction study involving the coadministration of fluoxetine with single doses of terfenadine (a CYP3A substrate), no increase in plasma terfenadine concentrations occurred with concomitant fluoxetine. In addition, in vitro studies have shown ketoconazole, a potent inhibitor of CYP3A activity, to be at least 100 times more potent than fluoxetine or norfluoxetine as an inhibitor of the metabolism of several substrates for this enzyme, including astemizole, cisapride, and midazolam. These data indicate that fluoxetine's extent of inhibition of CYP3A activity is not likely to be of clinical significance.

Effect of olanzapine on drugs metabolized by other CYP enzymes—In vitro studies utilizing human liver microsomes suggest that olanzapine has little potential to inhibit CYP1A2, CYP2C9, and CYP2C19. Thus, olanzapine is unlikely to cause clinically important drug interactions mediated by these enzymes.

The effect of other drugs on olanzapine—Fluoxetine, an inhibitor of CYP2D6, decreases olanzapine clearance a small amount (see CLINICAL PHARMACOLOGY, Pharmacokinetics). Agents that induce CYP1A2 or glucuronyl transferase enzymes, such as omeprazole and rifampin, may cause an increase in olanzapine clearance. Fluvoxamine, an inhibitor of CYP1A2, decreases olanzapine clearance (see Drug Interactions, Fluvoxamine). The effect of other CYP1A2 inhibitors, such as fluvoxamine and some fluoroquinolone antibiotics, on SYMBYAX has not been evaluated. Although olanzapine is metabolized by multiple enzyme systems, induction or inhibition of a single enzyme may appreciably affect olanzapine clearance. Therefore, a dosage increase (for induction) or a dosage decrease (for inhibition) may need to be considered with specific drugs.

Drugs highly bound to plasma proteins—The in vitro binding of SYMBYAX to human plasma proteins is similar to the individual components. The interaction between SYMBYAX and other highly protein-bound drugs has not been fully evaluated. Because fluoxetine is highly bound to plasma protein, the administration of fluoxetine to a patient taking another drug that is highly bound to protein (e.g., Coumadin, digitoxin) may cause a shift in plasma concentrations potentially resulting in an adverse effect. Conversely, adverse effects may result from displacement of protein-bound fluoxetine by other highly bound drugs (see CLINICAL PHARMACOLOGY, Distribution and PRECAUTIONS, Drug Interactions).

Carcinogenesis, Mutagenesis, Impairment of Fertility—

Carcinogenesis—Olanzapine: Oral carcinogenicity studies were conducted in mice and rats. Olanzapine was administered to mice in two 78-week studies at doses of 3, 10, and 30/20 mg/kg/day [equivalent to 0.8 to 5 times the maximum recommended human daily dose (MRHD) on a mg/m² basis]. Female mice received 20 mg/kg/day (equivalent to 0.06 to 2 times the MRHD on a mg/m² basis). Rats were dosed for 2 years at doses of 0.25, 1, 2.5, and 4 mg/kg/day (males) and 0.25, 1, 4, and 6 mg/kg/day (females) [equivalent to 0.1 to 1.5 and 0.1 to 1.5 times the MRHD on a mg/m² basis, respectively]. The incidence of liver hemangiomas and hemangiosarcomas was significantly increased in one mouse study in females dosed at 6 mg/kg/day (2 times the MRHD on a mg/m² basis). These tumors were not increased in another mouse study in females dosed at 10 or 30/20 mg/kg/day (2 to 5 times the MRHD on a mg/m² basis); in this study, there was a high incidence of early mortalities in males of the 30/20 mg/kg/day group. The incidence of mammary gland adenomas and adenocarcinomas was significantly increased in female mice dosed at 22 mg/kg/day and in female rats dosed at 2.4 mg/kg/day (0.5 and 2 times the MRHD on a mg/m² basis, respectively). Antipsychotic drugs have been shown to chronically elevate prolactin levels in rodents. Serum prolactin levels were not measured during the olanzapine carcinogenicity studies. However, measurements of circulating subchronic toxicity studies showed that olanzapine elevated serum prolactin levels up to 4-fold in rats at the same doses used in the carcinogenicity study. Increases in mammary gland neoplasms have been found in rodents after chronic administration of other antipsychotic drugs and is considered to be prolactin-mediated. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is unknown (see PRECAUTIONS, Hyperprolactinemia).

Fluoxetine—The dietary administration of fluoxetine to rats and mice for two years at doses of up to 10 and 12 mg/kg/day, respectively [approximately 1.2 and 0.7 times, respectively, the MRHD on a mg/m² basis], produced no evidence of carcinogenicity.

Mutagenesis—Olanzapine—No evidence of mutagenic potential for olanzapine was found in the Ames reverse mutation test, in vivo micronucleus test in mice, the chromosomal aberration test in Chinese hamster ovary cells, unscheduled DNA synthesis test in rat hepatocytes, or in the chromosomal aberration test in mouse lymphoma cells, or in vivo sister chromatid exchange test in bone marrow of Chinese hamsters.

Fluoxetine—Fluoxetine and norfluoxetine have been shown to have no genotoxic effects based on the following assays: bacterial mutation assay, DNA repair assay in cultured rat hepatocytes, mouse lymphoma assay, and in vivo sister chromatid exchange assay in Chinese hamster bone marrow cells.

Impairment of Fertility—SYMBYAX—Fertility studies were not conducted with SYMBYAX. However, in rodents, there was no toxicology study of more than duration, ovary weight was decreased in females treated with the low-dose [2 and 4 mg/kg/day (1 and 0.5 times the MRHD on a mg/m² basis), respectively] and high-dose [4 and 8 mg/kg/day (1 and 0.5 times the MRHD on a mg/m² basis), respectively] combinations of olanzapine and fluoxetine. Decreased ovary weight, and corpora luteal depletion and uterine atrophy were observed to a greater extent in the females receiving the high-dose combination than in females receiving either olanzapine or fluoxetine alone. In a 3-month repeat-dose dog toxicology study, reduced epididymal sperm and reduced testicular and prostate weights were observed in the high-dose combination of olanzapine and fluoxetine (5 and 5 mg/kg/day (9 and 2 times the MRHD on a mg/m² basis), respectively) and with olanzapine alone (5 mg/kg/day or 9 times the MRHD on a mg/m² basis).

Olanzapine—In a fertility and reproductive performance study in rats, male mating performance, but not fertility, was impaired at a dose of 22.4 mg/kg/day and female fertility was decreased at a dose of 3 mg/kg/day (11 and 1.5 times the MRHD on a mg/m² basis, respectively). Discontinuation of olanzapine treatment reversed the effects on male-mating performance. In female rats, the precoital period was increased and the mating index reduced at 3 mg/kg/day (1.5 times the MRHD on a mg/m² basis). Olanzapine was prolonged and estrous was delayed at 1 mg/kg/day (0.5 times the MRHD on a mg/m² basis); therefore, olanzapine may produce a delay in ovulation.

Fluoxetine—Two fertility studies conducted in adult rats at doses of up to 7.5 and 12.5 mg/kg/day [approximately 0.9 and 1.5 times the MRHD on a mg/m² basis] indicated that fluoxetine had no adverse effects on fertility.

Pregnancy—Pregnancy Category C—*SYMBYAX*—Embryo fetal development studies were conducted in pregnant rabbits with olanzapine and fluoxetine in low-dose and high-dose combinations. In the low-dose combination [low-dose] [1 and 0.5 times the MRHD on a mg/m² basis, respectively], and 4 and 8 mg/kg/day (high-dose) [2 and 1 times the MRHD on a mg/m² basis, respectively]. In rabbits, the doses were 4 and 4 mg/kg/day (low-dose) [4 and 4 times the MRHD on a mg/m² basis, respectively], and 8 and 8 mg/kg/day (high-dose) [2 and 2 times the MRHD on a mg/m² basis, respectively]. In these studies, olanzapine and fluoxetine were also administered alone at the high-doses (4 and 8 mg/kg/day, respectively, in the rat; 8 and 5 mg/kg/day, respectively, in the rabbit). In the rabbit, there was no evidence of teratogenicity; however, the combination produced decreases in fetal weight and retarded skeletal ossification in conjunction with maternal toxicity. Similarly, in the rat there was no evidence of teratogenicity; however, a decrease in fetal weight was observed with the high-dose combination.

In a pre- and postnatal study conducted in rats, olanzapine and fluoxetine were administered during pregnancy and throughout lactation in combination [low-dose: 2 and 4 mg/kg/day (1 and 0.5 times the MRHD on a mg/m² basis), respectively; high-dose: 4 and 8 mg/kg/day (2 and 1 times the MRHD on a mg/m² basis), respectively; and 4 and 8 mg/kg/day (2 and 1 times the MRHD on a mg/m² basis), respectively, and 8 and 5 mg/kg/day (4 and 2 times the MRHD on a mg/m² basis), respectively]. Administration of the high-dose combination resulted in a marked decrease in pup weight gain and survival. These effects were observed with olanzapine alone. The effects were observed with olanzapine alone. These effects were observed with olanzapine alone. These effects were observed with olanzapine alone. These

were a few cases of testicular degeneration and atrophy, depletion of epididymal sperm and infertility in the male progeny. The effects of the high-dose combination on postnatal ensymbix could not be assessed due to high progeny mortality.

There are no adequate and well-controlled studies with SYMBYAX in pregnant women.

SYMBYAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Olanzapine—In reproduction studies in rats at doses up to 18 mg/kg/day and in rabbits at doses up to 30 mg/kg/day (3 and 30 times the MRHD on a mg/m^2 basis, respectively), no evidence of teratogenicity was observed. In a rat teratology study, early resorptions and increased numbers of nonviable fetuses were observed at a dose of 18 mg/kg/day (9 times the MRHD on a mg/m^2 basis). Gestation was prolonged at 10 mg/kg/day (5 times the MRHD on a mg/m^2 basis) in a rabbit teratology study, fetal toxicity (manifested as increased resorptions and decreased fetal weight) occurred at a maternally toxic dose of 30 mg/kg/day (30 times the MRHD on a mg/m^2 basis).

Placental transfer of olanzapine occurs in rat pups.

There are no adequate and well-controlled clinical studies with olanzapine in pregnant women. Seven pregnancies were observed during premarketing clinical studies with olanzapine, including two resulting in normal births, one resulting in neonatal death due to a cardiovascular defect, three therapeutic abortions, and one spontaneous abortion.

Fluoxetine—In embryo fetal development studies in rats and rabbits, there was no evidence of teratogenicity following administration of up to 12.5 and 15 mg/kg/day, respectively (1.5 and 3.6 times the MRHD on a mg/m^2 basis, respectively) throughout organogenesis. However, in rat reproduction studies, an increase in stillborn pups, a decrease in pup weight, and an increase in pup deaths during the first 7 days postpartum occurred following maternal exposure to 12 mg/kg/day (1.5 times the MRHD on a mg/m^2 basis) during gestation or 7.5 mg/kg/day (0.9 times the MRHD on a mg/m^2 basis) during gestation and lactation. There was no evidence of developmental neurotoxicity in the surviving offspring of rats treated with 12 mg/kg/day during gestation. The no-effect dose for rat pup mortality was 5 mg/kg/day (0.6 times the MRHD on a mg/m^2 basis).

Benzodiazepines: Effects—Neonates exposed to fluoxetine and other SSRIs or serotonin and norepinephrine reuptake inhibitors (SNRIs), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see CONTRAINDICATIONS, Monoamine Oxidase Inhibitors).

Infants exposed to SSRIs in late pregnancy may have an increased risk for persistent pulmonary hypertension of the newborn (PPHN). PPHN occurs in 1-2 per 1000 live births in the general population and is associated with substantial neonatal morbidity and mortality. In a retrospective case-control study of 377 women whose infants were born with PPHN and 836 women whose infants were born healthy, the risk for developing PPHN was approximately six-fold higher for infants exposed to SSRIs after the 20th week of gestation compared to infants who had not been exposed to antidepressants during pregnancy. There is currently no corroborative evidence regarding the risk for PPHN following exposure to SSRIs in pregnancy; this is the first study that has investigated the potential risk. The study did not include enough cases with exposure to individual SSRIs to determine if all SSRIs posed similar levels of PPHN risk.

When treating a pregnant woman with fluoxetine during the third trimester, the physician should carefully consider both the potential risks and benefits of treatment (see DOSAGE AND ADMINISTRATION). Physicians should note that in a prospectively longitudinal study of 201 women with a history of major depression who were euthymic at the beginning of pregnancy, women who discontinued antidepressant medication during pregnancy were more likely to experience a relapse of major depression than women who continued antidepressant medication.

Labor and Delivery—*SYMBYAX*—The effect of SYMBYAX on labor and delivery in humans is unknown. Parturition in rats was not affected by SYMBYAX. SYMBYAX should be used during labor and delivery only if the potential benefit justifies the potential risk.

Olanzapine—Parturition in rats was not affected by olanzapine. The effect of olanzapine on labor and delivery in humans is unknown.

Fluoxetine—The effect of fluoxetine on labor and delivery in humans is unknown. Fluoxetine crosses the placenta; therefore, there is a possibility that fluoxetine may have adverse effects on the newborn.

Nursing Mothers—*SYMBYAX*—There are no adequate and well-controlled studies with SYMBYAX in nursing mothers or infants. No studies have been conducted to examine the excretion of olanzapine or fluoxetine in breast milk following SYMBYAX treatment. It is recommended that women not breast-feed when receiving SYMBYAX.

Olanzapine—In a study in lactating, healthy women, olanzapine was excreted in breast milk. Mean infant dose at steady state was estimated to be 1.8% of the maternal olanzapine dose.

Fluoxetine—Fluoxetine is excreted in human breast milk. In one breast milk sample, the concentration of fluoxetine plus norfluoxetine was 70.4 ng/mL. The concentration in the mother's plasma was 295.0 ng/mL. No adverse effects on the infant were noted. In another case, an infant nursed by a mother on fluoxetine developed crying, sleep disturbance, and vomiting. Plasma levels in the infant's plasma drug levels were 340 ng/mL of fluoxetine and 208 ng/mL of norfluoxetine on the 2nd day of feeding.

Pediatric Use—Safety and effectiveness in the pediatric population have not been established (see BOX WARNING and WARNINGS, Clinical Worsening and Suicide Risk). Anyone considering the use of SYMBYAX in a child or adolescent must balance the potential risks with the clinical need.

Fluoxetine—Significant toxicity, manifested by hyperactivity, lung, liver, neurobehavioral and reproductive toxicity, and impaired brain development, has been observed following exposure of juvenile animals to fluoxetine. Some of these effects occurred at clinically relevant exposures.

In a study in which fluoxetine (3, 10, or 30 mg/kg) was orally administered to young rats from weaning (Postnatal Day 21) through adulthood (Day 90), male and female sexual development was delayed at all doses, and growth (body weight gain, femur length) was decreased during the dosing period in animals receiving the highest dose. At the end of the treatment period, serum levels of creatine kinase (marker of muscle damage) were increased at the intermediate and high doses, and abnormal muscle and reproductive organ histopathology (skeletal muscle degeneration and necrosis, testicular degeneration and necrosis, epididymal vacuolation and hypospermia) was observed at the high dose. When animals were evaluated after a recovery period (up to 11 weeks after cessation of dosing), neurobehavioral abnormalities (decreased reactivity at all doses and learning deficit at the high dose) and reproductive functional impairment (decreased mating at all doses and impaired fertility at the high dose) were seen. In addition, testicular and epididymal microscopic lesions and decreased sperm concentrations were found in the high dose group, indicating that the reproductive organ effects seen at the end of treatment were irreversible. The reversibility of fluoxetine-induced muscle damage was not assessed. Adverse effects similar to those observed in rats treated with fluoxetine during the juvenile period have not

been reported after administration of fluoxetine to adult animals. Plasma exposures (AUC) in fluoxetine in juvenile rats receiving the low, intermediate, and high dose in this study were approximately 0.1-0.2, 1-2, and 5-10 times, respectively, the average exposure in pediatric patients receiving the maximum recommended dose (MRD) of 20 mg/day. Rat exposures to the major metabolite, norfluoxetine, were approximately 0.3-0.8, 1-8, and 3-20 times, respectively, pediatric exposure at the MRD.

A specific effect of fluoxetine on bone development has been reported in mice treated with fluoxetine during the juvenile period. When mice were treated with fluoxetine (5 or 70 mg/kg, intraperitoneal) for 4 weeks starting at 4 weeks of age, bone formation was reduced resulting in decreased bone mineral content and density. These doses did not affect overall growth (body weight gain or femoral length). The doses administered to juvenile mice in this study are approximately 0.3 and 2 times the MRD for pediatric patients on a body surface area (mg/m^2) basis.

In another mouse study, administration of fluoxetine (10 mg/kg intraperitoneally) during early postnatal development (Postnatal Days 4 to 21) produced abnormal behavioral deficiencies (decreased exploratory behavior in elevated plus-maze, increased shock avoidance latency) in adulthood (12 weeks of age). The dose used in this study is approximately equal to the pediatric MRD on a mg/m^2 basis. Because of the early dosing period in this study, the significance of these findings to the approved pediatric use in humans is uncertain.

Geriatric Use—*SYMBYAX*—Clinical studies of SYMBYAX did not include sufficient numbers of patients ≥65 years of age to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see DOSAGE AND ADMINISTRATION).

Olanzapine—Of the 2500 patients in premarketing clinical studies with olanzapine, 11% (263 patients) were ≥65 years of age. In patients with schizophrenia, there was no indication of any different tolerability of olanzapine in the elderly compared with younger patients. Studies in patients with dementia-related psychosis have suggested that there may be a different tolerability profile in this population compared with younger patients with schizophrenia. In placebo-controlled studies of olanzapine in elderly patients with dementia-related psychosis, there was a significantly higher incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack) in patients treated with olanzapine compared to patients treated with placebo. Olanzapine is not approved for the treatment of patients with dementia-related psychosis. If the prescriber elects to treat elderly patients with dementia-related psychosis, vigilance should be exercised (see BOX WARNING, WARNINGS, PRECAUTIONS, Potential for Cognitive and Motor Impairment, Seizures, and DOSAGE AND ADMINISTRATION, Special Populations).

As with other CNS-active drugs, olanzapine should be used with caution in elderly patients with dementia. Also, the presence of factors that might decrease pharmacokinetic clearance or increase the pharmacodynamic response to olanzapine should lead to consideration of a lower starting dose for any geriatric patient.

Fluoxetine—In fluoxetine clinical studies (10,782 patients) included 687 patients ≥65 years of age and 93 patients ≥75 years of age. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. As with other SSRIs, fluoxetine has been associated with cases of clinically significant hyponatremia in elderly patients.

ADVERSE REACTIONS: The information below is derived from a premarketing clinical study database for SYMBYAX consisting of 2666 patients with various diagnoses with approximately 1081 patient-years of exposure. The conditions and duration of treatment with SYMBYAX varied greatly and included (in overlapping categories) open-label and double-blind phases of studies, inpatients and outpatients, fixed-dose and dose-titration studies, and short- and long-term exposure.

Adverse events were recorded by clinical investigators using descriptive terminology of their own choosing. Consequently, it is not possible to provide a meaningful estimate of the proportion of individuals experiencing adverse events without first grouping similar types of events into a limited (i.e., reduced) number of standardized event categories.

In the tables and tabulations that follow, COSTART Dictionary terminology has been used to classify reported adverse events. The data in the tables represent the proportion of individuals who experienced, at least once, a treatment-emergent adverse event of the type listed. An event was considered treatment-emergent if it occurred for the first time or worsened while receiving therapy following baseline evaluation. It is possible that events reported during therapy were not necessarily related to drug exposure.

The prescriber should be aware that the figures in the tables and tabulations cannot be used to predict the incidence of side effects in the course of usual medical practice where patient characteristics and other factors differ from those that prevailed in the clinical studies. Similarly, the cited frequencies cannot be compared with figures obtained from other clinical investigations involving different treatments, uses, and investigators. The cited figures, however, do provide the prescribing clinician with some basis for estimating the relative contribution of drug and non-drug factors to the side effect incidence rate in the population studied.

Incidence in Controlled Clinical Studies—The following findings are based on the short-term, controlled premarketing studies in various diagnoses including bipolar depression.

Adverse events associated with discontinuation of treatment—Overall, 10% of the patients in the SYMBYAX group discontinued due to adverse events compared with 4.6% for placebo. Table 7 enumerates the adverse events leading to discontinuation in the SYMBYAX group for the use of SYMBYAX (incidence of at least 1% for SYMBYAX and greater than that for placebo). The bipolar depression column shows the incidence of adverse events with SYMBYAX in the bipolar depression studies and the "SYMBYAX-Controlled" column shows the incidence in the controlled SYMBYAX studies; the placebo column shows the incidence in the pooled controlled studies that included a placebo arm.

Table 7: Adverse Events Associated with Discontinuation*

Adverse Event	Percentage of Patients Reporting Event		
	SYMBYAX		Placebo
	Bipolar Depression (N=56)	SYMBYAX-Controlled (N=571)	(N=477)
Asthenia	0	2	0
Somnolence	0	2	0
Weight gain	0	2	0
Chest Pain	0	1	0

* Table includes events associated with discontinuation of at least 1% and greater than placebo

Commonly observed adverse events in controlled clinical studies—The most commonly observed adverse events associated with the use of SYMBYAX (incidence of ≥5% and at least twice that for placebo in the SYMBYAX-controlled database) were: asthenia, edema, increased appetite, peripheral edema, pharyngitis, somnolence, blinking abnormal, tremor, and weight gain.

Adverse events occurring at an incidence of 2% or more in controlled clinical studies—Table 8 enumerates the treatment-emergent adverse events associated with the use of SYMBYAX (incidence of at least 2% for SYMBYAX and twice or more that for placebo).

Table 8: Treatment-Emergent Adverse Events: Incidence in Controlled Clinical Studies

Body System/ Adverse Event[1]	Percentage of Patients Reporting Event		
	SYMBYAX		Placebo
	Bipolar Depression (N=56)	SYMBYAX-Controlled (N=571)	(N=477)
Body as a Whole			
Asthenia	13	15	3
Accidental Injury	5	3	2
Fever	4	3	1
Cardiovascular System			
Hypertension	2	2	1
Tachycardia	2	2	0
Digestive System			
Diarrhea	19	8	7
Dry mouth	16	11	6
Increased appetite	13	16	4
Tooth disorder	1	2	1
Metabolic and Nutritional Disorders			
Weight gain	17	21	3
Peripheral edema	4	8	1
Edema	0	5	0
Musculoskeletal System			
Joint disorder	1	2	1
Twitching	6	2	1
Arthralgia	5	3	1
Nervous System			
Somnolence	21	22	11
Tremor	9	6	3
Thinking abnormal	5	6	3
Libido decreased	4	2	1
Hypertonesia	2	1	1
Personality disorder	2	1	1
Sleep disorder	1	2	1
Amnesia	1	3	0
Respiratory System			
Pharyngitis	4	6	3
Dyspnea	1	2	1
Special Senses			
Amblyopia	5	4	2
Ear pain	2	1	1
Otitis media	2	0	0
Speech disorder	0	2	0
Urogenital System			
Abnormal ejaculation[2]	7	2	1
Impotence[2]	4	2	1
Anorgasmia	3	0	0

[1] Included are events reported by at least 2% of patients taking SYMBYAX except the following events, which had an incidence on placebo aSYMBYAX: abdominal pain, abnormal dreams, agitation, anaphylaxis, anorexia, anxiety, apathy, back pain, chest pain, constipation, cough increased, depression, dizziness, dysmenorrhea (adjusted for gender), dyspepsia, flatulence, flu syndrome, headache, hypertonia, insomnia, manic reaction, myalgia, nausea, nervousness, pain, palpitation, paresthesia, rash, rhinitis, sinusitis, sweating, vomiting.

[2] Adjusted for gender.

Additional Findings Observed in Clinical Studies—The following findings are based on clinical studies.

Effect on cardiac repolarization—The mean increase in QT_c interval for SYMBYAX-treated patients (4.9 msec) in clinical studies was significantly greater than that for placebo-treated (-0.9 msec) and olanzapine-treated (0.6 msec) patients, but was not significantly different from fluoxetine-treated (3.7 msec) patients. There were no differences between patients treated with SYMBYAX, placebo, olanzapine, or fluoxetine in the incidence of QT_c outliers (≥500 msec).

Laboratory changes—In SYMBYAX clinical studies, SYMBYAX was associated with asymptomatic mean increases in alkaline phosphatase, cholesterol, GGT, and uric acid compared with placebo (see PRECAUTIONS, Transaminase Elevations).

SYMBYAX was associated with a slight decrease in hemoglobin that was statistically significantly greater than that seen with placebo, olanzapine, and fluoxetine.

An elevation in serum prolactin was observed with SYMBYAX. This elevation was not statistically different than that seen with olanzapine (see PRECAUTIONS, Hyperprolactinemia).

Sexual dysfunction—In the pool of controlled SYMBYAX studies, there were higher rates of treatment-emergent adverse events, decreased libido, anorgasmia, impotence and abnormal ejaculation in the SYMBYAX group than in the placebo group. One case of decreased libido led to discontinuation in the SYMBYAX group. In the controlled studies that contained a fluoxetine arm, the rates of decreased libido and abnormal ejaculation in the SYMBYAX group were less than the rates in the fluoxetine group. None of the differences were statistically significant.

Sexual dysfunction, including priapism, has been reported with all SSRIs. While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects.

Vital signs—Tachycardia, bradycardia, and orthostatic hypotension have occurred in SYMBYAX-treated patients (see WARNINGS, Orthostatic Hypotension). The mean pulse in SYMBYAX-treated patients was reduced by 1.6 beats/min.

Additional findings—In a single 8-week randomized, double-blind, fixed-dose, study comparing 10 (N=199), 20 (N=200) and 40 (N=200) mg/day of olanzapine in patients with schizophrenia or schizoaffective disorder, statistically significant differences among 3 dose groups were observed in the following safety outcomes: weight gain, prolactin elevation, and QTc prolongation. Mean baseline to endpoint increases in weight were 0.3 kg, 1.5 kg, and 2.6 kg for olanzapine 5 mg, 10 mg, and 20 mg/day, respectively. Mean increases in prolactin were 1.6 ng/mL, 4.5 ng/mL, and 6.4 ng/mL (female) or 0.2 ng/mL, 0.4 ng/mL, and 1.0 ng/mL (male) for olanzapine 5 mg, 10 mg, and 20 mg/day, respectively. Mean increases in QTc were 1.2 msec, 3.0 msec, and 5.4 msec for olanzapine 5 mg, 10 mg, and 20 mg/day, respectively. The incidence of treatment-emergent prolactin elevations (≥24.2 ng/mL (female) or ≥20.0 ng/mL (male)) was 0.6%, 2.1%, and 3.6% for olanzapine 5 mg, 10 mg, and 20 mg/day, respectively.

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≥18.77 mg/kg, (male) at any time during the trial (10 mg/day: 31.2%; 20 mg/day: 42.7%; 40 mg/day: 61.1%) with significant differences between 10 vs 40 mg/day and 20 vs 40 mg/day; talipot (10 mg/day: 1.5%; 20 mg/day: 2.1%; 40 mg/day: 6.6%) (10 mg/day: 2.6%; 20 mg/day: 1.5%; 40 mg/day: 6.6%) with significant differences between 20 vs 40 mg, was observed.

Other Events Observed in Clinical Studies—Following is a list of all treatment-emergent adverse events reported at anytime by individuals taking SYMBYAX in clinical studies except (1) those listed in the body or footnotes of Tables 7 and 8 above or elsewhere in labeling, (2) those for which the COSTART terms were uninformative or misleading, (3) those events for which a causal relationship to SYMBYAX use was considered remote, and (4) events occurring in only 1 patient treated with SYMBYAX and which did not have a substantial probability of being acutely life-threatening.

Events are classified within body system categories using the following definitions: frequent adverse events are defined as those occurring on 1 or more occasions in at least 1/100 patients, infrequent adverse events are those occurring in 1/100 to 1/1000 patients, and rare events are those occurring in <1/1000 patients.

Body as a Whole—Frequent: asthenia, chills, infection, neck pain, neck rigidity, photosensitivity reaction; *Infrequent:* cellulitis, cyst, hernia, intentional injury, intentional overdose, malaise, moniliasis, overdose, pelvic pain, suicide attempt; *Rare:* death, tolerance decreased.

Cardiovascular System—Frequent: migraine, vasodilatation; *Infrequent:* arrhythmia, bradycardia, cerebral ischemia, electrocardiogram abnormal, hypertension, P-R interval prolonged; *Rare:* angina pectoris, atrial arrhythmia, atrial fibrillation, bundle branch block, congestive heart failure, myocardial infarct, peripheral vascular disorder, T-wave inverted.

Digestive System—Frequent: increased salivation, thirst; *Infrequent:* cholelithiasis, colitis, constipation, esophagitis, gastritis, gastroenteritis, gingivitis, hepatomegaly, nausea and vomiting, peptic ulcer, periodontal abscess, stomatitis, tooth caries; *Rare:* amebiasis, diverticulitis, fecal incontinence, gastrointestinal hemorrhage, gum hemorrhage, intestinal obstruction, liver fatty deposit, pancreatitis.

Endocrine System—Infrequent: hypothyroidism.

Hemic and Lymphatic System—Frequent: ecchymosis; *Infrequent:* anemia, leukocytosis, lymphadenopathy; *Rare:* coagulation disorder, leukopenia, purpura, thrombocythemia.

Metabolic and Nutritional—Frequent: decreased edema, weight loss; *Infrequent:* alcohol intolerance, dehydration, glycosuria, hyperlipemia, hypoglycemia, hypokalemia, obesity; *Rare:* acidosis, bilirubinemia, creatinine increased, gout, hypocalcemia, hypoglycemic reaction.

Musculoskeletal System—Infrequent: arthritis, bone disorder, generalized spasm, leg cramps, tendinous contracture, tenosynovitis; *Rare:* arthrosis, bursitis, myasthenia, myositis, osteoporosis, rheumatoid arthritis.

Nervous System—Infrequent: abnormal gait, ataxia, buccoglossal syndrome, cognitive rigidity, coma, confusion, depersonalization, dysarthria, emotional lability, euphoria, extrapyramidal syndrome, hostility, hyperkinesia, hypokinesia, incoordination, movement disorder, myoclonus, neuralgia, neurosis, vertigo; *Rare:* acute brain syndrome, aphasia, dysmenia, libido increased, subarachnoid hemorrhage, withdrawal syndrome.

Respiratory System—Frequent: bronchitis, lung disorder; *Infrequent:* apnea, asthma, epistaxis, hiccup, hyperventilation, laryngitis, pneumonia, voice alteration, yawn; *Rare:* emphysema, hemoptysis, laryngismus.

Skin and Appendages—Infrequent: acne, alopecia, contact dermatitis, dry skin, eczema, pruritis, psoriasis, skin discoloration, vesiculobullous rash; *Rare:* exfoliative dermatitis, maculopapular rash, seborrhea, skin ulcer.

Special Senses—Frequent: abnormal vision, taste perversion, tinnitus; *Infrequent:* abnormality of accommodation, conjunctivitis, deafness, diplopia, dry eyes, eye pain, mydriasis; *Rare:* eye hemorrhage.

Urogenital System—Frequent: breast pain, menorrhagia[1], urinary frequency, urinary incontinence, urinary tract infection; *Infrequent:* amenorrhea[1], breast enlargement, breast neoplasm, cystitis, dysuria, female lactation[1], fibrocystic breast[1], hematuria, hypomenorrhea[1], leukorrhea[1], menopause[1], metrorrhagia[1], oliguria, ovarian disorder[1], polyuria, urinary retention, urinary urgency, urination impaired, vaginal hemorrhage[1], vaginal moniliasis[1], vaginitis[1]; *Rare:* breast carcinoma, breast engorgement, endometrial disorder[1], gynecomastia[1], kidney calculus, uterine fibroids enlarged[1].

[1] Adjusted for gender.

Other Events Observed with Olanzapine or Fluoxetine Monotherapy—The following adverse events were not observed in SYMBYAX-treated patients during premarketing clinical studies but have been reported with olanzapine or fluoxetine monotherapy: splenic anemia, cholestatic jaundice, diabetic coma, dyskinesia, eosinophilic pneumonia, erythema multiforme, hepatitis, idiosyncratic hepatitis, jaundice, neutropenia, priapism, pulmonary embolism, rhabdomyolysis, serotonin syndrome, serum sickness-like reaction, sudden unexpected death, suicidal ideation, vasculitis, venous thromboembolic events (including pulmonary embolism and deep venous thrombosis), violent behaviors. Random cholesterol levels of ≥240 mg/dL and random triglycerides levels of ≥1000 mg/dL have been reported.

DRUG ABUSE AND DEPENDENCE: *Controlled Substance Class*—SYMBYAX is not a controlled substance.

Physical and Psychological Dependence—SYMBYAX, as with fluoxetine and olanzapine, has not been systematically studied in humans for its potential for tolerance, withdrawal, or physical dependence. While the clinical studies did not reveal any tendency for any drug-seeking behavior, these observations were not systematic and it is not possible to predict on the basis of this limited experience the extent to which a CNS-active drug will be misused, diverted, and/or abused once marketed. Consequently, physicians should carefully evaluate patients for history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of SYMBYAX (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

In studies in rats and rhesus monkeys designed to assess abuse and dependence potential, olanzapine alone was shown to have acute depressive CNS effects but little or no potential of abuse or physical dependence at oral doses up to 15 (rat) and 8 (monkey) times the MRHD (20 mg) on a mg/m² basis.

OVERDOSAGE: SYMBYAX—During premarketing clinical studies of the olanzapine/fluoxetine combination, overdose of both fluoxetine and olanzapine were reported in five study subjects. Four of the five subjects experienced loss of consciousness (3) or coma (1). No fatalities occurred.

Since the market introduction of olanzapine in October 1996, adverse event cases involving combination use of fluoxetine and olanzapine have been reported to Eli Lilly and Company. An overdose of combination therapy is defined as confirmed or suspected ingestion of a dose of olanzapine 20 mg or greater in combination with a dose of fluoxetine 80 mg or greater. As of 1 February 2002, 12 cases of combination therapy overdose were reported, most of which involved additional substances. Adverse events associated with these reports included somnolence; impaired consciousness (coma, lethargy); impaired neurologic function (ataxia, confusion, convulsions, dysarthria); arrhythmias; and fatality. Fatalities have been confounded by exposure to additional substances including alcohol, thioridazine, meperidine, and propoxyphene.

Olanzapine—In postmarketing reports of overdose with olanzapine alone, symptoms have been reported in the majority of cases. In symptomatic patients, symptoms with ≥10% incidence included agitation/aggressiveness, dysarthria, tachycardia, various extrapyramidal symptoms, and reduced level of consciousness ranging from sedation to coma. Among less commonly reported symptoms were the following potentially medically serious events: aspiration, cardiopulmonary arrest, cardiac arrhythmias (such as supraventricular tachycardia as well as a patient that experienced sinus pause with spontaneous resumption of normal rhythm), delirium, possible neuroleptic malignant syndrome, respiratory depression/arrest, convulsion, hypertension, and hypothermia. Eli Lilly and Company has received reports of fatality in association with overdose of olanzapine alone. In 1 case of death, the amount of acutely ingested olanzapine was reported to be possibly as low as 450 mg; however, in another case, a patient was reported to survive an acute olanzapine ingestion of 1500 mg.

Fluoxetine—Worldwide exposure to fluoxetine is estimated to be over 38 million patients (circa 1999). Of the 1578 cases of overdose involving fluoxetine, 378 million patients (circa 1999). Of the 1578 cases of overdose involving fluoxetine, 378 million patients (circa 1999), reported from this population, there were 195 deaths.

Among 633 adult patients who overdosed on fluoxetine alone, 34 resulted in a fatal outcome, 378 completely recovered, and 19 patients experienced sequelae after overdose, including abnormal accommodation, abnormal gait, confusion, unresponsiveness, nervousness, pulmonary dysfunction, vertigo, tremor, elevated blood pressure, impotence, movement disorder, and hypomania. The remaining 202 patients had an unknown outcome. The most common signs and symptoms associated with non-fatal overdose were seizures, somnolence, nausea, tachycardia, and vomiting. The largest known ingestion of fluoxetine in adult patients was 2 grams in a patient who took fluoxetine alone and who subsequently recovered. However, in an adult patient who took fluoxetine alone, an ingestion as low as 520 mg has been associated with lethal outcome, but causality has not been established.

Among pediatric patients (ages 3 months to 17 years), there were 156 cases of overdose involving fluoxetine alone or in combination with other drugs. Six patients died, 127 patients completely recovered, 1 patient experienced renal failure, and 22 patients had an unknown outcome. One of the 6 fatalities was a 9-year-old boy who had a history of OCD, Tourette's Syndrome with tics, attention deficit disorder, and fetal alcohol syndrome. He had been receiving 100 mg of fluoxetine daily for 8 months when he ingested approximately 1 gram of fluoxetine.

Mixed-drug ingestion or other methods of suicide complicated all 6 overdoses in children that resulted in fatalities. The largest ingestion in pediatric patients was 2 grams, which was non-lethal.

Other important adverse events reported with fluoxetine overdose (single or multiple drugs) included coma, delirium, ECG abnormalities (such as QT-interval prolongation and ventricular tachycardia, including torsades de pointes type arrhythmias), hypotension, mania, neuroleptic malignant syndrome-like events, pyrexia, stupor, and syncope.

Management of Overdose—In managing overdose, the possibility of multiple drug involvement should be considered. In case of acute overdose, establish and maintain an airway and ensure adequate ventilation, which may include intubation. Induction of emesis is not recommended as the possibility of subsequent seizures, or dystonic reactions of the head and neck following overdose may create a risk for aspiration. Gastric lavage (after intubation, if patient is unconscious) and administration of activated charcoal together with a laxative should be considered. Cardiovascular monitoring should commence immediately and should include continuous electrocardiographic monitoring to detect possible arrhythmias.

A specific precaution involves patients who are taking or have recently taken SYMBYAX and may have ingested excessive quantities of a TCA (tricyclic antidepressant). In such cases, accentuation of the parent TCA and/or an active metabolite may increase the possibility of serious sequelae and extend the time needed for close medical observation.

Due to the large volume of distribution of olanzapine and fluoxetine, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be beneficial. No specific antidote for either fluoxetine or olanzapine overdose is known. Hypotension and circulatory collapse should be treated with appropriate measures such as intravenous fluids and/or sympathomimetic agents. Do not use epinephrine, dopamine, or other sympathomimetics with β-agonist activity, since beta stimulation may worsen hypotension in the setting of olanzapine-induced alpha blockade.

The physician should consider contacting a poison control center for additional information on the treatment of any overdose. Telephone numbers for certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*.

DOSAGE AND ADMINISTRATION: SYMBYAX should be administered once daily in the evening, generally beginning with the 6 mg/25 mg capsule. While food has no appreciable effect on the absorption of olanzapine and fluoxetine given individually, the effect of food on the absorption of SYMBYAX has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with SYMBYAX in a dose range of olanzapine 6 to 12 mg and fluoxetine 25 to 50 mg (see CLINICAL STUDIES). The safety of doses above 18 mg/75 mg has not been evaluated in clinical studies.

Special Populations—The starting dose of SYMBYAX 3 mg/25 mg - 6 mg/25 mg should be used for patients with a predisposition to hypotensive reactions, patients with hepatic impairment, or patients who are receiving a combination of factors that may slow the metabolism of SYMBYAX (female gender, geriatric age, nonsmoking status) or those patients who may be pharmacodynamically sensitive to olanzapine. When indicated, dose escalation should be performed with caution in these patients. SYMBYAX has not been systematically studied in patients over 65 years of age or in patients <18 years of age (see WARNINGS, Orthostatic Hypotension, PRECAUTIONS, Pediatric Use, and Geriatric Use, and CLINICAL PHARMACOLOGY, Pharmacokinetics).

Treatment of Pregnant Women During the Third Trimester—Neonates exposed to fluoxetine, olanzapine, SYMBYAX, and other SSRIs or SNRIs, late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding (see PRECAUTIONS). When treating pregnant women with fluoxetine during the third trimester, the physician should carefully consider the potential risks and benefits of treatment. The physician may consider tapering fluoxetine in the third trimester.

Discontinuation of Treatment with SYMBYAX—Symptoms associated with discontinuation of fluoxetine, a component of SYMBYAX, and other SSRIs and SNRIs, have been reported (see PRECAUTIONS). Patients should be monitored for these symptoms when discontinuing treatment. A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate. Plasma fluoxetine and norfluoxetine concentration decrease gradually at the conclusion of therapy which may minimize the risk of discontinuation symptoms with this drug.

HOW SUPPLIED: SYMBYAX capsules are supplied in 3/25-, 6/25-, 6/50-, 12/25-, and 12/50-mg (mg equivalent olanzapine/mg equivalent fluoxetine*) strengths.

SYMBYAX	CAPSULE STRENGTH				
	3 mg/ 25 mg	6 mg/ 25 mg	6 mg/ 50 mg	12 mg/ 25 mg	12 mg/ 50 mg
Color	Peach & Light Yellow	Mustard Yellow & Light Yellow	Mustard Yellow & Light Yellow	Red & Light Yellow	Red & Light Yellow
Capsule No. Identification	PU3239 Lilly 3239 3/25	PU3241 Lilly 3241 6/25	PU3243 Lilly 3243 6/50	PU3232 Lilly 3232 12/25	PU3234 Lilly 3234 12/50
NDC Codes					
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Bottles 1000	0002 3239 04	0002 3241 04	0002 3243 04	0002 3232 04	0002 3234 04
Blisters (CP100	0002 3239 33	0002 3241 33	0002 3243 33	0002 3232 33	0002 3234 33

*Fluoxetine base equivalent

IDENTI-DOSE®, Unit Dose Medication, Lilly.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled Room Temperature].

Keep tightly closed and protect from moisture.

Literature revised October 1, 2007

PV 5418 AMP — PRINTED IN USA

Lilly — Eli Lilly and Company, Indianapolis, IN 46285 — www.SYMBYAX.com

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Medication Guide

Antidepressant Medicines, Depression and other Serious Mental Illnesses, and Suicidal Thoughts or Actions

Read the Medication Guide that comes with your or your family member's antidepressant medicine. This Medication Guide is only about the risk of suicidal thoughts and actions with antidepressant medicines. Talk to your, or your family member's, healthcare provider about:

- all risks and benefits of treatment with antidepressant medicines
- all treatment choices for depression or other serious mental illness

What is the most important information I should know about antidepressant medicines, depression and other serious mental illnesses, and suicidal thoughts or actions?

1. **Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.**
2. **Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a particularly high risk of having suicidal thoughts or actions. These include people who have (or have a family history of) bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions.**
3. **How can I watch for and try to prevent suicidal thoughts and actions in myself or a family member?**
   - Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed.
   - Call the healthcare provider right away to report new or sudden changes in mood, behaviors, thoughts, or feelings.
   - Keep all follow-up visits with the healthcare provider as scheduled. Call the healthcare provider between visits as needed, especially if you have concerns about symptoms.

Call a healthcare provider right away if you or your family member has any of the following symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling very agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

What else do I need to know about antidepressant medicines?

- Never stop an antidepressant medicine without first talking to a healthcare provider. Stopping an antidepressant medicine suddenly can cause other symptoms.
- **Antidepressants are medicines used to treat depression and other illnesses. It is important to discuss all the risks of treating depression and also the risks of not treating it. Patients and their families or other caregivers should discuss all treatment choices with the healthcare provider, not just the use of antidepressants.**
- Antidepressant medicines have other side effects. Talk to the healthcare provider about the side effects of the medicine prescribed for you or your family member.
- Antidepressant medicines can interact with other medicines. Know all of the medicines that you or your family member takes. Keep a list of all medicines to show the healthcare provider. Do not start new medicines without first checking with your healthcare provider.
- **Not all antidepressant medicines prescribed for children are FDA approved for use in children. Talk to your child's healthcare provider for more information.**

This Medication Guide has been approved by the U.S. Food and Drug Administration for all antidepressant medicines.

PV 5083 AMP

SYMBYAX® (olanzapine and fluoxetine HCl capsules) — PV 5418 AMP

Motion for Summary Judgment
Patient Information Exhibit No. 3
Case No. 3:06-cv-00524-JAN-POR
Date Entered: _____
By: _____
Deputy Clerk

008243

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NEW YORK

IN RE ZYPREXA PRODUCTS LIABILITY LITIGATION	)	MDL DOCKET No. 1596
THIS DOCUMENT RELATES TO:	)	
ALL ACTIONS	)	

EXPERT WITNESS REPORT AND DECLARATION
OF WILLIAM WIRSHING, M.D.

I. QUALIFICATIONS

A. Education

I graduated in 1978 from the College of Engineering at the University of California at Berkeley with highest honors (cumulative G.P.A. 3.93) and a Bachelors of Science degree in Electrical Engineering and Computer Science (minor in bioelectronic systems) (See CV attached hereto as Exhibit A.) During my tenure there, I was elected to membership in the Phi Beta Kappa and Tau Beta Pi honor societies. The former is traditionally reserved only for those pursuing a "liberal" educational experience (e.g., College of Letters and Science) and the latter is the equivalent entity for students in the science-intensive curriculum of the College of Engineering. Although I then began medical school at UCLA almost immediately, my education was interrupted when my youngest brother developed and then succumbed to brain cancer during my first and second years. During several protracted, though arranged, absences from school in southern California, I assisted my mother in caring for my brother and worked as an

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engineer in Mountain View (i.e., "Silicon Valley") California through the beginning of my third year at UCLA. Following John's death in the beginning of my third year, I stopped work and returned to Southern California and my schooling full time.

I completed my undergraduate medical schooling ("on time", despite my lengthy absences from campus) with a 3.97 GPA and was given the Sandoz award for "Excellence in the Behavioral Sciences" at graduation in 1982. In addition, I was elected to the Alpha Omega Alpha Medical Honor Society at the end of my third year. I remained at UCLA for both my rotating internship during which I focused on internal medicine, neurology, and pediatrics and for my three-year residency training in psychiatry. My final year of residency training I was the Chief Resident in Geropsychiatry at the West Los Angeles Veterans Affairs Medical Center. Over the next two years, I was a Post Doctoral Research Scholar at UCLA, a fellowship position through the National Institute of Mental Health during which I learned and applied clinical research techniques for the study of persons with severe schizophrenia. My mentors were Professors Van Putten, Goldstein (Principal Investigator), and Marder.

B. Clinical, Research, and Teaching Background

I remained at both UCLA and the affiliated West Los Angeles Veterans Affairs Medical Center until recently when a number of personal medical challenges have forced me into a period of semi-retirement. Over the two decades between 1986 and 2006 though, both my clinical work and research focus remained on the treatment of persons with schizophrenia. I was the Chief of the Schizophrenia Treatment Unit at the VA Medical Center during the vast bulk of this epoch, and was also the Co-Chief (with my wife Donna A. Wirshing, M.D.) of the Schizophrenia Outpatient Research Clinic during

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the last ten years. Though I rose through the traditional academic ranks at UCLA and even reached the level of full Professor over five years ahead of "schedule", I never lost my fascination with clinical care and never traded it for more administrative tasks as my career wandered through the decades.

However, as is usual among clinical academicians, my patient care tasks and research interests dovetailed consistently and have always taken place in a setting with medical trainees at every level of experience. Teaching these persons over the years has been the third major leg of my vocational life. Unlike most of my academic colleagues, I never thought of these teaching duties as on obligation to be tolerated and where possible shunted to my younger colleagues. In fact, it generally occupied the top spot in my personal emotional ranking of our traditional tasks (i.e., teaching, research, and patient care). My teaching has been honored over the years with several awards from both my students and colleagues, including 2006 when I was again nominated for the Golden Apple Award by the graduating medical school class (the highest teaching accolade in the School of Medicine, an honor I received in 1998).

Within the context of these various positions and responsibilities, I have been able to experience, study, and then teach others about the care of seriously mentally ill patients. While I have been most consistently compelled by and fascinated with the prototypic psychotic illness schizophrenia, persons with bipolar illness (i.e., "manic depressive disorder") have taken up a close second place over the years. Like any academician in my area, I have sought and received grants to continue my studies and have published in the peer reviewed literature (with the substantial aide of my colleagues and assistants—see my attached CV for the details). I believe that I have been fortunate

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in the extreme to have had these professional opportunities. They have permitted me to live an enviable work life that I was never able to master and was therefore neither predictable nor routine.

These sundry positions also brought me into contact with the pharmaceutical industry that coincidentally became increasingly interested in the treatment of psychotic persons at the very onset of my career in the mid 1980's. This time marked the beginning of the second significant epoch of pharmacologic treatment of psychosis (The first one having begun in the early 1950's but which had plateaued by the late 1960's). This latter period saw the development, testing, and subsequent marketing of what came to be known as the "Second Generation" or "Atypical" antipsychotic compounds. Though not truly revolutionary or even novel per se, they did constitute a significant advance in many (though not all) aspects over the older medications. This mutual interest in the treatment of psychosis allowed me to "test" potential medications in my patients under controlled protocol conditions from the beginning of their development by industry. Although not every medication that we tested over the years survived the gauntlet of clinical testing, we were able to test every medication that did receive the approval to market by the Food and Drug Administration.

The approval process for medications is a lengthy one that has become increasingly burdened by regulation and requirements over the years. As a consequence, it can take years for a given compound to move from first testing in patients to full marketing approval. Among the medications that we tested and studied that went on to receive approval have been risperidone (approval 1994), olanzapine (1996), ziprazadone (2000), aripiprazole (2002), and quetiapine (1998). The early and prolonged nature of

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this experience allowed us to develop a clinical knowledge of the real world effects of these drugs that was often at the very forefront of the entire field. And as is usual with pharmacologic compounds, our novel discoveries and observations generally involved the toxic effects rather than the therapeutic impacts of the drugs.

In the early to mid 1990's we were among the very first to report on the curious metabolic effects of the newer drugs. In particular, we noticed that many of our patients gained weight when first begun on these drugs and at a rate that was, on occasion, singular in our experience. We also noted that these patients soon began to suffer the usual downstream consequences of gaining weight (e.g., glucose intolerance, frank diabetes, and even severe hyperglycemia with resultant hyperosmolar coma). As is customary in the academic world, we described our experience in the peer-reviewed literature, reported it at any number of scientific meetings, and discussed it with the manufacturers. In addition, though, we worked with industry to extend, understand, and hopefully find ways to remediate these various toxicities. The increasingly high economic stakes of the field sometimes lead those in industry to confuse the message and the messenger (at least from my perspective). As a consequence, our relationships would, or at least could, sour and blossom suddenly, depending on the details of our latest report. As one might expect, our observations and conclusions were not infrequently challenged by one company only to be embraced and promoted by its competitor.

II. INFORMATION REVIEWED/RELIED UPON

I have treated mentally ill patients, including patients with Zyprexa induced diabetes and/or pancreatitis. I have worked as a consultant for Eli Lilly & Company, including

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consulting regarding the drug Zyprexa. Further, I have worked as a clinical investigator for Eli Lilly & Company during clinical trials of Zyprexa.

In the course of my work on this litigation, as well as my past work with Eli Lilly & Company regarding Zyprexa, I have reviewed, among other documents and information, the following materials:

a) conducted and analyzed clinical and scientific research, case reports and meta-analyses regarding Zyprexa and other antipsychotic drugs;

b) scientific literature relating to Zyprexa and other antipsychotic drugs;

c) internal Eli Lilly & Company documents relating to clinical and post-clinical trials regarding Zyprexa; and

d) labeling for Zyprexa and other antipsychotic drugs as provided in the Physician's Desk Reference.

III. WEIGHT GAIN ASSOCIATED WITH ZYPREXA AND OTHER ATYPICAL ANTIPSYCHOTICS

Overweight and obesity are widely accepted as causal factors to increase the risk for a number of diseases including diabetes, cardiovascular disease (e.g., coronary heart disease (CHD) and cerebrovascular disease), and hypertension, in both the adult and the pediatric populations. NIH/NHLBI guidelines. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report.* NIH Publication No. 98-4084 National Institutes of Health. September 1998. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. *The disease burden associated with overweight and obesity.* (1999) JAMA 282:1523-9. Ebbeling CB, Pawlak DB, Ludwig DS. *Childhood obesity: public-health crisis, common sense cure.* (2002) Lancet 360:473-82. In addition, marked weight gain and obesity are associated with abnormal

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metabolic changes such as insulin resistance and dyslipidemia, which are themselves risk factors for cardiovascular disease (CVD) and diabetes. Recent studies have reported increases in the risk of diabetes starting with a body mass index (BMI) as low as 25 kg/m—a risk that increases exponentially by approximately 25% for each (1 kg/m^2) increase in BMI over 25 kg/m. (Note: BMI is the standard measure of weight normalized for height. It is calculated by dividing an individual's weight in kilogram by the square of their height in meters) NIH/NHLBI guidelines. *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report.* NIH Publication No. 98-4084 National Institutes of Health. September 1998. Colditz GA, Willett WC, Stampfer MJ, Manson JE, Hennekens CH, Arky RA, Speizer FE. *Weight as a risk factor for clinical diabetes in women.* Am J Epidemiol 1990;132:501–13; Colditz GA, Willett WC, Rotnitzky A, Manson JE. *Weight gain as a risk factor for clinical diabetes mellitus in women.* Ann Intern Med 1995;122:481–6. The finding that insulin resistance increases with weight gain and decreases with weight loss indicates that fat accumulation is not just associated with insulin resistance but contributes to it. Boden, G. *Pathogenesis of type 2 diabetes: insulin resistance.* Endocrinol Metab Clin North Am 2001; 30: 801-815.

The introduction of atypical antipsychotic medications was trumpeted by the manufacturers of these pharmaceutical agents as a major advance in the treatment of schizophrenia with improved symptomatic control of the psychosis and a reduction in both tardive dyskinesia and extra pyramidal side effects. Without addressing this claim of enhanced efficacy and reduced neurotoxicity, I focus here on the issue of weight gain and its associated increased morbidity. Olanzapine, or Zyprexa, was the third member of the

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class of drugs known as the atypical antipsychotics (also known as second-generation antipsychotics (SGA)) to come to the U.S. market.

Weight gain is recognized as a "determinant of patient noncompliance" (Kurzthaler I., Fleischhacker WW. *The clinical implications of weight gain in schizophrenia.* (2001) J Clin Psychiatry 62: (suppl 7):32-37; Graham, K.A., et al. *Effect of Olanzapine on Body Composition and Energy Expenditure in Adults with First-Episode Psychosis.* (2005) Am J Psychiatry. 162:118-123) and this undesirable side effect may also lead to potential long-term health consequences. Almeras, N., et al. *Development of an atherogenic metabolic risk factor profile associated with the use of atypical antipsychotics.* (2004) J Clin Psychiatry. Apr;65(4):557-64. Olfson et al., reported that weight gain is 1 of 2 main side effects that will cause schizophrenic patients to discontinue treatment. Olfson M. et al., *Predicting medication noncompliance after hospital discharge among patients with schizophrenia.* (2000) Psychiatr Serv 51:216-222. Not all psychiatric medications are associated with weight gain and a few psychotropics, such as isocarboxazid, bupropion, topiramate and psycho-stimulants, may actually cause weight loss. Cantu TG et al. *Monoamine oxidase inhibitors and weight gain.* (1988) Drug Intel Clin Pharm 22:755-759; Weisler RH. *Comparison of Bupropion and Trazodone for the treatment of major depression.* (1994) 14:170-179; Chengappa RKN et al. *Long term effects of topiramate on bipolar mood instability, weight change and glycemic control: a case-series.* Eur Psychiatry 16:186-190.

Certain atypical antipsychotics are associated with greater weight gain liability than others. Allison et al. conducted a study "to estimate and compare the effects of antipsychotics – both the newer ones and the conventional ones – on body weight".

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Allison, DB et al. *Antipsychotic-induced weight gain: A comprehensive research synthesis.* (1999) Am J Psychiatry 156:1686-1696.

Weight gain was estimated by these researchers at 10 weeks because there was sufficient data for this time interval. Further, these researchers noted that "estimated weight gain while patients are taking a drug for longer periods would be expected to be substantially higher". This expectation is based on both the physics and the physiology of weight gain (Barnes-Josiah D et al. *Early body size and subsequent weight gain as predictors of breast cancer incidence (Iowa, United States* (1995); Cancer Causes Control 8:229-238) and empirical observations from studies of selected compounds for which longer-term data were available. Beasley CM Jr, Tollefson GD, Tran PV. *Safety of olanzapine.* (1997) J Clin Psychiatry 58(supp. 10):13-17:19-21.

Olanzapine and clozapine (the prototypic atypical that has been marketed in the US since the mid 1980's) are associated with the highest incidence of weight gain and as discussed below are the drugs associated with the highest diabetogenic potential. Note also that subjects in placebo conditions typically *lost* about 0.74 kg. These investigators noted that this loss of weight may be due to the fact that in placebo-controlled studies, subjects were taking some other neuroleptic drug before the trial (and therefore has some drug-induced tendency to gain weight).

What is the clinical significance of these degrees of weight gain? First, note that at 10 weeks, two and a half months time, patients exposed to olanzapine gained a mean of 4.15 kg (approximately 9.13 lbs), an amount only surpassed by the far-more infrequently prescribed clozapine which caused a mean of 4.45 kg. These researchers noted that if the therapeutic response and weight gain are correlated, then the fact that the shorter-term

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controlled studies usually included data on all subjects, whereas long-term use was usually restricted to individuals showing a positive therapeutic response to the drug, then this would imply that the 10-week weight gain might be higher than we have estimated. Thus, weight gains far in excess of 5 kg (11lbs) may be seen in patients on long-term therapy.

A 5kg or 11lb weight gain in a 10-week period of time is an astounding amount of weight-gain. The Institute of Medicine has suggested that weight losses of 5% in obese individuals can result in clinically meaningful reductions in morbidity and risk of early mortality. *Institute of Medicine: Weighing the Options: Criteria for Evaluating Weight-Management Programs.* Washington, D.C. National Academy press, 1995. As such, it is expected that increases in body weight of as much as 5% would result in corresponding increases in morbidity and risk of early mortality. In fact, it appears that weight gain of 5% or greater in adults are associated with important increases in risk. This is especially true for individuals who are obese to begin with.

Olanzapine was the third second-generation antipsychotic approved for use in the U.S., and has been widely used since its introduction in 1996. A large body of literature exists examining the association between olanzapine therapy and diabetes mellitus, hyperglycemia, abnormal glucose, lipid regulation and weight gain. This includes case reports, FDA MedWatch Drug Surveillance information, retrospective database analyses, and controlled experimental studies including randomized clinical trials.

That olanzapine is especially effective in producing weight gain is outlined by numerous studies discussed below. First, Goldstein et al., in their 1999 case-series reported on 7 cases of new-onset diabetes mellitus and diabetic ketoacidosis. Goldstein,

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LE et al. *New-Onset Diabetes Mellitus and Diabetic Ketoacidosis Associated with olanzapine Treatment.* Psychosomatics 40:5, September-October 1999. It is interesting to note the extent of the weight gain and clinical course in 5 of the 7 while the patients were on olanzapine: Case 1 gained 71 pounds after 6 months of olanzapine; Case 2 gained 10 to 15-pounds over 18 months; Case 4 gained "about 30 pounds" with only 5 weeks of therapy with olanzapine; Case 5 gained 25 pounds in approximately one year of therapy and, even though case 6 *lost* 6 pounds during 3_ months of olanzapine, it is noted that the patient presented to his endocrinologist with a random blood glucose of 686 mg/dL, polydipsia, polyuria and blurred vision and was, therefore diagnosed as having diabetes – which is often associated, initially, with weight loss.

Nemeroff, Kinon and Jones et al., conducted studies pertaining to the weight gain associated with the atypical antipsychotics agents, particularly Zyprexa. The data from these studies allow us to note the following: first, that the observation period is now a long-term period of 1 year. Furthermore, over this longer period of time, quetiapine, risperidone, ziprasidone, and aripiprazole all are associated with a modest increase weight over the year's time whereas 'all doses' of olanzapine were associated with a greater than 12lb weight gain (3 to 6 times more than the other SGAs) while the most commonly prescribed olanzapine doses of between 12.5 to 17.5 mg were associated with an astounding 24 lb weight gain (6 to 12 times that of the other SGAs).

Casey et al. conducted an analysis of the short-term weight gain data supplied in U.S. package inserts and found that "all of the first-line atypical antipsychotic medications tested (aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone) cause substantially different rates of clinically significant weight gain (defined by the

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U.S. FDA as ≥ 7% of baseline weight) compared to placebo." Casey DE, Haupt DW, Newcomer J, et al. *Antipsychotic-Induced Weight Gain and Metabolic Abnormalities: Implications for Increased Mortality in Patients With Schizophrenia.* J Clin Psychiatry 2004;65;(suppl 7):4-18. Olanzapine was associated with approximately 10 times the placebo-induced incidence of weight gain both compared to placebo and the other SGAs.

Furthermore, Simpson et al compared the mean weight change observed between those patients exposed to ziprasidone versus olanzapine. In a six-week long acute study 116 patients on ziprasidone gained a mean of 2.0 lbs from baseline while 122 patients on olanzapine gained a mean of 8.0 lbs. Simpson, G.M., Glick, I.D., Weiden, P.J., Romano, S.J., Siu, C.O. (2004), *Randomized, Controlled, Double Blind Multicenter Comparison of the Efficacy and Tolerability of Ziprasidone and Olanzapine in Acutely Ill Inpatients With Schizophrenia.* Am J Psychiatry 161:1837-1847.

Ebenbichler et al conducted a prospective, controlled, open study comparing body weight, fat mass, and indices of insulin resistance/sensitivity in 10 olanzapine-treated patients with schizophrenia with those of a group of 10 mentally and physically healthy volunteers. Ebenbichler CF, et al. *Olanzapine induces insulin resistance: results from a prospective study.* J Clin Psychiatry 2003; 64:1436-1439. Weight, fat mass, and indices of insulin resistance/sensitivity were assessed over individual 8-week observation periods.

Patients on olanzapine gained a mean of 7.6 lbs while the 'volunteers' gained a mean of 1.32 lbs. Furthermore, the olanzapine patients gained 4.84 lbs of 'body fat' versus 0.66 lbs gained in the volunteers. Finally, the BMI in the olanzapine patients increased a mean of 1.1 versus 0.2 in the volunteers. These investigators also noted that

some of their olanzapine-patients developed insulin resistance while not gaining fat, suggesting to them that an increase in fat mass is not the only factor contributing to the induction of insulin resistance. Ebenbichler at 1438. "According to large epidemiologic studies, weight gain of 1 BMI unit corresponds to an increase in relative risk to develop diabetes mellitus of 2.9 to 4.3 for women (Colditz GA et al., *Weight gain as a risk factor for clinical diabetes mellitus in women,* (1995) Ann Intern Med 122:481-486) and 1.0 to 1.5 for men (Chan JM et al. *Obesity, fat distribution and weight gain as risk factors for clinical diabetes in men,* (1994) Diabetes Care 17:961-969) .....thus, the increase in fat mass, itself, may be a factor leading to an increase in insulin resistance." Ebenbichler at 1438.

Haberfellner and Rittmannberger followed 27 outpatients with schizophrenia or schizoaffective disorder over a mean of 22 months (6-42 months), treating them with a mean dose of 8.52 mg of olanzapine at study entry and 8.70 mg at study end, doses significantly lower than those commonly used in this country. Haberfellner EM and Rittmannberger, A. *Weight gain during long-term treatment with olanzapine: a case series.* (2004) Int Clin Psychopharmacol 19:251-253. There were no control 'patients' in this case series. Nevertheless, over a two-year period, they noted that the mean BMI increased in their patients from 24.8 to 29.1. Eighteen (66.7%) of their patients gained more than 7% of their initial body weight and the weight gain was most pronounced in the first 3 months of treatment (mean weight change of 8.8 lbs). Haberfellner at 2

As reported within the ***Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes,*** which represents the opinions of the American Diabetes Association, the American Psychiatric Association, the American Association

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of Clinical Endocrinologists and the North American Association for the Study of Obesity, "there is considerable variability in weight gain among the various second-generation antipsychotics". *Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes.* Diabetes Care, (2004) 27(2):596-601. The authors of the Consensus Statement noted that at 10 weeks of therapy the average weight gain ranged from ~0.5 to 5.0kg (1.1 lbs to 11 lbs) and that "limited data suggest that in humans, most of the weight gained is fat" and data from a canine model indicate that certain (second-generation antipsychotics) increase total visceral fat mass and intrahepatic lipid content" (*Id.* at 597 and 598) while Eder at al, demonstrated that the olanzapine-induced weight gain was associated with an increase in body fat. Eder U., et al. *Association of olanzapine-induced weight gain with an increase in body fat.* (2001) Am J Psychiatry 158:1719-1722. According to the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists and the North American Association for the Study of Obesity ***Consensus Statement***, the infrequently prescribed clozapine and the frequently prescribed olanzapine were associated with the greatest weight gain while aripiprazole and ziprasidone were both associated with equivocal weight gain. Also note that both clozapine and olanzapine were associated with an increased risk of diabetes and a worsening lipid profile while the data pertaining to the other drugs was "discrepant" or had no effect.

The authors of the ***Consensus Statement*** suggested that both hunger and satiety may be altered in people taking olanzapine and clozapine because of their known affinities to serotonin, norepinephrine, dopamine and particularly histamine-H1 receptors, all of which have been implicated in the control of body weight. Eder at 598. The

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blockade of the serotonin and histamine receptors has been linked to weight gain and, the second-generation antipsychotics with the strongest affinity for the H_1 receptor are clozapine and olanzapine. Kroeze WK, et al. *H1-histamine receptor affinity predicts short-term weight gain for typical and atypical antipsychotic drugs.* Neuropsychopharmacology. 2003 Mar; 28(3):519-26.

McQuade et al presented data at the 2003 annual meeting of the American Psychiatric Association in San Francisco. They compared the weight gain associated with both olanzapine and aripiprazole, observed over approximately 26 weeks. These researchers found that there was a net difference of 5.6kg (12.32 lbs) during this period of time for olanzapine patients, while those exposed to aripiprazole showed little to no weight gain at all.

Most recently, Graham et al reported on their study involving nine adults (six men and three women) experiencing their first psychotic episode who had no previous history of antipsychotic drug therapy who were begun on a regimen of olanzapine and studied within 7 weeks and approximately 12 weeks after olanzapine initiation. Graham, K.A., et al. *Effect of Olanzapine on Body Composition and Energy Expenditure in Adults with First-Episode Psychosis.* (2005) Am J Psychiatry. 162:118-123. After approximately 12 weeks of olanzapine therapy, the median increase in body weight was 4.7 kg (10.3lbs), a significant increase of 7.3% from first observation. Body fat, measured by dual-energy x-ray absorptiometry, increased significantly, with a propensity for central fat deposition. The patients in this study experienced a significant increase of 15.3% in their body fat in addition to a 26.0% increase in 'fat mass'.

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As Schwartz et al reported "Early intervention is the key to preventing significant drug-related weight gain and treating obesity if it occurs. Patients should be told about weight gain as a potential adverse effect before they begin treatment and their weight should be monitored as long as they continue taking drugs that may increase weight." Schwartz, TL et al. *Psychiatric medication-induced obesity: treatment options.* (2004) Obesity Reviews 5:233-238.

Further, although the medical literature is replete with studies linking obesity to the development of diabetes, the risks associated with weight gain or changes in body fat distribution is less well reported. Hanson RL, Narayan KMV, McCance DR, et al. *Rate of weight gain, weight fluctuation, and incidence of NIDDM.* Diabetes 1995;43:261–6; Ford ES, Williamson DF, Liu S. *Weight change and diabetes incidence: findings from a national cohort of U.S. adults.* Am J Epidemiol 1997;146:214–22; Wannamethee GS, Shaper AG. *Weight change and duration of overweight and obesity in the incidence of type 2 diabetes.* Diabetes Care 1999;22:1266–72; Holbrook TL, Barrett Connor E, Wingard DL. *The association of lifetime weight and weight control patterns with diabetes among men and women in an adult community.* Int J Obes 1989;13:723–9; Colditz GA, Willett WC, Rotnizky A, et al. *Weight gain as a risk factor for clinical diabetes mellitus in women.* Ann Intern Med 1995;122:481–6; Flegal KM, Carroll MD, Ogden C, et al. *Prevalence and trends in obesity among U.S. adults,* 1999–2000. JAMA 2002;288:1723–7. In order to evaluate this risk, Koh-Banerjee et al prospectively examined the relationship between changes in body weight and body fat distribution and the subsequent risk of diabetes in a large population of U.S. men. Koh-Banerjee et al. *Changes in body weight and body fat distribution as risk factors for clinical diabetes in*

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U.S. men. (2004) Am J Epidemiol 159:1150-1159. These researchers noted that long-term weight gain was strongly related to the risk of diabetes. "Men who gained 7-11 kg had an increased risk of 2.1 (95 percent CI: 1.2, 3.6), while those who gained 12-18 kg had a relative risk of 3.0 (95 percent CI: 1.8, 5.2). Men who experienced the highest degree of weight gain (≥19 kg) had an 8.8 times (95 percent CI: 5.2, 14.7) greater risk of diabetes than those men whose weight remained stable.

IV. DIABETES AND HYPERGLYCEMIA ASSOCIATED WITH OLANZAPINE

There are numerous relevant case reports and epidemiological studies linking diabetes, ketoacidosis, hyperglycemia and dyslipidemia with olanzapine. I will outline some of the highlights. The above referenced ***Consensus Statement*** by the American Psychiatric Association and the American Diabetes Association relied on many of these references for their observations that olanzapine is associated with an increased risk of diabetes, hyperglycemia and dyslipidemia.

In their groundbreaking article, Koller and Doraswamy reviewed data from the FDA MedWatch Drug Surveillance System (January 1994 to mid-May 2001), published reports (Medline, to mid-May 2001), and meetings abstracts over a similar period and identified a total of 237 cases of diabetes or hyperglycemia associated with olanzapine therapy. Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52. These reports included 188 cases (79%) of newly diagnosed hyperglycemia, and 44 cases (19%) of exacerbation of pre-existing diabetes. In the remaining 5 cases, this distinction was unclear. Of the 188 patients with new-onset hyperglycemia, 153 met diagnostic criteria for diabetes based on blood glucose (fasting,

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>126 mg/dL; non-fasting, >200 mg/dL) or HbA_{1c} levels, and 20 were either receiving anti-diabetic medication, and/or were acidotic or ketotic at the time of hyperglycemia. Gallagher D, Ruts E, Visser M, Heshka S, Baumgartner RN, Wang J, Pierson RN, Pi-Sunyer FX, Heymsfield SB. *Weight stability masks sarcopenia in elderly men and women.* Am J Physiol Endocrinol Metab 2000;279:E366–75.

For the 153 patients with newly diagnosed diabetes, their mean age at onset of the disease was 39.8 (± 12.4) years. Over two-thirds of cases (68%) occurred before patients reached 45 years of age. Among patients experiencing exacerbation of their pre-existing diabetes, mean age was 51.7 ± 15.4 years. Time from initiation of olanzapine therapy to the onset of hyperglycemia ranged from 2 days to 45 months among the 209 patients with available data. For 73% of patients, onset occurred within 6 months of starting olanzapine. For patients with definitive, newly-diagnosed diabetes, 47% of cases occurred within 3 months and 70% within 6 months of starting therapy. For those patients with exacerbation of disease, 84% of events occurred within 3 months of starting olanzapine therapy. Among 10 patients rechallenged with olanzapine therapy, 8 experienced worsening glycemic control. For 4 patients, this occurred within 8 days of the resumption of olanzapine therapy.

The severity of hyperglycemia ranged from mild glucose intolerance to diabetic ketoacidosis and nonketotic hyperosmolar coma. In 69 cases (64 with new-onset diabetes), blood glucose levels ≥700 mg/dL were recorded; in 41 cases (38 with new-onset diabetes), blood glucose values exceeded 1000 mg/dL. Changes in mental state accompanied hyperglycemia in 43 cases, while for 17 patients, pancreatitis or hyperamylasemia were associated with hyperglycemia. Overall, there were 15 deaths

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reported among identified olanzapine cases, with 13 occurring during or shortly after a hyperglycemic episode.

Diabetic ketoacidosis was a frequent occurrence in the reported cases of diabetes or hyperglycemia associated with olanzapine therapy. Metabolic acidosis or ketosis was reported in 80 of the 237 cases (33.8%) and 92% of these cases were new-onset diabetes. In addition, the proportion of fatalities among the cases of diabetic ketoacidosis was high (11.3%) with acidosis or ketosis reported in 9 of the 15 deaths observed in the olanzapine cases.

In an addendum to the paper, the authors reported on an additional 52 cases of hyperglycemia (newly diagnosed, n=35; exacerbation, n=12), identified by extending their FDA MedWatch search to February 2002. Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52. Again the incidence of diabetic ketoacidosis was relatively high, with 20 reports of ketosis or acidosis associated with hyperglycemia (38.5%). There were also 5 reports of pancreatitis among the cases. In all, 10 deaths occurred among these 52 patients. the nature of the reports, however, it is difficult to conclude much about the relative rates of these very bad outcomes. It is likely, for example, that the more severe outcomes (e.g., death, or ketoacidosis) would be over reported relative to less severe outcomes (e.g., uncomplicated diabetes).

In a recent review, Ananth et al analyzed 26 cases of diabetes associated with olanzapine treatment identified from the literature. Ananth J, Venkatesh R, Burgoyne K, Gunatilake S. *Atypical antipsychotic drug use and diabetes.* Psychother Psychosom 2002;71:244–54. The mean duration of olanzapine treatment prior to detection of

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diabetes was 18.26 weeks (range, 4–68 weeks), with 43% of cases occurring within 12 weeks. The mean age of patients at detection was 41.5 years (range, 19–56 years); 17 patients (65%) were aged 45 years or below. Approximately one-third of patients (9 cases) experienced ketoacidosis.

In the review by Melkersson, et al, it was noted that patients treated with olanzapine had significantly higher median insulin levels than those receiving clozapine or typical antipsychotics ($p<0.05$). Melkersson KI, Hulting AL. Insulin and leptin levels in patients with schizophrenia or related psychoses--a comparison between different antipsychotic agents. Psychopharmacology (Berl) 2001;154:205–12. Ten patients (71%) in the olanzapine group had elevated insulin levels compared with 7 (50%) in the clozapine group and 6 patients (32%) treated with typical agents. Two other studies have also examined glucose and insulin levels in patients with schizophrenia or related psychoses treated with olanzapine. Melkersson KI, Dahl ML. *Relationship between levels of insulin or triglycerides and serum concentrations of the atypical antipsychotics clozapine and olanzapine in patients on treatment with therapeutic doses.* Psychopharmacology (Berl) 2003; 170(2):157–66; Melkersson KI, Hulting AL, Brismar KE. *Elevated levels of insulin, leptin, and blood lipids in olanzapine-treated patients with schizophrenia or related psychoses.* J Clin Psychiatry 2000;61:742–9 Elevated insulin levels were reported for 5 (31%) of the 16 olanzapine-treated outpatients included in the study (mean treatment duration, 1.2 years). Melkersson KI, Dahl ML. *Relationship between levels of insulin or triglycerides and serum concentrations of the atypical antipsychotics clozapine and olanzapine in patients on treatment with therapeutic doses.* Psychopharmacology (Berl) 2003; 170(2):157–66

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Retrospective database analyses from epidemiological and health service databases have investigated the association between olanzapine therapy and diabetes. In all except one of the studies, the risk of developing diabetes was increased significantly with olanzapine treatment.

The largest analysis involved 38,632 outpatients with schizophrenia, treated with first (n=15,984) or second-generation (n=22,648) antipsychotic therapy, from the Veteran's Health Administration database. Sernyak MJ, Leslie DL, Alarcon RD, Losonczy MF, Rosenheck R. *Association of diabetes mellitus with use of atypical neuroleptics in the treatment of schizophrenia.* Am J Psychiatry 2002;159:561–6. Of the patients receiving second-generation antipsychotics, 10,970 (48.4%) were treated with olanzapine.

A smaller retrospective analysis of the VISN-10 Veteran's Administration database assessed the risk of developing diabetes in patients receiving olanzapine, risperidone, haloperidol, or fluphenazine therapy between the start of 1997 and the end of 2000. Fuller MA, Shermock KM, Secic M, Grogg AL. *Comparative study of the development of diabetes mellitus in patients taking risperidone and olanzapine.* Pharmacotherapy. 2003;23(8):1037–43. Female patients, ethnic groups other than Caucasian or African-American, patients treated with clozapine, and those with pre-existing diabetes were excluded from the analysis. After controlling for age, race, diagnosis, and use of other antipsychotic medication, this study showed that the risk of developing diabetes was significantly higher with olanzapine therapy than with risperidone (relative risk 1.37; 95% CI, 1.06–1.76; p=0.016).

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An analysis of medical claims data from two health plans showed that olanzapine treatment was associated with a significant increase in the risk of new-reported diabetes compared with untreated patients. Gianfrancesco FD, Grogg AL, Mahmoud RA, Wang RH, Nasrallah HA. *Differential effects of risperidone, olanzapine, clozapine, and conventional antipsychotics on type 2 diabetes: findings from a large health plan database.* J Clin Psychiatry 2002;63:920–30. A total of 4308 individuals with psychosis who had received at least 60 contiguous days of antipsychotic therapy (first or second generation), and 3625 who received no antipsychotic treatment were identified from the database. Patients with a type 2 diabetes diagnosis were then identified. Those with pre-existing disease were excluded from the two analyses, based on screening at either 4 months or 8 months prior to the observation period. The ***one-month*** odds ratios for risk of developing diabetes with olanzapine therapy were statistically significant ($p<0.001$) using both the 4-month (1.082) and 8-month (1.099) cut-off period. Similarly, analysis according to treatment dose produced a significant odds ratio using both screening periods (4-month, 1.161; 8-month, 1.222; $p<0.002$). The 12-month odds ratio for olanzapine, based on the treatment duration and the 8-month cut-off, was 3.10, suggesting that 12 months of treatment increases the odds of diabetes by 210% compared with no treatment. Compared with risperidone therapy, the 12-month odds ratio for olanzapine was 3.53 ($p<0.05$). Similar methodology was used in a second study analyzing medical claims data from a Blue Cross/Blue Shield database encompassing nearly 2 million individuals. Gianfrancesco F, White R, Wang RH, Nasrallah HA. *Antipsychotic-induced type 2 diabetes: evidence from a large health plan database.* J Clin Psychopharmacol 2003;23(4):328–35.

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Data available from April 1997 to October 2000 were used to compare the risk of diabetes in patients with psychosis receiving antipsychotic therapy compared with those not receiving treatment. In this study, however, the presence of type 2 diabetes was based solely on prescription claims for anti-diabetic medication, and only an 8-month screening period for existing diabetes was used. Overall, the database analysis identified 6528 individuals with psychosis who had received at least 60 contiguous days of antipsychotic therapy (first or second generation), and 10,296 who had received no antipsychotic treatment. Among the 1719 patients treated with olanzapine, 15 developed diabetes. Logistic regression analysis showed that the risk of developing diabetes was significantly greater with olanzapine than with no antipsychotic therapy (odds ratio, 1.03, p=0.0247), *based on 1 month of treatment.* Adjusting this value to 12 months of treatment gave an odds ratio for olanzapine of 1.426 (95% CI, 1.046–1.955), compared again with no antipsychotic therapy, suggesting that the likelihood of diabetes was 42.6% greater with olanzapine than for untreated individuals.

Case control analysis, in which each case of diabetes is matched to control cases (i.e., patients with schizophrenia who had not developed diabetes), showed a significant increase in risk of diabetes with olanzapine therapy compared with no antipsychotic therapy (OR, 5.8; 95% CI, 2.0–16.7; p=0.001). Koro CE, Fedder DO, L'Italien GJ, Weiss SS, Magder LS, Kreyenbuhl J, Revicki DA, Buchanan RW. *Assessment of independent effect of olanzapine and risperidone on risk of diabetes among patients with schizophrenia: population based nested case-control study.* BMJ 2002;325(7358):243. Typical antipsychotic therapy (OR, 1.4; 95% CI, 1.1–1.7; p=0.004), and less significantly risperidone treatment (OR, 2.2; 95% CI, 0.9–5.2; p=0.079), was associated with increases

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in the risk of diabetes compared with no therapy. When compared with typical antipsychotic therapy, olanzapine therapy showed a significant increase in the risk of developing diabetes (OR, 4.2; 95% CI, 1.5–12.2; p=0.008). The level of risk associated with risperidone therapy was not significantly different as compared with that of typical agents (OR, 1.6).

Lambert et al., published the result of the case-controlled analysis of California medicaid claims in March of 2005 in *Pharmacoepidemiology and Drug Safety.* Lambert BL, Chia-Hung C, Ken-Yu C, Eskinder T, Carson W. *Antipsychotic exposure and type 2 diabetes among patients with schizophrenia - a matched case-control study of California Medicaid claims.* Pharmacoepidemol Drug Safety 2005; March 22 (Published on-line in Wiley InterScience (www.interscience.wiley.com.) Utilizing a 12-week exposure window these researchers noted that olanzapine was associated with an Odds Ratio of 1.36 (95% CI 1.20 – 1.53) of developing diabetes. Changing to a 24-week exposure, the OR increased to 1.38 (95% CI 1.31 – 1.90) and with a 52-week exposure the OR increased to 1.41 (95% CI 1.24 – 160). Using the 52-week exposure data these researchers observed a significant dose response with an OR of 1.25 (95% CI 1.00-1.57) for doses $\leq$ 7.5 mg, an OR of 1.84 (95% CI 1.53 – 2.22) for doses 7.5 mg $\leq x \leq$ 12.5 mg, and an OR of 1.87 (95% CI 1.58 – 2.21 for doses >12.5 mg. These researchers observed that their findings were largely consistent with other published epidemiological studies.

A number of prospective, controlled clinical studies, including randomized clinical trials have examined the impact of olanzapine treatment on direct measures of glucose regulation, in contrast to surrogate measures used in the retrospective database analyses, with the majority of the controlled studies reporting significant increases in

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plasma glucose and/or insulin levels during olanzapine treatment in comparison to different control conditions.

A significant increase in fasting glucose levels was observed during olanzapine therapy in a 14-week prospective study of antipsychotic therapy. Lindenmayer JP, Czobor P, Volavka J, Citrome L, Sheitman B, McEvoy JP, Cooper TB, Chakos M, Lieberman JA. *Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics.* Am J Psychiatry 2003;160:290–6. Patients with schizophrenia or schizoaffective disorder were randomized to one of four treatments: clozapine, olanzapine, risperidone, or haloperidol. Patients in the olanzapine group had a significant mean increase from baseline in fasting glucose after 14 weeks of treatment (n=22, +14.3 mg/dL, $p<0.02$); this increase was greater than that observed in the other groups. Four patients receiving olanzapine treatment had elevated fasting glucose levels (≥126 mg/dL) during the study. This compared with 6 patients in the clozapine group, 3 on risperidone, and 1 on haloperidol.

Newcomer et al compared glucose regulation in non-diabetic patients with schizophrenia treated with first or second-generation (clozapine, olanzapine, or risperidone) therapy and untreated healthy subjects. Newcomer JW, Haupt DW, Fucetola R, Melson AK, Schweiger JA, Cooper BP, Selke G. *Abnormalities in glucose regulation during antipsychotic treatment of schizophrenia.* Review Arch Gen Psychiatry 2002; 59:337–45. Patient groups were well matched for age and BMI – mean age and BMI were 37.4 years and 28.6 kg/m^2, respectively, in the 12 olanzapine treated individuals, with groups also balanced for gender and ethnicity. Despite the exclusion of patients with diabetes, significant elevations in plasma glucose levels were observed in the olanzapine

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group at fasting, and at all time points (15, 45, and 75 minutes) after the glucose load, compared with untreated healthy subjects (n=31) and with patients treated with typical antipsychotics (n=17) (all comparisons, $p<0.005$). Insulin resistance, calculated from fasting plasma glucose and insulin levels, was increased significantly in association with olanzapine compared with typical antipsychotic treatment ($p<0.05$).

Ebenbichler et al, as discussed above, conducted a prospective, controlled, open study comparing body weight, fat mass, and indices of insulin resistance/sensitivity in 10 olanzapine-treated patients with schizophrenia and a group of 10 mentally and physically healthy volunteers. Ebenbichler CF, Laimer M, Eder U, Mangweth B, Weiss E, Hofer A, Hummer M, Kemmler G, Lechleitner M, Patsch JR, Fleischhacker WW. *Olanzapine induces insulin resistance: results from a prospective study.* J Clin Psychiatry 2003;64:1436–9. Weight, fat mass, and indices of insulin resistance/sensitivity were assessed over individual 8-week observation periods. They found that fasting serum glucose and fasting serum insulin increased significantly in the olanzapine-treated patients leaving the investigators to conclude that the disturbances in glucose homeostasis during treatment with olanzapine was due to insulin resistance. These researchers caution that "(D)ue to the induction of insulin resistance within weeks of the initiation of olanzapine intake, prescribing clinicians should consider close monitoring of the parameters of glucose homeostasis early in treatment. Ebenbichler noted that the insulin resistance induced by olanzapine treatment was rapid, occurring within days, suggesting to them that a potent factor distinct from weight gain directly induces insulin resistance.

In October, 2004, at the annual meeting of the American Academy of Child and Adolescent Psychiatry in Washington, D.C., researchers from the Johns Hopkins

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Children's Center reported that the atypical antipsychotics "commonly used to treat children with aggression, bipolar disorder, and schizophrenia", specifically olanzapine, may trigger insulin resistance, "a condition that increases the risk of developing Type 2 diabetes and heart disease later in life". (http://www.eurekalert.org/pub_releases/2004-10/jhmi-adl101704.php.)

The Hopkins team evaluated 11 children, some overweight and others obese, who gained "significant amounts of weight" (a 10 percent weight increase) while taking olanzapine, quetiapine, and risperidone. The researchers noted that all six children on "moderate or high doses of one of these drugs, and three of five children on low doses" had evidence of insulin resistance. This evidence included hypertension, high levels of triglycerides, low levels of high density lipoprotein cholesterol and increased levels of protein in the urine – three criteria of the metabolic syndrome, discussed below.

The study's lead author stated that "The insulin resistance seen in these children was greater than what would be expected from weight gain alone, suggesting there is a factor distinct from excess weight that directly induces insulin resistance". If the study's findings are confirmed by larger follow-up studies, Dr. Mark Riddle, the lead author, says he would expect monitoring of metabolic side effects to become standard practice among clinicians prescribing atypical antipsychotics to children.

Reaven et al published a follow-up evaluation of a cohort of Mexican-American and non-Hispanic white children 5.5 years after the previous study to determine whether the increased features of insulin resistance observed in Mexican Americans at age 11 years were still present at age 17. Reaven, P.D. *Cardiovascular Risk Factor Associated with Insulin Resistance in Children Persist Into Late Adolescence.* January 2005 Diabetes

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Care, 28;1:148-150. These investigators noted that the "strong relationships between fasting insulin and cardiovascular risk factors (HDL, triglycerides, and blood pressure) observed in this group at age 11 years were also observed at age 17 years." These children also had significantly elevated levels of C-reactive protein (CRP) at age 17. At least one study found CRP to be an independent predictor of both brachial artery reactivity and carotid artery intimal thickness in 11-year-old subjects (an early indication of the vascular damage of the type seen in typical coronary artery disease). Jarvisalo, M.J., et al. (2002) *Elevated serum C-reactive protein levels and early arterial changes in healthy children.* Arterioscler Thromb Vasc Biol. 22:1323-1328.

Glucose, insulin, and lipid parameters were also assessed in a randomized, double-blind, 6-week study comparing olanzapine and ziprasidone therapy in 269 inpatients with acute exacerbation of schizophrenia or schizoaffective disorder. Glick ID, Romano SJ, Simpson G, Home RL, Weiden P, Pigott T, Bari M. *Insulin resistance in olanzapine- and ziprasidone-treated patients: results of a double-blind, controlled 6-week trial.* Presented at: Annual Meeting of the American Psychiatric Association, May 5–10, 2001, New Orleans, LA. Significant increases from baseline in median fasting plasma insulin levels ($p<0.0001$) and HOMA calculated insulin resistance ($p<0.0001$) were observed with olanzapine therapy, but not ziprasidone. Median body weight increased by 7.2 lb (3.3 kg) from baseline with olanzapine treatment compared with 1.2 lb (0.5 kg) with ziprasidone – median body weight was significantly higher in the olanzapine group than the ziprasidone group at endpoint ($p<0.0001$).

Considered together, the case reports, the vast majority of the retrospective database analyses, and controlled experimental studies including randomized clinical

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trials consistently demonstrate that olanzapine treatment increases the risk of significant weight gain, insulin resistance, hyperglycemia, and/or diabetes mellitus.

The majority of the large retrospective database analyses showed a significant increase in the risk of developing diabetes with olanzapine therapy. The risk of diabetes increased significantly with olanzapine therapy compared with no antipsychotic treatment and compared with treatment with typical antipsychotics. Three database analyses also showed a significantly greater risk of developing diabetes with olanzapine therapy compared with risperidone.

In contrast to these findings, one analysis, which used prescription claims data, reported no significant increase in the risk of diabetes with olanzapine treatment compared with haloperidol therapy. Buse JB, Cavazzoni P, Hornbuckle K, Hutchins D, Breier A, Jovanovic L. *A retrospective cohort study of diabetes mellitus and antipsychotic treatment in the United States.* J Clin Epidemiol 2003;56(2):164–70. The study, however, did show a significantly higher risk of diabetes in olanzapine-treated patients compared with the general population cohort, similar to other first and second-generation antipsychotics studied. This study was authored by Lilly.

Analysis of cases identified from the FDA MedWatch system also provides support for an association between olanzapine therapy and diabetes development. Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52. The large number of reported cases, the temporal relationship between initiation of olanzapine therapy and onset of hyperglycemia, the rapid reversibility on treatment discontinuation, and the younger age of affected patients are all indicative of causality. The larger number of olanzapine-treated cases reported to

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the FDA MedWatch System and in the literature contrasts with the fewer reports of diabetes or hyperglycemia associated with risperidone, quetiapine or ziprasidone therapy. Further, since risperidone was approved for use years before olanzapine, and the total number of risperidone prescriptions at the time of the Medwatch reports were significantly larger than the total number for olanzapine, the number of case reports associated with olanzapine treatment cannot be understood simply as a function of greater exposure.

Further support for a link between olanzapine and diabetes comes from the temporal association between olanzapine treatment and the occurrence of events. Almost half of the cases of diagnosed, new-onset diabetes identified from the MedWatch System occurred within 3 months of the start of treatment, while 70% occurred within 6 months. Six cases were seen within one week of starting treatment. Similarly, in a review of published case reports from the literature, 43% of cases occurred within 12 weeks of olanzapine initiation. Ananth J, Venkatesh R, Burgoyne K, Gunatilake S. *Atypical antipsychotic drug use and diabetes.* Psychother Psychosom 2002;71:244–54. An important feature of the cases analyzed by Koller and Doraiswamy was the high proportion of patients under 45 years old. Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52. The mean age at onset for new-diagnosed diabetes was 39.8 years, with 68% of cases occurring in those under 45 years. This is in contrast to the age distribution of prevalence of diabetes in the U.S. population. Data from the U.S. National Health Interview Surveys (NHIS) show that 81% of diabetes cases occur in individuals over 44 years old, with prevalence increasing with age. Kenny SJ, Aubert RE, Geiss LS. *Prevalence and incidence of non-*

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insulin dependent diabetes. In Harris MI, Cowie CC, Stern MP, Boyko EJ, Reiber GE, Bennett PH, eds. Diabetes in America, 2nd ed. Publication no. 95-1468. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1995:47–67. For individuals aged 65–74 years and ≥75 years, 10% and 11%, respectively, have diabetes. An indirect comparison presented by Koller and Doraiswamy showed that the frequency of newly diagnosed diabetes among olanzapine-treated patients aged 0–44 years was double that in the U.S. population (66% vs. 33%). Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52

A comparison of the age distributions between the study and U.S. populations showed that the difference was statistically significant ($p<0.0001$). This suggests that diabetes occurs earlier in olanzapine-treated patients than in the general population, with a marked increase in those younger than 44 years. Analysis of the age distribution for all olanzapine prescriptions suggests that this does not simply reflect large numbers of olanzapine prescriptions in younger individuals.

Published case reports also contain a high proportion of younger individuals. The review by Ananth et al reported a mean age of patients of 41.5 years, with 65% of patients aged 45 years or below. Ananth J, Venkatesh R, Burgoyne K, Gunatilake S. *Atypical antipsychotic drug use and diabetes.* Psychother Psychosom 2002;71:244–54. Analysis of healthcare data according to age showed that the greatest increase in the risk of diabetes with olanzapine therapy occurred among patients less than 40 years old (odds ratio, 1.64). Wirshing DA, Boyd JA, Meng LR, Ballon JS, Marder SR, Wirshing WC.

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The effects of novel antipsychotics on glucose and lipid levels. J Clin Psychiatry 2002;63:856–65.

Another notable feature of the MedWatch study and the case reports was the significant number of cases of diabetic ketoacidosis. Overall, 34.6% of the cases of hyperglycemia reported in the MedWatch analysis were associated with metabolic acidosis or ketosis. Koller EA, Doraiswamy PM. *Olanzapine-associated diabetes mellitus [review].* 41: Pharmacotherapy 2002;22:841–52.

Diabetic ketoacidosis is typically an indicator of profound insulin deficiency, and is therefore commonly thought of in association with type 1 diabetes rather than with type 2 disease. Diabetic ketoacidosis is not typically observed as a first manifestation of type 2 diabetes, as the disease is characterized initially by peripheral insulin resistance and hyperinsulinemia, followed by gradual and progressive decline of beta-cell function with diabetic ketoacidosis typically occurring in the later phases of the disease, if at all. While most type 2 diabetics will not experience diabetic ketoacidosis, most cases of diabetic ketoacidosis in the population in fact occur in type 2 rather than type 1 diabetics, given the higher frequency of type 2 disease and the contributions of acute insults to beta-cell function such as glucose toxicity. In the MedWatch analysis of olanzapine cases, the majority of cases of diabetic ketoacidosis (92%) were associated with new onset of type 2 diabetes. Published case reports of abnormal glucose regulation with olanzapine therapy also suggest a significant incidence of diabetic ketoacidosis. The clinical significance of diabetic ketoacidosis is illustrated by the number of fatalities in the MedWatch study and among the case reports. Ketosis or acidosis was reported in 9 of the fatalities reported in

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the main MedWatch study. Thus, more than 10% of the cases of diabetic ketoacidosis were associated with patient fatality.

Weight gain and obesity, and increased adiposity in general, are well-established risk factors for diabetes. This strongly suggests that the well-documented occurrence of significant weight gain with olanzapine therapy is a key factor in the increased risk of diabetes seen with this agent. Allison DB, Mentore LJ, Heo M, Chandler PL, Cappelleri CJ, Infante CM, Weiden JP. *Antipsychotic-induced weight gain: a comprehensive research synthesis.* Am J Psychiatry 1999;156:1686–96; Sussman N. *Review of atypical antipsychotics and weight gain.* J Clin Psychiatry 2001;62(Suppl 23):5–12. However, several observations suggest that at least in some cases, weight gain may not play a primary role. A significant minority of reported cases of new-onset diabetes were not accompanied by substantial weight gain or obesity. Among the cases identified from the MedWatch System, 24% of patients did not appear to be overweight or have sustained weight gain. While no significant correlation between weight gain and increased blood glucose levels was reported in the two studies in which this was analyzed, this may reflect a number of critical host factors (e.g., beta-cell function) that can intervene between changes in weight and plasma glucose. Lindenmayer JP, Czobor P, Volavka J, Citrome L, Sheitman B, McEvoy JP, Cooper TB, Chakos M, Lieberman JA. *Changes in glucose and cholesterol levels in patients with schizophrenia treated with typical or atypical antipsychotics.* Am J Psychiatry 2003; 160:290–6; Meyer JM. *A retrospective comparison of weight, lipid, and glucose changes between risperidone- and olanzapine-treated inpatients: metabolic outcomes after 1 year.* J Clin Psychiatry 2002; 63:425–33.

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The rapid onset of diabetes following olanzapine initiation and prompt resolution with treatment withdrawal in some cases also do not suggest that the effects of olanzapine on glucose regulation in these individuals occur simply through actions on weight and adiposity.

V. OLANZAPINE AND PANCREATITIS

The medical literature is also replete with reports of olanzapine being associated with pancreatitis, an acute or chronic inflammation of the pancreas resulting in autodigestion of the organ. Further, I have witnessed patients experience Zyprexa-induced pancreatitis. The condition may be asymptomatic or associated with debilitating pain and can result in hypotension and death.

Reports of pancreatitis were first reported with clozapine in 1992 (Frankenburg FR, Kando J. *Eosinophilia, cloazapine, and pancreatitis [letter]*, Lancet 1992; 340:251; Martin A. *Acute pancreatitis associated with clozapine use [letter]*. Am J Psychiatry 1992;149:714) and were followed by reports of pancreatitis associated with olanzapine. Nishawala MA, Callaghan M, Malatack JJ, et al. *Pancreatitis associated with serotonin-dopamine antagonists.* J Child and Adolscent Psychopharmacol 1997;7:211-13. Doucette et al, in 2000 reported on a 72-year-old woman admitted to the intensive care unit six days after beginning olanzapine therapy and was diagnosed with acute hemorrhagic pancreatitis and unintentional verapamil overdose. According to the Naranjo probability scale, olanzapine was considered to be the probable cause of the acute pancreatitis.

Also in 2000, Hagger, Brown and Hurley reported on two patients with chronic schizophrenia with acute pancreatitis. Hagger R, Brown C, Hurley P. *Olanzapine and*

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pancreatitis. Br J Psychiatry (2000) 177:567. The authors noted that clozapine has been associated with pancreatitis and has a similar structure to olanzapine, therefore one might suspect that olanzapine might cause pancreatitis. It is important to note that one these patients experienced a further episode of pancreatitis upon 'rechallenge' with olanzapine.

Ragucci and Wells in 2001 reported on a 46-year-old woman with no previous history of diabetes begun on olanzapine therapy in 1999. The patient was admitted to the hospital with a diagnosis of diabetic ketoacidosis. The authors noted that the Naranjo probability scale indicated a possible relationship between olanzapine and the DKA, which probably led to the development of the pancreatitis.

Waage et al, in 2004 reported on a 42-year-old man "in good physical condition" who gradually developed hypertriglyceridemia, high cholesterol levels, diabetes and, "ultimately, acute pancreatitis after 19 months of olanzapine monotherapy. Waage C, Carlsson H, Waage Nielsen E. *Olanzapine-Induced Pancreatitis: A Case Report. J Pancreas,* (Online) 2004, 5;5:388-391. Although there may be other causes of pancreatitis, these authors ruled out "the common causes" including trauma, gall stones, alcohol, elevated calcium levels and other drugs as the source of their patient's acute pancreatitis.

"To gain further insight into the clinical characteristics and the relative risk of pancreatitis associated with atypical antipsychotic agents...." Koller et al "queried the Food and Drug Administration MedWatch database to identify reports of pancreatitis..." Koller EA, Cross JT, Doraiswamy PM, Malozowski SN. *Pancreatitis Associated with Atypical Antipsychotics: From the Food and Drug Administration's MedWatch Surveillance System and Published Reports.* Pharmacotherapy 2003;23(9):1123-1130.

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Clozapine and olanzapine were specifically selected because of "published case reports"; risperidone was also assessed because "it is widely prescribed." *Id.* at 1124. Haloperidol was selected as the control drug because it is not generally associated with pancreatitis "despite its long prescription history and because it continues to be prescribed for many of the same patient populations". These researchers identified 192 cases of pancreatitis, 18 of which were reported in 17 publications. Sixty-two cases of pancreatitis occurred in patients receiving only olanzapine. The complication was reported most frequently in the less-frequently-prescribed clozapine followed next by olanzapine and then risperidone.

VI. EFFICACY

In addition to the risks associated with olanzapine as described above, the perceived 'efficacy' of olanzapine vis-á-vis the other drugs in the class requires analysis. Lilly, in a 1997 article, reported that "(T)he data submitted to regulatory agencies for approval of olanzapine were from February 14, 1995" and that "olanzapine had been investigated in 50 studies in 22 countries, resulting in a total of 3139 persons exposed to at least one dose of olanzapine". Beasley, C.M., et al. *Efficacy of Olanzapine: An Overview of Pivotal Clinical Trials.* J Clin Psychiatry 1997;58[suppl 10]:7-12. However, of interest is the fact that, for a drug anticipated to be used for lifetime treatment of an incurable disease, only 301 patients received at least 1 year of treatment while only 876 received at least 6 months of treatment. *Id.* at 7.

The U.S. Clinical Trial was a multi-center study that involved only 152 in-patients with a diagnosis of schizophrenia. This randomized, double-blind placebo-controlled, parallel study compared olanzapine at doses of 1mg/day and 10mg/day with placebo. The acute phase of this clinical trial lasted but 6 weeks. Positive and negative scores on the

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Brief Psychiatric Rating Scale on the 10mg dose were not reported as statistically significant over placebo for any efficacy measurement. *Id.* at 8.

The North American Clinical Trial was a multicenter conducted at 22 sites in the U.S. and Canada that involved 335 patients with a diagnosis of schizophrenia with acute exacerbation. This study compared olanzapine in the dosage ranges of 5.0 ± 2.5 mg/day, 10.0 ± 2.5 mg/day, and 15 ± 2.5 mg/day with haloperidol in the dosage range of 15 ± 5 mg/day and with placebo. The acute phase of this study was also 6 weeks in length although "(T)reatment responders could continue double-blind for up to 12 months." *Id.* at 8. Based on the results from the 6 week acute phase study, olanzapine in the dosage range of 7.5 mg/day to 17.5 mg/day was shown to be effective with respect to "overall psychopathology" and "core positive psychotic psychopathology". *Id.* at 7-8.

The Eastern Hemisphere Clinical Trial was a multicenter study conducted in Europe, South Africa, Israel and Australia involving 431 inpatients with a diagnosis of schizophrenia with acute exacerbation. This randomized, double-blind, active-controlled and parallel study looked at olanzapine 5.0 ± 2.5 mg/day, 10.0 ± 2.5 mg/day and 15.0 ± 2.5 mg/day with one dosage range of haloperidol (15 ± 2.5 mg/day) and olanzapine 1.0 mg/day). The acute phase of this clinical study was 6 weeks in length. There was no statistically significant difference observed in the three dosage ranges of olanzapine as compared to the 1.0 mg/day dosage. In addition there was no statistically significant difference detected when comparing the three olanzapine treatment groups with the haloperidol group. *Id.* at 9

The International Clinical Trial involved 1996 inpatients or outpatients with schizophrenia, schizophreniform disorder or schizoaffective disorder to current therapy.

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This randomized, double-blind, active-controlled, parallel study compared olanzapine (5.0 to 20.0 mg/day) with haloperidol (5.0 to 20.0 mg/day). Again, this was a 6-week active phase of treatment. For the active phase of treatment, the olanzapine treatment group had a statistically greater mean improvement in BPRS total score compared to the haloperidol treatment group. *Id.* at 10. Duggan et al, writing for the Cochrane Library, conducted a meta-analysis of "(A)ll randomised clinical trials comparing olanzapine to placebo or any antipsychotic treatment for those with schizophrenia or schizophreniform psychoses". Duggan L, Fenton M, Dardennes RM, El-Dosoky A, Indran S. *Olanzapine for schizophrenia (Cochrane Review). The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd. Twenty trials were included in this meta-analysis. Attrition from olanzapine versus placebo studies was so great (olanzapine - 61%, placebo - 73% by 6 weeks, RR 0.85 CI 0.7-0.98, NNT 8 CI 5-40) that interpretation of results was problematic. Olanzapine appeared superior to placebo at six weeks for the outcome of 'no important clinical response' (RR 0.88 CI 0.8-0.98, NNT 8 CI 5-27), but trial data regarding negative symptoms were equivocal for this comparison.

Ten studies presented data on short-term follow-up (less than 3 months). Three of these were acute phase studies. Beasley CM Jr, et al. *Olanzapine versus placebo and haloperidol: acute phase results of the North American double-blind olanzapine trial.* Neuropsychopharmacology. 1996;14:111-23; Beasley CM, et al. *Safety of olanzapine.* J Clin Psychiatry. 1997;58 [Suppl 10]:13-7; Tollefson GD, Sanger TM. *Negative symptoms: a path analytic approach to a double-blind, placebo- and haloperidol-controlled clinical trial with olanzapine.* Am J Psychiatry. 1997;154-466-74) lasted 6 weeks with 'responders' entering a 46-week extension. Tran PV, Dellva MA, Tollefson

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GD, Wentley AL, Beasley C Jr , *Oral olanzapine versus oral haloperidol in the maintenance treatment of schizophrenia and related psychoses.* British Journal of Psychiatry 1998;172:499-505. Dellva MA, Tran P, Tollefson GD, Wentley AL, Beasley CM Jr. *Standard olanzapine versus placebo and ineffective-dose olanzapine in the maintenance treatment of schizophrenia.* Psychiatric Servives. 1997;48:1571-77. Nine studies fell into the 'medium term' (3-12 months) category and only one trial fulfilled criterion for 'long-term' (more than one year). Jones B, Crawford AMK, Beasley CM Jr, Tollefson GD. *The acute and long-term effect of olanzapine compared with placebo and haloperidol on serum prolactin concentrations.* Schizophrenia Res. 1998;29(1-2):204.05.

In comparing olanzapine to the other atypical antipsychotic medications, these Cochrane investigators reported that there were no clear differences between olanzapine and typical drugs for the outcome of no important clinical response at 6-8 weeks. Relapse and Clinical Global Impression endpoint score data support the suggestion that olanzapine is not conclusively clinically more effective than older typical drugs.

What is also important to note from the published clinical trials is that most trials only reported adverse events if their incidence was either statistically significant or had a frequency of 10% or greater. This will result in rare adverse effects being ignored. If this policy had been implemented rigorously in other drug trials the agranulocytosis of clozapine and ocular problems associated with thioridazine would have gone unreported.

Furthermore, when evaluating the olanzapine versus placebo it is important to note that "(S)o many people left these studies early (olanzapine 61%, placebo 73%) that all results, except the one of leaving the study early, are so full of assumptions that confident interpretation is impossible." Duggan L, Fenton M, Dardennes RM, El-Dosoky

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A, Indran S. *Olanzapine for schizophrenia (Cochrane Review).* In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd., at 19. Over a six-week period less people left the study early if allocated to olanzapine (61%) than if given placebo (73%, NNT 8 CI 4-40) "but the proportions are enormous". *Id.* Even if this result is secondary to clinical improvement, this degree of loss must suggest that there was some factor within the design of the study that was unacceptable to participants. By one year almost everyone had left the key study in this area making any other data impossible to interpret. Beasley CM Jr, et al. *Olanzapine versus placebo and haloperidol: acute phase results of the North American double-blind olanzapine trial.* Neuropsychopharmacology. 1996;14:111-23.

Conley et al published the results of their study comparing olanzapine to chlorpromazine in the treatment of treatment-resistant schizophrenia. Robert R. Conley, M.D., et al., *Olanzapine Compared With Chlorpromazine in Treatment-Resistant Schizophrenia*, Am J. Psychiatry 1998; 155: 914-920. The numbers of subjects who showed a 20%, 30%, or 40% improvement on their total BPRS scores were not different between the drug groups. The mean weekly total BPRS scores of the patients who completed the study did not differ between the olanzapine group and the chlorpromazine group. No other primary efficacy measures showed a difference between drug groups. Olanzapine-treated patients showed a greater therapeutic response on the BPRS anxiety-depression subscale than did chlorpromazine-treated patients in the last-observation-carried-forward database. However, this effect did not meet the a priori value for significance of 0.01 for a secondary analysis. There were no between-site differences in any of the outcome measures.

The authors stated that the results of this study demonstrate no difference in efficacy between olanzapine and chlorpromazine in the treatment of psychotic symptoms in patients with treatment-resistant schizophrenia. Overall, neither drug group showed a substantial change in their level of psychosis from their pre-randomization baseline, and no differences between groups emerged in the analysis of the primary efficacy variables.

Rosenheck et al conducted a study looking at patients randomly assigned to receive flexibly dosed olanzapine, 5 to 20 mg/day, with prophylactic benztropine, 1 to 4 mg/day; or haloperidol, 5 to 20 mg/day, for 12 months. Robert Rosenheck, M.D., et al., *Effectiveness and Cost of Olanzapine and Haloperidol in the Treatment of Schizophrenia A Randomized Controlled Trial*, JAMA, 2003; 290:2693-2702. The authors stated that although olanzapine has been widely adopted as a treatment of choice for schizophrenia, its long-term effectiveness and costs have not been evaluated in a controlled trial in comparison with a standard antipsychotic drug. The authors hypothesized that olanzapine would outperform haloperidol on 3 primary outcomes, as demonstrated by fewer symptoms, better quality of life, and lower costs in patients with schizophrenia.

Although 177 patients (57.3%) discontinued the assigned study medication because of lack of efficacy, adverse effects, or other reasons (54.1% in the olanzapine group and 60.7% in the haloperidol group) efforts were made to follow up all patients for a full 12 months and to record nonstudy medications; 26.7% of olanzapine discontinuers and 32.1% of haloperidol discontinuers were followed up for the entire 12 months.

This 12-month double-blind study found no statistically or clinically significant advantages of olanzapine for schizophrenia on measures of compliance, symptoms, or overall quality of life, nor did it find evidence of reduced inpatient use or total cost.

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Olanzapine treatment did result in modestly reduced symptoms of akathsia, in less tardive dyskinesia in one secondary analysis, and in small but significant improvements in measures of memory and motor function. The authors noted that cognitive gains with olanzapine were insufficient to improve QOLS functioning or employment earnings. Olanzapine was also associated with more frequent reports of weight gain and with significantly greater total VA costs, ranging from $3000 to $9000 per patient annually.

Perhaps the most unexpected difference in this study was the lack of any significant advantage for olanzapine on measures of retention, termination due to adverse effects, or EPS other than akathsia. The authors concluded that olanzapine does not demonstrate advantages compared with haloperidol (in combination with prophylactic benztropine) in compliance, symptoms, extrapyramidal symptoms, or overall quality of life, and its benefits in reducing akathsia and improving cognition must be balanced with the problems of weight gain, its higher cost and morbidities.

Volvaka et al looked at the use of clozapine, olanzapine, risperidone, and haloperidol in the treatment of patients with chronic schizophrenia and schizoaffective disorder. Volavka, J., et al., *Clozapine, Olanzapine, Risperidone, and Haloperidol in the Treatment of Patients With Chronic Schizophrenia and Schizoaffective Disorder*, Am J Psychiatry 2002; 159:255-262. These authors noted that "clozapine is the established treatment for patients with schizophrenia who do not respond adequately to other antipsychotic medications". The authors indicated that olanzapine was not more effective than chlorpromazine in an 8-week trial of very ill, chronically institutionalized patients with schizophrenia and "because of methodological differences, it is difficult to interpret the results of [the previous] studies and draw conclusions across them in terms of the

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comparative efficacy and safety of the atypical drugs with respect to conventional agents and each other." Geddes et al performed systemic overview and meta-regression analyses of the published randomised controlled trials looking at 12,649 patients in 52 trials. Geddes, J., et al. *Atypical antipsychotics in the treatment of schizophrenia: systemic overview and meta-regression analysis.* BMJ. 2000; 321:1371-1376. They concluded that there was "no clear evidence that atypical antipsychotics are more effective or are better tolerated than conventional antipsychotics" and suggested that "(C)onventional antipsychotics should usually be used in the initial treatment of an episode of schizophrenia unless the patient has previously not responded to these drugs or has unacceptable extrapyramidal side effects."

They found "no difference in pooled efficacy in two trials comparing olanzapine and risperidone". Tran PV, Hamilton SH, Kuntz AJ, Potvin JH, Andersen SW, Beasley C, et al. *Double blind comparison of olanzapine versus resperidone in the treatment of schizophrenia and other psychotic disorders.* J Clin Psychopharmacol; 1997;17: 407-18; Conley RR, Brecher M, Risperidone/Olanzapine Study Group. *Risperidone versus olanzapine in patients with schizophrenic or schizoaffective disorder.* Paris, European College of Neuropsychopharmacology, 1998. (After internal review, Janssen Cilag have re-evaluated the quality of data collection (www.futur.com/CompanyStatement.STM) accessed 30 December 1999). They also found "no reliable evidence of differential effects between atypical antipsychotics". Furthermore, when they controlled for the higher than recommended dose of conventional antipsychotics used in some trials, a modest advantage in favor of atypical antipsychotics in terms of extrapyramidal side effects remains, but the differences in efficacy and overall tolerability disappear,

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suggesting that many of the perceived benefits of atypical antipsychotics are really due to excessive doses of comparator drug used in the trials. "Taking these points into account, we think it inappropriate to advocate the first line use of a new drug without clear evidence of overall superior efficacy or tolerability." Geddes, J., et al. *Atypical antipsychotics in the treatment of schizophrenia: systemic overview and meta-regression analysis.* BMJ. 2000; 321: at 1374.

Davis et al conducted a meta-analysis of the second-generation atypical antipsychotics and indicated that their meta-analysis focused on overall differential efficacy and pointed out that almost all studies have been sponsored by the pharmaceutical industry and that it was possible that bias arose from this source which could be present despite randomized double-blind methods. John M. Davis, M.D., *et al.*, *A Meta-analysis of the Efficacy of Second-Generation Antipsychotics*, Arch Gen Psychiatry. 2003; 60:553-564. Consequently, trials independent of the pharmaceutical industry were recommended.

Bhana et al conducted a study finding that the efficacy of olanzapine was equal to that of fluphenazine. Nila Bhana, *et al., Olanzapine An Updated Review of its Use in the Management of Schizophrenia*, Adis Drug Evaluation, Drugs 2001: 61 (1): 111-161, citing Dossenbach M, *et al., Olanzapine vs fluphenazine-6 weeks treatment of acute schizophrenia* [abstract no, P.2.095]. Eur Neuropsychopharmacol 1997 Sep; 7 Suppl.2:S222. Bhana et al indicated that in 3 studies, olanzapine was shown to be at least as effective as haloperidol against the positive and negative symptoms of schizophrenia. They noted that "[M]ost of the comparative studies of olanzapine and risperidone for the treatment of schizophrenia (published as abstracts and consisting of small randomized

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trials, naturalistic studies, meta-analyses or retrospective reviews) have failed to detect any significant differential effects between the 2 drugs on overall psychopathology."

Furthermore, "[P]reliminary results...from a shorter...controlled, randomized study showed that risperidone 2 to 6 mg/day was superior to olanzapine 5 to 20 mg/day according to the PANSS positive and anxiety/depression subscale scores at week 8, but not at end-point. However, olanzapine and risperidone were similar on the PANSS total score and other subscales."

Tohen et al conducted a study sponsored by Lilly Research Laboratories. There were no significant differences between treatment groups in baseline-to-endpoint mean change in scores on the extrapyramidal symptoms rating scales. Mauricio Tohen, M.D., Dr.P.H., *et al.*, *Olanzapine Versus Divalproex in the Treatment of Acute Mania*, Am J Psychiatry 2002; 159: 1011-1017. Sponsored by Lilly Research Laboratories. There were no statistically significant differences between treatment groups in the incidence rates of potentially clinically relevant changes in vital signs. Patients in the olanzapine treatment group had a significantly larger mean weight gain, compared to the patients in the divalproex treatment group.

However, Zajecka et al indicated that in the Tohen et al trial, while the results suggested that the efficacy of olanzapine was superior to that of divalproex, the divalproex dosages used were lower than those used in other trials. John M. Zajecka, M.D., *et al.*, *A Comparison of the Efficacy, Safety, and Tolerability of Divalproex Sodium and Olanzapine in the Treatment of Bipolar Disorder*, J Clin Psychiatry 2002; 63: 1148-1155.

Zajecka's study showed no significant differences in the efficacy of divalproex and olanzapine for the treatment of bipolar mania. There were no significant differences in efficacy between treatment groups for the subset of subjects displaying psychotic symptoms. While both treatments were associated with weight gain, divalproex was associated with significantly less weight gain than olanzapine. Furthermore, significantly fewer divalproex-than olanzapine-treated subjects reported weight gain as an adverse event. In short, this study suggest that divalproex and olanzpine, when administered in dosages that reflect current clinical practice, demonstrate equivalent efficacy in the treatment of acute mania in bipolar disorder. Divalproex exhibited a more favorable long-term safety and tolerability profile than olanzapine, specifically with respect to weight gain, reported adverse events, and lipid profile.

Simpson et al conducted a 6-week, flexible dose trial to compare the tolerability and efficacy of ziprasidone and olanzapine in acutely ill, recently admitted inpatients with a primary psychiatric diagnosis of schizophrenia or schizoaffective disorder. Their study was a 6-week, multicenter, double-blind, and parallel-design, randomized, controlled trial involving inpatients. George M. Simpson, M.D., *et al., Randomized, Controlled, Double-Blind Multicenter Comparison of the Efficacy and Tolerability of Ziprasidone and Olanzapine in Acutely Ill Inpatients With Schizophrenia or Schizoaffective Disorder*, Am J Psychiatry 2004; 161: 1837-1847.

The results demonstrated that ziprasidone was comparable in efficacy to olanzapine in improving all measures of psychosis, depressive symptoms, and disease severity. Ziprasidone demonstrated efficacy equivalent to olanzapine in controlling

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symptoms of schizophrenia, while being associated with a lower incidence of weight gain and more favorable effects on lipid profile and other metabolic parameters.

Most recently, Buchanan et al examined the comparative efficacy and safety of olanzapine and haloperidol in 63 outpatients with partially responsive schizophrenia in a 16-week double-blind study. Buchanan, R.W. et al. *Olanzapine Treatment of Residual Positive and Negative Symptoms.* Am J Psychiatry 2005;162:124-129.These investigators found that there were no significant differences between the two drugs in their effect on positive or negative symptoms. There were no significant differences between the two treatment groups on measures of social and functional outcome. Olanzapine-treated patients had a significant reduction in extrapyramidal symptoms and subjective measures of stiffness and dry mouth, but the increases in systolic blood pressure and weight gain in olanzapine-treated patients were significantly greater than they were in haloperidol-treated patients.

These investigators concluded that olanzapine has limited differential benefit for either positive or negative symptoms in patients with treatment-resistant schizophrenia and "although olanzapine is associated with fewer extrapyramidal symptoms, other side effects may offset this benefit".

Finally, it is also important to note while evaluating the 'efficacy' of olanzapine that in these trials more people treated with olanzapine reported an increase in appetite compared to those taking conventional antipsychotics, which supports the clinical experience. The data on weight gain is equivocal in the short-term studies and shows a statistically significant difference in the medium term, with those on olanzapine gaining more weight. Duggan L, Fenton M, Dardennes RM, El-Dosoky A, Indran S. *Olanzapine*

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for schizophrenia (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd

VII. CONCLUSION/SUMMARY

As the above recitation of credentials demonstrates, I have studied and written extensively in the fields of schizophrenia and the effects on patients with this illness of the administration of various antipsychotic medications, including olanzapine. The papers which I have authored, co-authored or otherwise contributed to are peer reviewed papers. The research I have conducted has been conducted in accordance known and accepted professional standards in my field.

In addition to treating patients diagnosed with schizophrenia, bipolar disorder and other mood disorders, through consulting work with various pharmaceutical companies, including Eli Lilly and Company, I am aware of the requirements on the part of these companies to properly advise treating doctors of the various side effects, adverse event information and safety concerns that have been discovered during the course of the clinical trial and post marketing processes of these types of drugs. This information can substantially affect the decisions of the treating doctors in their choice of drugs for the treatment of certain psychiatric disorders and in turn substantially affect the outcome of the treatment efforts.

I offer the following opinions concerning the drug olanzapine. The opinions offered are within a reasonable degree of medical probability.

1. There is a direct and indirect causal connection between the administration of olanzapine and certain adverse effects observed in some patients treated with this drug. These adverse affects include, among other things, significant weight gain,

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hyperlipedemia, hyperglycemia, pancreatitis, and the development of diabetes. Moreover, the data indicate that while some of these adverse events may occur with the use of any of the atypical antipsychotic medications, the degree of the adverse effect on some patients using olanzapine is substantially greater than the adverse affects observed in patients on other atypical antipsychotic medications.

2. According to my personal consulting work for the manufacturer of olanzapine, Eli Lilly and Company, including clinical trial investigator, the considerable risk of significant weight gain and its potential adverse effects on patients being given olanzapine was known to Lilly as early as 1995. Studies, including some conducted by Lilly itself, indicate that olanzapine is substantially more likely than other atypical antipsychotic medications to cause weight gain, pancreatitis, hyperglycemia, and diabetes. There is no credible evidence that olanzapine is more efficacious than typical or other atypical antipsychotic medications. Lilly had a duty to notify health care providers and consumers when it knew or had reason to know of the clinically significance of the weight gain to patients who had been prescribed olanzapine, and to warn physicians that olanzapine carries a greater risk of diabetes than typical antipsychotics and all other atypical antipsychotic drugs other than clozapine.

3. It is therefore my opinion that olanzapine should not be used as a first line drug of choice for the treatment of the disorders for which it has been marketed. It is further my opinion that had Lilly provided full disclosure to the treating

physicians of the actual potential consequences to their patients of the use of olanzapine over other atypical antipsychotic medications, and of olanzapine's lack of enhanced efficacy to justify the increased serious risk, a reasonably prudent doctor would not, given the fact that there are choices of typical antipsychotics and other atypical antipsychotics available to treat the same illness for which olanzapine is used, choose olanzapine as the drug of first choice for treatment of any of the illness for which the drug has been marketed.

4. It is further my opinion that Lilly was grossly negligently in allowing physicians to prescribe this drug without necessary and essential information of serious medical complications to a patient population that is already at an elevated risk for the development of diabetes and/or pancreatitis.

William C. Wirshing, M.D.

31 Jan 2007
Date

CONSENSUS STATEMENT

Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes

American Diabetes Association
American Psychiatric Association
American Association of Clinical Endocrinologists
North American Association for the Study of Obesity

Antipsychotic medications are an important component in the medical management of many psychotic conditions. With the introduction of the second-generation antipsychotics (SGAs) over the last decade, the use of these medications has soared. Although the SGAs have many notable benefits compared with their earlier counterparts, their use has been associated with reports of dramatic weight gain, diabetes (even acute metabolic decompensation, e.g., diabetic ketoacidosis [DKA]), and an atherogenic lipid profile (increased LDL cholesterol and triglyceride levels and decreased HDL cholesterol).

Because of the close associations between obesity, diabetes, and dyslipidemia and cardiovascular disease (CVD), there is heightened interest in the relationship between the SGAs and the development of these major CVD risk factors. To gain a better understanding of this relationship, the American Diabetes Association, the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity convened a consensus development conference 19–21 November 2003 on the subject of antipsychotic drugs and diabetes. An eight-member panel heard presentations from 14 experts drawn from the areas of psychiatry, obesity, and diabetes. Presentations were also made by a representative from the U.S. Food and Drug Administration (FDA) and by representatives from the AstraZeneca, Bristol-Myers Squibb, Janssen, Lilly, and Pfizer pharmaceutical companies. In addition, before the conference, the consensus panel was given copies of most of the known peer-reviewed, English language clinical studies published in this area, as well as additional articles from animal studies; other papers and abstracts were reviewed at the conference.

With this information, the panel developed a consensus position on the following questions:

1. What is the current use of antipsychotic drugs?
2. What is the prevalence of obesity, prediabetes, and type 2 diabetes in the populations in which the SGAs are used?
3. What is the relationship between the use of these drugs and the incidence of obesity or diabetes?
4. Given the above risks, how should patients be monitored for the development of significant weight gain, dyslipedemia, and diabetes, and how should they be treated if diabetes develops?
5. What research is needed to better understand the relationship between these drugs and significant weight gain, dyslipedemia, and diabetes?

1. WHAT IS THE CURRENT USE OF ANTIPSYCHOTIC DRUGS?— Antipsychotic medications (Table 1) are the mainstay of treatment for psychotic illnesses and are also widely used in many other psychiatric conditions. Introduced ~50 years ago, these medications have helped millions of people manage their symptoms. For people who respond well, antipsychotics can mean the difference between leading an engaged, fulfilling community life and being severely disabled.

The first-generation antipsychotics (FGAs) are still widely available and are effective at treating positive symptoms of psychosis, such as hallucinations and delusions. FGAs do not, however, adequately alleviate many other common and important aspects of psychotic illness, such as negative symptoms (e.g., withdrawal, apathy, poverty of speech), cognitive impairment, and affective symptoms. In addition, all FGAs can produce significant extrapyramidal side effects at clinically effective doses. These side effects, which include dystonic reactions, drug-induced parkinsonism, akathisia, and tardive dyskinesia, can make treatment intolerable for some people, leading to subjective distress, diminished function, stigma, and nonadherence.

The effort to find more effective medications with fewer and less-severe side effects led to the development of the SGAs, often referred to as the "atypical antipsychotics." SGAs have fewer or no extrapyramidal side effects at clinically effective doses. Many of these newer medications are also more effective than the older agents at treating the negative, cognitive, and affective symptoms of psychotic illnesses.

The six currently available SGAs vary in their efficacy, formulation, biochemistry, receptor binding, and side effect profiles. One of them, clozapine, is clearly the most effective antipsychotic. However, clozapine is only indicated after other medications have failed or in patients at high risk for suicidal behavior, largely because it can cause agranulocystosis.

In general, SGAs are better tolerated and more effective than the FGAs. Aside from clozapine, they have become the first-line agents for their indicated use and

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Abbreviations: CVD, cardiovascular disease; DKA, diabetic ketoacidosis; FDA, Food and Drug Administration; FGAs, first-generation antipsychotics; SGAs, second-generation antipsychotics.

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Table 1—Antipsychotic medications

	Generic name	Trade name	Year approved
Commonly used FGAs	Chlorpromazine	Thorazine	—
	Perphenazine	Trilafon	—
	Trifluoperazine	Stelazine	—
	Thiothixene	Navane	—
	Haloperidol	Haldol	—
	Fluphenazine	Prolixin	—
SGAs	Clozapine	Clozaril	1989
	Risperidone	Risperdal	1993
	Olanzapine	Zyprexa	1996
	Quetiapine	Seroquel	1997
	Ziprasidone	Geodon	2001
	Aripiprazole	Abilify	2002

are increasingly being used off-label. In current practice, people who are likely to be treated with an SGA include those with schizophrenia spectrum disorders, bipolar disorder, dementia, psychotic depression, autism, and developmental disorders and, to a lesser extent, individuals with conditions such as delirium, aggressive behavior, personality disorders, and posttraumatic stress disorder. These psychiatric conditions are common and often require lifelong treatment. In the U.S., the prevalence of schizophrenia and related conditions is ~ 1%, the prevalence of bipolar disorders is ~ 2%, and the prevalence of major depression is ~ 8%. The SGAs are therefore widely used medications, and their use has important public health ramifications.

2. WHAT IS THE PREVALENCE OF OBESITY, PRE-DIABETES, AND TYPE 2 DIABETES IN THE POPULATIONS IN WHICH THE SGAs ARE USED?

— It is difficult to determine whether the prevalence of these metabolic disorders is increased in these psychiatric populations independent of drug treatment. Most of the available data are derived from studies of individuals with schizophrenia, and even in this condition, the evidence is very limited. Data from most studies suggest that the prevalence of both diabetes and obesity among individuals with schizophrenia and affective disorders is ~1.5–2.0 times higher than in the general population. Many characteristics of people with schizophrenia, such as sedentary behavior, may contribute to the apparently higher prevalence of metabolic abnormalities. However, none of these studies controlled for all of the major diabetes risk factors. For example, BMI and family history of diabetes were rarely determined, nor were the control populations appropriately matched for these and other variables. Thus, it is unclear whether psychiatric conditions per se, independent of other known diabetes risk factors, account for the increased prevalence.

There are limited data evaluating the metabolic profile and diabetes risk of drug-naïve subjects with schizophrenia. In a small cohort of adults with schizophrenia untreated with medications, visceral fat content (which is correlated with insulin resistance) was threefold higher than in age- and BMI-matched control subjects. In another study, the same investigators found that drug-naïve patients presenting with their first episode of schizophrenia had an increased prevalence of impaired fasting glucose, were more insulin resistant, and had higher plasma levels of glucose, insulin, and cortisol than did matched control subjects.

Overall, the limited amount of epidemiological data suggest an increased prevalence of obesity, impaired glucose tolerance, and type 2 diabetes in people with psychiatric illness. Whether this is a function of the illness itself versus its treatment is unknown. Studies using the proper diagnoses of glucose intolerance and more complete risk factor characterization are necessary in order to resolve this issue.

3. WHAT IS THE RELATIONSHIP BETWEEN THE USE OF THESE DRUGS AND THE INCIDENCE OF OBESITY OR DIABETES?

— Recognition of an association between SGAs and diabetes was first derived from case reports of severe, sometimes fatal, acute diabetic decompensation, including DKA. Subsequent drug surveillance and retrospective database analyses suggest there is an association between specific SGAs and both diabetes and obesity. This potential relationship is of considerable clinical concern because obesity and diabetes are important risk factors for CVD, and the relative risk of CVD mortality is significantly greater in people with psychiatric disorders than in the general population. High rates of smoking and physical inactivity may also contribute to the excess mortality. Therefore, if SGA therapy further increases the risk for obesity and type 2 diabetes, this should be of major clinical concern.

Although there are significant shortcomings in many of the studies examining the relationships between the SGAs and obesity or diabetes, clear-cut trends can be identified.

Obesity

There is considerable evidence, particularly in patients with schizophrenia, that treatment with SGAs can cause a rapid increase in body weight in the first few months of therapy that may not reach a plateau even after 1 year of treatment. There is, however, considerable variability in weight gain among the various SGAs (Table 2). At 10 weeks of therapy, estimated average weight gain with drug treatment compared with placebo varies from ~0.5 to 5.0 kg. Limited data suggest that in humans, most of the weight gained

Table 2—*SGA's and metabolic abnormalities*

Drug	Weight gain	Risk for diabetes	Worsening lipid profile
Clozapine	+++	+	+
Olanzapine	+++	+	+
Risperidone	++	D	D
Quetiapine	++	D	D
Aripiprazole*	+/−	−	−
Ziprasidone*	+/−	−	−

+ = increase effect; − = no effect; D = discrepant results. *Newer drugs with limited long-term data.

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is fat. Data derived from a canine model indicated that certain SGAs increase total visceral fat mass and intrahepatic lipid content.

The mechanism(s) responsible for weight gain associated with SGA therapy are unknown. Weight gain occurs when more energy is ingested than is expended. Therefore, weight gain is due to increased energy intake, decreased energy expenditure, or both. Even a small, chronic imbalance between energy intake and expenditure can lead to large changes in body weight over time. For example, ingestion of ~500 kcal/day more than is expended can account for the largest average weight gain reported with SGA therapy (4.5 kg at 10 weeks). This amount of daily increase in energy intake represents the calories in a normal-size candy bar plus a soda or in an ice cream dessert. Hunger and satiety may be altered in people taking SGAs because of the known binding affinities of these drugs to serotonin, norepinephrine, dopamine, and particularly histamine-H1 receptors. All of these receptors have been implicated in the control of body weight.

Weight gain and changes in body composition may account for many of the purported metabolic complications associated with SGA therapy, e.g., insulin resistance, pre-diabetes, diabetes, and dyslipidemia. A possible direct effect of SGAs on β-cell function and insulin action in liver and muscle tissue could also be involved, as discussed below.

Diabetes

Numerous case reports have documented the onset or exacerbation of diabetes, including the occurrence of hyperglycemic crises, following initiation of therapy with many of the SGAs.

Several of these events occurred within a few weeks of initiating drug treatment. In some, but not all cases, hyperglycemia promptly resolved after the medication was discontinued. Several reports documented recurrent hyperglycemia after another challenge with the same drug. Additional cases of diabetes or hyperglycemia have been reported through MedWatch into the FDA's Adverse Event Reporting System.

Large retrospective cohort studies have been reported that estimate the prevalence of diabetes in patients using SGAs. These reports relied on a variety of methods for determining the diagnosis of diabetes, such as ICD-9 codes and data on prescriptions for diabetes medications. In addition, several cross-sectional studies of patients taking different SGAs, "switch studies" of patients changed from one medication to another, and one prospective randomized controlled trial evaluating SGA therapy on parameters of insulin sensitivity and glycemic control have been conducted. Despite limitations in study design, the data consistently show an increased risk for diabetes in patients treated with clozapine or olanzapine compared with patients not receiving treatment with FGAs or with other SGAs. The risk in patients taking risperidone and quetiapine is less clear; some studies show an increased risk for diabetes, while others do not. The two most recently approved SGAs, aripiprazole and ziprasidone, have relatively limited epidemiological data, but available clinical trial experience with these drugs has not shown an increased risk for diabetes (Table 2).

One possible mechanism for hyperglycemia is impairment of insulin action (i.e., insulin resistance). Drug-induced insulin resistance may occur because of weight gain or a change in body fat distribution or by a direct effect on insulin-sensitive target tissues. Patients treated with olanzapine and clozapine have higher fasting and postprandial insulin levels than patients treated with FGAs, even after adjusting for body weight. To date, studies in humans have not shown adverse effects of any antipsychotic medication on β-cell function, but this issue has not been adequately studied in individuals with psychiatric illnesses.

Dyslipidemia

An additional related consequence of SGA use is their effect on serum lipids. Although the data are limited, the available evidence suggests that changes in serum lipids are concordant with changes in body weight. Clozapine and olanzapine, which produce the greatest weight gain, are associated with the greatest increases in total cholesterol, LDL cholesterol, and triglycerides and with decreased HDL cholesterol. Aripiprazole and ziprasidone, which are associated with the least amount of weight gain, do not seem to be associated with a worsening of serum lipids. Risperidone and quetiapine appear to have intermediate effects on lipids (Table 2).

Risk-benefit assessment

Despite the adverse effects cited above, a number of factors should be considered when choosing among the antipsychotic medications. These include the nature of the patient's psychiatric condition, specific target signs and symptoms, past history of drug response (both therapeutic and adverse), patient preference, history of treatment adherence, medication effectiveness, psychiatric and medical comorbidities, availability of appropriate formulations (e.g., fast-dissolving oral, short- or long-acting intramuscular), need for special monitoring, and cost of and access to medications. Nonetheless, the risks of obesity, diabetes, and dyslipidemia have considerable clinical implications in this patient population and should also influence drug choice.

Even for those medications associated with an increased risk of metabolic side effects, the benefit to specific patients could outweigh the potential risks. For example, clozapine has unique benefits for treatment-refractory patients and those at significant risk for suicidal behavior. Since treatment response in many psychiatric conditions is heterogeneous and unpredictable, physicians and patients can benefit from the availability of a broad array of different therapeutic agents.

4. GIVEN THE ABOVE RISKS, HOW SHOULD PATIENTS BE MONITORED FOR THE DEVELOPMENT OF SIGNIFICANT WEIGHT GAIN, DYSLIPIDEMIA, AND DIABETES, AND HOW SHOULD THEY BE TREATED IF DIABETES DEVELOPS?—

Given the serious health risks, patients taking SGAs should receive appropriate baseline screening and ongoing monitoring. Clinicians who prescribe SGAs for patients with psychiatric illnesses should have the capability of determining a patient's height and weight (BMI) and waist circumference. These values should be recorded and tracked for the duration of treatment. Clinicians should also encourage patients to monitor and chart their own weight. It is particularly important to monitor any alteration in weight following a medication change. The patients' psychiatric illness should not discourage clinicians from addressing the metabolic

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Table 3—*Monitoring protocol for patients on SGAs**

	Baseline	4 weeks	8 weeks	12 weeks	Quarterly	Annually	Every 5 years
Personal/family history	X					X	
Weight (BMI)	X	X	X	X	X		
Waist circumference	X					X	
Blood pressure	X			X		X	
Fasting plasma glucose	X			X			X
Fasting lipid profile	X			X			

*More frequent assessments may be warranted based on clinical status.

complications for which these patients are at increased risk.

Baseline monitoring

The panel recommends that baseline screening measures be obtained before, or as soon as clinically feasible after, the initiation of any antipsychotic medication (Table 3). These include

- Personal and family history of obesity, diabetes, dyslipidemia, hypertension, or cardiovascular disease
- Weight and height (so that BMI can be calculated)
- Waist circumference (at the level of the umbilicus)
- Blood pressure
- Fasting plasma glucose
- Fasting lipid profile

These assessments can determine if the patient is overweight (BMI 25.0–29.9) or obese (BMI ≥30), has pre-diabetes (fasting plasma glucose 100–125 mg/dl) or diabetes (fasting plasma glucose ≥126 mg/dl), hypertension (blood pressure >140/90 mmHg), or dyslipidemia. If any of these conditions are identified, appropriate treatment should be initiated. Psychiatrists should not hesitate to refer the patient to the appropriate health care professional or specialist knowledgeable about these disorders.

The panel recommends that nutrition and physical activity counseling be provided for all patients who are overweight or obese, particularly if they are starting treatment with an SGA that is associated with significant weight gain. Referral to a health care professional or program with expertise in weight management may also be appropriate.

Health professionals, patients, family members, and caregivers should be aware of the signs and symptoms of diabetes and especially those associated with the acute decompensation of diabetes such as DKA (Table 4). The latter is a life-threatening condition and always requires immediate treatment. Patients, family members, and caregivers also need to know that treatment with some SGAs may be associated with significant weight gain and a heightened risk of developing diabetes and dyslipidemia. For patients with, or at higher risk for, diabetes and in those treated with other medications that may increase these risks (e.g., valproate, lithium, Depo-Provera), it may be preferable to initiate treatment with an SGA that appears to have a lower propensity for weight gain and glucose intolerance (Table 2). Potential for weight gain should also be considered in the choice of other psychiatric and nonpsychiatric medications.

Table 4—*DKA clinical presentation*

Rapid onset of:
- Polyuria, polydipsia
- Weight loss
- Nausea, vomiting
- Dehydration
- Rapid respiration
- Clouding of sensorium, even coma

Follow-up monitoring

The patient's weight should be reassessed at 4, 8, and 12 weeks after initiating or changing SGA therapy and quarterly thereafter at the time of routine visits (Table 3). If a patient gains ≥5% of his or her initial weight at any time during therapy, one should consider switching the SGA. In such a situation, the panel recommends cross-titration to be the safest approach; abrupt discontinuation of an antipsychotic drug should generally be avoided. When switching from one antipsychotic drug to another, it is preferable to discontinue the current medication in a gradual fashion. The profile of the subsequent drug will determine the initial dose and escalation strategy. Particular consideration should be given before discontinuing clozapine because of the potential for serious psychiatric sequelae.

Fasting plasma glucose, lipid levels, and blood pressure should also be assessed 3 months after initiation of antipsychotic medications. Thereafter, blood pressure and plasma glucose values should be obtained annually or more frequently in those who have a higher baseline risk for the development of diabetes or hypertension. In those with a normal lipid profile, repeat testing should be performed at 5-year intervals or more frequently if clinically indicated.

Although limited data are available in children and adolescents regarding the risks of diabetes when SGAs are given, these patients should have their height, in addition to weight, measured at regular intervals and their BMI calculated. BMI percentile adjusted for age and sex should be used to determine if excessive weight gain has occurred, and if present, a change in therapy should be considered.

For people who develop worsening glycemia or dyslipidemia while on antipsychotic therapy, the panel recommends considering switching to an SGA that has not been associated with significant weight gain or diabetes (Table 2). All patients with diabetes should be referred to an American Diabetes Association–recognized diabetes self-management education program, if available. Referral to a clinician with experience treating people with diabetes is recommended. These patients should carry diabetes identification.

Immediate care or consultation is required for patients with symptomatic or severe hyperglycemia (glucose values ≥300 mg/dl), symptomatic hypoglycemia, or glucose levels ≤60 mg/dl, even in the absence of symptoms. The presence of

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symptoms of DKA (Table 4), requires immediate evaluation and treatment.

Blood pressure, lipid, and glycemic goals of therapy for people with diabetes apply equally to those who also have psychiatric disorders. However, all goals need to be individualized. The benefits and risks of different therapeutic agents used in the treatment of diabetes and its comorbidities should be considered in the context of the patient's psychiatric condition and treatment.

In summary, the panel recommends the following:

- Consideration of metabolic risks when starting SGAs
- Patient, family, and care giver education
- Baseline screening
- Regular monitoring
- Referral to specialized services, when appropriate

5. WHAT RESEARCH IS NEEDED TO BETTER UNDERSTAND THE RELATIONSHIP BETWEEN THESE DRUGS AND SIGNIFICANT WEIGHT GAIN, DYSLIPIDEMIA, AND DIABETES?— Evidence for weight gain and abnormalities of glucose and lipid metabolism in patients taking SGAs is in part derived from case-control studies, pharmacovigilance (e.g., through MedWatch), and database reviews. Many of these studies suffer from their retrospective nature, heterogeneity of methodology, selection or ascertainment bias, and absence of appropriate or well-characterized control subjects. Comparison studies among SGAs are also limited by relatively short periods of study, by failure to control for a possible treatment sequence bias in "switchover" studies, and by not always using clinically equivalent dosages of the medications.

Trials with SGAs should be randomized and controlled, preferably using drug-naive subjects. Weight gain and measures of glucose and lipid metabolism should be thoroughly evaluated. Study subjects should be well-characterized in terms of their baseline risk factors for diabetes, obesity, and lipid disorders and their degree of baseline impairment in insulin sensitivity and β-cell function. The duration of exposure to the various SGAs should be carefully controlled. Future research studies should focus on the following:

- Baseline body composition in untreated patients with psychiatric disorders and changes that occur during treatment with SGAs need to be better characterized. This would include measures of fat versus fat-free mass and visceral and subcutaneous adipose stores, using valid methods to measure body fat (e.g., magnetic resonance imaging, computed tomography, dual-energy X-ray absorptiometry).
- The contribution of altered neuroendocrine function (e.g., hypothalmic-pituitary-adrenal axis activation) to alterations in body composition and abnormalities in glucose and lipid metabolism needs further study to distinguish the acute effects of stress from the underlying disease process.
- Studies are needed that examine glucose and lipid metabolism as they relate to alterations in insulin sensitivity in peripheral and hepatic tissues (e.g., euglycemic-hyperinsulinemic clamp with labeled glucose infusions), alterations in β-cell function (hyperglycemic clamp or frequently sampled intravenous glucose tolerance test), and alterations in lipid metabolism (using tracer infusions).
- Large prospective studies should be conducted to identify baseline and early treatment factors that predict the later occurrence of abnormalities in body weight and composition and disorders of glucose and lipid metabolism during treatment with these drugs.
- Additional studies are needed to identify whether there are baseline characteristics that predict acute, life-threatening complications (e.g., DKA, pancreatitis).
- Additional data are needed to determine whether the risks of therapy are increased in certain ethnic groups (e.g., African Americans).
- Studies determining the effect of SGAs in various psychiatric disorders are needed to clarify the disease-related risk for the development of weight gain and metabolic disturbances.
- Alterations in energy intake and expenditure as contributors to weight gain in the psychiatric population and how these processes are altered by treatment with SGAs should be studied.
- Studies are needed to determine whether the disorders of body weight and glucose and lipid metabolism are due to central nervous system or peripheral tissue actions of the SGAs. Valuable information on the direct effects of SGAs on different body tissue compartments might be obtained from studies in appropriate animal models.
- Studies of the genetic markers that are associated with, and may be causally related to, the metabolic disturbances occurring in treated patients with psychiatric disorders (e.g., 5-HT_{2C}, histamine-H1 receptor alleles) are needed.

SUMMARY— The SGAs are of great benefit to a wide variety of people with psychiatric disorders. As with all drugs, SGAs are associated with undesirable side effects. One constellation of adverse effects is an increased risk for obesity, diabetes, and dyslipidemia. The etiology of the increased risk for metabolic abnormalities is uncertain, but their prevalence seems correlated to an increase in body weight often seen in patients taking an SGA. Direct drug effects on β-cell function and insulin action could also be involved, since there is insufficient information to rule out this possibility. In the general population, being overweight or obese also carries a much higher risk of diabetes and dyslipidemia.

These three adverse conditions are closely linked, and their prevalence appears to differ depending on the SGA used. Clozapine and olanzapine are associated with the greatest weight gain and highest occurrence of diabetes and dyslipidemia. Risperidone and quetiapine appear to have intermediate effects. Aripiprozole and ziprasidone are associated with little or no significant weight gain, diabetes, or dyslipidemia, although they have not been used as extensively as the other agents.

The choice of SGA for a specific patient depends on many factors. The likelihood of developing severe metabolic disease should also be an important consideration. When prescribing an SGA, a commitment to baseline screening and follow-up monitoring is essential in order to mitigate the likelihood of developing CVD, diabetes, or other diabetes complications.

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APPENDIX

Consensus panel

Eugene Barrett, MD, PhD, Chair; Lawrence Blonde, MD, Stephen Clement, MD, John Davis, MD, John Devlin, MD, John Kane, MD, Samuel Klein, MD, William Torrey, MD.

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Presenters at the conference

David Allison, PhD, Richard Bergman, PhD, John Buse, MD, PhD, Patrizia Cavazzoni, MD, Fred Fiedorek, MD, Rohan Ganguli, MD, Andrew Greenspan, MD, David Kendall, MD, Ron Leonge, MD, Antony Loebel, MD, Patrick Lustman, PhD, Herbert Meltzer, MD, John Newcomer, MD, Judy Racoosin, MD, Bryan Roth, MD, Michael Sernyak, MD, Jogin Thakore, MB, Donna Wirshing, MD, William Wirshing, MD.

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Lilly

Memo

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285
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Neuroscience Products

July 1, 2002

Dr. J. Lechleiter
Mr. G Mayr
cc: Mr. A. Mascarenhas

JAPAN TRIP SUMMARY – JUNE 23-27, 2002

This is a summary of issues and proposed actions in follow up to our previous update on Japan. It is clear that the impact of the label change in Japan has been very profound. We concluded we have lost substantial ground and trust in our relationships with the MHLW. Market research shows we have also lost quite a bit of credibility with prescribers and opinion leaders, basically because they felt left in the dark with what they perceived as the late sharing of safety information. As a result, there has been a 75% drop in new patients who are being put on the drug, and a continuing fairly high drop-out rate. That's going to lead to a significant performance impact, probably over and above the 10% assumed on the sales line in the short term, although we think we will be able to stem the tide and turn this around.

Another area of concern is in the sales force. As a result of the label changes, there is substantial lack of alignment and integration in the internal organization. There is a disparity of views on how to address the safety issues and how to integrate marketing, sales, market research, medical, regulatory, etc. Andrew Mascarenhas is staying very close to this himself in the short term, and is considering making a change in the business unit leadership role to get a more integrative leader in place. We have pointed this out to the Japanese leadership team and gotten agreement that obtaining enhanced internal integration is crucial. For the time being, he will take personal responsibility for leading that integration effort.

A further issue is team motivation and turnover in the sales organization and lack of trust both from a sales force and a customer level. We have recommended, in line with the affiliate's proposal, to adjust promotional strategy to reflect the reality of the new label in Japan, enhance confidence by our message for the appropriate use of the product within the label, and point out how to specifically address concerns about hyperglycemia and the potential use of the product in patients with diabetes. We need to also revise our forecast for the year to reflect the post label change environment and discuss how to communicate it to the sales force because it is very unlikely the affiliate will make plan. This is an issue that needs to be resolved with sales management very quickly.

Exhibit 6, Page 1 of 1
SOA Opposition to Lilly
Motion for Summary Judgment
Case No. 3AN-06-05630 CI
Zyprexa MDL 1596: Confidential-Subject to Protective Order
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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA, Plaintiff, vs. ELI LILLY AND COMPANY, Defendant.	)	Case No. 3AN-06-5630 CIV

NOTICE OF FILING PLEADING AND EXHIBITS UNDER SEAL

On this date the State of Alaska is filing a pleading titled "Plaintiff's Response to Defendant's Motion to Compel Discovery." Because one or more exhibits filed with these pleadings may be confidential documents under the Court's April 6, 2007 oral ruling, the State of Alaska is submitting this pleading and the attached exhibits under seal.

See Judge Rindner's 6/13/08 order page 23 and 24 #23 documents unsealed

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Lmade 8/11/08

008301

DATED this 20 day of December, 2007.

FELDMAN ORLANSKY & SANDERS
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BY _____
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Certificate of Service
I hereby certify that a true and correct copy of **Notice of Filing Pleading and Exhibits Under Seal** was served by messenger on:

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008302

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Case No. 3AN-06-05630 CI
	)	
ELI LILLY AND COMPANY,	)	
	)	
Defendant.	)	
	)	

PLAINTIFF'S RESPONSE TO DEFENDANT'S MOTION TO COMPEL DISCOVERY

I. INTRODUCTION

Eli Lilly and Company has filed a Motion to Compel which seeks further responses to its Fourth Interrogatories and Requests for Production. Those discovery requests seek specific evidence underlying the State's claims brought pursuant to the Unfair Trade Practices and Consumer Protection Act ("UTPCPA").

First, the State does not agree it has to provide Lilly with a detailed evidentiary roadmap of its theories of recovery at this juncture of the case, and it has responded with the general nature of the proof underlying its claims that it will present at trial. Second, the immediate necessity of some of the information Lilly seeks that is specific to the State's damages under the UTPCPA is obviated by this Court's recent order bifurcating the trial of this case into liability and damages phases. Finally, much of the discovery

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relevant to these issues is in fact ongoing as pointed out by Lilly in its motion, and the delay in the progress of that discovery has been brought about by Lilly itself.

Notwithstanding these objections, the State will provide further responsive information as noted below. However, the State reserves the right to supplement its discovery responses when it receives and has had a chance to analyze all relevant discovery still due from Lilly underlying the State's claims.

II. ARGUMENT

In response to Lilly's First Interrogatories and Requests for Production, the State provided a general description of the kinds of proof it would offer underlying its claims in this case. In response to Lilly's Fourth Interrogatories and Requests for Production, the State provided a description of similar information. What Lilly apparently seeks is a recitation of each piece of evidence the State intends to offer on its UTPCPA claims at the trial of this case.

The State does not agree that it must provide Lilly with the particular documents and testimony it will rely on at trial on particular issues at this juncture, as this invades the mental impressions, conclusions, opinions and legal theories of counsel. Further, to the extent the discovery Lilly seeks focuses on damages – i.e., the specific number of violations of the UTPCPA – it is entirely unnecessary for Lilly to have this information immediately in light of the Court's recent bifurcation order. Most importantly, the evidence is incomplete at this point because of Lilly's refusal to produce meaningful

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discovery in response to the State's discovery requests. The Court will recall that Lilly delayed the production of virtually any such evidence until ordered by the Discovery Master to produce it. Even when producing the evidence in response to the Court's Order, Lilly has done so in a way to render it as meaningless as possible.[1] Additionally, at Lilly's request, key depositions regarding such evidence have been delayed.[2] For these reasons, the State respectfully suggests it should not be compelled at this time to provide more specific responses to Lilly's discovery requests than those contained herein.[3]

As a practical matter, the parties must exchange deposition designations and exhibits pursuant to the Court's pretrial order in January and February 2008. At that time, Lilly will know precisely what testimonial and documentary evidence the State will be using to prove its case. At present, the State reserves the right to use any and all evidence produced by any party in discovery in this case or in the Zyprexa Multidistrict Litigation ("MDL"). As for the specific evidence in support of its UTPCPA claims, the State provides the following by way of additional response.

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[1] Exhibit 1, Memorandum in Support of Plaintiff's Renewed Motion to Compel and Motion for Sanctions, *State of Alaska v. Eli Lilly and Company*, Case No. 3AN-06-5630 CI, December 11, 2007, at 2-4.

[2] Exhibit 2, Letter of Christiaan A. Marcum to Eric Rothschild dated December 3, 2007.

[3] In apparent acknowledgment that what it seeks at this time is premature, Lilly alternatively requests in its motion that the State be compelled to respond "after the State's completion of discovery." Lilly Motion to Compel at 6.

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A. Evidence of Lilly conduct in violation of the UTPCPA previously disclosed.

On several occasions, the State has provided Lilly with evidence it proposes to use to prove Lilly's conduct violated the UTPCPA. The State provided a recitation of facts in response to one of Lilly's first interrogatories early on in the litigation.[4] Further, the State provided an extensive "backgrounder" of facts based upon documentary evidence developed in the MDL.[5] The facts and documents referenced in the "backgrounder" provide extensive evidence of Lilly's conduct nationwide which also form the basis of violations of the UTPCPA in Alaska. While the State has alleged specific statutory violations of the UTPCPA, as indicated in its responses to Lilly's interrogatories, the evidence the State intends to present revolves around several general areas of misconduct: (1) Lilly's minimization of the magnitude and hazards of weight gain with Zyprexa; (2) Lilly's failure to warn of and outright denial of a causal relationship between Zyprexa and hyperglycemia or diabetes; (3) Lilly's claim that hyperglycemia or diabetes occurred with Zyprexa use at rates comparable to other antipsychotic medications; and (4) Lilly's promotion of Zyprexa as safe and efficacious for uses not indicated on its labeling – e.g., for "complicated mood disorders." The State has alleged from the beginning of the litigation that Lilly's conduct in Alaska would be similar to that

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[4] Exhibit 3, Plaintiff's Responses to Defendant's First Set of Interrogatories, at 5-8.

[5] Exhibit 4, Plaintiff's Zyprexa Backgrounder, *State of Alaska v. Eli Lilly and Company*, Case No. 3AN-06-5630 CIV, May 25, 2007, at 1.

nationwide. The State has been able to develop evidence – and is continuing to do so – of Lilly's conduct in Alaska that clearly mirrors the evidence from the MDL discovery that the State has previously alleged violates the UTPCPA.

B. Evidence of Lilly conduct in Alaska in violation of the UTPCPA.

There is evidence of a carefully orchestrated, company-wide policy of engaging in the general conduct noted above. That evidence is plentiful in the MDL discovery cited in the State's "backgrounder." It is clear that Alaska-based Lilly representatives were engaging in that same conduct. Perhaps the most telling evidence of this comes from the sampling of 4,000 "call notes" produced by Lilly to date.[6] In the call notes produced by Lilly, all four of the general categories of misconduct enumerated above are well-documented.

There are many instances of Zyprexa sales representatives minimizing the magnitude and risks of weight gain on Zyprexa. For example, Alaska sales representatives told physicians that weight gain was "manageable," provided "strategies" and "solutions" for combating weight gain, and generally touted Zyprexa's "superior" or "broad spectrum" efficacy as a benefit which outweighed the risk of weight gain. This conduct occurred regularly from 1999 to 2004, a time during which Lilly acknowledged

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[6] A "call note" is a business record which contemporaneously details a Lilly sales representative's visit to a physician. Lilly was supposed to produce a random sample of 10 percent of its call notes to the State. However, Lilly has refused to produce a single call note generated after August of 2004 despite the fact that its liability for unfair trade practices and failure to warn persists to the present day. The State's Motion to Compel filed on December 11, 2007 (Exhibit 1) seeks production of call notes up to the present.

internally that it did not know how to effectively manage weight gain, that weight loss programs worked only five percent of the time in healthy – i.e., mentally stable – volunteers, that it was actively attempting to "minimize the liability of weight gain while at the same time increasing the focus on Zyprexa's superior efficacy," and that it would be "ludicrous" to state that some patients who gained clinically significant weight on Zyprexa would not be at long-term increased cardiac risk as a result.[7]

Lilly's Alaska sales representatives also misrepresented to physicians on numerous occasions that there was no causal relationship between Zyprexa and diabetes, or between weight gain on Zyprexa and diabetes. These detailing visits occurred between 2000 and 2004, coming at a time when the company was attempting to "eliminate this risk [diabetes] from the risk/benefit equation."[8] It is clear from the call notes that when Lilly representatives shared diabetes information with physicians in Alaska, it was the same tortured data claiming there was no causal link between Zyprexa and diabetes. Sales representatives in Alaska even used a "Q&A" letter from chief Lilly scientist Dr. Alan Breier, which, when distributed internally, admitted that Zyprexa-induced weight gain was a substantial contributing factor in pushing some patients into diabetes, but

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[7] Exhibit 4, at 14-15.

[8] *Id.*, at 14. The State believes that production of call notes after 2004 will demonstrate that Lilly engaged in such misconduct up to the present.

when placed into final form for distribution to physicians toed the company line that there was no causal link between Zyprexa and diabetes.[9]

Lilly sales representatives also used the "comparable rates" message with Alaska physicians. While the name of the message may have changed over time, the thrust remained the same: that diabetes occurred in other antipsychotics at rates comparable to Zyprexa. The two-fold purpose of the message was to "reduce the perception that diabetes is specifically linked to Zyprexa" and to "eliminate this risk from the risk/benefit equation."[10] The message was delivered with frequency to Alaska physicians, beginning in 2001 and continuing through at least January 2004.[11] However, at all times Lilly had relevant information belying the "comparable rates" message that it refused to share with physicians. Even after Lilly was required to change its label in September 2003, Lilly continued to trumpet the message to physicians – this time referring to it as "equal footing" – to minimize the negative effect of the label change on Zyprexa.[12] Not only was this message belied by available data – a point made clearly in 2004 by the ADA Consensus Statement, which ranked the atypicals by weight gain and diabetes risk – but Lilly was forced in October of this year to acknowledge in a revised Zyprexa warning

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[9] *Id.*, at 19-20.

[10] *Id.*, at 14.

[11] The State has every reason to believe this message was repeated beyond 2004, but as noted herein, Lilly has not produced any documents beyond that date.

[12] The message is also known at times as "no consistent differences."

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that "the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics."[13] Not only do internal company documents cited in the State's "backgrounder" make it clear the company knew this for years prior to 2007, but in a recent 30(b)(6) deposition of Lilly regarding the label change, the company admitted as much.[14]

Finally, there are numerous instances in the "call notes" of Lilly sales representatives promoting Zyprexa as safe and efficacious for uses far beyond its approved indications. Often through the use of patient exemplars with names like "Donna," "Martha," "Marty" and "Melvin," the representatives would promote Zyprexa for use in combating non-indicated mood and thought disorders such as depression, anxiety, and "complicated mood disorder," and for use in patient populations such as the elderly for whom Zyprexa had not been established as safe or effective.

Clearly, in all of these categories there is evidence that Lilly's Alaska sales force was totally aligned with its overall national marketing plan for Zyprexa: to minimize its risks while over promoting its efficacy for both indicated and off-label uses. This

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[13] Exhibit 5, Letter from Eli Lilly and Company to health care professionals dated October 5, 2007, at 1, 3.

[14] Transcript of 30(b)(6) Deposition of Eli Lilly and Company, December 11, 2007, 15-19.

conduct violates both general and specific prohibitions of the UTPCPA, and the State will present evidence of this nature at trial in support of its allegations.

C. The number of UTPCPA violations in Alaska.

As noted above, with discovery ongoing the State should not be forced at this time to disclose to Lilly what it believes to be exact number of violations of the UTPCPA committed by Lilly. Lilly has unilaterally refused to provide discovery beyond 2004 as to the majority of discovery sought by the State. The State has a pending motion to compel discovery of such matters and there are several key depositions remaining which will help elucidate the extent and magnitude of Lilly's violations continuing to the present. Moreover, in light of the Court's bifurcation order, damages discovery such as this is not of the essence at this time.

Nevertheless, it is clear that Lilly engaged in a decade-long scheme to promote the prescription of Zyprexa to Alaska citizens without giving truthful information about its safety risks and proper uses. As a result, the scope and number of violations of the UTPCPA is enormous. Each and every prescription of Zyprexa to any Alaska resident is a violation of the provisions of the UTPCPA, because each prescription failed to warn of the true nature and extent of Zyprexa's risks. Through the year 2006, there were 208,780 prescriptions to Alaska Medicaid patients alone. The State believes the total number of prescriptions (to both Medicaid and non-Medicaid patients) will be significantly higher

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but is still in the process of discovering the total number prescriptions to all Alaska residents.

In addition to each prescription without an adequate warning being a separate violation of UTPCPA, it was also a separate violation of the Act for any sales call in which the sales representative minimized the hazards with weight gain and diabetes, misrepresented the facts about the drug, or improperly promoted the drug off-label. However, the State has only received a 10 percent sampling of call notes up through August of 2004. It will require a full production of all call notes through the present to fully address the spectrum and magnitude of UTPCPA violations in Alaska

III. CONCLUSION

For the foregoing reasons, and in light of the information provided herein, the State respectfully requests the Court deny Lilly's motion to compel.

Dated this 20 day of December, 2007.

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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Case No. 3AN-06-05630 CI
	)	
ELI LILLY AND COMPANY,	)	
	)	
Defendant.	)	
	)	

MEMORANDUM IN SUPPORT OF PLAINTIFF'S RENEWED MOTION TO COMPEL AND MOTION FOR SANCTIONS

I. INTRODUCTION

On February 8, 2007, the State served its first sets of Interrogatories and Requests for Production, which were followed on May 31, 2007, by the State's Second Interrogatories and Requests for Production. After Lilly stone-walled any meaningful response to most of the State's discovery requests, the State filed motions to compel on both sets of discovery. After extensive briefing and a day long hearing in front of the Discovery Master, Lilly withdrew some objections to certain requests and was ordered by the Discovery Master to respond to others. While Lilly has responded to some of those requests, it has failed to meaningfully respond to others and has effectively evaded the Orders of the Discovery Master.

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PLAINTIFF'S EXHIBIT
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OA Response to Dilly Motion to Compel 3314

This memorandum is submitted in support of Plaintiff's Renewed Motion to Compel and Motion for Sanctions. The issues requiring legal discussion are addressed below along with the specific discovery issues which remain outstanding.

II. SPECIFIC RESPONSE DEFICIENCIES

A. Interrogatory Nos. 1 and 3 and Corresponding Request for Production Nos. 1 and 3.

The State's interrogatories and requests for production sought information regarding Lilly's marketing of Zyprexa for use in Alaska's Medicaid program and communications by Lilly employees regarding the efficacy, benefits, risks or costs associated Zyprexa use. Specifically, the State requested the identities of individuals responsible for communicating on such topics with representatives of Alaska's Medicaid program (Interrogatory No. 1, Request for Production No. 1) and members of any organization, committee or authority responsible for determining which prescription drugs will be on any Alaska formulary, pharmaceutical and therapeutics list or preferred drug list (Interrogatory No. 3, Request for Production No. 3). Lilly withdrew its objection to these requests at the hearing in front of the Discovery Master, as noted in the Discovery Master's September 24, 2007 Order.[1] Further, on the record at that hearing Lilly committed to producing witness names and documents related to those topics.[2] To

[1] Discovery Master Order, September 24, 2007, pp. 9, 10 (Exhibit 1).

[2] September 11, 2007 Hearing Transcript, pp. 64-66 (Exhibit 2).

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Exhibit 1
SOA Response to Lilly
Motion to Compel
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this date, Lilly has only identified and produced documents for two such witnesses. The State has taken the depositions of those witnesses, and it is abundantly clear that Lilly has failed to meaningfully respond to the State's discovery requests.

The first witness identified was Nathaniel Miles, a manager of Public Affairs. At his deposition, Miles made it clear that he did not communicate with members of the Alaska Medicaid department or any DUR or P&T committees regarding any of the issues of inquiry in the State's discovery requests.[3] His communications were primarily with legislators, and communications with persons falling within the categories of individuals covered by the State's requests would have been handled by others, including sales representatives and outcomes liaisons.[4]

The second identified witness was Kevin Walters, a Public Health Division account executive. Walters denied ever discussing any Lilly product with Alaska Medicaid representatives, and indicated that communications regarding the issues raised in the State's requests would have been by sales representatives and Lilly employees referred to as "outcomes liaisons."[5]

Lilly has identified its Alaska sales representatives, and the State has issued deposition notices for some of them. However, Lilly never identified any Alaska

[3] Deposition of Nathaniel Miles, pp. 216-218 (Exhibit 3).

[4] *Id.* (Exhibit 3).

[5] Deposition of Kevin Walters, pp. 86-93 (Exhibit 4).

[redacted]

Exhibit 1
SOA Response to Lilly
Motion to Compel

outcomes liaisons as witnesses, nor produced any documents from those individuals' custodial files. The witnesses above both identified Trina Clark as an Alaska outcomes liaison for the relevant time period,[6] and Walters further identified Jeff Hill as an Alaska outcomes liaison for the relevant time period.[7] Lilly should be required to immediately produce the custodial files, including but not limited to all relevant documents and emails, for these witnesses and to produce them both for deposition as soon thereafter as possible.

B. Request for Production No. 7.

The State requested the database of "call notes" generated by Lilly sales representatives. The Discovery Master ordered the production of a random sampling of 4,000 such call notes as urged by Lilly during the hearing. However, counsel for Lilly also represented during the hearing that Lilly would produce call notes for any physician whose deposition Lilly sought to take in this case, as was the practice in the MDL proceedings.[8] Lilly has now noticed the depositions of seven physicians: Dr. Carolyn Rader; Dr. Lucy Curtiss; Dr. Alexander Von Hafften; Dr. Jeffrey Magee; Dr. Ramzi

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[6] Deposition of Nathaniel Miles, p. 51 (Exhibit 5); Deposition of Kevin Walters, p. 87 (Exhibit 6).

[7] Deposition of Kevin Walters, p. 87 (Exhibit 6).

[8] September 11, 2007 Hearing Transcript, pp. 88-89 (Exhibit 7).

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Exhibit 1
SOA Response to Lilly Motion to Compel

008317

Nassar; Dr. Robert Schults; and Dr. Verner Stillner. Lilly should immediately produce any and all call notes detailing sales visits to those physicians.

In addition, the sampling of only 4,000 call notes produced to the State does not include any call notes which occurred after August 5, 2004. The State asserts that Lilly is liable for negligence, strict liability and statutory causes of action up to the present day and Lilly should therefore be required to provide call notes reflecting its conduct with Alaska physicians through the present day.

C. Interrogatory Nos. 12 and 13.

The State requested specific financial information on an annual basis related to sales of Zyprexa both globally and in Alaska. The Discovery Master ordered Lilly to produce publicly available data responsive to both requests. While Lilly provided such data through the year 2004, it has refused to do so for 2005 to the present arguing that its objection to providing information after September 2004 was not overruled by the Discovery Master. However, in reviewing the transcript, the issue of the date scope of production on financial issues was not argued, and the Discovery Master certainly did not sustain any objection to scope related to date or limit Lilly's production obligation in that manner.[9] Lilly should be required to produce the responsive financial information for 2005 to the present.

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[9] *Id.* pp. 95-97 (Exhibit 8).

Exhibit 1
SOA Response to Lilly Motion to Compel

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III. Conclusion

For the reasons stated above and in its Renewed Motion to Compel and Motion for Sanctions, the State requests that the Court grant its motion in all respects and set a deadline by which Lilly must supplement its discovery responses with all information and documents responsive thereto, and by which it must produce witnesses for deposition. Further, the State requests the Court grant it fees and costs related to the depositions of Nathaniel Miles and Kevin Walters, as well as those associated with bringing this motion.

Dated this 11 day of December, 2007.

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Exhibit 1
SOA Response to Lilly
Motion to Compel

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December 3, 2007

VIA US MAIL AND EMAIL
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Re: State of Alaska v. Eli Lilly and Company
Case No.: 3AN-06-5630CIV

Dear Eric:

I am in receipt of your letter dated November 30th regarding the State's Responses to Lilly's Fourth Sets of Interrogatories and Requests for Production.

We have provided you with the basis for our allegations in previous discovery responses and briefing in this case, including a recitation of facts and citation of documents developed in the MDL discovery. However, Lilly has delayed the production of every piece of Alaska-specific discovery the State has requested and which would allow the State to provide more detailed responses to your Fourth Interrogatories. As stated in our responses, we have only recently received this discovery and have just begun the depositions of Alaska-specific witnesses. Moreover, we have agreed to delay some of these depositions at *your* request. Thus, it is not appropriate for the State to answer these interrogatories at this time, and it will not do so until the discovery on these issues is fully developed.

With kindest regards, I remain,

Sincerely yours,

Christiaan Marcum

cc: Matthew L. Garretson, Esq.
Joseph W. Steele, Esq.
Eric T. Sanders, Esq.
David Suggs, Esq.
Brewster Jamieson, Esq.

PLAINTIFF'S EXHIBIT 2 SOA Response to Lilly Motion to Compel

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA, Plaintiff,	)	
v.	)	Case No. 3AN-06-05630 CI
ELI LILLY AND COMPANY, Defendant.	)	

PLAINTIFF'S FIRST AMENDED RESPONSES TO DEFENDANT'S FIRST SET OF INTERROGATORIES

Pursuant to Rules 26(e)(2) and 33 of the Alaska Rules of Civil Procedure, Plaintiff hereby amends it's Responses to Defendant's First Set of Interrogatories as follows. Plaintiff specifically reserves the right to further supplement and or amend these responses as discovery continues and as provided for by the applicable rules of procedure.

INTERROGATORIES

INTERROGATORY NO. 1: Identify each Medicaid State Plan in effect for the State of Alaska since 1996, and for each plan:

a. state whether pharmacy benefits are offered as part of the coverage;

b. state whether pharmacy benefits are offered for Zyprexa prescriptions; and

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PLAINTIFF'S EXHIBIT 3

ANSWER: The State of Alaska has engaged the services of a PBM, First Health Services Corporation. First Health's services have been limited to administrating the pharmacy program. It has had no responsibility for selecting drugs to include on the formulary or PDL. David Campana and Lynda Walsh are the State's employees with responsibility for communicating with First Health. Plaintiff objects to the interrogatory to the extent it requests Plaintiff to identify any documents exchanged with the PBM(s) regarding Zyprexa since 1996 on the grounds that the request is overbroad, vague, and burdensome.

INTERROGATORY NO. 8: Identify any false or misleading statements alleged to have been made to Alaska by Lilly.

ANSWER: The State reserves the right to supplement this response as discovery progresses in this case. The following is a general description of the types of false or misleading statements made by Lilly regarding Zyprexa. As discovery has only begun in this case, it is neither intended to be exhaustive nor exclusive.

Lilly's false and misleading statements regarding Zyprexa span a decade beginning with the launch of the drug in 1996 and continuing through the FDA mandated label change for all atypical antipsychotics in 2003.

In 1995, a prelaunch analysis by Lilly of data from its HGAJ study of Zyprexa showed a statistically significant increased incidence of high blood glucose in Zyprexa patients as compared to patients using Haldol. This analysis has never been disclosed to

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prescribing physicians. In October 1996, Lilly began its Zyprexa marketing campaign by characterizing weight gain on Zyprexa as "therapeutic" instead of an adverse event. By 1998, despite Lilly's knowledge of significant numbers of post-marketing adverse event reports related to weight gain and hyperglycemia, Lilly continued to refer to these adverse events as "infrequent" events seen in clinical studies and made no mention of them in post-marketing reports. Also, by 1998 Lilly employees were internally discussing the link between atypical antipsychotics, weight gain and diabetes, but declined to notify physicians or the public of their concerns.

In 1999, Lilly knew there was a reasonable association between Zyprexa and treatment-emergent hyperglycemia, yet it refused to provide any such information to physicians or the public because it would be damaging to Zyprexa. In early 2000, however, Lilly's Global Product Labeling Committee was reviewing information in consideration of a labeling change regarding hyperglycemia. The information indicated that analyses of Lilly's clinical trial data showed an incidence of treatment-emergent hyperglycemia in Zyprexa patients that was 3 ½ times higher than in patients treated with placebo. Rather than providing this information to physicians, however, Lilly engaged in a tortured reanalysis of the data and in may May of 2000 issued a label change without prior FDA approval claiming there was no significant difference in treatment-emergent hyperglycemia rates between Zyprexa and placebo. Lilly had its sales force actively promote this tortured data nationwide. Five months later, in October 2000, FDA demanded that Lilly remove the

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language from the label claiming there was no difference in the rates of treatment-emergent hyperglycemia, noting that the changed label inappropriately implied that Zyprexa was safe.

In 2000, while trumpeting the supposedly superior efficacy of Zyprexa and falsely stating that it carried no significant risk of treatment-emergent hyperglycemia, Lilly additionally began a nationwide campaign to promote Zyprexa to primary care physicians for non-indicated or off-label uses. Lilly not only falsely promoted Zyprexa as safe and effective, it promoted it for a wide array of intentionally broad and vague mental disorders. At the same time, outside Lilly consultants were warning the company to "come clean" on the hyperglycemia issue, yet Lilly failed to do so. Instead, in 2001 Lilly tripled its direct-to-physician promotion of Zyprexa using a "sell sheet" which featured its tortured clinical trial data analysis and a "comparable rates" message claiming Zyprexa patients had rates of hyperglycemia and diabetes comparable to those treated with other antipsychotics. Internally, however, Lilly acknowledged that appropriate analysis of clinical trial data showed that Zyprexa treatment resulted in statistically significant mean increases in random glucose compared with both placebo and other antipsychotics.

Regardless, in 2002 Lilly's position was that diabetes occurred at comparable rates across antipsychotics. While it knew this position was false, it believed that advancing it would help eliminate diabetes concerns from the risk-benefit equation. Further, Lilly advanced the position that weight gain on Zyprexa was manageable for most patients even though it knew that position was false. Lilly instructed its sales force to avoid the issue of

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hyperglycemia altogether if possible, and if confronted with it, to use the "comparable rates" story.

In July 2003, Lilly intensified its efforts to influence the public that Zyprexa did not cause diabetes and that if diabetes occurred with Zyprexa use it did so at "comparable rates" with other antipsychotics. While admitting internally that weight gain caused by Zyprexa could be a substantial contributing factor pushing some patients into diabetes, Lilly falsely represented to the public that there was no causal link, that weight gain was manageable, and that diabetes occurred at "comparable rates" across all antipsychotics. Even after the September 2003 label change mandated by the FDA, Lilly continued to trumpet its "comparable rates" message, even though subsequent pronouncements by the ADA Consensus Conference and the Veterans Healthcare Administration clearly demonstrated that the consensus of the medical community most knowledgeable on this issue was that use of Zyprexa resulted in more weight gain and a higher risk of diabetes than most other atypical antipsychotics..

INTERROGATORY NO. 9: Identify any false or misleading statements alleged to have been made to Alaska's PBM(s) by Lilly.

ANSWER: See response to Interrogatory No. 8 above.

INTERROGATORY NO. 10: Identify every on-label Zyprexa prescription that you reimbursed or paid for as a result of Lilly's alleged wrongful conduct.

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SOA Response to Lilly
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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA

THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA, Plaintiff, vs. ELI LILLY AND COMPANY, Defendant.	)	Case No. 3AN-06-5630 CIV

PLAINTIFF'S ZYPREXA BACKGROUNDER

The State provides the following backgrounder on Zyprexa and Lilly's specific acts and omissions related thereto. This backgrounder is based upon confidential documents produced in *In re Zyprexa Products Liability Litigation*, MDL 1596 (E.D.N.Y. – J.B.W.). The State has provided this factual summary of information it has gleaned from documents produced in the federal multi-district litigation to date in an effort to provide the Court with factual context in which to review its claims, and to provide balance in light of the factual summary provided by defendant Eli Lilly and Company.

In October 1995, Lilly submitted its New Drug Application ("NDA") to the FDA seeking approval to market Zyprexa in the United States. In December 1995, while FDA review of the NDA continued, top Lilly scientists Charles Beasley, M.D. and Gary

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PLAINTIFF'S EXHIBIT 4

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glucoses relative to placebo and haloperidol." *See* Tab 22. In a March 15, 2001 email, Dr. Beasley further acknowledged the impact that weight gain could have on individual patients, but in doing so made it clear Lilly had no intention of "coming clean" with this information to physicians:

> Unfortunately, I believe it will be a while before we have a clear, ***definitive*** position developed regarding hyperglycemia, hyperlipidemia, obesity, the metabolic syndrome long-term cardiovascular risk and olanzapine. We have 2 physicians primarily dedicated to these issues and a host of others working on them as well. One thing we can say definitively is that olanzapine causes weight gain and for approximately 50% of patients in trials who remained on the drug for >6 months, the amount of gain was >10 pounds. Some patients, in clinical trials gained as much as 80+ pounds. Lacking empirical data to the contrary, it would be ludicrous to state that such a patient is not at long-term, increased cardiac risk relative to prior to gaining that weight, especially, if in temporal association with that weight gain the patient developed an increase in fasting glucose and lipid levels. Therefore, much research is ongoing.

Tab 23 at 2 (emphasis in original).

In a November 2001 "Issues Management Planning," Lilly set forth the position it would take with physicians and the public, regardless of its knowledge.

> Our Position
> - Diabetes/Hyperglycemia may occur in patients taking antipsychotics and/or mood stabilizers, including Zyprexa, at comparable rates, with the possible exception of Clozapine.
>
> ***
>
> Rational [sic] for Position
> - Showing that diabetes is a common occurrence for all antipsychotics, and not just Zyprexa, will help reduce the perception that diabetes is linked specifically to Zyprexa and intern [sic], will help to eliminate this risk from the risk/benefit equation.

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Tab 24 at 2. Lilly knew the "comparable rates" message was untrue, yet continued to advance it. The strategy was similar with weight gain:

> Our Position
> - Weight gain can occur with Zyprexa as with other antipsychotics and mood stabilizers. For most patients, this can be managed allowing them to receive the overwhelming benefits Zyprexa offers.
>
> Rational [sic] for Position
> - To minimize the liability of weight gain while at the same time increasing the focus on Zyprexa's superior efficacy.

Tab 25 at 2. Lilly knew Zyprexa caused more weight gain than other antipsychotics, and Lilly knew that for most patients, weight gain could not be managed. For example, in this same document, Lilly admitted that weight loss programs only worked approximately five percent of the time in normal volunteers. *Id.* at 4. Moreover, a similar "Issues Management Planning" document previously mentioned stated that the company did not know how to effectively deal with the weight gain associated with Zyprexa. *See* Tab 24 at 4.

In April 2002 – after nine serious cases of hyperglycemia, diabetic ketoacidosis and coma, including two cases of death, occurred in less than a year of marketing in Japan – the Japanese Ministry of Health, Labor and Welfare ("MHLW") required Lilly to issue an "Emergency Safety Information" letter to physicians. *See* Tab 26. The warnings required by the Japanese agency included a contraindication against use of Zyprexa by diabetics and instructions to monitor blood glucose with an initial fasting blood glucose

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the issue did arise, Lilly instructed the sales persons to give the "comparable rates" story Lilly knew to be false. *Id.* at 4.

By June 2003, however, Lilly was seeing an observable shift in physicians' attitudes about Zyprexa. A June 9, 2003 report to the Policy Committee noted that Lilly's market research conducted during an American Psychiatric Association convention revealed that some customers were beginning to disproportionately associate Zyprexa, weight gain and diabetes. *See* Tab 33 at 2. A month later, Dr. Breier and various marketing executives told the Policy Committee they would intensify their efforts to influence physicians, patients, Wall Street, the media and even their own sales representatives that Zyprexa did not cause diabetes and that the rates of diabetes with Zyprexa were comparable to other antipsychotic drugs. *See* Tab 34. The principle method of redoubling this effort was the use of a letter signed by Dr. Breier to be distributed to all physicians by the Lilly sales representatives. In an email, dated May 6, 2003, Breier responded to a series of questions ostensibly asked by physicians. The first two questions and answers distributed internally are as follows:

> 1. **Does Zyprexa cause diabetes?** *The most straight forward answer is we do not think so.* Why do I not say Zyprexa definitely does not cause diabetes. In part because it is very difficult to prove a negative. When anyone develops diabetes in the general population it is often impossible to say definitively why they developed diabetes. We have been intensively investigating this issue for several years with clamp studies, animal studies, epidemiology studies and clinical trial studies and have found *no direct link* between diabetes and Zyprexa, or any other antipsychotic drug for that matter, i.e., we have found no smoking gun.

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Moreover, the numerous research groups around the world have also not found a *direct causal link* to diabetes.

2. **Why do I say no direct link as opposed to any link at all?** *We know and have well characterized that Zyprexa and all antipsychotics causes [sic] weight gain and weight gain is an established risk factor for diabetes. Thus in some patients the weight gain of Zyprexa could predispose them to diabetes, particularly if those patients have other risk factors for diabetes.* However, and this is very important, most people who gain weight do not develop diabetes. Diabetes is an illness with multiple pathways leading to and contributing towards its development. Thus a patient who gains weight on Zyprexa or other antipsychotic drugs and mood stabilizers is probably like anyone else who gains weight [sic] the general population. For the vast majority of individuals, their pancreases are healthy and the weight gain will not precipitate diabetes. *For those in the minority whose pancreases are functioning suboptimally weight gain could push them over to diabetes... and that is weight gain caused by any means, over eating in the general population or weight gain produced by any antipsychotic, antidepressant or traditional mood stabilizer.*

Tab 35 (bold emphasis in original, italics emphasis added). Dr. Breier thus admitted in this hypothetical "exchange" that weight gain caused by Zyprexa could be a substantial contributing factor for pushing some patients into diabetes. However, the letter ultimately provided to physicians by sales representatives was much different.

Does Zyprexa cause diabetes? The available data do not establish a causal link between diabetes and Zyprexa – or any other antipsychotic, for that matter. We have been intensely investigating this question for several years from multiple vantage points: preclinical studies, head-to-head clinical trials, epidemiological surveys, and endocrinological challenge or "clamp" studies. Our conclusions have been confirmed by studies conducted by others from around the world. Two clamp studies conducted by Lilly found that Zyprexa did not decrease pancreatic insulin release or, unlike other medicines (e.g., prednisone, protease inhibitors), have a direct

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www.lilly.com

Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285
U.S.A.

Phone 317 276 2000

October 5, 2007

Re: Safety data on Zyprexa® (olanzapine) and Symbyax® (olanzapine and fluoxetine HCl capsules) – Hyperglycemia, Weight Gain, and Hyperlipidemia

Dear Health Care Professional,

Eli Lilly and Company would like to inform you of important information being added to the Zyprexa® (olanzapine) and Symbyax® (olanzapine and fluoxetine HCl) labels. These labeling updates include new WARNINGS for Weight Gain and Hyperlipidemia and updated information in the WARNING for Hyperglycemia. These changes reflect results of recently completed pooled analyses of clinical trials in adults and adolescents as well as information from two published large studies of atypical antipsychotics, CATIE[1] and CAFE[2].

The new labeling language is detailed below. Monitoring of glucose, weight, and lipids is recommended during olanzapine and olanzapine/fluoxetine combination treatment. Guidelines published by the American Diabetes Association (ADA) following the consensus development conference[3] provide recommendations for the monitoring of blood glucose, weight, and lipid levels in those treated with atypical antipsychotics. Other highlights of the updated labeling include:

- Abnormal or borderline glucose levels at baseline are an important risk factor for further glucose increase.
- While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.
- Significantly greater mean increases in total cholesterol, LDL cholesterol, and triglycerides were observed in Zyprexa-treated patients compared with placebo-treated patients both with and without evidence of dyslipidemia at baseline.
- Labeling provides information on magnitude and distribution of weight gain over a two year period in Zyprexa-treated patients.
- Labeling also provides information on glucose, weight gain, and lipids from studies of Zyprexa for adolescent patients. Please note that Zyprexa and Symbyax are not approved currently for use in children and adolescents aged less than 18 years old.

PLAINTIFF'S EXHIBIT 5

Eli Lilly and Company remains committed to providing you with the most current product information available for the management of your patients and we will continue our ongoing research and analyses in these areas.

Please refer to the full prescribing information for Zyprexa and Symbyax included with this letter.

Should you have any questions or would like additional information regarding this important safety information, please contact the Lilly medical department at 1-800-Lilly-Rx or your Eli Lilly and Company sales representative.

The Medical Community can further our understanding of adverse events by reporting all cases to the Agency via the MedWatch program by phone at 1-800-FDA-1088, by fax at 1-800-FDA-0178, via the MedWatch website at www.fda.gov/medwatch or by mail:

MEDWATCH
Food and Drug Administration
5515 Security Lane
Suite 5100, HFD-001
Rockville, MD 20852

Sincerely,

Tim Garnett, M.D.
Vice President,
Global Patient Safety
Eli Lilly and Company

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The following are the updated Hyperglycemia WARNINGS and the new Hyperlipidemia and Weight WARNINGS included in the Zyprexa label.

WARNINGS:

Zyprexa:
The following is updated language in the WARNINGS section of the Zyprexa package insert, and will be reflected in other materials.

Hyperglycemia — Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. While relative risk estimates are inconsistent, the association between atypical antipsychotics and increases in glucose levels appears to fall on a continuum and olanzapine appears to have a greater association than some other atypical antipsychotics.

Mean increases in blood glucose have been observed in patients treated (median exposure of 9.2 months) with olanzapine in phase I of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). The mean increase of serum glucose (fasting and nonfasting samples) from baseline to the average of the two highest serum concentrations was 15.0 mg/dl.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled adult olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine was associated with a greater mean change in fasting glucose levels compared to placebo (2.76 mg/dL versus 0.17 mg/dL). The difference in mean changes between olanzapine and placebo was greater in patients with evidence of glucose dysregulation at baseline (patients diagnosed with diabetes mellitus or related adverse events, patients treated with antidiabetic agents, patients with a baseline random glucose level ≥200 mg/dL, and/or a baseline fasting glucose level ≥126 mg/dL). These patients had a statistically significantly greater mean increase in HbA_{1c} compared to placebo. In patients with baseline normal fasting glucose levels (<100 mg/dL), 2.2% (N= 543) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 3.4% (N= 293) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 17.4% (N=178) of those treated with

olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 11.5% (N=96) of those treated with placebo.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine was associated with a statistically significantly greater mean change in fasting glucose levels compared to placebo (2.68 mg/dL versus -2.59 mg/dL). In patients with baseline normal fasting glucose levels (<100 mg/dL), zero out of 124 (0%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus 1 out of 53 (1.9%) of those treated with placebo. In patients with baseline borderline fasting glucose levels (≥100 mg/dL and <126 mg/dL), 2 out of 14 (14.3%) of those treated with olanzapine were found to have high glucose levels (≥126 mg/dL) during olanzapine treatment versus zero out of 13 (0%) of those treated with placebo.

Physicians should consider the risks and benefits when prescribing olanzapine to patients with an established diagnosis of diabetes mellitus or having borderline increased blood glucose level (fasting 100–126 mg/dL, non-fasting 140–200 mg/dL). Patients taking olanzapine should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug.

Hyperlipidemia — Undesirable alterations in lipids have been observed with olanzapine use. Clinical monitoring, including baseline and follow-up lipid evaluations in patients using olanzapine, is advised.

Significant, and sometimes very high (>500 mg/dL), elevations in triglyceride levels have been observed with olanzapine use. Modest mean increases in total cholesterol have also been seen with olanzapine use.

Olanzapine Monotherapy in Adults — In an analysis of 5 placebo-controlled olanzapine monotherapy studies with treatment duration up to 12 weeks, olanzapine-treated patients had statistically significant increases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 5.3 mg/dL, 3.0 mg/dL, and 20.8 mg/dL respectively compared to decreases from baseline in mean fasting total cholesterol, LDL cholesterol, and triglycerides of 6.1 mg/dL,

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4.3 mg/dL, and 10.7 mg/dL for placebo-treated patients. For fasting HDL cholesterol, no statistically significant differences were observed between olanzapine-treated patients and placebo-treated patients. Mean increases in fasting lipid values (total cholesterol, LDL cholesterol, and triglycerides) were greater in patients without evidence of lipid dysregulation at baseline, where lipid dysregulation was defined as patients diagnosed with dyslipidemia or related adverse events, patients treated with lipid lowering agents, or patients with high baseline lipid levels. Table 1 shows categorical changes in fasting lipid values.

Table 1. Changes in Fasting Lipids Values from Adult Placebo-Controlled Olanzapine Monotherapy Studies with Treatment Duration up to 12 Weeks

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	745	39.6%*
		Placebo	402	26.1%
	Normal to High (<150 mg/dL to ≥200 mg/dL)	Olanzapine	457	9.2%*
		Placebo	251	4.4%
	Borderline to High (≥150 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	135	39.3%*
		Placebo	65	20.0%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	745	21.6%*
		Placebo	402	9.5%
	Normal to High (<200 mg/dL to ≥240 mg/dL)	Olanzapine	392	2.8%
		Placebo	207	2.4%
	Borderline to High (≥200 mg/dL and <240 mg/dL to ≥240 mg/dL)	Olanzapine	222	23.0%*
		Placebo	112	12.5%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	536	23.7%*
		Placebo	304	14.1%
	Normal to High (<100 mg/dL to ≥160 mg/dL)	Olanzapine	154	0%
		Placebo	82	1.2%
	Borderline to High (≥100 mg/dL and <160 mg/dL to ≥160 mg/dL)	Olanzapine	302	10.6%
		Placebo	173	8.1%

* Statistically significant compared to placebo.

In phase 1 of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), over a median exposure of 9.2 months, the mean increase in triglycerides in patients taking olanzapine was 40.5 mg/dL. In phase 1 of CATIE, the mean increase in total cholesterol was 9.4 mg/dL.

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 3 placebo-controlled olanzapine monotherapy studies of adolescent patients, including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), for fasting HDL cholesterol, no statistically significant

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differences were observed between olanzapine-treated patients and placebo-treated patients. Table 2 shows categorical changes in fasting lipid values in adolescent patients.

Table 2. Changes in Fasting Lipids Values from Adolescent Placebo-Controlled Olanzapine Monotherapy Studies

Laboratory Analyte	Category Change from Baseline	Treatment Arm	N	Patients
Fasting Triglycerides	Increase by ≥50 mg/dL	Olanzapine	138	37.0%*
		Placebo	66	15.2%
	Normal to High (<90 mg/dL to >130 mg/dL)	Olanzapine	67	26.9%
		Placebo	28	10.7%
	Borderline to High (≥90 mg/dL and ≥130 mg/dL to >130 mg/dL)	Olanzapine	37	59.5%
		Placebo	17	35.3%
Fasting Total Cholesterol	Increase by ≥40 mg/dL	Olanzapine	138	14.5%*
		Placebo	66	4.5%
	Normal to High (<170 mg/dL to ≥200 mg/dL)	Olanzapine	87	6.9%
		Placebo	43	2.3%
	Borderline to High (≥170 mg/dL and <200 mg/dL to ≥200 mg/dL)	Olanzapine	36	38.9%*
		Placebo	13	7.7%
Fasting LDL Cholesterol	Increase by ≥30 mg/dL	Olanzapine	137	17.5%
		Placebo	63	11.1%
	Normal to High (<110 mg/dL to ≥130 mg/dL)	Olanzapine	98	5.1%
		Placebo	44	4.5%
	Borderline to High (≥110 mg/dL and <130 mg/dL to ≥130 mg/dL)	Olanzapine	29	48.3%*
		Placebo	9	0%

* Statistically significant compared to placebo.

Weight Gain — Potential consequences of weight gain should be considered prior to starting olanzapine. Patients receiving olanzapine should receive regular monitoring of weight.

Olanzapine Monotherapy in Adults — In an analysis of 13 placebo-controlled olanzapine monotherapy studies, olanzapine-treated patients gained an average of 2.6 kg, which was statistically significantly different compared to an average 0.3 kg weight loss in placebo-treated patients with a median exposure of 6 weeks; 22.2% of olanzapine-treated patients gained at least 7% of their baseline weight, which was statistically significantly different compared to 3% of placebo-treated patients, with a median exposure of 8 weeks; 4.2% of olanzapine-treated patients gained at least 15% of their baseline weight, which was statistically significantly different compared to 0.3% of placebo-treated patients, with a median exposure of 12 weeks. Clinically significant weight gain was observed across all baseline Body Mass

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Index (BMI) categories. Discontinuation due to weight gain occurred in 0.2% of olanzapine-treated patients and in zero placebo-treated patients.

During long-term continuation therapy with olanzapine (238 median days of exposure), 56% of olanzapine patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 5.4 kg.

Table 3 includes data on weight gain with olanzapine pooled from 68 clinical trials. The data in each column represent data for those patients who completed treatment periods of the durations specified.

Table 3. Weight Gain with Olanzapine Use

Amount Gained kg (lb)	6 Weeks (N=2976) (%)	6 Months (N=1536) (%)	12 Months (N=778) (%)	24 Months (N=422) (%)
≤0	27	21	20	22
0-5 (0-11 lb)	57	34	25	22
5-10 (11-22 lb)	15	26	25	22
10-15 (22-33 lb)	2	12	16	18
>15 (>33 lb)	0	6	14	16

Olanzapine Monotherapy in Adolescents — The safety and efficacy of olanzapine have not been established in patients under the age of 18 years. In an analysis of 4 placebo-controlled olanzapine monotherapy studies of adolescent patients (ages 13 to 17 years), including those with schizophrenia (6 weeks) or bipolar disorder (manic or mixed episodes) (3 weeks), olanzapine-treated patients gained an average of 4.6 kg, which was statistically significantly different compared to an average of 0.3 kg in placebo-treated patients, with a median exposure of 3 weeks; 40.6% of olanzapine-treated patients gained at least 7% of their baseline body weight, which was statistically significantly different compared to 9.8% of placebo-treated patients, with a median exposure of 4 weeks; 7.1% of olanzapine-treated patients gained at least 15% of their baseline weight, compared to 2.7% of placebo-treated patients, with a median exposure of 19 weeks. Clinically significant weight gain was observed across all baseline Body Mass Index (BMI) categories, but mean changes in weight were greater in adolescents with BMI categories above normal at baseline. Discontinuation due to weight gain occurred in 1% of olanzapine-treated patients, compared to zero placebo-treated patients.

During long-term continuation therapy with olanzapine, 65% of olanzapine-treated patients met the criterion for having gained greater than 7% of their baseline weight. Average weight gain during long-term therapy was 7.4 kg.

Information for Patients:

Hyperglycemia — Patients should be advised of the potential risk of hyperglycemia-related adverse events. Patients should be monitored regularly for worsening of glucose control.

Weight Gain — Patients should be counseled that olanzapine is associated with weight gain. Patients should have their weight monitored regularly.

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IN THE SUPERIOR COURT FOR THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,	)	
	)	
Plaintiff,	)	
	)	
-v-	)	CAUSE NO.
	)	3AN-06-5630 CIV
ELI LILLY & COMPANY,	)	
	)	
Defendant.	)	

The videotaped deposition upon oral examination of ROBIN PITTS WOJCIESZEK, a witness produced and sworn before me, Nancy M. Kottenstette, Notary Public in and for the County of Marion, State of Indiana, taken on behalf of the Plaintiff at the offices of Ice Miller, One American Square, Suite 3100, Indianapolis, Indiana, on December 11, 2007, at 9:37 a.m., pursuant to all applicable rules.

C O N F I D E N T I A L

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this supplemental application.

Q And who were those key members responsible for the supplemental application?

A They would be the medical director of the Zyprexa team.

Q Who was?

A Sara Corya.

Q Okay. How does she spell her last name?

A C-O-R-Y-A.

Q Okay.

A The Zyprexa global brand development team leader at the time was Eric Baclet.

Q Anyone else?

A Of course, my supervisor, Greg Brophy.

Q Okay.

A And, again, those -- there was a core team of probably over 20 individuals, too, who are involved in just the overall data package who were also communicated, but those were the key individuals.

Q Now, the letter from FDA makes reference to a number of regulatory filings with FDA by Lilly regarding Symbyax; correct?

A Correct.

Q And Symbyax is a combination drug containing both Zyprexa and Prozac; correct?

A That's correct.
Q Or, I guess, the generic terms would be containing both olanzapine and fluoxetine; correct?
A That's correct.
Q Did I pronounce that last one correctly?
A Yes, you did.
Q Okay. And in those regulatory submissions, Lilly was seeking approval from FDA to market the combination drug Symbyax for use in treatment resistant depression or TRD; is that correct?
A That's correct.
Q Okay. And it indicates that these prior submissions had occurred in September of 2006, in November of 2006, December of 2006, and February of 2007; correct?
A That's correct.
Q Okay. And am I correct that those submissions made by Lilly to FDA included information from clinical studies of the combination drug?
A That's correct.
Q Okay. And among other things, that clinical data included information regarding changes in the blood glucose of patients who were exposed to the combination drug as compared to people who were just receiving placebo; is that correct?

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A That's correct.
Q And since those submissions occurred in the fall of 2006, the studies that contained that data would have been concluded sometime before that; correct?
A That's correct.
Q And do you know when it was that those clinical studies were done which contained the data that was submitted to FDA in the submissions that are referenced here?
A They had completed over numerous years, but the last study that completed, which was to support the indication which was HDAO, completed in the fall of 2005.
Q Fall of 2005. And that was the latest of those studies; correct?
A That's correct.
Q And what was -- what would have been the earliest of those studies?
A I don't recall. They were -- some of the studies that we included in the submission were also submitted with the original application for Symbyax in 2002.
Q Okay. I want to make sure I understand. So that the submissions that occurred in the fall of 2006 to support the additional indication for

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treatment resistant depression included data from studies that had been conducted in support of the original Symbyax submission in 2002 as well as other studies after that point, the last of which had been completed by the fall of 2005. Is that a fair statement?

A That's a fair statement, yes.

Q Okay. And the earliest of those studies that had been done in support of the 2002 submission, I presume, would have been completed sometime before 2002; is that correct?

A That's correct.

Q Do you know when it was that they would have been completed?

A I don't know the exact dates, but, typically, they're done about six months prior to a submission.

Q So probably 2001 sometime?

A Some of them were, yes.

Q Okay. Do you know what the date -- at least a month, date of the 2000 submission for Symbyax?

A If I recall, it was November of 2002. It was prior to my responsibility --

Q Okay.

A -- around the application.

Q Okay. So it'd be fair to say that the data that's being referenced here in this letter is the data that was generated between, say, early 2002 and 2005 in that time frame; correct?

A Majority of the data, yes.

Q Okay. Now, in order to approve Symbyax for use in treatment resistant depression, FDA needed to approve the labeling for the drug; correct?

A Correct.

Q Okay. And on the first page of the letter in -- there's a bolded heading that states "Updated Information on Risks of Weight Gain, Hyperglycemia, and Hyperlipidemia." Do you see that?

A Yes, I do.

Q In the first paragraph right after that heading, it states "A primary concern with this application and the primary basis for our not taking a final action is our view that we lack important safety information needed to adequately update the labeling with all relevant risk information. In particular, we are concerned that the labeling is deficient with regard to information about weight gain, hyperglycemia, and hyperlipidemia that is associated with olanzapine use, whether taken alone or in combination with fluoxetine. You