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

VOLUME 10

TRANSCRIPT OF PROCEEDINGS

March 14, 2008 - Pages 1 through 252

BEFORE THE HONORABLE MARK RINDNER

Superior Court Judge

A-P-P-E-A-R-A-N-C-E-S

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PROCEEDINGS

THE COURT: We're on the record in State of Alaska vs. Eli Lilly and Company, 3AN-06-05630. Counsel are present; we're out of the presence of the jury. I understand there's a motion to take up.

MR. ALLEN: Yes, sir, Your Honor. Scott Allen.

Can I approach?

THE COURT: Sure.

MR. ALLEN: Your Honor, I handed you excerpts from John Lechleiter's deposition of yesterday, along with your rulings on the deposition, as well as an e-mail that was sent to me on March 8th from Adam Michaels, with a carbon copy to Mr. Lehner, concerning the deposition, asking me to include certain portions of the Lechleiter deposition in our cuts. Included within that was 300 -- Page 365, Line 24 to 366, Line 6.

Yesterday, as you recall, in the deposition we were asked to stop the tape -- actually, the second time I asked the tape to be stopped. We were asked to stop the tape twice because there was an alleged error that had

occurred in the presentation of the testimony. Those errors occurred at Pages 110, Line 4 to 110, Line 15 and 110, Line 18 to 111, Line 6. That was the first time we had to stop the tape. I -- I worked hard on getting these depositions ready.

By the way, Your Honor, I -- for the record, we're going to try to present five of them today that will take less than two hours, and I was up till 3:00 a.m. to look at them, and I hope nothing happens, but anyhow. I wanted the Court to note, just for the record, because I understood the Court was upset, justifiably, if I had put something in the record. But at one -- the first time it happened I was playing -- the objections by the defendants were overruled and that's why the material was in the tape.

And the last time, when I stood up and stopped it, that material was included at the request of Eli Lilly. So I didn't want to have two strikes going against me today if -- if, in fact, another event occurs. And Mr. Lehner -- I like Mr. Lehner -- but he did say yesterday, "Mr. Allen has two strikes," and so I want the record to be clear. But more importantly, Your

Honor, I would like to be able to present not the -- I'll go ahead and just read the question and answer at Page 110, Line 4 through 111, Line 6, and present that to the jury concerning Dr. Lechleiter's testimony.

MR. LEHNER: Your Honor, I stood up yesterday with respect to this piece of -- these two items here on Page 110, because what was on the screen at that time, as you recall, was the document that you had sustained our objection to. And I think that was the cause of concern, and that was the harm. The jury saw a Wall Street Journal article -- what they saw certainly was on the screen, but that was what was presented to the jury, and you had, as you recall, sustained our objection to that.

And with respect to the last piece here, that counterdesignation was designed to be included, indeed, provided that the previous parts of the deposition had been played and those had not been played. So I think that's really a nonissue. But I think the harm was the document being shown to the jury.

THE COURT: Again --

MR. LEHNER: And just for the

record, I was not -- and I told Mr. Allen this morning. This has been a confusing process. It's difficult -- we said, I appreciate all the work that everybody is doing on our team and on theirs to get this right, and my point yesterday is we need to get the technicians working together so this is done in the way you want it done.

THE COURT: Again, nobody is in trouble with me.

MR. ALLEN: Okay.

THE COURT: Nobody has strikes.

MR. ALLEN: Okay.

THE COURT: I'll take some of the heat, because if I had done what I probably should have done, which is brought in all the material that you had, I probably could have seen that I included that portion, but I agree with Mr. Lehner that the exhibit, I do recall, was not permitted.

MR. ALLEN: Yes, Your Honor, but let me --

THE COURT: And so my understanding is what you want to do is read the --

MR. ALLEN: Yes, sir, the question

and answer.

THE COURT: -- from 110, 04 to 110, 15 and 110, 18 to 111, 06.

MR. ALLEN: Yes, sir.

THE COURT: And since I had overruled the objection to that and just for the record, it's because it's dealing with the issue of the stock dropping in response to the Prozac patent --

MR. ALLEN: Yes.

THE COURT: -- which, as I understand, is part of the motive allegation in this case, that because of the loss of the Prozac patent, there was more desire on Lilly to promote Zyprexa. I'll allow that to be read to the jury, and I'll give them an explanation that a portion of the thing was excluded that I've permitted, and that it's now going to be read.

MR. ALLEN: Thank you, Your Honor. I do want the record to reflect -- I mean, we've had our differences, Mr. Lehner and I, but they're professional, and I just want to make sure everybody understands that.

THE CLERK: If I think people are unduly sniping at each other, I'll let you know.

I don't foresee anything that's been going on other than there's been some good-natured banter and there's probably been a little tension and stress, but I understand the stakes in this case and I don't feel anyone has crossed my lines.

MR. ALLEN: Right. Thank you, Your Honor. I appreciate it.

THE COURT: Again, as I've said, I believe that I have excellent attorneys in this case, all of whom are acting quite professionally to my satisfaction.

MR. ALLEN: Thank you, Your Honor. I appreciate it.

I'll let the Court know, but I -- we need to get Dr. Wirshing on. I'm -- I've given -- or getting copies to the defense lawyers now. I gave them the original exhibits. We forgot to introduce some exhibits at the time of Ms. Eski's deposition, and at some point today I'm going to try to do that, and then I want to bring up another issue, but it's premature, but I appreciate the Court's time.

THE COURT: Okay. Before we start -- we bring in the jury and start taking

testimony, Lilly yesterday filed a renewed motion for mistrial concerning the rendering of treatment by doctors, one of whom has now been a witness in this case for the State, and one of whom, I guess, today will be a witness for the State, citing to me a number of cases. After questioning the jurors and all the jurors indicating that nothing about the incident would affect their ability to evaluate those doctors' testimony in the exact same way as anybody else's testimony, I denied the oral motion for a mistrial. Lilly cited to me a number of cases.

I find the cases generally to be distinguishable. There's the case of Campbell versus Fox, which is 498 Northeast 2d 1145. In that case the doctor rendered a -- it was actually the defendant and it was in a medical malpractice case, in which the doctor's competency was at issue.

Same as to Reome, R-e-o-m-e, versus Portland Memorial Hospital, which is at 152AD 2d 773. It's a New York appellate case, and, again, the doctor admin -- the defendant doctor in a med mal administered to the jury. an unpublished decision in Hochadel versus Saint Luke's

Hospital. That's found at 1993 WestLaw 496681, Ohio Appellate, Sixth District, also a med mal defendant doctor.

State versus Rideout, 143 New Hampshire, 363, a Supreme Court of New Hampshire case from 1999. In that case the jury was in the middle of its deliberations and a sheriff, I believe, went out to help a juror get something out of the car or something and the concern there was communications with the juror. There's been no indications of that in this case. And, again, that was in the process of deliberation.

In State of Minnesota vs. Schwartz, which is a Supreme Court of Minnesota case, at 122 Northwest 2d 769, again, it was a criminal case. There were many assignments of errors that led to the reversal and the mistrial in that case, or actually the reversal, I guess. And the decision, it says, with the exception of the admission of the testimony of a particular witness who was allowed to testify about something improperly, we would not consider any assignment of error herein before referred to as sufficient in itself to justify a new trial.

In other words, the issue that came

up with the juror wasn't going to be sufficient in itself to render -- to require a new trial. It was only the cumulative effect in a criminal case.

Likewise, State of New Jersey versus Hunt, which is a -- at 138A 2d 1, it was a murder case. Nonemergency treatment was rendered, unlike this particular case. Other doctors would have been available other than the witness to do that, which is apparently -- the trial judge even referred to that as being an unfortunate choice, and again the Court found an aggregate of errors in the criminal case.

The case that the State has cited to me, Partlow versus State, 453 Northeast 2d 259, was a criminal case and they still allowed -- did not require a mistrial and affirmed the conviction. The witness was on the stand and had to attend to a juror. The juror ended up remaining on the jury, which is not our case, and still they allowed that. In some ways that may be the closest of the cases, although there are facts and issues there that are probably different.

But having reviewed the case law

authority, and, again, having questioned the jurors, I do not believe that the case law supports requiring a mistrial in this case based on the record before the Court, and I'll deny the renewed motion for mistrial.

I've also reviewed the case law as well as the transcript concerning the motion to strike the testimony of Duane Hopson. Two cases were cited to me. One is the Miller versus Phillips case, in which it wasn't error to allow a witness who wasn't necessarily designated as an expert to testify as to expert opinions. The Court found no surprise, and also noted, I think, something that I note here, that the witness's testimony to the extent that there were hybrid opinions expressed, in many ways was cumulative of other witnesses and certainly a lot of the -- I don't think there's surprise here, having read the transcript of his deposition.

The other case was Zaverl, Z-a-v-e-r-l, versus Hanley. That's at 64 P3d 809, an Alaska case of 2003. The Miller case is at 959 P2d 1247, a 1998 Alaska case. In that case there was an affirmative statement, and doctor's or expert's lawyer had refused to allow

the expert to testify on the subject matter that then he eventually was testifying to in court. And I don't believe that that's the same situation here, having -- the witness was fully deposed, and while not all the questions were asked, certainly the subject matter was gone into in a general sense and could have been asked or followed up.

And, again, given what I've seen from other witnesses in this case, and particularly witnesses who were the first two witnesses, experts in this case, I don't believe that Dr. Hopson's testimony can in any way be seen as surprising. What may have been surprising was that the State took up the challenge of the defense in opening statement that they weren't going to bring on any witnesses from the State and the defense was.

In that regard, I note that having heard the testimony of Dr. Hopson, had he testified in Lilly's case and then all these questions been asked in cross, I would have found the cross to be entirely proper. I realize there's a difference in allowing him to go first, particularly in light of the opening statements,

but I don't think find that a sufficient reason to strike his testimony, so I will deny the motion to strike his testimony as well.

Dr. Breier's going to be our first --

MR. ALLEN: No, Your Honor. It will be Dr. Wirshing.

THE COURT: Sorry.

MR. ALLEN: Yeah. And then I'm -- I may leave and go get these depositions ready at some point, but I'd like to -- the first thing I'd like to do is read Dr. Lechleiter's deposition --

THE COURT: So we're going to do -- I'll explain to the jury that -- what we're doing with Dr. Lechleiter, and then Dr. Wirshing will be on live here.

MR. ALLEN: Yes, sir.

THE COURT: Mr. Suggs, you're going to question him?

MR. SUGGS: Yes, sir.

THE COURT: Okay.

Then we'll go off record; take about two minutes to let the jury get ready.

We'll be off record.

THE CLERK: Please rise. Superior Court stands in recess. Off record.

(Short recess.)

THE COURT: We're back on the record and all members of the jury are present, as are counsel.

Ladies and gentlemen of the jury, we're going to start our testimony in a second. The first thing you're going to hear is yesterday -- I believe it was yesterday, you saw the videotape deposition of Dr. Lechleiter. And during the course of that testimony, a portion of the video that I had indicated could be played, we -- we stopped the playing of inadvertently.

And Mr. Allen is going to read that short portion to you that was left out of the video, and you should consider his reading of that deposition testimony -- again, this is the same deposition that you saw the video of. The doctor was under oath, and you should consider that as you would any other deposition testimony or any other testimony in this matter, leaving it up to you as to what the weight that you'll give to the testimony and the fact that it's -- was a videotaped deposition.

Following that, my understanding is that the State is going to present a live witness, and then after that live witness you've got two --

MR. ALLEN: Well, I'm going -- after I read this, I'm going back to the hotel and get the videos together, and I'll -- I have less than -- I'll tell you this, I know it's less than two hours of total videos left, and it may be less than an hour and a half, and I just got to go work on it.

THE COURT: There will be some video depositions, and then after the video depositions my understanding is the State's case will be done.

MR. ALLEN: Yes, sir. Subject to our --

THE COURT: If it looks like we can get those video depositions in by 2:00ish or a little bit like that in order to finish up the State's case today, we'll probably go a little bit long, but we'll see where we are depending on how long the live witness takes and how long the editing of the videos goes down to, but that's what the process is. So I expect that the

State's case may end today and certainly will end early on Monday.

MR. ALLEN: No question.

THE COURT: And then the defense will begin the presentation of its case. So that just kind of gives you an idea of where we are in this process.

Mr. Allen, do you want to read the portions of Dr. Lechleiter's --

MR. ALLEN: Yes, sir.

Question to Dr. Lechleiter: Sir, I've handed you what's been marked as Deposition Exhibit No. 6. This is an online 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 the 10th. On August 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 to cause this stock price fall?

Answer of Dr. Lechleiter: 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.

That concludes it, Your Honor.

THE COURT: Thank you.

Mr. Suggs, who is your next witness?

MR. SUGGS: Your Honor, the State of Alaska calls as its next witness Dr. William Wirshing.

THE COURT: Dr. Wirshing, if you could come forward, please, and if you could stand behind the witness chair, we'll administer an oath.

(Clerk swears witness.)

THE CLERK: For the record, would you please state your full name, spelling your first and last name, sir?

THE WITNESS: Full name is William, spelled conventionally, C., last name Wirshing, W-i-r-s-h-i-n-g.

EXAMINATION

Q. (BY MR. SUGGS) Good morning, Dr. Wirshing.

A. Good morning, David.

Q. How old are you, sir?

A. 51.

Q. And you live in the Los Angeles area?

A. I do.

Q. And you are a physician, correct?

A. That is correct.

Q. And you've been a doctor for over 25 years?

A. Yes, it has been over 25 years.

Q. And have we retained you as an expert witness to testify about your opinions as to whether Zyprexa can cause diabetes and whether Eli Lilly adequately warned about the risks of Zyprexa?

A. Yes, sir, you have.

Q. And before we go into your opinions about Zyprexa, I'd like to first go over your educational background and your personal experience with Zyprexa.

A. Fine.

Q. First, you received your bachelor's degree in electrical engineering and computer

science in 1978 from the University of California in Berkeley; is that correct?

A. That's correct. I did a subspecialization in bioelectronic systems.

Q. And you received your medical degree from the University of California at Los Angeles or UCLA in 1982; is that right?

A. That is correct.

Q. And you've been licensed to practice medicine in California since 1983?

A. Yes. June of 1983.

Q. And you took your internship and residency in psychiatry at the Neuropsychiatric Institute at UCLA; is that right?

A. Not quite. My -- my internship was a combined medical, pediatric and neurologic internship, and I did that at the West Los Angeles VA and at UCLA.

Q. Okay.

And that internship and residency was another four years after medical school?

A. That is correct.

Q. And you completed the residency in 1986?

A. That's correct. I was chief resident in geropsychiatry right before I finished up, but I

completed it in June of 1986.
Q. Okay.
And then you spent an additional two years in a postdoctoral research fellowship; is that correct?
A. That's correct.
Q. And we've heard some prior testimony from Dr. Brancati and I believe others, Dr. Gueriguian, as well, about postdoctoral fellowships. Am I correct that generally those are for folks who are considering going into academic medicine?
A. Yes. It's -- mine was through the NIMH. My mentor and professor was the late Dr. Michael Goldstein, and it was specifically to study schizophrenia. It's obligatory when you're involved in a research fellowship that you pay back month for month, year for year, in academia the time that you spent in the fellowship, so you -- yes, it's anticipated, indeed. It's obligatory, at least for a time.
Q. Okay.
And the focus of your research fellowship was in the field of schizophrenia; is that correct?

A. Specifically schizophrenia, yes, sir.
Q. Okay. And has schizophrenia continued to be a particular focus of your practice and research since that time?
A. It has continued to fascinate me to the present day.
Q. And why is that your focus, sir? Why do you like to work with schizophrenia?
A. Oh, that's -- that's a very good question. It is -- in all of medicine, which I dearly love just about every single aspect of it, but in all of medicine it is the -- it is the particular mollusk in the tidal pool which fascinates me beyond all others. It is endlessly interesting, maddeningly impossible to comprehend, and it is -- it is a challenge every single day to deal with it. And it is -- it has always been an honor to be in the presence of these people.
Q. Okay. And, sir, you were board certified in psychiatry in 1988; is that correct?
A. Yes. I think it was 1988. Yes, sir.
Q. Okay.
And then you received an additional qualification in geriatric psychiatry in 1991; is

that right?
A. Yes. That was the first year that that designation was actually instituted, was in 1991.
Q. Okay.
A. I was the inaugural -- among the inaugural class.
Q. And after your medical training and residency and postdoctoral training, did you then become a professor at the medical school at UCLA?
A. Not quite. They don't start you out at the professor level. They torture you for a good number of years before you get to that rank. But I -- you start out -- I was an assistant processor there -- in the UC system there are five separate steps for assistant professor, each of which takes two to three years. There are then three steps at the associate professor, each of those taking -- taking three years, and then you make full professor.
Q. Okay.
A. There are nine ranks of full professor.
Q. Okay.
Sounds like peeling an onion.
A. It is indeed.
Q. Okay.

And you were a full professor at UCLA?
A. I was. I made full professor by the time I was 40.
Q. Okay. And for how long were you a professor at UCLA?
A. Well, counting up all the various onion layers?
Q. Yes.
A. From 19 -- I guess it would be 1988 until 2006, 2007.
Q. Okay.
And was your professorship at UCLA in conjunction with employment at the VA hospital in Los Angeles?
A. No, it was dependent upon it. UCLA and the VA are basically across the 405 Freeway from one another, and my site of my clinical work, my research interest, my teaching, took place at the VA, and that's where my paycheck came from, but I had the academic appointment at UCLA, and I taught medical students and indeed undergraduate students at the university. So it was a -- a shared interrelationship, but it was completely dependent upon my employment at the VA.

Q. Okay.
And am I correct that you left your position at the VA in late 2006?
A. I did. Yes, sir.
Q. Okay.
And you are now a vice president of a -- an entity called Exodus; is that correct?
A. That's correct, sir.
Q. Can you tell the jury what is involved with that?
A. Exodus is a -- an entity, a business that has six separate sites, five of which are in Los Angeles County in California and one of which has just now opened up in North County San Diego, which is just south of -- south of Los Angeles. And it is largely taking care of county-type patients, so seriously, chronically mentally ill, the exact kind of patients I've spent my career with.
And it is -- my job is -- I'm vice president actually in charge of continuing medical education and research, but the vast majority of my work just continues to be the -- the clinical work that's fascinated me my whole life. It's -- though I never believed that I

would ever say this, but I actually don't miss my patients at the VA. I'm very, very much enjoying my new position.
Q. Very good. I think you told me that you spend about three-fourths of your time doing clinical care and the other quarter of the time is about teaching; is that correct?
A. Teaching and writing and research, yeah. It's probably closer to 80 percent, but around that price category.
Q. The jury has heard about what peer-reviewed medical journals are. Have you served as an editorial reviewer for any peer-reviewed medical journals?
A. Yes, many.
Q. How many, roughly?
A. I'm an ad hoc reviewer on the -- the journals, which means they call me when they -- they get an article that has my expertise in it, but I would say over the course of the years two dozen.
Q. Okay.
And have you yourself published any articles in the peer-reviewed medical journal?
A. Oh, it's one of the obligatory aspects

about being in academia. Publish or perish, as they say.
Q. And about how many articles have you published in peer-reviewed journals?
A. Oh, probably about 80 articles, 120 abstracts, 25 chapters.
Q. Okay.
And how many of the articles that you've published have dealt with schizophrenia or the properties of drugs used to treat schizophrenia?
A. Effectively all of them.
Q. Okay.
And how many of your published medical articles studied the effects of Zyprexa?
A. Toxic efficacy? Both? Either?
Q. Either way.
A. Well, counting the abstracts, probably a dozen and a half. Something along those lines Pure articles, probably half a dozen.
Q. Okay.
And did any of those articles deal with the metabolic properties or metabolic effects of -- of Zyprexa, with respect to blood glucose, lipids, weight gain, that sort of thing?

A. I believe that all of them did.
Q. Okay.
And did any of your medical articles regarding Zyprexa -- strike that.
Those articles that you did that did address the metabolic issues, were they published in peer-reviewed journals?
A. Yes, sir.
Q. When did you publish your first article about whether or not Zyprexa is linked with weight gain and hyperglycemia or diabetes?
A. Well, the first abstract was -- was 1996. I think the first article came out in 1998.
Q. And was that the first article ever to link Zyprexa and diabetes?
MR. LEHNER: Objection. This is going beyond, I think, his qualifications here. This is getting into the substantive testimony.
MR. SUGGS: I'm just talking about the timeline of his activity. I can -- I'll withdraw the question.
THE COURT: I'll allow it.
Before you do that, Doctor, you've used the term abstracts as opposed to articles.

THE WITNESS: Correct.
THE COURT: Could you let us know what the differences are?
THE WITNESS: Sure. When you go to, say, a scientific conference, the APA or some meeting of nerds like myself, you have to submit a condensed description of the project that you're going to present, either verbally or in what we call poster fashion. And that abstract is -- is literally a paragraph or two long, and as I say, summarizes in formalized fashion exactly what was done in the little project that you're going to -- that I'm going to present.
Those abstracts are then published; just the abstracts, not the full article, not the full description, but just the abstracts are published in like the proceedings of that particular conference. And sometimes a full paper is written as a consequence of that abstract. Sometimes you never get around to it. Sometimes it -- it just falls apart -- your findings fall apart down the road. So abstracts usually antedate a formal full publication, but both are published, just different sizes, different formats.

Q. (BY MR. SUGGS) Besides your own articles, are there other peer-reviewed scientific articles addressing the issue of whether or not Zyprexa and other atypical antipsychotic drugs are associated with an increased risk of diabetes?
A. Oh, literally hundreds.
Q. And are you familiar with that literature?
A. I'm -- yes, quite.
Q. Okay.
Did you review that literature in preparation for your appearance here as an expert witness?
A. Not in its absolute entirety, again, but, yes, I did go over it.
Q. And have you reviewed that literature as it came out, as it was published?
A. Yes. I mean, it's -- it's something that fascinates me; it's of interest to me. It's ongoing upkeep of my knowledge in that situation, yes.
Q. Okay.
And the jury has heard some testimony about something referred to as a

consensus statement, and a consensus conference that was convened in November of 2003.
Were you a presenter at that conference?
A. I was, yes, sir.
Q. And were you invited to speak as a presenter at that conference?
A. I was, yes, sir.
Q. And were you invited to speak or be a presenter because of your expertise in the area?
A. Yes. Absolutely.
Q. Okay.
And I believe you gave presentations regarding the blood monitoring protocol and also in the area of lipids; is that correct?
A. That's correct. Yes, sir.
Q. Now, in addition to reviewing the published medical articles and being familiar with that literature, in any event, as a result of serving as an expert witness in this case, have you had the opportunity to review internal Lilly company documents?
A. Yes, sir.
Q. And attorneys gave you those documents,

correct?
A. They did. Yes, sir.
Q. And you would have had no other way of obtaining access to those documents but for your role as an expert witness in this litigation; is that correct?
A. I presume the answer -- the answer is no. I never have tried to get access to them, but I wouldn't offhand have any idea how to go about it.
Q. Okay.
Do you recall that the documents you reviewed were stamped with a confidentiality stamp?
A. Over and over again.
Q. Okay.
The jury has heard about the testing that drugs undergo before they're released on the market here in the U.S., and the jury has also heard testimony about first-generation antipsychotics and second-generation antipsychotics. Behind you is a list of second-generation antipsychotic drugs.
Were you personally involved as a clinical investigator in the premarket clinical

testing of any of those second-generation antipsychotics on behalf of the drug companies that were developing them?
A. Yes, sir.
Q. And which, if any, were you a clinical investigator on?
A. All except for quetiapine.
Q. And have you prescribed both first- and second-generation antipsychotic drugs to your patients?
A. Tens of thousands of times.
Q. Are there any first- or second-generation antipsychotic drugs here in the U.S. that you have not prescribed to your patients at one time or another?
A. Absolutely not.
Q. Okay.
In addition, have you also prescribed other first- or second-generation antipsychotics that are available in other countries but are not available here?
A. In desperate circumstances, yes, I've obtained medications from overseas for my patients.
Q. And are you knowledgeable regarding the

risks and benefits of first- and second-generation antipsychotic drugs?
A. I certainly like to think so.
Q. And are you familiar with the labeling of those drugs?
A. Yes, sir.
Q. And have you reviewed, in particular, for purposes of testifying in this litigation the labeling of Zyprexa from 1996 to the present?
A. I have.
Q. Okay.
How many --
MR. LEHNER: Your Honor, may we approach for a minute?
THE COURT: You may.
(Bench discussion.)
MR. LEHNER: It's the same issue that we had previously that he gave his deposition on May 1, 2007. He --
MR. SUGGS: Your Honor, he's not going to testify about the 2007 label. He just happens to be a practicing physician and --
THE COURT: Just so that we're clear, I assumed that too.
(End bench discussion.)

Q (BY MR. SUGGS) Okay. I believe that you testified that you have reviewed the Zyprexa labeling from 1996 to the present?
A. Yes, sir, I did.
Q. Okay.
And how many premarket clinical studies involving Zyprexa were you engaged in?
A. Olanzapine, I think we did -- we did one fairly large premarketing study comparing 10 milligrams of olanzapine to 1 milligram olanzapine in a blinded fashion.
Q. And was that study conducted on behalf of Lilly or for Lilly before Zyprexa went on the market?
A. Yes, sir. Before -- before a compound is available on market, even clinical investigators, researchers like myself, are dependent upon drug companies to provide those medications, because they're simply not available. They're proprietary.
Q. Okay.
And how much did Lilly pay your research facility to conduct those scientific studies?
A. I don't recall exactly, but

approximately $150,000.
Q. Okay.
And did you personally profit from that money, or does it go to the -- to the university as --
A. No. The university locks you up for doing something like that.
Q. Okay.
A. No, you -- very much forbidden, at least, in the place that I was working for that to occur. The money goes to a research institute and is very carefully monitored and has to specifically go for specific things, and a pile of ponderous paperwork that you have to follow. Too many regulations for me to even recount.
Q. Okay.
And during your involvement in that premarket clinical study, did you have discussions with in-house Lilly physicians regarding the data from Lilly's clinical studies of Zyprexa?
A. Oh, absolutely. One of my -- the favorite aspects of my career at that point was actually to interact with industry prior to a drug reaching market. It's very exciting; it's

very interesting. You're learning things that nobody else in the world has ever learned before. You're discovering things, and it's really what I like to do. Once -- once things are known I get bored and I want to leave the room.

Q. And the jury has heard testimony from Dr. Charles Beasley by way of videotape.

Was he one of the individuals that you had discussions with?

A. Yes, I worked with Charles dating back to probably 1993.

Q. Okay.

And the jury is going to hear videotaped testimony from Dr. Gary Tollefson later this afternoon or perhaps a little bit later. Was he another one of the individuals that -- at Lilly that you spoke with regarding Zyprexa before it went on the market?

A. Yes. I don't -- I think I first had interactions with Dr. Tollefson in -- it was regarding actually Prozac, and that was in 1990.

Q. Okay.

And was Dr. Winston Satterlee, another Lilly in-house physician that you had discussions with about Zyprexa before it went on

the market?

A. Yes. Winston was one of my favorite people at Lilly.

Q. Okay.

And did you also have discussions with nonphysicians, but people in the marketing group at Lilly before Zyprexa went on the market?

A. No. No.

Well, just before it goes on the market, but I have no knowledge of who's going to be in marketing prior to the drug being marketed. The team tends to change dramatically, at least in general, on average, when a drug goes from the scientist sorts to the marketing people, and it -- the game, if you will -- I don't mean to speak pejoratively, but the stuff that happens is not as interesting to me, and I tend to not have as much to do with the marketing people.

Q. Okay.

Did you continue to do clinical studies on Zyprexa on behalf of Lilly after Zyprexa went on the market in October of 1996?

A. Well, the answer is sort of yes and sort of no. I continued to do research on olanzapine, really, continuously till about 2005 or so, but

it was in -- in large part of my design, so I would go hat in hand to ask for research support from Lilly to study their compound in a certain way in my clinical population. And had many hundreds of discussions with them trying to -- trying to fine-tune exactly what -- what we could both agree to. Those are -- were very, very, very lengthy discussions.

Q. And did Lilly pay your research facility for conducting those studies?

A. Yes, sir.

Q. And did you also have any consulting relationships with Lilly regarding Zyprexa?

A. Both with Zyprexa and with fluoxetine.

Q. Okay.

With respect to Zyprexa, what did your consulting for Lilly involve?

A. Oh, in general, the consulting prior to release would be get together the clinical investigators at a meeting or two and we would discuss the results, give the feedback to the -- to the scientist sorts and they would occasionally gather usually as a satellite to some meeting that we were already holding, some national meeting of one sort or another, and I

would be reimbursed to a certain degree for that participation.

Q. Okay.

And you also mentioned that you were a consultant for Lilly in connection with fluoxetine, and the trade name for that is Prozac; is that correct?

A. Yes, sir.

Q. And what were your consulting duties with Lilly about with respect to Prozac?

A. Well, in 19 -- 1989 there was a -- an issue as to whether or not Prozac led to the development of suicidal ideation. I was extremely fascinated by this report, and elaborated a case series of six patients that I published in the Archives of General Psychiatry what I thought explaining how this could actually occur, and I thought it was a recognizable toxic consequence, understandable, treatable consequence of it.

And as a result of that small letter to the editor, it came to the attention of legal's Lilly team that -- Lilly's legal team -- sorry, excuse me -- and I worked for years with them on cases across the world. I mean, it was

unbelievably interesting and fascinating. Perhaps north of a hundred cases.

Q. Okay.

And I presume you were paid for your time consulting for Lilly on those cases?

A. As far as I know, they were quite good at paying their bills.

Q. Okay.

MR. SUGGS: Your Honor, the State of Alaska tenders Dr. Wirshing as an expert in the fields of psychiatry in general, in particular with respect to the treatment of schizophrenia, bipolar disorder and geriatric psychiatry. In addition, we tender him as an expert in the risks and benefits of both first-generation and second-generation antipsychotic drugs and the labeling of those drugs.

We also tender him as a -- an expert regarding the relationship between Zyprexa and weight gain, hyperglycemia, diabetes and hyperlipidemia, and also as an expert with respect to the issue of whether Lilly adequately warned about the risks of Zyprexa.

THE COURT: Do you wish to voir

dire?

MR. LEHNER: No, we'll save our questions for cross-examination. Thank you very much.

THE COURT: I will so recognize the doctor as an expert in the field -- in the areas that you have just designated.

MR. ALLEN: Thank you.

THE WITNESS: Thank you, Your Honor.

Q. (BY MR. SUGGS) Dr. Wirshing, in Lilly's opening statement Ms. Gussack played a video clip from a deposition you gave, in which you stated that -- and I think I'm quoting this: The second-generation antipsychotics are among the most powerful disease modifiers in all of medicine and are a godsend to most people. And she also said that you testified that they could be the closest thing to magic one might see in medical practice.

Do you recall giving testimony like that at any time?

A. Well, it certainly does sound like my turn of phrase.

Q. Okay.

And was that testimony -- did it arise in a Zyprexa case for the first time, or did it arise in a case involving a -- another antipsychotic drug?

A. Well, I -- I believe that one was from a risperidone or Risperdal class-action suit that I was involved in, so it -- I don't -- it had nothing to do with olanzapine at all.

Q. Okay.

And when you were giving that testimony, the second-generation antipsychotics are among the most powerful disease modifiers, were you referring to the class of second-generation antipsychotics as a whole or any particular drugs within that class or --

A. Well, I mean, at the time, what I was -- what I was -- was thinking of and what was going on in my head, it was -- was the prototype of the class, which is the first one up there, clozapine, which was elaborated in 1959. It is the -- as I say, the prototypic atypical, and -- and it is -- unequivocally the most toxic and unequivocally the most powerful of the antipsychotics. So, that's what was in my mind.

Q. Okay.

And, sir, despite the fact that you're here to testify on behalf of the State of Alaska and against Eli Lilly, you continue to prescribe Zyprexa for some of your patients even today, correct?

A. Well, I'm in Alaska today and I'm not allowed to practice medicine in Alaska. But I left -- when I left home on Monday or left home on Tuesday -- on Monday, I had prescribed olanzapine to, I think, two of my patients.

Q. Okay.

If you're still prescribing Zyprexa for at least some of your patients, why are you here testifying against Lilly? What, if anything, did they do wrong with Zyprexa?

A. Well, that's a fair question. I think the truthful answer is twofold. Firstly, it is my opinion that Lilly has consciously, deliberately and continuously denied, obfuscated or simply given short shrift to the true toxic profile of olanzapine. But quite honestly, that is not enough to get me to Alaska and to have kept me focused on this issue literally for more than 10 years.

The second reason, which is more

emotional for me, is that in their defense of their compound, Lilly has blamed the patients, at least in part, for the toxic consequences that are directly due to their drug, and you know, this is unconscionable to me.

Q. When you say that they've blamed the patients, how have they done that?

A. Well, I mean, I -- I -- I recall -- I recall the moment it happened. After our -- after articles first started -- first started to come out, my -- my wife at the time, Donna, and I were quite close, not just as a married couple, but quite close colleagues. And we were listening to a presentation from Lilly and they highlighted the fact that, quote, "People with schizophrenia are known to have an increased risk of diabetes."

I've been studying diabetes -- I mean, I'd been studying schizophrenia for 20 years at that point, and I turned to my wife Donna and I said, how come I didn't know that?

And this was never talked about beforehand, and it had -- it got repeated over and over and over again, to the point that it became almost axiomatic.

Schizophrenia is diabetes.

There's not one shred, not one microscopic, nothing, bit of evidence to suggest that the illness schizophrenia itself is associated with an increased risk of endocrinologic disturbance. None, zero. And that has been repeated over and over.

In effect, blaming the patient for the condition which the drug caused, and this -- this is emotionally very upsetting to me.

Q. Okay.

Doctor, you've told us your bottom line. Now let's start back at the beginning of your story with Zyprexa and your involvement with Lilly.

A. Yes, sir.

Q. Am I correct that your first involvement with Lilly and Zyprexa was back during the clinical studies that were conducted on the drug before it went on the market?

A. Yes, sir, approximately 1993.

Q. And as a result of your involvement in Zyprexa's clinical study and the data that you were collecting, did you have concerns about weight gain?

A. Yes, sir.

Q. And did you discuss those concerns with people at Lilly?

A. Of course. Yes, sir.

Q. Okay.

MR. SUGGS: Can you pull up Exhibit 1586, please, and go to Page 8.

By the way, this is the -- this is a memorandum describing the third United States Schizophrenia Advisory Panel meeting in December of 1995. It's been previously admitted.

A. Yeah, this is one of the satellite meetings I referenced. This was around the American College of Neuropsychopharmacology, which is held in Puerto Rico every year at that time.

MR. SUGGS: Can you go to Page 8, please.

THE COURT: Just so that I can be clear on the record, I'm not sure whether you said 1586 or 1596.

MR. SUGGS: It's 1586, Your Honor, and it has been admitted.

THE COURT: Looks like -- oh, I see. At the bottom there's also a 1596. Okay.

Go on.

MR. SUGGS: Your Honor, that 1596 is --

THE COURT: The MDL number. That's where my confusion was.

MR. SUGGS: I've been confused by that many times myself.

Chris, can you pull up the last couple lines of the first paragraph.

Q. (BY MR. SUGGS) The last two sentences state in there, Patients who remained on olanzapine for 12 months gained an average of 24 pounds at the end of 12 months.

Do you see that language, sir?

A. Yes, sir.

Q. And at any time in your involvement with Lilly's premarket testing of Zyprexa, did Dr. Beasley or anyone else inform you that the average weight gain on Zyprexa was 24 pounds?

A. No, sir. I -- I was at the ACNP, but I was not part of this advisory panel.

Q. Okay.

MR. SUGGS: And, Chris, can you pull up AK10008.

Your Honor, this is the 1998 PDR,

which I believe the evidence shows was the first PDR for Zyprexa, and it has not been previously admitted. Do you have any objection to admitting that?

It's the 1998 PDR.

MR. LEHNER: No, Your Honor.

THE COURT: 1008 (sic) may be admitted.

MR. SUGGS: And can you go to, I believe, Chris, it's Page 3, the page regarding weight gain in the adverse reactions section.

Q. (BY MR. SUGGS) And Doctor, you have reviewed -- you testified that you've reviewed the 1996 labeling through 2006; is that correct?

A. More times than I like to remember, yes, sir.

Q. Okay.

And if I could direct your attention to the last sentence in the section -- in the adverse reactions regarding weight gain, it states, Average weight gain during long-term therapy was 5.4 kilograms. Do you see that?

A. Yes, sir.

Q. And if we do the math, am I right that

5.4 kilograms works out to about 11.8 pounds?

A. That's correct, 2.2046 pounds per kilogram.

Q. Okay.

And that's less than half of the 24 pounds weight gain that we saw in the other document; is that correct?

A. Yes, 11.8 is less than half of 24.

Q. And throughout the time period from 1996 through 2006, did the Zyprexa labeling state in the adverse reactions section that the average weight gain during long-term therapy was 5.4 kilograms?

A. Yeah, as far as I know, that particular sentence never altered a single letter.

Q. Did the labeling ever advise physicians that the average weight gain over the course of a year was twice that or 24 pounds?

A. No, it said precisely what it says here, 5.4 kilograms.

Q. And in your opinion, sir, is it a material fact that the average weight gain with Zyprexa is 24 pounds over a year's time?

A. Again, are we talking about the average --

Q. Yes.

A. -- weight gain?

Q. Well, let me restate my question.

Was it -- in your opinion is it a material fact that the average weight gain on Zyprexa over -- for those who use it for a year, is 24 pounds?

A. It has enor -- it has enormous range. The -- the average is at least 24 pounds, but it -- it varies enormously from individual to individual. It -- literally from a slight weight loss to patients gain 125 pounds in the first year. I mean, it -- it has enormous variance, but on average, yeah, it's around 25 pounds.

Q. And do you believe that practicing physicians should have been made aware that the average weight gain over the course of a year on Zyprexa was 24 pounds?

A. Physicians should be aware of whatever the data is.

Q. Okay.

A. Absolutely.

Q. Now, is there a rule of thumb that applies to be able to figure out how much weight gain results in an increased risk of diabetes?

A. Yeah. Other things being equal, the single most powerful and pertinent determinant of diabetes is excess adipose tissues, excess fat, certain kind of fat, but excess fat in general. If you look at large populations, like the Framingham Heart Study population, for instance, where you have huge numbers, you can show that a one-pound change in adiposity, a one-pound change in fat translates to a 4 percent increased risk of diabetes in that same population. A five-pound change in fat translates to a 25 percent increased risk of diabetes.

Q. So is it just a straight linear relationship, then?

A. No. No, even those numbers are not quite linear, but it tends to go up aggressively, so that people that have more weight have progressively more risk. It goes up in a decidedly nonlinear fashion.

Q. And if, in fact, the average weight gain for folks who used Zyprexa for a year was on the order of 24 -- well, was 24 pounds, as we saw in Exhibit 1586, what would that translate into in terms of an increased risk of diabetes?

24 pounds in one year.

A. There's -- there's a problem in that 24 pounds is such an unusual weight change in a single year that there aren't good statistics for large numbers of people because folks don't do that very often. However, extrapolating from what we do know about weights from populations, I would say -- it's different for males, different for females, sort of an averaging -- sort of an average male/female thing, if you will. It would be three to four and a half, so 300 to 450 percent.

Q. Okay.

A. Approximately. Higher for the -- higher for women, lower for men, but kind of in that average.

Q. Okay.

So an increased risk of diabetes with Zyprexa for those who use it for a year on the order of three to four times higher?

A. Correct, due only to the increase in adiposity.

Q. And do you believe that physicians should have been warned about that at the outset when this drug went on the market?

A. Should have been warned about the

magnitude or the --

Q. Yes.

A. Of course. Of course.

MR. SUGGS: Chris, can you go back to Exhibit 1586 and that same page. I believe it was Page 8.

And can you blow up the italicized paragraph there in the middle.

Q (BY MR SUGGS) At this 1995 meeting, after the advisers were informed of the 24-pound weight gain in a year, the document states, quote, "Several advisers 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 2 diabetes."

Do you see that language, sir?

A. Of course.

Q. Now, even though you were not aware of the 24 pounds weight gain, but had seen weight gain in your own patients that you were involved in, did you express concerns to Lilly at that time about increased blood pressure, increased

cholesterol and the risk of type 2 diabetes as a result of the weight gain?

A. Yes, but it is simply axiomatic that if you are going to increase fat to that degree, even -- even the -- the 5.4-kilogram degree, but if you're going to increase fat to that degree, it's simply axiomatic, you will induce severe problems with lipids, blood pressure and glucose regulation in a population.

Q. Let's talk specifically about who it was that you told about your concerns with this.

A. Okay.

Q. Did you talk with Dr. Beasley about this?

A. Yes, sir.

Q. Did you talk with Dr. Tollefson about this?

A. Dr. Tollefson?

Oh, yes, we did. Yes.

Q. How about Dr. Winston Satterlee?

A. Yes, Winston Satterlee I had a number of conversations with.

Q. And when would you have had your conversations with those individuals?

A. Oh, that was probably subsequent to the

first presentation, so '95ish, early '96.

Q. Okay.

And when you told them about your concerns -- by the way, these three people that we've talked about so far, they were all medical doctors in-house at Lilly, correct?

A. Medical doctors/scientists.

Q. Okay.

A. Yeah.

Q. And what was their reaction when you told them about your concerns with diabetes being a risk with the use of Zyprexa?

A. They were receptive, interested, polite, collegial. I mean -- they were the same as bringing any other of our observations. We had a number of different things that we talked to them about. This was but one of them.

We talked about neurocognitive measures that we had noticed. We -- we talked about subjective tolerability. We talked about sexual functioning on the drug. I mean, we had a lot of good and interesting and some -- some bad and interesting findings with respect to olanzapine.

Q. Okay.

I believe you testified earlier that you also had a discussion with an individual named J. R. Richards shortly before Zyprexa went on the market?

A. Yes. I met Mr. Richards -- he was marketing, so he was not a part of the scientific folks that we had been working with prior to that, and had met Mr. Richards, took me to this -- my oldest daughter, my wife and I went to a prelaunch celebratory meeting at one of these really cool Italian restaurants in New York City -- it was a magnificent meal -- and had a lengthy discussion with him about two particular issues that I was concerned about.

Q. And did you tell him at that meeting -- well, at that dinner that you were concerned that Zyprexa was going to have potential problems with diabetes?

A. I -- I told him about two things at that dinner. The two items that I was concerned with was that, one, the clinical studies that had been done focused on a primary drug dose of 10 milligrams, and that it was my belief the drug had elevated efficacy above that dose and they were going to screw it up and tell people to dose

the drug improperly, dose too low. That's what I was worried about. That was my first concern.

And my second concern was the weight gain and the attendant problems, diabetes included, associated with the drug. By '96 we had had -- we had begun instituting a whole bunch of -- I designed it, but a whole bunch of strategies to try and control the weight gain, and that was what I was mostly interested in.

Q. What was the reaction of the marketing person when you told him about the risk of diabetes with Zyprexa?

A. Marketing --

MR. LEHNER: Objection, Your Honor; mischaracterizes the testimony. He didn't say that.

Q. (BY MR. SUGGS) Let me restate the question.

Did you express to Mr. J. R. Richards, a marketing person at Lilly at that dinner in New York, concerns that Zyprexa could have problems with diabetes?

A. Yes, and I specifically presented -- I think Latrell was her name -- was a nurse practitioner from the south, I believe -- a plan

to try and help people with the weight gain that occurred. I mean, this was a known, recognized fact of olanzapine, and what I was interested in was setting up a strategy to deal with it.

Q. And what was the reaction from Mr. Richards in marketing?

A. Dismissive.

Q. Pardon?

A. Dismissive.

Q. Okay.

A. Marketing people, in general, are dismissive of people like me. We're scientific nerds and, you know, go away sort of thing, but it's a -- it's a common situation. As I say, I tend to lose interest in him and I'm probably just as dismissive of him as he was of me.

Q. After you told various people at Lilly about your concerns about potential safety problems with Zyprexa, did anybody at Lilly show you any computer analyses indicating that Zyprexa, in fact, had a statistically significant increased incidence of hyperglycemia or cholesterol as compared to haloperidol?

A. No. Quite the contrary. I recall that after this -- not the first article we've talked

about, but I believe it was the second article, they were quite adamant that -- that our drug may cause a little problem with weight gain, but it doesn't cause diabetes.

Q. Have you seen documents for the first time in this litigation reflecting computer analyses of data from the HGAJ study and the relationship between Zyprexa and hyperglycemia?

A. The HGAJ was the 1,996 patient study?

Q. Yes.

A. Yes. Yes, sir.

MR. SUGGS: Can you pull up Exhibit 1605, please. And 1605 has already been admitted into evidence, Your Honor.

THE COURT: Thank you.

Q. (BY MR. SUGGS) And, Dr. Wirshing, this document is described as a Table of Treatment-Emergent Abnormal, High or Low Laboratory Values at Any Time, from the HGAJ Acute Phase.

Are you familiar with a study known as the HGAJ study?

A. Yes, sir. It was -- it's one of the cool studies in the profession. It's a study involving literally the largest number of

psychotic patients ever enrolled in a single study; 1,996. I believe they were shooting for 2,000, but they got 1,996; 2 to 1 randomization. Two patients put into olanzapine, one patient put into the comparator haloperidol; 5 to 20 milligrams of olanzapine and the equivalent number in the haloperidol. The acute phase lasted for eight weeks, but then there was an open phase which lasted a total of a year, and that's where that 24 pounds, for instance, came from.

Q. And this particular computer analysis is dated June 19, 1995. Do you see that up in the upper right-hand corner of the box?

A. Yes, sir, I do.

Q. Okay.

And would this have been at or around the time that you had expressed concerns to Lilly about weight gain and potential risks of hyperglycemia?

A. Yeah, this -- essentially coincident.

MR. SUGGS: Okay.

And could you go to Page 11, Chris. And can you pull up the Glucose Nonfasting Chart there, or that portion of the chart.

Q. (BY MR. SUGGS) And, Dr. Wirshing, can you tell us what this chart shows in connection with the -- the high line there?

A. Yeah. Well, it -- it shows that of a very large number of samples, 1,284 collected, that 34 met their criteria for, quote, unquote, high, which is two standard deviations above, and that translated at 2.6 in the olanzapine group. And of the 625 samples in the haloperidol group, 7, or 1.1 percent in the haloperidol group also met that criteria, so two and a half times as much in the olanzapine group.

Q. And was that finding statistically significant?

A. Yeah, at the -- at the .03 level, yes, sir.

Q. Okay.

In your opinion is that a red flag for diabetes?

A. It -- it certainly is -- is suggestive of it. I mean, it's -- this was only an eight-week study, and to actually have hyperglycemia emerge in that period of time is -- that's interesting. That's difficult to explain, quite honestly.

Q. Can you also pull up --

Well, pardon me. Back when you expressed your concerns to Lilly about a possible problem with diabetes in 1995, did they show you this data?

A. No, sir. As we talked about, I had not seen this data until the preparation for coming up here to Alaska.

Q. Okay.

MR. SUGGS: Can you go to the following page, Chris, and pull up the data regarding cholesterol there.

Q. (BY MR. SUGGS) And can you tell us, Doctor, what does that show with respect to high cholesterol?

A. This -- so this is, again, taking total cholesterol, so the total lipid cholesterol pool in your blood, and it shows that 5 of 622 patients in haloperidol or 0.8 percent, and 29 of 1,272, or 2.3 percent. Again, about a threefold difference, significant .02 level.

Q. And did they show you this data back in 1995?

A. No, they did not, though this is a little less difficult to explain and a little

more expected, given what I know.

Q. What is the relationship between hyperglycemia, weight gain and high cholesterol, if there is one?

A. Oh, yes, there is. As our -- in gen- -- is not for an individual, but for the prototypic human in general, as you increase adiposity and you increase fat, particularly certain kinds of fat, what the -- we call omental adiposity, so the fat around your midsection, that is a -- the researchers call it brown fat.

It's a particularly bad kind of fat, and that is associated both with endocrinologic disturbance through insulin resistance. The insulin just doesn't work as well as it used to. The pancreas has to work harder, and it's just harder to keep your sugars down and they tend to drift up.

Though the fat causes a -- that particular fat causes a toxicity in certain individuals, again, not in everybody. If you're the type of person that carries your fat elsewhere, doesn't do anything but cause you to have joint problems, but it does not impact your endocrinologic situation.

In terms of circulating lipids, when you expand the fat pools in your -- in your body so that the cholesterols or the so-called phospholipids, they're the way that we transport fats in our blood. Imagine -- our blood is like seawater, and when you put oil on seawater, it floats and you can't transport it anywhere. It -- you have to -- to make it miscible with water, you have to do some tricky things to it and that involves cholesterol.

So the transport of lipids to all the various tissues, to and from all the various tissues in the body requires cholesterol. When you expand those fat stores, you got more stuff on your freeway, so your cholesterol goes up. It's a direct relationship between increasing adiposity and total cholesterol. You lose weight, your cholesterol goes down; you gain weight, your cholesterol goes up. You gain fat, not just weight. You gain fat.

Q. The jury's seen this section of the CFR a number of times, which says that -- under this section heading, the labeling shall describe serious adverse reactions and potential safety hazards, limitations in use imposed by them, and

steps that should be taken if they occur. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug. A causal relationship need not have been proved.

Do you see that language, sir?

A. I'm quite familiar with it. Yes, sir.

Q. And you are familiar with that requirement, right?

A. Of course.

Q. Well, sir, if Lilly was aware back in 1995 that the average weight gain of patients on Zyprexa who used it for a year was 24 pounds, and they were aware that there was a statistically significant higher incidence of high blood glucose even after as little as eight weeks, as reflected in Exhibit 1605, and they were also aware that there was a statistically significant higher incidence of high cholesterol, even after as little as eight weeks, is that reasonable evidence of an association, in your mind, that would trigger the duty to warn?

A. I would say that the mere presence of weight gain would cause me to answer the question in the affirmative. I'd have to say, absolutely.

Increasing weight to that degree, it is simply axiomatic that you will cause diabetes and you will cause cholesterol dysregulation. That is an absolute incontrovertible medical fact.

Q. But, Doctor --

MR. SUGGS: Chris, can you pull up the labeling that we were looking at, again, before. And go to the adverse reactions section.

Q. (BY MR. SUGGS) And, Dr. Wirshing, doesn't the -- the labeling list diabetes in the adverse reactions section?

A. Absolutely. It has since the very beginning.

MR. SUGGS: Chris, can you pull up that part of the labeling. Do you know where it is?

I think it's on Page 4, in the right-hand column. I believe so, yes.

Q. (BY MR. SUGGS) Are you able to read that, Dr. Wirshing?

Can you blow it up some more, Chris?

A. Endocrine system. Infrequent diabetes mellitus and goiter, rare. Diabetic acidosis -- I assume that's ketoacidosis. I can't read that.

And lymphatic system. I can't quite figure out what that is. Infrequent cyanosis, leukocytosis, lymphadenopathy and thrombocytopenia.

Q. Dr. Wirshing, doesn't that listing of diabetes back in the adverse reactions section -- isn't that good enough?

A. No, the adverse reactions section is not the warnings section.

Q. No. We're talking -- this is in the adverse reactions section.

A. No -- yeah, this -- no, this -- the adverse reactions section is -- is very different and very distinct from the warnings section. The vast majority of that which is in the adverse experience section -- adverse reactions section has nothing to do with the compound.

It's -- when you do these studies, remember, these -- these studies last from eight weeks to a year, and you're the clinical investigator. You're responsible for -- you're the doctor. You're responsible for the patient for that period of time. Anything that happens to that patient while they're in your care, that gets listed as an adverse experience. You get a cold, that gets in. You get the flu, you -- you

break your arm, you get divorced, whatever the heck it is, that gets put down in the adverse reactions section. And so you have no idea whether it has anything to do with the drug. Indeed, you don't know whether your patient was on a placebo or the drug or a comparator. You just simply list it in the adverse experience section.

That then gets translated to this ponderous list, and this is useful for clinicians and it should be here. It's required to be here, because if something happens to your patient on a -- on a drug and you go, my, I wonder if this has anything to do with the drug, you can at least look it up here in the adverse experience and say, has anybody else ever seen that?

And it's helpful sometimes, confirmatory to see that, oh, yes, back pain has been reported with olanzapine. Oh, yes, edema of the lower -- swelling -- edema of the lower extremities has been reported. But it's -- it's not a -- you wouldn't warn people about this because this -- this is everything and its grandmother here.

Q. Well, is it your opinion that the risk

of weight gain, hyperglycemia and diabetes should have been in the warning section of the labeling as early as '96?

A. Absolutely. I mean, it is -- it is my belief that the single most prominent clinical consequence of taking olanzapine by far and away, head and shoulders, is the fact that it causes weight gain. I mean, that's the most interesting thing from a scientist's perspective.

How it does that, why it does that, I mean, it is -- it is startling, but it is also the most clinically pertinent toxicity of the molecule by far.

Q. Doctor, did you and your colleagues publish an article in 1998 which discussed a link between diabetes and Zyprexa?

A. I think so, yes.

MR. SUGGS: Chris, can you pull up Exhibit 10 -- pardon me -- AK10141.

For the record, Your Honor, this is an article entitled Novel Antipsychotics and New Onset Diabetes, published by Donna A. Wirshing, Brad Spellberg, Stephen Erhart, Stephen Marder and William Wirshing, in the Society of Biological Psychiatry in 1998.

And, Your Honor, we would move for the admission of AK10141 for the purposes of notice.

MR. LEHNER: Your Honor, consistent with the Alaska rule on scientific theses and medical articles, this could be admitted as an exhibit.

THE COURT: I didn't hear you, Mr. Lehner.

MR. LEHNER: I think we discussed earlier, Your Honor, about admitting scientific articles. This is one of those, and we would admit it for that purpose. Notice to the --

THE COURT: Yeah. Ladies and gentlemen, this article is being admitted to -- for the purpose of showing that this was being discussed in the literature and there was notice to people of the contents of this document.

Q. (BY MR. SUGGS) And, Dr. Wirshing, is the Journal of Biological Psychiatry, is -- is that a peer-reviewed journal?

A. Yes, sir.

Q. And it notes that the article was received in September of 1997. That would have been less than an year after Zyprexa had been on

the market; is that correct?

A. That's correct.

Q. And your article was actually published a little bit later, in 1998; is that correct?

A. Also correct, yes, sir.

Q. And the article describes six patients who developed diabetes after they were on either clozapine or Zyprexa. I believe there were four patients on clozapine and two on Zyprexa; is that right?

A. As I recall, yes, sir.

Q. And did you regard this as additional evidence of an association between Zyprexa and the risk of diabetes?

A. Yeah, that's precisely why we published the case series.

Q. Okay.

Was it your opinion at the time you published your article in 1998 that the patient -- that these particular patients' use of either clozapine or Zyprexa was a substantial contributing factor in the development of their diabetes?

A. For these six patients?

Q. Yes.

A. Yes.
Q. Okay.
And why was that?
A. Well, somewhat of a tortured answer, and I will try and -- try to get it across. In -- in -- as a scientist, I require and I teach my students -- I require only believe other people's double-blind placebo and active comparison trials of sufficient duration and adequate power. In other words, don't trust anybody else unless you did a really good experiment.
Unfortunately, I'm also a clinician, and as a clinician, I'm -- I'm a person and I'm a human being, and I am compelled by the end of one experiment that I just did this morning with my patient; I gave him this drug and this is the stuff I saw. And those are overwhelming.
So as a clinician, yes, it was my conclusion, absolutely, these drugs were the cause of this condition, and it was my thought that it was because it caused weight gain.
As a scientist, I have to admit that I can't -- I can't know that, but as a -- as a clinician, I'd bet the farm on it.

Q. By this point in time, back in 1998, how many publications had you had in the field of psychiatry? Just ballpark.
A. Oh, I -- 80.
Q. Pardon?
A. 80.
Q. 80?
Would it be fair to say that you were a well-known psychiatric researcher at that point in time, 1998? Don't be modest.
A. Yeah, I had -- I'd irritated a sufficient number of people that folks knew who I was, yeah.
Q. What was the -- why did you publish this article?
A. Well, also a good question. My wife at the time, Donna, God bless her fuzzy little heart, is -- really likes to be first, and this was -- this was one of her pet projects. She's had a -- she's had an abiding and longstanding interest in -- in basically metabolism, dating back to her -- her college years. She was an Olympic alternate in the 1980 national fencing team, and also a runner, and she became interested in metabolism back then. So it was

really her focus on weight that prompted all this interest.
And when we saw this diabetes, she was very -- very keen to publish it, to let other people know. But in large part to display -- to demonstrate that weight gain is a substantial difficulty and you have to pay attention to it.
Q. And was this the first published medical article in the world linking Zyprexa with weight gain?
A. Yes, sir, it was.
Q. Okay.
And what was the reaction after you published this article?
A. It definitely got attention. This is -- this is the -- the lowest quality, if you will, in the -- in my profession, in academics, this is the lowest quality of publication. This is the stuff we saw. What do you guys think? No control, no -- no research. Case series is what it's called. So people take that for what it's worth. But this -- this really attracted an awful lot of attention.
There was lots of focus from the company; lots of focus from other people that

began reporting similar things. There was an increasing amount of publication and interest in this specific -- specific arena, which culminated a few years later in the consensus conference that we've already talked about.
Q. Okay.
And you said you had focus from Lilly. Did you have communications with Lilly after this article was published in 1998?
A. Most certainly.
Q. Who was your -- who were your first conversations with?
A. Well, at that point, you remember, we had -- we had changed over from -- from the premarketing scientist sorts and -- I don't think in 1998 we were actually participating actively in any specific protocols, as I recall. So my communication was with -- mostly with Mel Hamm, who was our regional district sales representative, and -- and his boss, a man named Anderson. I don't recall his first name. But many meetings about this.
Q. And what -- what was their reaction to your publication of this article linking Zyprexa with diabetes?

A. It was -- it was twofold, and I -- I recall specifically that at first -- I had a very good relationship with Mel. At first it was receptive, interesting. We'll take it back to the guys in Indianapolis, blah, blah, blah. You know, it was just collegial.

Mel is a -- a very capable man. He is -- was a retired captain from the U.S. Navy and was in charge of the worldwide formulary for the Navy. He was a pharmacist by training. So, you know, very capable, cool guy, very interesting personality.

On follow-up, after he had come back from what I presume to be corporate, again, my presumption, but Mel was adamant -- I mean, in my face adamant that -- might cause a little weight gain, does not cause diabetes, and --

Q. Fair to say you were --

A. I'm at a loss --

Q. -- shocked at his reaction?

A. I don't -- I don't know how to -- how to respond to that. I mean, it's -- it's -- it's tantamount to saying, you know, you could throw a person down an elevator shaft, but damn it, it's not going to hurt him when they hit the floor.

It just makes no sense. We can't have a rational conversation if you have that posture. It's just absolutely counterintuitive medically speaking.

Q. Did they show you any -- when Mr. Hamm came back after -- the second time and had the adamant reaction to you, did he show you any data at that time?

A. Well, he -- he came back with the big dog after that, with Mr. Anderson, and they showed me this ponderous dataset, which was a -- which -- which Lilly had elaborated -- I don't think it was directly in response to our publications, but in response to the mounting public interest or -- in the -- in the academic community about this issue, where they had -- where they had taken this literally thousands of patients in their controlled clinical trials and summarized it and showing that there was -- that there was no difference among placebo, haloperidol and olanzapine and what they idiosyncratically called impaired glucose tolerance.

And it was this -- as I say, just a tortured dataset, but it was -- it was a heck of a lot of data and we went over and over and over

that.

Q. Did they later -- I'm sorry.

A. I was just going to say that there were -- there were meetings following that, however.

Q. Did they later show you any data indicating that Lilly was, in fact, aware of the risk of diabetes --

Strike that.

Did they later -- did Mr. Hamm or Mr. Anderson later show you any data indicating that Lilly was, in fact, aware of a higher risk of hyperglycemia with Zyprexa as compared to placebo?

A. No, he did not show me any data. He didn't see that the written compilation like I described from that summary gemish, but he did say -- and this was, well, I'm guessing now, but six, eight months down the road, that from the HGAJ study, that there was a 0.5 versus 2.0 percent difference between haloperidol, 0.5, and olanzapine 2.0, of diabetes. I'm not sure -- I'm not sure whether it was diabetes or -- impaired glucose tolerance, but it was involving endocrinologic function, at any rate,

between haloperidol and olanzapine.

Q. And was the Zyprexa the 2 percent and the haloperidol the 0.5 percent?

A. That's correct, about four times difference.

Q. About four times difference?

A. Yes, sir.

Q. And would that four times difference, would that be consistent with the weight gain results from the HGAJ study that we talked about earlier --

A. It -- it would be --

Q. -- the 24 pounds weight gain?

A. Yeah, it would -- it would -- it would depend on several factors. Even though I said that there's an ironclad association between weight gain and diabetes, it depends on the details. It depends on what race we're talking about, what gender we're talking about, what age we're talking about, what your genetic background is. But, on average, a fourfold difference. Let's assume that haloperidol caused no change. That's smaller than I would anticipate, but in the price category.

Q. Why if he was so adamant in the first

meeting after -- by the way, let's get the timeline on this down.

Your article was published in '98.

A. Correct.

Q. When was your -- when was your first conversation with Mr. Hamm? Would that have also been in '98?

A. It would have -- my guess would have been before the publication came out. Because we had presented this, as I say, in this abstract form that we'd alluded to earlier, half a dozen times or so at various conferences over the previous year and a half. So my guess would be at least early '98, if not late '97, something like that.

Q. Okay.

And your second conversation with him --

A. Was --

Q. -- and this was the conversation where you said he told you orally about results showing a higher risk of -- with Zyprexa.

A. That was not Mr. Hamm; that was Mr. Anderson. And that would have been -- that would have been definitely down the road. And my

guess would be late '98, early '99.

Q. Okay.

But why would he first tell you adamantly there is no association and then later tell you orally of this evidence, showing that there was an increased risk?

A. Well, I could -- I can only tell you what my guess is as to what his motivation was. My motivation -- he believed the first one, and that there was the data -- additional data he had for the second one. That -- it's -- in the business of academics you -- we change our mind all the time based on what the data tells us. You can't get wedded to any -- any one fact. That -- that doesn't surprise me.

Q. Did --

I'm sorry.

A. So -- so my -- my assumption is that -- is that, you know, these studies were not done to specifically address and look at the question of does it cause problems with diabetes, weight gain, lipid, et cetera, et cetera.

These studies were done to investigate the primary impact of these compounds on psychotic symptoms. And these other things

had to be pretty big if they came up. So the -- it's -- it might seem like a trivial thing. Well, go back and check their weights, go back and check this. It might seem an easy thing, but it is really difficult to go back and exhaustively check those datasets.

So my assumption was that they just got better data as time went on, that they had cleaned up the datasets, more reliably established the integrity of that dataset, and that's what they -- that's what they showed. Didn't surprise me, I mean --

Q. Sir, you said you studied the labeling from '96 to 2006. Did they -- did the labeling ever warn physicians that there was a fourfold increased incidence of impaired glucose with Zyprexa as compared to Haldol?

A. No. As we've talked about, it's in the adverse experiences, not as a -- not as a fourfold difference, but it has the infrequent listing and consistently throughout that period you referenced.

Q. My question is very specific.

Did -- did the labeling ever at any time, in any part of the labeling, ever tell

physicians that there was a fourfold increased incidence of impaired glucose with Zyprexa as compared to Haldol?

A. No, sir.

Q. Okay.

MR. SUGGS: Chris, could you pull up Exhibit 988, please.

Your Honor, I believe Exhibit 988 is already admitted.

Q. (BY MR. SUGGS) And this is a document entitled Census of Spontaneous Reports for Olanzapine During the First Two Years of Marketing, September, '96 to September, '98. And if I could direct your attention to --

Can you pull up Page 14, please, Chris.

On this page there is a heading of -- well, it's a description, Census of Adverse Events from Clintrace Database, Olanzapine, Spontaneous Reports.

Do you see that language, sir?

A. I do.

Q. Okay.

And an adverse event or spontaneous report, am I correct that that is a report that

can come from a patient or a physician or from anyone, really, describing an adverse event that occurs in a patient after they've used the drug?
A. That's correct. I mean, the vast majority come from clinicians.
Q. Okay.
And this particular page has grouped together under the endocrine section about -- I guess it's six different items, all of which are related to blood sugar elevation, those being hyperglycemia, diabetes mellitus, diabetic acidosis, diabetic coma, ketosis and glucose tolerance decreased, and Chris, could you highlight the -- there's also -- it's hard to read because of the -- I guess it's highlighting that was in the original document, but it says unduplicated reports.
That's clearer. I wish you would have kept it there.
Chris, can you undo that, because it's even less visible now than it was.
Doctor, how many unduplicated reports are there total for the -- for the two years there that is described in this report?
A. Obviously on the far right-hand column

you see there's 194.
Q. 194. Okay.
We've had testimony from Dr. Gueriguian that it's estimated that the number of adverse events that actually occur in the real world is somewhere on the order of one percent to --
Strike that.
We've heard testimony from Dr. Gueriguian that the number of adverse events that are reported are only about one percent to perhaps 10 percent of those that are -- actually occur out in the real world. Is that your understanding, as well?
A. Yeah, those numbers are usually quoted for new drugs. For instance, once a -- once an adverse experience is obvious and everybody knows that this occurs, they drop way down, so it gets even lower than that. So those numbers -- particularly that 10 percent number, that would only occur when a drug is brand new and people were just completely unfamiliar with the side effects.
Once you get familiar with the side effects you just -- you don't -- you don't --

nobody bothers phoning in my patient on penicillin got a rash. It's like thank you, Doctor. We'll write it down.
Q. Now, if those estimates of 1 percent to 10 percent are correct, what would this 194 unduplicated reports represent out in the real world?
A. At 10 percent it would be 2,000, at 1 percent it would be 20,000, so 2- to 20,000.
Q. And is the potential for almost 20,000 cases of blood sugar elevation of one sort or another -- is that additional further reasonable evidence of an association of the drug with a serious hazard, in your view?
A. Well, of course. I mean, again, this is what you would expect in a drug that causes -- causes weight gain. This is -- I would be very surprised if you didn't have these reports.
Q. Okay.
Now, your 1998 article was the first publication ever identifying any cases of diabetes related to Zyprexa; is that correct?
A. That -- that's correct, but -- but remember, the process of getting a publication in peer review is -- nobody goes through that effort

except for -- except for academicians. It's just so much work. The process of reporting an adverse experience is hello, this is Bob, this is what I saw. Good-bye. It doesn't take -- it doesn't take anything -- you can do it on the Net now, actually. So it's a trivial process.
So the fact that there were this many clinicians, it's just so much easier to notice and then to present this. It doesn't surprise me at all. Publication and peer reviewed is much more arduous and much more time consuming.
Q. Whether you had your meetings with Mr. Hamm and Mr. Anderson after you published your article, did they ever tell you that by 1998 they had almost 200 reports of adverse events --
A. No.
Q. -- relating to blood sugar elevation?
A. No. Yeah, these -- these type of reports are generally kept by the company.
MR. SUGGS: Chris, can you blow up that bottom word there in the middle The "Confidential."
Q (BY MR. SUGGS) Sir, do you believe it's appropriate to keep confidential the number of

adverse events with a drug?
A. Do I personally believe that?
Q. Yes.
A. I think it's downright ridiculous. It's why you report them, so people will know about them. That's the whole point.
MR. SUGGS: Chris, could you pull up Exhibit 1215, please.
For the record, Exhibit 1215 is admitted, Your Honor. It's a -- an e-mail chain. All the e-mails are in late 1998.
And Chris, could I have you pull up the second physical page of this document. This is an e-mail from Peter Clark to Jack E. Jordan, Bruce Kinon, John R. Richards, with copies to Jeffrey Ramsey, Robert P. Schmidt, subject the Wishing/Goldstein articles. And also, Chris, could you pull up the -- there's some bulleted points below that, and could you pull up the second and the third bulleted points.
Q (BY MR. SUGGS) Dr. Wirshing, at the time of this page the e-mail starts off by saying, 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 article, published in the Society of Biological Psychiatry. They misspelled your name there, but that is you and that is the article that you published in 1998, is it not?
A. My wife and I, yes.
Q. Okay.
And they also referred to another article that was published -- or soon to be published, apparently, at that time by Goldstein, that was soon to be published in Psychosomitics Journal. I believe that's a misspelling of --
A. Psychosomatics.
Q. And are you familiar with that article by Goldstein?
A. Yes.
Q. Okay.
And if can direct your attention to the two bullet points that are blown up there, which is apparently what they were saying that they were going to use to respond to your report and that of Mr. Wishing (sic). They state the, quote, "use of antipsychotics may result in weight gain. Patients who gain weight may develop insulin resistance, which may lead to hyperglycemia and diabetes." Do you see that

language, sir?
A. Of course.
Q. And was that consistent with the thrust of your article?
A. Obviously.
Q. Okay.
Was that also consistent with the thrust of the Goldstein article?
A. Definitely.
Q. Okay.
MR. SUGGS: Now, could you turn to the previous page, Chris, which is actually the response to that e-mail suggestion. And just go ahead -- actually, could you also include the name of the person who sent the e-mail.
Q (BY MR. SUGGS) Okay. This is the e-mail response from Bruce Kinon. Do you know Mr. Kinon or Dr. Kinon?
A. It's Dr. Kinon. Yes, got to know Bruce when he was working with John Kane at Long Island Jewish Hospital in New York. It's a collaborative group we've worked with for decades. Bruce actually did one of my -- one of my favorite studies in antipsychotic treatment that I talk about all the time.

Q. And Dr. Kinon responds to Peter Clark with copies to Jack Jordan, Jeffrey Ramsey, John R. Richards and Robert Schmidt. Is that correct?
A. That's what it says, yes.
Q. And is that John R. Richards the same person that you met with back two years earlier and -- at the Italian restaurant in New York and told you -- you told him you had concerns about Zyprexa?
A. I always refer to him as J. R., but yes.
Q. Okay.
And in his e-mail, Dr. Kinon says, 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."
Do you see that language, sir?
A. I do.
Q. And is Dr. Kinon's recommendation what you would expect from a reasonably prudent drug manufacturer?

A. I don't -- I don't know how to explain at all Bruce -- Bruce's response. I mean, it just -- it just makes no sense medically. It just makes no sense. So it's -- it's not the recommendation that anybody would give.
Q. At least no reasonable manufacturer, correct?
A. Absolutely not.
Q. Okay.
Now, the following year, in 1999, did you and your colleagues publish another paper which further linked Zyprexa with weight gain?
A. Zyprexa and other compounds, yes.
Q. Okay.
MR. SUGGS: Chris, can you pull up Exhibit AK10142, please.
For the record, this is a medical article published in the Journal of Clinical Psychiatry in June of 1999, entitled Novel Antipsychotics, Comparison of Weight Gain Liabilities, by Donna Wirshing, other -- and Dr. William Wirshing, as well as other authors. Your Honor, we also offer Exhibit AK10142 for the purposes of notice.
MR. LEHNER: That's fine, Your

Honor.
THE COURT: And again, ladies and gentlemen, this document is offered for the purpose of notice to Lilly of the information contained in the article. 10142 is admitted.
Q (BY MR. SUGGS) And this was published in the Journal of Clinical Psychiatry. Is that a peer-reviewed journal, Dr. Wirshing?
A. Yes, sir.
Q. And is it well respected?
A. It's very -- very commonly read.
Q. Okay.
A. Almost all psychiatrists get it.
Q. And what did you do in this study?
A. This study was very long in coming about. This -- involves looking, as I recall, at 92 different subjects in one or another controlled experiments that we had done in -- in our research center over six years. Wait. No. Probably close -- went back even further. Probably eight years.
So studies were already done, we went back and looked at the changes in weight of patients who were put on one or another of these compounds over time, and looked at the -- looked

at the pattern, what happened to that weight gain, did it persist, did it increase, did it go down, did it change, and looked at the differences between -- or among various antipsychotic compounds. Most of these were in the atypical class --
Q. Okay.
A. -- but I think there was a comparison typical drug also involved.
Q. And do we have a slide that helps illustrate the results from the study?
A. I think we've got a couple of them, yes.
MR. SUGGS: Can you pull up Slide 14, Chris.
Q (BY MR. SUGGS) Okay, it appears that the colors for the various drugs that you were studying here were blue for clozapine, yellow for olanzapine, green for Risperdal, blue for --
A. Sertindole.
Q. Sertindole?
A. Yeah, it's a compound that was marketed briefly in Europe but because of some very interesting cardiotoxicity never made it to market here. Very interesting compound, though.
Q. Okay.

And the HAL, does that stand for haloperidol?
A. It does, yes.
Q. And this chart, does it accurately reflect the -- the findings from your study?
A. Right. So this is a summary of those 92 subjects, kind of a complex statistical analysis, but controlling for baseline weight, gender, age, race, et cetera, and so that you can make a reasonable comparison, because you don't always put the same kind of patients in each study, so this is as best we could do, controlling for all the variables that we know that might impact weight, so to just selectively live look at the drug's impact on weight alone. At least that was our attempt.
Q. Okay.
And what does it show -- so you've got the data chunked out between one group for no change in weight or lost weight, then the middle category is for less than 10 percent weight gain, and then to the right it's greater than 10 percent weight gain; is that correct?
A. It's a little weird here, but --
Q. If I gave you a light pen, would that

help point things out?
A. You'd probably just get me into trouble. But -- no.
If you -- three sets of histograms, and dividing the 100 percent of patients up into three separate groups. The first group, the group on the left there is no change observed or weight loss during the protocol, and you can -- during the protocols, which ranged, by the way, from eight weeks to six months.
So you can see that the vast majority of people do change their weight over the course of time. It is a fact of life in general for us Americans, but, but there -- sertindole was rather interesting. 25 percent of patients either lost weight or remained the same, and that was kind of interesting, and you could see that the haloperidol group, about 10 percent don't change. It means that 90 percent do change.
The middle set of histograms -- the middle set of bars, is at the 10 percent line. Now, that's going to take a moment to explain that. The FDA considers that a seven percent increase in weight constitutes clinical

pertinence, but to tell you the truth, they just pulled that number right out of the frigging sky. I mean, it just -- you can't find any basis for that. I happen to like the nice round number 10 so we chose 10 percent. So, you know, for a 150-pound person, that means that a 15-pound weight change. A 200-pound person, that's a 20-pound weight change. Obviously, a 10-pound weight difference.
So you can see that that's where the majority of people fell into it, ranging from a low of 50 percent on clozapine to a high of around 80 percent on haloperidol gained less than 10 percent. So it's a -- it's -- again, shifting your weight by 10 percent is a significant difference. These were all less than 10 percent.
Now, the one on the right there is people that gained more than that, so in excess of 15 pounds for a prototypic 150-pound male and the vast majority -- I worked at the VA so the vast majority, 95 percent of these patients are male.
You could see that for the clozapine treatment, 40 percent of patients on clozapine gained more than 10 percent. I mean,

that's a startlingly large number. 35 percent on olanzapine, 10 percent on risperidone and none of the patients on sertindole, which I will tell you was of enormous interest to the manufacturer of sertindole at the time. And about 10 percent of the patients on Haldol, which is fairly typical of what we see over the years on haloperidol.
Q. Pardon me. Has your finding that olanzapine causes more weight gain than -- well, does this indicate that olanzapine results in more weight gain than most other antipsychotics but for clozapine?
A. Well, no, this -- this simply compares it to two drugs, to risperidone and haloperidol, because sertindole is not available. So it says that it's more than risperidone and haloperidol and yes, that's been confirmed over and over again. The things that -- this dataset differs from most in the literature in that risperidone, the green there at the far right, risperidone in general causes about twice the weight gain of Haldol and about half the weight gain of olanzapine, and in our dataset it caused approximately the same as haloperidol. So that's a little different.

But other than that difference, clozapine, olanzapine, risperidone, haloperidol, that rank order has been confirmed by literally hundreds of different researchers.
MR. SUGGS: Your Honor, would this be a good time for a morning break?
THE COURT: Yes, it is. Ladies and gentlemen of the jury, we will take our morning break, and we'll be in recess for about 15 minutes.
THE CLERK: Off record.
(Short recess.)
THE COURT: Would counsel please approach for a second.
I'm told that one of the jurors is having stomach problems, so it's possible we may need to take some more frequent recesses. He knows to raise his hand if he needs to take a break before we do. I just want to let you know that that's what's going on. We'll -- I just wanted to let you know.
MR. LEHNER: Okay.
THE COURT: Please, Mr. Suggs.
MR. SUGGS: Thank you, Your Honor.
Q. (BY MR. SUGGS) Dr. Wirshing, there's

one thing I meant to you ask earlier about your background. Am I correct that you've had three different types of cancer?
A. Yes, sir, I have.
Q. And based on that experience, are you anti or pro drug company, and anti or pro pharmaceutical products?
A. I'm -- I can say unequivocally and without question I would not be alive if I did not take medications from one, two, three separate manufacturers every single day of my life. They are life-sustaining for me. They've allowed me to have three children, allowed me to have a career.
Q. Okay. Thank you, Dr. Wirshing.
Dr. Wirshing, were you aware in 2000 that Lilly was claiming in a paper prepared for publication that the rate of impaired glucose intolerance (sic) and diabetes with Zyprexa was comparable to the rates with placebo, haloperidol and risperidone?
A. I was, yes, sir.
Q. And how is it that you became aware of that position?
A. A couple of different ways. One, that

was the basis of the data that I referenced with regard to Mr. Hamm and Mr. Anderson, and secondly, I was actually a reviewer on the paper -- I think it was sent -- Biological Psychiatry or The Journal of Clinical Psychiatry, one of those two. I recall I reviewed the paper twice, first after it was rejected and then once again, I think.
MR. SUGGS: Can you pull up AK3645, Chris.
For the record, this is a -- a paper entitled Incidence and Rate of Treatment-emergent Potential Impaired Glucose Tolerance and Potential Diabetes with Olanzapine Compared to Other Antipsychotic Agents and Placebo. The authors are Charles Beasley, Kenneth Kwong, Paul Berg, Cindy Taylor, Jamie Dananberg and Alan Breier.
Your Honor, the State of Alaska would move for the admission of AK3645, not for notice but for the purpose of motive and intent.
MR. LEHNER: Your Honor, we weren't giving notice that that was going to be the purpose, so we'll take a look at that with that in mind.

THE COURT: Okay.
MR. SUGGS: Your Honor, I will note that I provided this to them 24 hours ago.
MR. LEHNER: I agree. It's a scientific article --
THE COURT: Now the testimony about this point, subject to rulings about admissibility of the document.
MR. SUGGS: Very well, Your Honor.
Q. (BY MR. SUGGS) Is this the paper that you reviewed?
A. Yes, sir.
Q. Okay.
MR. SUGGS: And Chris, could you pull up the third physical page and conclusion of the paper.
Q (BY MR. SUGGS) The conclusion of this paper -- oh, by the way, the authors were all Lilly employees, were they not?
A. As far as I'm aware. I'm only personal familiar with two of them, though.
Q. Okay.
The conclusion of this paper was the rate of development of IGT -- let's stop right there. What is IGT, least --

A. IGT is idiosyncratically defined in this -- in this article. It stands for impaired glucose tolerance. It has no acceptable meaning to anybody. As I say, it was ad hoc, defined for the purposes of this particular article as a random glucose, so blood drawn irrespective of whatever time you had eaten, and a level of 160. So it's just -- it's a number without meaning in the -- in the diabetic literature.
Q. Okay.
It states, the rate of development of IGT and diabetes during the course of severe neuropsychiatric illness is higher than perhaps heretofore appreciated. The estimated rate with olanzapine is comparable to the rates with placebo, haloperidol and risperidone. Olanzapine was associated with a lower estimated rate than clozapine. Did I read that correctly?
A. Yes, sir.
Q. Okay.
And I believe you testified that you have -- you reviewed this article that was submitted to the Journal of Biological Psychiatry; is that correct?
A. That is correct, sir. Yes, sir.

MR. SUGGS: And Chris, could you pull up Exhibit 1440.

And I believe this -- this Exhibit 1440 is already admitted. I'll need to check with Mr. Borneman later.

Q. (BY MR. SUGGS) And you've blown up the top of the page. It appears to be a fax dated November 3, 2000, from Biological Psychiatry, regarding a manuscript, and it gives the title and then the authors, and is that the same manuscript that we looked at just moments ago, Exhibit 3645?

A. Yes, sir, it is.

Q. Okay.

And were you one of the reviewers of this paper?

A. I was, yes, sir.

Q. And were there three reviewers on this paper?

A. As I recall. Usually the -- depends on the particular journal, from three to the hoity-toity journals, seven, but three's a usual number.

Q. Okay.

MR. SUGGS: And Chris, could you

pull up the second page.

And blow up the text of the review.

Q (BY MR. SUGGS) And is this the review that you wrote?

A. Yes, sir. Yes, sir, it is.

Q. Okay.

You stated -- and by the way, which would have been back in November of 2000; is that correct?

A. Yes, sir, November 3rd, 2000.

Q. Okay.

The authors present a highly curious dataset. Since their own work has shown that olanzapine is associated with a clinically and statistically pertinent increase in weight compared to both haloperidol and placebo, they seem to be suggesting that olanzapine exerts a sizable antidiabetic power. It is estimated 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.

Did I read that correctly?

A. Yes, sir, you did.

Q. And did you write that with tongue in cheek?

A. Yes, sir, it was somewhat nastily sarcastic.

Q. Okay.

And I believe you said that this article was rejected by the Journal of Biological Psychiatry?

A. Yes. I mean, that's a -- my review is a frank rejection.

Q. And do the other two -- did the other two authors also have criticisms of the methodology of the paper?

A. They did.

Q. Okay.

I believe you said that you reviewed this for some other journal, as well. Do you remember what the journal is?

A. Yes, I remember the second journal it

got sent to was -- the order was either Biological Psychiatry, then Journal of Clinical Psychiatry, or vice versa, but I reviewed it for both of them, as I recall.

Q. Why would you have been selected to review this paper from Lilly twice?

A. Oh. As -- when you send a manuscript in -- it's a little different now, but back then you send a manuscript in and the editor, editor's assistant, assistant assistant, gets the manuscript and goes who the heck can we send this to. And it's a fairly short list of people that have this particular interest that I had. I had a relationship with the editors of these journals. They knew my work, they knew I was interested in this. I don't write big ponderous reviews. I tend to cut to the chase fairly quickly so they use me a lot.

Q. Despite the fact that this paper was not published, did Lilly use the dataset from this analysis to make presentations to physicians about the safety of Zyprexa?

A. Well, they -- I can't -- can't guarantee what Lilly did with other physicians. I've already talked about them doing it with me. And

so I know they did it with me, with Scott, Donna, Steve --
Q. Let me stop you for a second. Who are all these other folks?
A. Sorry. Donna, my ex and colleague, Wirshing, Steve Erhart, Steve Marder, C. Scott Saunders, Joe Pierre, all psychiatrists, all research psychiatrists in my -- in my group. And to the -- I mean, to the nonprescribers, my research assistants, you know, the Ph.D. candidates, medical students and whatnot, but not prescribers.
Q. Do you recall who it was that would have made those presentations?
A. Yes. I've already mentioned two of them, Mr. Hamm and Mr. Anderson.
Q. Let me stop you for a second. Mr. Hamm was a sales rep, correct?
A. That's right.
Q. And he was making a presentation of this dataset?
A. He and Mr. Anderson, that's correct. And the second one was a delightful young man with a very memorable name, Thomas Hardy, and he was an endocrinologist, a young guy who was

recently out of residency training in endocrinology, very bright guy.
He came and presented to the department at UCLA, so I remember he was actually -- he actually presented in the chairman's office, as I recall.
Q. It was the same dataset that was --
A. Same -- same dataset.
And a good guy. As I say, it was a very memorable afternoon.
Q. In the course of reviewing internal -- well, why was it such a memorable afternoon?
A. Well, he was -- he was clearly sent around by Lilly. This was his job. He worked for Lilly. He sent around by Lilly to debrief us about these data, and to -- to in a sense, I think, counter some of the escalating evidence from the literature, the mounting evidence from the literature that olanzapine was in fact associated with endocrinologic disturbance.
I guess we've talked about it, presumably through its impact on weight. That's just the simplest and most parsimonious explanation for that observation. And I -- believe it or not, I was relatively polite during

the presentation and just waited for him to finish. And afterward I talked to Tom and I said, how can you say that the drug that causes weight gain doesn't have a commensurate increase in the risk of developing diabetes? Why are you sticking to that statement? And I -- you know, I didn't do this in front of my colleagues. I -- I really did like the man. And he just shook his head and he said, I don't know.
Q. And when would that conversation have taken place?
A. '99.
Q. Okay.
In the course of reviewing internal Lilly documents in this case, did you review any e-mails discussing a meeting with outside endocrinology experts in October of 2000 in Atlanta, regarding Lilly's hyperglycemia dataset?
A. Yes, I reviewed the e-mails. I was not at the meeting but I reviewed the e-mails.
Q. Okay.
MR. SUGGS: And can you pull up Exhibit 1453, please.
And go to the last page.
This is a series of e-mails

regarding a meeting in Atlanta that various representatives of Lilly had with the North American Diabetes Advisory Board or NADAB.
Can you go to the next page, please, Chris. And blow up that biggest paragraph there.
And I'm not going to go into this in detail because the jury has heard about this meeting through numerous witnesses, but just to refresh the recollection briefly, this is the one where in one e-mail the person I do believe they made a very strong point that unless we come clean on this, referring to hyperglycemia, it could get much more serious than we might anticipate.
Q (BY MR. SUGGS) You reviewed this e-mail, correct?
A. I have, but it's my belief that that refers to the combination of weight gain and diabetes.
Q. Okay.
A. Both of those effects.
Q. Okay.
MR. SUGGS: And since this e-mail has been discussed with numerous witnesses, I'm

not going to go into it in detail, but could you back up one page, please, Chris.

And the last paragraph of that top e-mail, could you blow that up, please.

This particular section of an e-mail was from e-mail by Dr. Beasley, and he says, 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.

Q (BY MR. SUGGS) Do you see that language, sir?

A. Yes, sir, I do.

Q. And do you know who Dan Casey was?

A. Dan Casey is.

Q. I'm sorry. Do you know who Dan Casey is?

A. Yes, sir. Dan -- Daniel is a professor up in Oregon. Sorry. Down in Oregon. He works in Portland. One of the -- one of the grand men

in the profession; was, in fact, was usually the chair of the FDA's ad hoc committee for each of the new antipsychotic compounds. I mean, very bright, capable man.

Q. And apparently Dan Casey was giving that same message as described up above there?

A. Oh, yeah. Dan -- Dan worked quite closely with Donna, my ex and myself in this issue. We had exactly overlapping interests in this arena. He began to publish after -- and lectured, research and whatnot, in this various topic after we had made our original observations.

Q. And did his publications also indicate that there was an increased risk of diabetes with Zyprexa?

A. Oh, yes, sir. He had a -- a study where he looked at his veteran population, he worked in Portland, as I mentioned, and he had a diabetic risk on -- related to antipsychotics in general and olanzapine in particular that had extraordinarily high rates in his population.

Q. Do you recall offhand what --

A. Yeah, 64 percent.

Q. Wow.

A. But it was -- it was in a highly selected sample but it was really quite startling.

Q. Okay.

Did you have the opportunity to personally observe whether, after receiving this message, Lilly went ahead and did indeed get too aggressive about denial, blaming it on schizophrenia, or claiming no worse than other agents?

A. That is in lockstep with my observation of precisely what they did.

Q. And how is it that you were able to observe what they did?

A. In any number of different ways. In their presentations, in their interactions with me, in their responses to publications, in their response to the consensus panel meeting held in -- in 2003, whenever it was. 2003. This has been their message, no worse than other agents. It's high rate in schizophrenia, people with schizophrenia are obese, people with schizophrenia have diabetes, over and over and over again. This was their message.

Q. And are those messages right or wrong,

sir?

A. Those messages, as I've talked about already, are -- they are just frustratingly wrong.

Q. And did you yourself personally advise Lilly, don't get too aggressive about denial. Don't blame it on schizophrenia, don't claim no worse than other agents?

A. I was within the chorus of academicians giving that advice.

Q. Did you and your colleagues also publish a retrospective analysis in 2002 entitled The Effects of Novel Antipsychotics on Glucose and Lipid Levels?

A. We did. This would have been sort of Metabolic Consequences Part 3. This would be the next -- next chapter.

Q. Okay.

And Chris, can you pull up AK10140, please.

(Phone interruption.)

THE WITNESS: I apologize. Excuse me. I thought I had it turned off. I apologize, Your Honor.

THE COURT: That's all right. I

told one of the jurors he won't be the last one. I suspect you won't, either.

THE WITNESS: I've gotten punished a lot in my life for that. I know better than that.

MR. SUGGS: Your Honor, for the record, Exhibit AK10140 is an article published in The Journal of Clinical Psychiatry in October 2002, entitled The Effects of Novel Antipsychotics on Glucose and Lipid Levels. The authors were Donna Wirshing, Jennifer Bird --

THE WITNESS: Boyd.

MR. SUGGS: Pardon?

THE WITNESS: Boyd.

MR. SUGGS: Boyd?

THE WITNESS: Yes.

MR. SUGGS: Oh, I'm sorry. Laura Meng, Jacob Ballon, Steven Marder and Dr. Wirshing.

And we would move for the admission of Exhibit AK10140 for purposes of notice, Your Honor.

MR. LEHNER: No objection, Your Honor.

THE COURT: 10140 is admitted for

the purposes of notice.

Q (BY MR. SUGGS) And Dr. Wirshing, did you intend to imply by the title of this article that the antipsychotic drugs you studied caused the effects that you observed?

A. Yes -- yes, sir, I did.

Q. And can you tell the jury briefly how it was you went about doing this study?

A. Yes. This -- as -- retrospective study, so after all is said and done we decided to ask the question, what is the -- what is the effect on the number of parameters; blood glucose, cholesterol, the various components of cholesterol, et cetera, and we wanted to do weight. I'm embarrassed to tell you that at the VA we didn't have weights, so although we had all these fancy measures, I didn't have patients' weights. It was extremely frustrating. But -- because that would have tied it together very nicely. But we did have those measures.

So we asked those questions, what is the impact, so we went back and collected patients from our already collected data who had been on this agent, that agent, the next agent, and compared them over time to see what happens

to these parameters over time. So baseline before they get on the drug, and during various follow-up periods after they get on the drug.

This was primarily from our research database that had lots of variants, kind of messy, dirty data, that is to say, it's not rigorously controlled experimentation, just sort of general clinical work that we -- that we had done over the previous 10 years. And -- had hundreds of patients that we were looking at trying to find these data, and then compared across those -- those various -- this drug, drug two, drug three, drug four, controlling for everything we could think of; time on the drug, age of the patient, gender of the patient, race of the patient, et cetera.

Q. Okay.

And do we have some PowerPoint slides that would help you show the jury what it was you found in this study?

A. I think so. Yes, sir.

MR. SUGGS: Chris, can you pull up Slide 34, please.

Mr. Borneman, is there any way we can dim the light just a tad up there by the --

THE WITNESS: We need that one off. There we go.

MR. SUGGS: Okay. Thanks.

Q. (BY MR. SUGGS) Could you explain to us what is shown in this -- by the way, does this graph fairly and accurately depict the data from your article that was published in 2002?

A. Yes. Yes, sir, it does.

Q. And can you describe for us what it shows?

A. Well, so if you look -- look down at the X axis, the one horizontal that's not actually drawn, but running across the bottom there you see the designation for the type of drugs. The first one, I'm not going to even try and tell you what the color is, I'll just let you guess, but clozapine, olanzapine, risperidone, quetiapine, haloperidol and fluphenazine.

Haloperidol and fluphenazine are what we call the typical or first-generation class and the first four are the atypical drugs, clozapine being the prototypic one that I mentioned earlier, the olanzapine being the one that we've discussed all morning. And this shows that a zero would be they had no change from

baseline and going up 5, 10, 15, 20 percent change, and remember, the average glucose, yours, mine, anybody without diabetes, fasting sugar runs around a hundred, just -- that's a ballpark. It goes from 60 to 110, but -- but kind of picture 100 in your head.

So that would be a change of -- of, say, 15 for clozapine or a change of 22 for olanzapine, and to put that in context for you, the definition of diabetes is 126. So that's -- if it -- if a person on olanzapine started out at a hundred and they -- the average person ended up at 122, so just kind of put -- put it in perspective for you.

The little asterisk on top indicates statistical pertinence, meaning that it looks like a real statistical change, and you can see that even haloperidol, which showed a change of 7.5 percent or 7 and a half units on the -- on that mythical 100-point scale that I mentioned, it also was statistically pertinent, so there's a tendency for all of these drugs over time to increase a person's fasting glucose ratings.

Q. Let me ask you, what period of time did this involve?

A. It -- it varied, but it -- but it was -- these data, as I say, are controlled for the length of time, but it varied from six months to -- to a couple of years.

Q. Okay.

So these would definitely be long-term studies, correct?

A. Correct. I mean, again, they're not strictly studies, these are long-term retrospective observations.

Q. Okay.

A. You know, we're not really controlling people to the degree that you would in a study, but they were on the drug, they continued to pick it up from the pharmacy, they continued to refill it at a regular time, so it looked like they were taking it, and as best we could in clinical practice, determine, yeah, this is -- this is the drug they were taking and this is the effects that we noticed in the course of their taking this drug.

Q. And given the way that you collected the data and the types of patients that you collected it on, did you have comfort that this was reflecting real world experience?

A. Oh, yes. Yeah, this -- apart from the other -- as distinct, rather, from the other datasets that we've talked about so far, this was a more real world dataset. This was real world practice.

Q. Okay.

MR. SUGGS: Can you pull up the next slide, please, Chris.

Q (BY MR. SUGGS) And this shows the percent change in triglycerides, and can you first tell us what triglycerides are and why we should care what they are?

A. Okay. Sure. Sure. Triglycerides are the main fat energy component that humans eat and that we store and that we rely on when we go to access those fat stores. Triglycerides are structurally very different than cholesterol, and historically -- we haven't really cared too much about them. They aren't nearly as clearly associated with cardiovascular complications like atherosclerosis as something like the cholesterols.

We now know, even though we've given short shrift to them over the years and little attention, we now know that elevated

triglycerides are -- have a minor impact on cardiovascular health, and if sufficiently high can have a major impact on things like your pancreas. So this -- this is looking -- and it also -- triglycerides, for instance, when you -- you eat a fat-laden meal, you have a McDonald's quintuple double cheeseburger kind of a thing, your triglycerides go way up. Your cholesterol doesn't change much after the meal but your cholesterol can go way, way up. So that's why it's important to get these fasting and all these are fasting.

THE COURT: You just said your cholesterol can go way, way up. Did you mean triglycerides?

THE WITNESS: Thank you. Absolutely. Just like you said.

Yeah, your cholesterol changes marginally, your triglycerides just rocket up tremendously after a fat-laden meal.

Q. (BY MR. SUGGS) You said that there's evidence that the triglycerides can have a negative effect on the pancreas. Is that in connection with insulin production or insulin regulation or --

A. Yeah, actually -- did I say -- extremely good question. The answer is absolutely true. If you compare a diet which is high in triglycerides, fat, to a diet that's slow in saturated fats, say, the person on the high-saturated fat diet has a great deal of difficulty maintaining their insulin regulation. They require more insulin.

It's as though the diet itself induces a temporary state of insulin resistance, and one of the characteristics -- the reason that's important for the -- our purposes here is that patients with schizophrenia tend to be at the lower socioeconomic spectrum in our society and they eat terrible diets. That is absolutely true.

And it's a curious fact of our -- of our moment in historical context that for the first time in our history that less -- having less money allows you access to diets that have a higher fat content. That has never occurred before in the history of man. It's somewhat pedantically an aside, but it means that if you have a drug which increases it, increases triglyceride metabolism, that the worst person

you want to give it to is a person that has access to an awful lot of dietary fats, which happens to be patients with schizophrenia. They tend to eat very bad diets.

MR. SUGGS: Can you pull up the next slide.

THE WITNESS: I'm getting quite --

MR. SUGGS: I'm sorry.

THE WITNESS: We hadn't quite finished. This shows an absolutely startling increase in triglycerides, and to me, apart from everything else we've talked about except for weight, this is the most amazing data -- or these are the most amazing data, rather. And you see for clozapine and olanzapine you see 35 and 40 percent increase in triglycerides. It's due to a drug that's -- that's almost an unbelievably high level. That is -- that is so dramatic.

You'll also see quetiapine is -- shows a decrease. And I will tell you the patients on quetiapine gained weight and had some difficulties with glucose problems. And the explanation I have for this decrease is because most quiet -- the study was done shortly after quetiapine came to market and the patients who

were put on quetiapine had come from clozapine and olanzapine. They were treatment failures, and so they -- I think this is -- this was my attempt to show this effect appears separate from simply weight gain causes increase in triglycerides.

This looks like there was something else selectively happening for certain compounds that caused an elevation in triglycerides that was distinct from simple weight gain.

Q. Okay.

Anything else we need to talk about in this slide or should we move on to the next one?

A. I believe I've beaten it to death.

Q. Okay.

MR. SUGGS: Could I have the next slide, please?

This one is entitled Percent Change in Cholesterol Values, HDL, and I can never remember. I know that there's a good cholesterol and a bad cholesterol.

Q (BY MR. SUGGS) Is this the good one or the bad one?

A. In general if you're trying to remember

things, remember, don't get cholesterol. But if you're going to have one this is -- this is the good one. High density lipoproteins, so-called because they have lots of lipoproteins and not much fat are the transport system, remember, we're in aqueous medium of the blood, fats don't -- aren't admissible until they are accompanied. You have to go escorted by these lipoproteins.

So the fat stores are from the tissues after repair, after tissue building, after all the stuff is done -- the body is done with it, going back to the liver and to the enterohepatic circulation for recycling. So this is conceptualized as the good direction. So if you have high HDL, this protects you a lot from having high LDL, which is the so-called bad cholesterol.

Picture it like a two-way road; one road going out to the tissues, that would be the so-called bad cholesterol, LDL. And one road leading back from the tissues, that would be the HDL or the good cholesterol. If you have a good flow of HDL you can tolerate a higher flow of LDL, but if your HDL drops, that's bad, then you

really got to push down that LDL, otherwise you're in big trouble. And what this showed is that even though the triglycerides were going up, as we saw 30 and 40 percent, the HDL was going down. That's weird.

Q. And olanzapine, am I correct, was the worst offender, not only with respect to this HDL dimension but also with respect to the triglycerides and to the glucose; is that correct?

A. That's correct, yes, sir.

Q. Okay.

By the way, did Lilly -- this was published in 2002; is that correct?

A. That's correct.

Q. Before 2007 did Lilly ever include any language in its warning section of its labeling about cholesterol or triglycerides?

A. No, sir.

MR. SUGGS: Can we turn the lights back up, Mark?

Q (BY MR. SUGGS) Dr. Wirshing, we've already talked a lot -- about a lot of the facts you've considered and some of your opinions, but I want to make sure we have a clear record of --

of your opinions. Based on your review of the published scientific literature, including your own research, do you have an opinion as to whether Zyprexa can cause weight gain?

A. Yes, sir, I do.

Q. And what is that opinion?

A. That it unequivocally does.

Q. And do you have an opinion Zyprexa can cause diabetes?

A. Yes, I do.

Q. And what is that opinion?

A. That it -- it causes diabetes in direct proportion to its impact on weight.

Q. And do you have an opinion as to whether Zyprexa can cause hyperlipidemia?

A. I do.

Q. And what's that opinion?

A. That it causes hyperlipidemia through two separate mechanisms, one of which we've talked about and one of which we haven't. But the first mechanism is that it, as your weight goes up, your transport of lipids goes up and your cholesterol, triglycerides and whatnot rise commensurately.

The second way that olanzapine --

and it's a much more unusual way, I hasten to add. The second way that olanzapine induces predominantly hypertriglyceridemia, separate from the cholesterol transport system, hypertriglyceridemia is through its impact on the liver. This occurs early on and can be startlingly high, but fortunately occurs -- it occurs relatively uncommonly. An estimate would be less than 0.5 percent of the population exposed to it. But it can be severe and potentially fatal.

Q. Do you have an opinion, sir, as to whether Lilly adequately warned of the risks of weight gain, diabetes, hyperglycemia, hyperlipidemia before October of 2007?

A. Yes, sir, I do.

Q. And what's that opinion?

A. They did not.

Q. Do you have an opinion, sir, as to whether the incidence of weight gain, hyperglycemia, diabetes and hyperlipidemia with Zyprexa is comparable to the incidence of those adverse reactions with other atypical antipsychotics or not comparable?

A. Well, it's comparable to some and not

comparable to others, so I guess the answer to the question would be not comparable.

Q. Okay.

And do you have an opinion as to whether Zyprexa should be used as a first line antipsychotic drug, sir?

A. I do.

Q. And what's that opinion?

A. Well, the opinion has really been the same since -- since the -- since the very beginning. I wrote the regulations for my VA in this regard. My opinion is that you should fail less toxic before resorting to more toxic technologies, other things being equal.

And the second thing, the reason I was asked to write the regulations actually, by the VA, is to -- other things being equal, you should fail cheaper technology before resorting to more expensive technology.

Q. Sir, do you know whether it is generally accepted in the medical community that Zyprexa can cause weight gain, diabetes, hyperglycemia and hyperlipidemia?

A. Absolutely.

Q. How do you know that, sir? How do you

know that it's generally accepted in the medical community?
MR. LEHNER: Objection, Your Honor.
THE COURT: What's the objection?
MR. LEHNER: No foundation.
THE COURT: I think that was a foundation question.
MR. SUGGS: It was.
THE COURT: So I'll overrule the objection.
Q (BY MR. SUGGS) How do you know that, sir?
A. I am part of the community. I continue to -- to lecture frequently. I give at least one CV lecture per week, and my reading of the -- the literature suggests that the rest of the world has kind of finally caught up to my way of thinking.
Q. Sir, do you know of any doctors other than those retained by Lilly in this litigation who claim that Zyprexa does not cause diabetes?
MR. LEHNER: Objection, Your Honor. No foundation. How would he know that?
THE COURT: He was asked if he knows any doctors. I'll overrule the objection.

THE WITNESS: I don't -- I don't -- I don't know of anyone who -- who believes that. I don't -- I don't know that Lilly has any doctors that -- that say that olanzapine is not associated with increased risk of diabetes.
MR. SUGGS: I guess we'll find that out later.
Just a couple other quick points I wanted to bring up.
Could you pull up Exhibit 2368.
This is the consensus development conference. It's already been admitted into evidence. There's been a lot of testimony about this. I'm not going to belabor the details here.
Q (BY MR. SUGGS) But you were invited to present at this conference, were you not?
A. Yes, sir, both my wife, Donna, and I were presenters at that conference.
Q. And can you go to -- and by the way, you were presenting there on two topics, the first of them being lipids?
A. Lipid -- correct.
Q. And the lipid presentation that you gave -- let's see. This would have been in November of 2003. Your publication that we were

talking about just a moment ago was a year before that. Would it be fair to say that your presentation here in 2 -- there in 2003 included at least the topics that you talk about here to the jury just a few moments ago regarding your 2002 paper?
A. Yes, very much so. I mean, that's why I was asked to do it.
Q. And was there other scientific literature available at the time of this conference that was confirmatory of your findings that you described in 2002 in that paper?
A. Absolutely. There was animal research, primarily canine, dog model, epidemiologic research, basic science receptor, chemistry research, and clinical research like my own.
MR. SUGGS: Thank you.
And Chris, could you go to Table 3. It's at the top of Page 4.
THE WITNESS: Excuse me for interrupting, but the second thing I actually was asked to speak on was the monitoring protocol, so lipids and the monitoring protocol.
MR. SUGGS: And that's the part I was going to pull up here, Doctor.

Table 3 is entitled Monitoring Protocol for Patients on SGAs.
Q (BY MR. SUGGS) That refers to second generation antipsychotics; is that correct?
A. It does.
Q. And it calls -- did you -- did you make a proposal to this consensus panel as to monitoring of patients on second-generation antipsychotics?
A. I did.
Q. And this calls for monitoring of personal family history, weight, waist circumference, blood pressure, fasting plasma glucose, fasting lipid profile at baseline and various points in time; is that correct?
A. That's correct.
Q. And was this the proposal --
Strike that.
Was the proposal that you made to the conference, was it what was adopted here in Table 3?
A. Almost. The differences that I suggested, which is why I think this is wrong. The differences that I suggested were measurements of weight at two weeks, the first

weight change in two weeks.
The -- it was adopted at four weeks because it was felt that most people don't see their patients that frequently, but I felt rather strongly and I continue to do so today that at two weeks. I also suggested, though I didn't argue with this, I also suggested that the first lipid check be at eight weeks rather than 12 weeks, but there's really no difference. I don't have an objection to that. Other than those two differences, this was the monitoring suggestion that I made.
Q. And this monitoring program is now --
Strike that.
At any time before October 2007, did Lilly's -- by the way --
Strike that.
Did you propose that this monitoring be put in place for every patient who was using a second-generation antipsychotic?
A. Yeah, this was -- except for those changes that I alluded to earlier, this was the monitoring that I had done since 1996 and continue to do so today.
Q. And did you ever recommend this

monitoring system to Lilly?
A. Yes. This -- in those protocols that we talked about, the ones that -- one versus 10 milligrams of olanzapine, premarketing study, for instance, embedded within those protocols were the monitoring strategies that had all of these elements in them. We added those, graphed those onto the protocol.
That's why we knew about all this stuff before anybody else did, because we were gathering these data selectively for ourselves, because we had specific interest in them. So this was routine part of our clinical and research work for a decade before this.
Q. When was the first time you told Lilly about this monitoring protocol of yours?
A. Well, I -- when I -- when you do extra things on an industry-sponsored protocol you ask for more money, and so I said, would you give me more money if I did these extra things, and they said sure, so I presented the monitoring protocol to them before the drug was released.
Q. And before October 2007 was that monitoring protocol ever part of the labeling for Zyprexa?

A. No, sir.
MR. SUGGS: May I take a moment, Your Honor?
THE COURT: Sure.
(Discussion off the record.)
Q (BY MR. SUGGS) Dr. Wirshing, I have just one more question for you.
A. Sure.
Q. During the entire period that you were raising issues about weight gain and diabetes, before you got involved in this litigation, did the folks at Lilly ever question your competence, character or scientific standards that led to your conclusions and opinions?
A. Not to my face.
MR. SUGGS: Okay. Thank you, Dr. Wirshing. I have no further questions at this time.
THE COURT: Mr. Lehner?
MR. LEHNER: Do you want to take a break now?
THE COURT: How is the jury doing? Anybody need a break?
Why don't we continue for a while.
CROSS-EXAMINATION

Q (BY MR. LEHNER) Hi, Dr. Wirshing. How are you?
A. Good morning. Fine, sir.
Q. Good. We've met before; I had the opportunity to take your deposition. Is that correct?
A. Yes, sir, that's true.
Q. We spent about six hours or so, six or seven hours at your apartment talking about Zyprexa; is that correct?
A. We did.
Q. And we talked pretty much nothing else except about Zyprexa at that time; isn't that correct? It was a long day about Zyprexa.
A. We had a few other topics, but it was definitely obsessionally focused on olanzapine.
Q. Absolutely.
Doctor, you started working, I think you said, with Lilly on olanzapine during the Phase II clinical trials, and then you also worked on some Phase III clinical trials. That's what you have told us before; is that correct?
A. Phase II and III, yeah. Some of their -- some of their trials were kind of combined Phase II-III trials, but yeah.

Q. And these were the trials that were conducted before the product was on the market; is that correct?
A. That's correct.
Q. And the information, as you've described, was shared with Lilly, everything that you were gathering you were turning over to Lilly at the time; is that correct?
A. Everything we've talked about, yes, sir.
Q. That's right.
And essentially the information that goes into the label ultimately is the information that is derived from those clinical trials; isn't that correct?
A. Absolutely, sir. Yes, sir.
Q. That's how the process works. The investigators like yourself do these studies, turn over the data to Lilly, and then information is gathered and put together and then ultimately is conveyed in the label; isn't that correct?
A. Yes, sir, that's my understanding too.
Q. And as you know, the product Zyprexa first came on the market in 1996; is that right?
A. Yes, sir.
Q. Can we take a look at the 1996 label for

a minute.
And let's turn to the section on weight gain that we've looked at a number of times. I think that's about Page 7, 8. If you blow it up there, the table at the back. A couple more pages back?
MR. SUGGS: Your Honor, can I get a stipulation that this is not from the PDR but is, rather, a separate document? On the screen there?
MR. LEHNER: You can get -- it's not from the PDR. It is Lilly's label. You will stipulate to that; is that correct?
MR. SUGGS: Well, it's not the PDR. Will you stipulate to that?
MR. LEHNER: I'll stipulate that it's not the PDR if you'll stipulate to it that it's Lilly's label.
MR. SUGGS: I'll stipulate to that.
THE COURT: So this exhibit, ladies and gentlemen, is not from the PDR. It was Lilly's first label?
MR. LEHNER: Yes, the 1996 label.
THE COURT: 1996 label.
And it's EL2954A.

Q (BY MR. LEHNER) And the section that describes --
MR. SUGGS: Excuse me. Do you have copies? I gave you copies.
MR. LEHNER: Yes. Go to Page 16, and if you can bring up the language under there that says weight gain under the table, please. The jury has seen this language before, Dr. Wirshing.
Q (BY MR. LEHNER) And let's just go through that, if you don't mind. Would you read that to the jury, the first couple sentences there.
A. Beginning with weight gain?
Q. Yes.
A. Yes, sir.
In placebo-controlled six-week studies weight gain was reported in 5.6 percent of olanzapine patients compared to 0.8 percent of placebo patients. Olanzapine patients gained an average of 2.8 kilograms compared to an average of 0.4-kilogram weight loss in placebo patients. 29 percent of olanzapine patients gained greater than 7 percent of their baseline weight, compared to 3 percent of placebo patients.

A categorization of patients at baseline on the basis of body mass index (BMI) revealed a significantly greater effect in patients with low BMI compared to normal or overweight patients. Nevertheless, weight gain was greater for all three olanzapine groups compared to the placebo group.
Q. Why don't you stop there. That described what Lilly learned from investigators like yourself in what is described as short-term trials; is that correct?
A. In the -- the six-week trials, yes.
Q. Right. In the short-term trials.
Why don't you go on and read the next paragraph. That deals with the longer term continuation therapy.
A. During long-term continuation therapy with olanzapine, 238 median days of exposure, 56 percent of olanzapine patients met criteria for having gained greater than 7 percent of their baseline weight. An average weight gain during long-term therapy was 5.4 kilograms.
Q. Okay.
Now, it's fair to say that all the information in that original label concerning

weight gain is accurate; is that right?
A. I have -- I have no -- no idea if it's accurate. I mean, I --
Q. You have no idea?
A. I mean, I -- I didn't see any original data. I mean, I -- I -- I can't comment on its accuracy. These are the same data I've seen over and over and over again.
Q. But you have no idea whether it's accurate; is that right?
Well, let's turn to -- as you remember, I just said I took your deposition; isn't that correct?
A. That's correct.
Q. Let's turn to your deposition, if we would -- we could and Page 57. And let's go to Line 16.
A. Okay.
Q. And if you could blow up Line 16, and --
MR. SUGGS: Excuse me, Your Honor. I think the correct procedure is to show the witness the deposition and to see if that refreshes his recollection.
THE COURT: I don't know if he's refreshing his recollection at this point. It

may be impeachment.
MR. LEHNER: I think I'm going to impeach him.
Q. (BY MR. LEHNER) On Line 16, and let's just start beginning to read there. Let me ask -- let me make sure that my question is focused. I was suggesting and asked --
What I was asking you was whether or not any of the information contained in the label was inaccurate, as far as you know. Not whether it could be supplemented or whether more information could be included, but whether or not the information contained in the label was accurate as far as your recollection of what was demonstrated through the clinical trials. And let's go to the next page, if you wouldn't mind.
And you asked, in terms of weight gain, and I said yes, and you said no, meaning that it was not inaccurate. That was your answer at the time; isn't that correct?
A. Yes, I didn't know whether it was inaccurate or accurate.
Q. You said it was not inaccurate; is that right?
A. To my knowledge it was not inaccurate,

correct.
Q. And you would agree, Doctor, that weight gain is seen in all the atypical antipsychotics, correct?
A. In short-term trials?
Q. Short-term, long trials. That all atypicals have weight gain associated with them in some degree or another, isn't that correct?
A. No. Short-term trial with ziprasdone does not show significant weight difference.
Q. Long-term trials?
A. Long-term trials too.
Q. Thank you very much.
But the weight gain in -- among the atypicals varies; is that correct?
A. Absolutely, yes, sir. Quite widely.
Q. And indeed some people might gain a fair amount of weight, some people may gain no weight, some people might even lose weight; it really depends on the individual; isn't that correct?
A. Now we're talking about for an individual compound or for across the group?
Q. I asked the question, it's true that these vary across the group and you said yes, and I said for an individual, in any particular

medication the weight gain may vary; isn't that correct?
A. Clearly.
Q. Right. And in fact in some cases, the weight gain may have a therapeutic benefit, particularly for people who are on schizo- -- people who may be underweight, people whose bad diet has caused them to be on the street, people whose lifestyle has led them to not have the proper nutrition; isn't that correct?
A. It's a fair question. In clinically underweight people, does the addition of an atypical compound promote a more favorable weight profile. It's -- it's a very good question, and I can't answer it actually from the schizophrenic population. I can answer it from people who have eating disorders, and the answer is yes.
Q. Yes.
And --
A. Can be favorable.
Q. But there are people who are underweight who come into these trials and if they happen to gain weight that could be a therapeutic benefit in some instances; isn't that correct?
A. Again, usually, if -- if you gain

adiposity, almost irrespective of what your baseline weight is, that's not good. If you gain lean muscle mass, yeah, absolutely, that's very good. That's extremely good. To the extent that it would cause lean muscle mass, no, that would be very favorable to a person's -- to an underweight person's health profile.

Q. Doctor, you, as we've seen, have written about this topic since 1999 or 1996, 1997, 1998. You've been actively involved in studying and researching the issues of weight gain. When did you first learn -- when did you first come to the conclusion that, as you said earlier on, there could be 24 pounds of weight gain on average per year for people on Zyprexa?

A. When did I --

Q. When did you first come to that conclusion? When did you first --

A. Well, we -- on Zyprexa, we -- we had -- our longer-term data would -- would probably have supported that, so when did I personally become aware of it? I would say I probably became aware of that in '96, '97. Because the way we do protocols, as you recall, is that people are put on open label extensions following their

protocol, and I probably had 15 patients by the time the drug was marketed who were on olanzapine, sometimes for as much as a couple of years, before the drug had been marketed.

Q. That was a -- that was a piece of information that you knew very early on; is that correct?

A. From my data, yes. I mean, I hadn't heard from other people's data but from my data that wouldn't have been surprising at all.

Q. Right.

So when Mr. Suggs asked you about the '96 label that we just looked at and pointed your attention to the 5.4 kilograms or about 11 pounds, and you said you didn't think there was anything in the label that was inaccurate, how does that conform to what you then thought you believed many years ago about the fact that a gain -- people on Zyprexa would gain 24 pounds?

A. Oh. As a -- as a scientist, there's -- or as a clinician there's two different datasets. One is my patients who are an N of 15 and another one is a completely different dataset. I didn't have any reason to think that their dataset was -- would be identical to mine.

Q. So your dataset was based on an N, meaning a number of 15 patients, is that correct?

A. Yeah, it was a much smaller dataset. Absolutely right.

Q. Much smaller dataset. That's right. And their dataset was based on how many patients?

A. The long -- the long-term trials, I'm not quite sure. I think -- and I'm not quite sure where the 5.4 comes from. If it was -- if it was the extension of the haloperidol versus olanzapine protocol, there were 2 -- 335 in the olanzapine group and 118 or so in the haloperidol group, so hundreds of patients at the very least.

Q. So the Lilly data was based on hundreds of patients and your conclusion was based on an N of 15 as you said, is that correct?

A. Yeah, so much more faith in the larger number.

Q. Thank you very much.

You said you had been provided a number of documents from the -- by the attorneys; is that correct?

A. Yes, sir.

Q. That's right. Boxes of them full?

A. That's correct.

Q. And I think you said you had never seen them before they were given to you by the attorneys; is that correct?

A. Most of them I hadn't seen before.

Q. Most of them?

A. Yeah. I mean, some -- I've been involved in this -- as you very well know, I've been involved in this whole experience for some time and have been consulted at a number of different points in the legal meandering, so I've only come into contact with Mr. Suggs and his group in the last year or so, but I've had contact with other attorneys and so other attorneys have provided me with other things.

Q. So most of -- most of the documents that you said that you had seen that you reviewed you had not seen before the attorneys, that's what you testified here today, before the attorneys, these attorneys provided you --

A. That's correct. Certainly the ones we've talked about today.

Q. And you hadn't seen this material I think and you really hadn't done much work on it until you said to prepared to come to Alaska to testify. Is that correct as well?

A. Hadn't done much done --
Q. On looking at the documents that had been prepared --
A. Before the last year, certainly, no.
Q. Let's look at Page 209 of your deposition, if we could.
MR. LEHNER: Line 5, please.
MR. SUGGS: Your Honor, unless Mr. Lehner needs to lay a foundation for this before putting it up on the screen?
MR. LEHNER: I think the witness testified as I just did that he had not seen any of these documents until the attorneys had given them to him.
Q (BY MR. LEHNER) Isn't that correct?
A Many of them, yes, sir.
Q. And would you look at line 5 of your deposition. This was in answer to a question.
THE COURT: Are you suggesting, Mr. Suggs, that he should just go through the -- had his deposition taken, when it was taken, is that the foundation you're talking?
MR. SUGGS: No, Your Honor, I think if he's going to refresh his recollection --
THE COURT: I don't think he's

refreshing his recollection, he's impeaching.

MR. LEHNER: I'm not refreshing his recollection.
MR. SUGGS: Okay.
Q BY MR. LEHNER) Would you look at Line 5, please. There was -- I don't think that there was a single thing that counsel provided to me that I had not seen before. Is that correct?
A. That's correct.
Q. That's not -- that's your testimony a year ago; isn't that correct?
A. That's --
Q. In May '07.
A. That's correct.
Q. It's not consistent with your testimony today; is that correct?
A. That is not correct.
THE COURT: Do you want to explain that?
THE WITNESS: Yeah. I start -- I started this -- working with Rachel and -- Rachel Abrams and Mr. Suggs aggressively on this -- on this case about a year ago. December of 2006 or so. And it was at that -- prior to that I hadn't

seen -- seen only about 25 percent of the material, and that dates back to the summer of 2006, when attorneys for a consortium of -- of insurance companies who were, as I recall, suing Lilly had retained me and I saw quite a large number of documents from them.
Q (BY MR. LEHNER) Do you recall when your deposition was taken here in May '07; is that correct?
A. Of course do I.
Q. And at that time you said there was not a single thing that counsel provided to me that I had not seen before; is that correct?
A. That's correct.
Q. That's what your testimony is.
A. That's correct.
Q. And your testimony provided us with a list of what they had provided to you, and we talked about that list at your deposition; isn't that correct?
A. That's correct.
Q. All right.
Why don't we look at a few of those documents.
A. Certainly.

Q. Let's bring up Document 320. This is the Dear Doctor letter from Japan. According to your testimony --
THE COURT: This is -- this is --
MR. LEHNER: This is --
THE COURT: AK --
MR. LEHNER: AK320.
THE COURT: Thank you.
Q (BY MR. LEHNER) According to your testimony, you had seen this before the attorneys provided it to you; is that correct?
A. I had.
Q. Okay.
Let's bring up Document 988. This is a document that AK998, that you've been shown today. You'd seen this before the attorneys had provided it to you; is that correct?
A. No.
Q. No.
Let's bring up 990.
Let's go to the next page. This is a document that has been seen in this litigation. This is a report to the Global Product Labeling Committee. Had you seen that before the attorneys provided it to you?

A. Yeah, this was provided for me by the insurance company attorneys.
Q. When was that litigation?
A. I don't know when the litigation was. They -- they fired me.
Q. All right.
A. But I was --
Q. And then let's go on to Document 1110. That's a document that you had seen before these attorneys provided it to you; is that correct?
A. I didn't even recognize this one yet.
Q. And let's go on to Document 1111. That's a document that you'd seen before; is that correct?
A. What's the date on this one?
Q. Well, had you seen this document --
A. I don't -- I don't recognize this. I don't have it identified in my head as being I've ever seen it before so --
Q. Let's go on to Document 1449. This is a series of e-mails that you've been shown and I think Mr. Suggs showed you some of these e-mails; is that correct?
A. Yes.
Q. Had you seen these before these

attorneys had showed it to you?
A. Yes, I have.
Q. So, in fact, you had seen a number of the documents in this case before these attorneys showed them to you; is that correct?
A. The ones that you've talked about were shown to me by the attorneys from the insurance companies.
Q. What about Lilly's -- what about other data, for example, from the J data run, had you seen any of that? You were an investigator; you were a clinical investigator. Had you been supplied data from that?
A. No, sir. It was not -- on the -- olanzapine versus haloperidol?
MR. LEHNER: That's correct.
THE WITNESS: I was not a clinical investigator on that protocol.
Q. (BY MR. LEHNER) Had you seen that data before the attorneys showed it to you?
A. Well, before these attorneys, yes, but not -- not the insurance company attorneys.
Q. You were asked to disclose in your expert report matters by which -- for which you'd been retained in litigation. Did you disclose

that you'd been retained by any insurance attorneys in connection with the Zyprexa litigation?
A. I don't recall.
Q. You did not -- you don't have any recollection of disclosing that on your report, do you?
A. I mean, it -- my involvement with them was a single day.
Q. Oh. Okay.
A. They did not allow me to retain any of the documents. I had to go to their office in downtown Los Angeles and they made me look at them there in the course of a 10-hour day.
Q. You said you were retained by them.
A. For that day.
Q. And your obligation was to disclose all the matters in which you've been retained; is that correct, to give an opinion?
A. I presume the answer is yes. It was oversight on my -- in case if I left it off.
Q. Let me ask you a little bit about your opinions on weight gain and diabetes.
A. Yes, sir.
Q. There is a difference between weight

gain and obesity; isn't that correct?
A. There is, absolutely.
Q. And one can gain weight and not be obese; isn't that correct?
A. Governor of our state is a case in example.
Q. And you can already be obese and not gain any more weight; is that right?
A. I'm sorry?
Q You can be obese and that's sort of the condition you are and you're not going to gain more weight. You've sort of reached your sort of high-level weight; is that right?
A. Absolutely. Of course.
Q. And we all know that obesity is a risk factor for diabetes; is that right?
A. That's correct, sir.
Q. And weight gain can be a risk factor for diabetes; is that correct?
A. That's also correct.
Q. And doctors learn about all this in medical school. You were certainly taught that; isn't that correct?
A. Absolutely. Yes, sir.
Q. And that's true of primary doctors as

well as -- primary care doctors, as well?
A. It's true of all doctors.
Q. In fact, primary care doctors spend a lot more time treating people who may have problems with their weight and diabetes. They're very attuned to these particular issues; isn't that correct?
A. It's one of the most common conditions afflicting our society today.
Q. And because doctors know that, you would agree with me that you don't need to warn doctors specifically about the risk of diabetes if you're talking about weight gain; isn't that true?
A. You know, ideally I would like to say -- say that that's true, but unfortunately, I think the truth is that you do have to remind them. It should be axiomatic that weight gain causes diabetes; look out for it, Doctor. It should be unnecessary, just has your question suggests, but my experience is that my colleagues are not quite as reliable as you might anticipate.
Q. Well, you're not prepared to say here today that there's a direct causal relationship between Zyprexa and the development of diabetes other than through weight gain that might occur

around the central part of the body; isn't that correct?
A. I am absolutely not.
Q. That's your belief?
A. My belief is that -- is that the evidence -- the cumulative evidence to date is that olanzapine's impact on endocrinologic dysfunction, on diabetes, is directly due to its impact on weight, yes, sir.
Q. That's right. And that's -- and that's how it happens, there's no direct relationship between Zyprexa and diabetes, no effect on the pancreas that you've been able to identify, no effect on insulin resistance that you've been able to identify, other than through weight gain; is that right?
A. We are in agreement. Yes, sir.
Q. Great.
Lets talk a little bit about the differential risk for diabetes. All right?
A. Yes, sir.
Q. Now, I think it was your opinion when you wrote a report that you gave in this case that there was not enough information to determine whether there was a differential rate

for diabetes among the atypicals separate from weight gain; is that correct?
A. That's correct.
Q. And, in fact, in December 2004 you wrote an article in the Psychiatric Times. Remember we talked about that article?
A. Yes, sir.
Q. And that was an article you wrote with your wife Donna and others?
A. Yes, sir.
Q. And at that time you said that our field, and this is December 2004. Our field, and you're referring to the field of psychiatry --
A. Medicine.
Q. -- is currently grappling with insufficient information to date to determine their impact, and you were referring to the second-generation antipsychotics, on weight gain and diabetes; is that correct?
A. That's correct.
Q. There wasn't enough information out there to make any definitive conclusion at that time about the relationship between the second-generation antipsychotics and diabetes at that time; is that correct?

A. That -- that is correct. In particular that was because other people were saying of the belief that drugs had a selective toxicity on the endocrinologic system. It was not my belief.
Q. And that article accurately reflected your views at the time when you wrote it, in December 2004, right?
A. It did. It did. Yes, sir.
Q. So it would be fair to say that there was insufficient information at least as of 2004 to say that there was a differential risk between each of the second-generation antipsychotics with respect to this impact they might have on diabetes; is that correct?
A. Yes. Again, that's --
Q. That's a yes?
A. That's a yes, and it's referring to the -- to the -- this nonobesity related factor.
Q. Right.
A. I still don't think there is today.
Q. So it's only through whatever weight gain somebody may gain?
A. That's correct.
Q. That's correct.
Now, you were -- you said you

attended the consensus panel; is that correct?
A Yes, sir.
Q. Is that right and we saw that. And you were a presenter, and along with your wife you were a presenter; is that correct?
A. Yes, sir.
Q. And did you have an opportunity to review the correspondence that the FDA sent to the journal that printed the consensus statement?
A. I did, yes, sir.
Q. And the FDA came to the same view that you did, didn't they, that there was really insufficient information as of that time to determine whether or not there was a differential risk among the atypical antipsychotics with respect to diabetes. That's what they told the journal; isn't that correct?
A. That is indeed what they said.
Q. Now, Doctor, let's talk a little bit about the label, if -- if we could.
A. Yes, sir.
Q. And you would agree with me and we had a little bit of a discussion here that the product label, whether it's the label that the manufacturer may send to a doctor or whether it's

in the PDR, that the label is not a medical textbook, is it?
A. Absolutely not.
Q. I mean, it's not designed to teach doctors basic information about what they learn in medical school?
A. No, sir. It is not.
Q. It's designed to communicate information that's going to be clinically significant to doctors; isn't that right?
A. That is correct.
Q. And there's a difference -- and we heard Dr. Brancati the other day talk about the difference between statistically significant information and clinically significant information.
A. Yes, sir.
Q. You would agree that there is a difference between the two; isn't that correct?
A. There can be an enormous difference.
Q. And doctors, when they're looking at a label are going to want this clinically significant information, and that's the kind of information that allows them to make the kind of decision they need to make to treat their

patients; isn't that correct?
A. That's not only correct, in my experience, most doctors don't even know what statistically significant means.
Q. So a statistically significant piece of information may not provide any useful information to a doctor?
A. Potentially so. Yes, sir.
Q. All right.
And you certainly, I assume, wouldn't go to a doctor who -- for some condition and if the doctor said, you know, I just read the label and I haven't read anything else but I want to give you this medicine. That's not the kind of doctor you would go to, would you? You'd expect a doctor to sort of seek out some information from other sources and that's what doctors always do before they prescribe a medication; isn't that correct?
A. Clearly.
Q. Clearly. In fact, doctors get information from all sorts of sources, talking to their fellow physicians, going to the Web, going to some of the seminars that you may teach and others may teach; isn't that correct?

A. Yeah. My -- it's my hope that people would get a -- have a mosaic educational experience.
Q. So that they could be best informed about the full benefits and the full risks that might be associated with the product before they would prescribe it to one of their patients; isn't that correct?
A. Before, during, after, and -- and also, I mean, the -- one of the crucial things about continuing education is so that you don't fall victim to your own idiosyncratic small experience. I did it yesterday, this is what I saw, therefore that's what I'm going to see today. And so the -- you have to -- you have to reach out, you have to get other people's experience. The broader that experience and the more varied that education, the better you are going to be taking care of patients.
Q. Doctor, you looked at a lot of materials we said before, you prepared your report here, not only the material that the attorneys had given you but apparently some other additional material, as well; is that right?
A. That's correct.

Q. And looking at that material that was -- formed the basis for your report; is that correct? Conclusions you reached; is that right?
A. I think that, my clinical experience, my intellectual experience over time. Kind of the sum total of what I've gone through.
Q. And, in fact, I think you were qualified as an expert in labeling and whether the label would be adequate. You heard that, as well?
A. I did.
Q. And you're familiar with the regulations of the FDA, you've told us you're very familiar with that. You read labels all the time, you're very familiar with what should be contained in labels and what would be accurate and what would be inaccurate as far as the information that may be contained; is that right?
A. I don't know that I would be an expert in what would be accurate and inaccurate. But I certainly read labels all the time.
Q. And you certainly studied the labels with respect to the antipsychotics that are on the board behind you; isn't that correct?
A. These and many others, yes, sir.
Q. In fact, you specifically reviewed the

labeling for each of the six antipsychotic medications from the year they were first put out by the FDA up at least until the time you were deposed in May 2007; isn't that correct?
A. That's correct.
Q. And you did that specifically in connection with this litigation; isn't that right?
A. Back a year ago, yes, sir.
Q. Right.
Now, that would include the original 1996 label for Zyprexa; isn't that right?
A. About the oldest one I went back to is '97 or '98, I think, but yeah, it -- well, as early as I could get to.
Q. But the label hadn't changed between '96 and '98?
A. No.
Q. And you reviewed the 2000 label; is that correct?
A. Yes, sir.
Q. And you reviewed the label change that was made in 2003?
A. Yes, sir, I did.

Q. All right.
Now, I'm going to ask you whether or not you found anything in reviewing the label when you reviewed specifically the 1996 label that was erroneous or inaccurate.
A. That was erroneous or inaccurate?
Q. Correctly.
A. To my knowledge?
Q. Yes.
A. No. I don't -- I don't think I can -- I can point to anything that I -- that I knowingly know was inaccurate at the time.
Q. All right.
And when you reviewed the 2000 label, did you find anything there that was erroneous or inaccurate?
A. Given my state of knowledge at the time in 2000?
Q. No. When you reviewed that label in connection with this litigation.
A. Correct.
Q. Right?
After you had an opportunity to review all the material that the attorneys provided to you because you said you just

reviewed these labels in connection --
A. Okay. I'm sorry. I answered the question improperly, then. I was trying to go back to my state of my knowledge in 1996.
Well, the only thing that would be -- that would be inaccurate in the label was the -- the long-term weight gain, which was the difference between 12 and 24 pounds, but other than that -- let's see.
Well, if you -- no, I mean, the label did contain hypertriglyceridemia, the label did contain hypercholesterolemia. It didn't it quantify it, but what was in there was not decidedly incorrect.
Q. It was not -- it wasn't inaccurate. and indeed, if you were to prepare a report and deliberately leave something out, you would certainly view that as being inaccurate, your report; isn't that right?
A. I guess I wasn't thinking about in that context. But to answer your question, yes, I think I would.
Q. So when you looked at the 2000 label for Zyprexa, you didn't see anything there that you found was erroneous or inaccurate? Is that

right?
A. Well, in the context of having left -- left things out, there was not a quantification of those abnormalities. That is to say, the hypertriglyceridemia, the hypercholesterolemia, and the changes in glucose, they were mentioned, so in that sense they weren't inaccurate. They were there, but they weren't quantified, so the fact that they weren't quantified to the degree they were in the dataset, is that inaccurate by your definition? I guess so. But I -- I didn't quarrel with it. It said hypercholesterolemia, hyperglyceridemia, you know, it had all those side effects in it.
Q. When you reviewed, then, Doctor, the 2003 label in connection with this litigation, and indeed you sat down and looked at the label in connection with this litigation, in light of all the information that had been provided to you by these attorneys, it was your conclusion that the label was neither erroneous or inaccurate; isn't that right?
A. No --
Q. Isn't that right? Yes or no, Doctor?
A. No, that is not correct.

Q. Well, then let's go to your deposition, please.
A. Okay.
Q. Page 214, and again, this is the deposition that was taken on May 1st, I think, 2007; is that correct? By the way, Doctor, when you had your deposition taken, and after your deposition you certainly were aware that you had an opportunity to change your testimony, to add to it, to make any corrections, additions or deletions that you thought were necessary; isn't that correct?
A. That is correct. However, I was not sent my deposition.
Q. By these attorneys; is that right?
A. By Rachel.
Q. Attorneys representing the plaintiffs; is that --
A. That's correct. I had not seen it for many months.
Q. All right.
But you were certainly given that opportunity. That's your opportunity under the law to make any corrections --
A. Absolutely.

Q. -- additions or changes. And you did not take advantage of that opportunity; is that correct?
A. That's correct.
Q. All right.
Now, let's look at Line 20, please, on Page 214.
A. Yes, sir.
Q. And the question was that -- and you specifically reviewed the labeling of each of the six antipsychotic medications from the year they received FDA approval to the present, and that includes the label for olanzapine that was approved in October 1996; is that correct?
A. Right.
Q. And can we go to the next page, and you answered: That is correct. And then the question is: And as we've already talked about the information that was included in the label about weight gain, and I think you indicated again that there is nothing erroneous about that. You had some opinions about whether or not more information may have been conveyed in some fashion to other physicians.
In review of the label, did you

find anything else in the label -- did you find anything in the label that you viewed as erroneous?
And you asked, did I -- and then the question was did you find anything in the label, when you reviewed the Zyprexa label from 1996 to present, that you found erroneous or inaccurate and your answer was, No, I don't think there was anything frankly wrong. That was your testimony at the time; is that correct?
A. That is correct.
Q. Thank you.
Would this be a good time to take a break?
THE COURT: Sure. Why don't we take a -- our second break for the day. We'll be off record for about 15 minutes.
(Short recess.)
THE COURT: We're back on the record and all members of the jury are present. Mr. Lehner?
Q. BY MR. LEHNER: Dr. Wirshing, you know what a medical letter is; isn't that correct?
A. Yes, sir.
Q. And a medical letter is what doctors

receive from pharmaceutical companies from time to time warning doctors about new findings, new good things, new bad things, new data that they may find, new facts that they want to bring to the attention of the medical community. That's what the purpose of a medical letter is; isn't that correct?

A. Yes, sir.

Q. And you get them pretty regularly; isn't that right?

A. Quite frequently. They're not regular, but quite frequently.

Q And you recall receiving medical letters from Lilly from time to time on issues related to weight gain, diabetes and weight gain management; isn't that correct.

A. Yes, sir. Several.

Q. And again, I think you've told me that you have reviewed the medical letters that you have received from Lilly on these various topics in connection with the deposition that you gave in May 2007; is that correct?

A. Yes, sir.

Q. And I want to show you some of those medical letters.

A. Certainly.

Q. I'd be happy to give counsel a pack here.

Let's start with EL3003.

MR. SUGGS: Your Honor, I don't believe these are in evidence.

MR. LEHNER: Your Honor, these are on our exhibit list. They were not objected to. I certainly entitled to cross-examine the witness on these matters, I believe. He testified he'd has seen them.

THE COURT: That's fine. I just want to get -- I'd like to get things admitted before the jury shows them so we don't have a problem down the road with things that are shown to the jury and then they're not admitted and then I've got to tell the jury that they've got to forget about it.

MR. LEHNER: Well, and they've made no objection to them, Your Honor.

THE COURT: So can we just get the numbers and we'll get them admitted.

MR. LEHNER: Yes. You're going to admit them in your case? This is your case.

MR. SUGGS: Are you admitting

that -- is it -- are these being offered for the purpose of showing that Dr. Wirshing received these particular letters?

MR. LEHNER: These are being shown because Dr. Wirshing said he reviewed these medical letters as part of his expert report. That's absolutely right.

MR. SUGGS: Well, I think you need to show them to him and see if these are indeed the ones that he saw.

MR. LEHNER: I'd be happy to show them to him first.

THE COURT: Why don't you show them to him first, and then we'll get what --

Q (BY MR. LEHNER) Dr. Wirshing, there's a series of medical letters that I'm giving you while I'll identify them for the record --

MR. SUGGS: Objection. Your Honor, can we approach the bench, please?

THE COURT: You may.

(Bench discussion.)

MR. LEHNER: I'm certainly entitled to cross-examine him on these medical letters. He said --

THE COURT: You can cross-examine

him all you want to. Don't put them up on the screen if you're not going to admit them. If you're going to admit them -- if you are going to put them up on the screen, I want them admitted. That's my problem. I don't know what your problem is.

MR. SUGGS: The nature of the objection I have is that he referred to these as letters, and there's no -- he calls them letters but there's no -- there's no addressee, there's no nothing.

Did he get this?

MR. LEHNER: He's going to tell us.

THE COURT: He's going to tell us, and if you want to point that out and stuff but my understanding is you've asked him he can follow --

MR. SUGGS: Is this part of the letter?

MR. LEHNER: I asked him whether he received this material. He testified as a medical letter is what it is. It's communications --

MR. SUGGS: Are you saying that this summary here is part of the letter?

MR. LEHNER: I'm saying he described what a medical letter is. I don't think we need to argue that now.
MR. SUGGS: See, you're describing this as a medical letter and I don't think this is a medical letter. It doesn't look like a letter.
THE COURT: You can cross-examine him on that. My concern is if you want to show them to the jury, I want to get them admitted and we can deal with if you need to voir dire to do that we can do that.
MR. LEHNER: The real issue we have, Your Honor, is I would certainly think I'm entitled to show the jury whether or not we admit it into evidence. I don't want to admit -- any Rule 50 motion that we may have. I mean, that's really the issue here. We're not introducing any affirmative evidence at this time. And, you know, if he's -- if he reviewed medical letters as he said he did --
THE COURT: Again, you don't have to offer them at this time if you don't want to, but if you want to show them to the jury, I don't want to be in the position of showing the jury

stuff that isn't in evidence. They should see it when it's been admitted into evidence.
MR. SUGGS: And my objection is I don't want there to be the implication this is actually a letter that he received when it doesn't look like a letter.
THE COURT: Well, you can cross-examine as to that.
(End of bench discussion)
Q (BY MR. LEHNER) Dr. Wirshing, you're looking through a series of documents now. I'll just identify them for the record while you're doing that, just so it's clear for the record. This is EL3003, EL3008, EL 2991, EL 2996, EL 2990, EL3004. Those are the documents you have in front of you.
And Doctor, having looked at these, these are what are vernacularly referred in the medical community as medical letters, is that correct?
A. That's correct, yes, sir.
Q. And these are the kind of communications that pharmaceutical companies send to physicians like to you inform them, as we said, about matters related to their product and in these

particular cases these relate to body weight changes --
A. Glucose.
Q. -- glucose and cholesterol and diastolic blood pressure; is that correct?
A. That's correct.
Q. And then there's some on weight gain reduction and management; is that correct?
THE COURT: Mr. Suggs?
MR. SUGGS: Objection, Your Honor, as to the time.
THE COURT: Well, that --
MR. SUGGS: The date of these communications.
THE COURT: That can be established by either of you.
Q (BY MR. LEHNER) And these are -- you recall receiving these letters or letters similar to this from Lilly; is that correct?
A. Certainly.
Q. Certainly you do?
A. Certainly I recall receiving letters of similar ilk. As to exactly when, I'm not sure, but I certainly recognize them all.
Q. You recognize them all.

A. Yes, sir.
Q. Thank you very much.
So you recall receiving them at some point in time; is that correct? Before you gave your report in this litigation; is that right?
A. I -- I can't guarantee that it -- that it was before. I've certainly seen them before.
Q. And before you gave your report in this case; is that right? Before May of 2007; is that right?
A. I'm fairly certain I've seen them all before then.
Q. Thank you very much.
And let's just go through the titles of them.
A. Okay.
Q. The first one, EL3003, is called summary body weight changes, and that's a -- sort of a -- looks like a 12-page letter, as it were; is that right?
A. Got it.
Q. Do you have it?
And it sets out in detail, is that correct, certain information about weight changes

associated with Zyprexa; is that right?
A. It does.
Q. And it gives data on mean changes in weight over three years in patients treated with HGAJ -- treated with Zyprexa from the J trial; is that correct? See that on Page 5?
A. Right. HGAJ trial.
VENIREPERSON: Can we see it on overhead?
THE COURT: No, at this point you just have to stick with the testimony. At some point that document may or may not be provided to you, but at this point I can't allow it.
Q. BY MR. LEHNER: And turn to Page 7, if you will.
A. Okay.
Q. There you'll see there's comparative information about the effect of weight gain that is seen in Zyprexa compared to clozapine and risperidone; is that right?
A. Yeah, it has a bunch of information, including the ones that you listed, yes.
Q. Right.
And at the end there is a summary and then following the summary there's a list of,

what, 19 different journal articles that deal with this topic of weight gain associated with neuroleptic medication, antipsychotic-induced weight gain, all from various medical journals; is that correct?
A. Journal articles, Lilly data file on -- on file with -- with Lilly and presentations at scientific meetings. Yes, sir.
Q. And there's two articles I see from -- that were authored by Dr. Allison. See that?
A. Yes, I know David.
Q. Dr. Allison -- you know Dr. David Allison?
A. Yes, sir.
Q. And he's an expert that the plaintiff intends to call in this case. Do you understand that?
A. I did not know David was going to be here, no.
Q. And let's look at the title of the next one.
A. 3004?
Q. 3008.
A Check.
Q. Again, a 12-page document dealing with

body weight changes; is that correct?
A. Yes.
Q. And there is a summary page, a summary of this information so that doctors could -- to get the summary of the information quickly, and that's what the first two pages are, right?
A. That's correct. Very similar to the last one.
Q. And then the 10 following pages are a more detailed analysis of the information on body weight changes; is that correct?
A. Correct.
Q. And again, there's at the end a bibliography of references that is included in this; is that correct?
A. There is. Much the same bibliography as the last one, but yes.
Q. Let's --
A. In fact, identical.
Q. Let's look at 2996.
A. 2996.
Check.
Q. And can you read the title of that one?
A. Yes.
Zyprexa: Effective Long-term Treatment on Weight

Change in Association with Changes in Glucose, Cholesterol and Diastolic Blood Pressure.
Q. And this is -- this document is how long?
A. This document goes to -- looks like there are two pages in this particular one, second of which goes to 5 and the first one goes to -- I guess it's -- did you copy it for me twice?
Q. No, I think they're a little bit different, but these are five-page documents that deal with this topic of glucose, correct?
A. So two separate five-page documents that have the same EL2996 on it, the same title.
Q. And again include table of information about weight gain, cholesterol and glucose; is that correct? See the table, for example, down on the bottom of Page 2?
A. Page 2? Yeah. Again, they -- the two that -- two that you've given me appear to be identical.
Q. Look at 2990.
THE COURT: When you say the two appear to be identical, what two by numbers.
THE WITNESS: It's a 10-page -- 10

pages that were given to me, both entitled EL2996, and both -- they appear to be five identical pages.
Q. They may have been Xeroxed twice, Your Honor.
A. So -- yeah, looks like five pages, 2996. The next one is 2990?
Q (BY MR. LEHNER) Yeah.
A. Yes, sir. Check.
Q. Weight Reduction and Management. Have you had a chance to look at this one --
A. Yeah.
Q. This document is about information that Lilly's providing to physicians on how to manage weight gain and some certain strategies for reducing weight gain; is that correct?
A. I was actually consulted on this one.
Q. You were actually consulted on this one?
A. Yes, sir.
Q. And helped contribute to this information?
A. To the ideas, yeah. I mean, we'd had some pretty good success at helping people lose weight who had gained weight on olanzapine. So they were very interested in our work.

Q. And so Lilly took some of your ideas and circulated it to physicians; is that correct?
A. Yeah. Honestly, I'd stolen the ideas from other people, but yeah.
Q. Well, when you -- when you looked at these medical letters, both now -- well, when you looked at them before you gave your deposition in May and then preparing the report, again, I take it you didn't see anything in these medical letters that was inaccurate or misleading; is that correct?
A. I -- with respect to the data presented, no, I had no reason to believe that the -- the data presented was inaccurate. As far as the misleading, I have a -- I have a little bit different take on it. You know, there's much when you read these letters, much which blames weight gain on a whole host of other nondrug related problems, including the illness schizophrenia itself. And to me that is a little misleading. That distracts from the primary purpose of the -- of the -- of the teaching, which should be drug-related obesity. So it's not inaccurate, no, but it is a little misleading.

Q. Well, when -- when I took your deposition -- and you were under oath at the time and you knew you were to tell the truth, the whole truth, nothing but the truth, that's the oath you took when you took your deposition. That was not your testimony when you gave your deposition, is it? Is that correct?
A. I have no specific recollection at this time.
Q. Doctor, you mentioned that one of the concerns you had was that Lilly was blaming the -- blaming schizophrenics for diabetes, and you thought that was wholly inappropriate and you thought it was insensitive; is that correct?
A. I did indeed.
Q. Yes.
And because you were not aware of any information that linked the disease of schizophrenia with diabetes and you thought this was a real sort of red herring; is that your sense?
A. That's precisely my sense.
Q. But you reviewed, I take it, Doctor, and indeed I saw it in materials that you reviewed again -- that you reviewed before you gave your

deposition under oath in this case, you reviewed the submission that Lilly made to the FDA in May 2000. It was a very large submission?
A. Yes, sir.
Q. And you had that. And I'm just wondering whether you noticed in there the various articles which discussed that the association between abnormalities and glucose homeostasis and the serious mental illness, including schizophrenia, was first described in the early part of the 20th century. Did you notice those articles?
A. Of course I did, and I have personally reviewed those articles.
Q. You said you weren't aware of any literature on the topic. That was your testimony earlier?
A. I'm not aware of any literature which demonstrates there is an effect -- none of that literature does.
Q. So you disagree with all of those?
A. I totally disagree with them. There is no effect aside from changes in obesity, which can contribute to the association between schizophrenia and endocrinologic perturbations.

Q. And so you would disagree with the Canadian Diabetes Association Which has recognized schizophrenia as a risk factor for diabetes, as well?
A. As a risk factor, they are wrong. They know something about diabetes, they don't know about schizophrenia.
Q. And you would disagree with the FDA, as well in the 2003 label change which they recognized that there may be an increased risk among this population for diabetes?
A. It wouldn't be the first time. Associated only with the illness schizophrenia. Not with concomitant obesity. Concomitant obesity is absolutely a risk factor.
Q. The disease state itself, you disagree with all those other people who believe that there may be some relationship between the disease state.
A. Absolutely. Absolutely. In point of fact, for females with schizophrenia, for instance, there's a good percentage of them which are underweight. They have a decidedly lower risk of diabetes than average. So in that case it would be an inverse relationship.

Q Now, Doctor let's take a look, if we could, to EL2399, and I believe this was an article that we've seen already.
MR. SUGGS: Can I have a copy, George?
MR. LEHNER: I think you used it in your presentation, Dave, actually.
THE WITNESS: Yes, you did.
MR. LEHNER: And this is part of the Wirshing --
MR. SUGGS: Oh, it's a different number. I see it.
Q (BY MR. LEHNER) And this is, again, an article that we've seen previously; is that correct?
A. It is, yes, sir.
Q. And your wife, again, was the lead author on that; is that correct?
A. Yes, sir.
Q. And you were the second author on this, correct?
A. Yes, sir.
Q. All right.
Now, you know that Lilly submitted this paper to the FDA, again, as part of the

July 2000 submission; is that right?
A. I am aware of that.
Q. And I want to turn to Page 361. It's the fourth page in. There were some conclusions there that I just wanted to ask you about.
A. Yes, sir.
Q. And if we go down, where it begins fourth page in, clozapine effect on weight gain was sustained. See that?
A. Yes, sir. It was.
Q. Clozapine's effect weight gain was sustained and unresponsive to interventions, whereas olanzapine's weight gain effect was somewhat reversible with dietary and other behavioral maneuvers. That was one of the conclusions you came to in this study, correct?
A. And I think one of the important ones, yes, sir.
Q. And so the kind of weight gain that one sees among these atypical antipsychotics is different in some respects; is that correct?
A. In my experience the weight gain with clozapine is particularly resistant to change.
Q. Right. And I take it this conclusion you reached in this article you repeated again in

a subsequent article that you and, again, your wife wrote a couple years later, where you said that our previous research demonstrated that simple behavioral measures to lose weight were effective in patients treated with risperidone and olanzapine? Do you remember that conclusion?
A. Absolutely. And continue to be effective to the present day.
Q. And one of the things that I think you talked about was -- and some have these conversations you reported having with people at Lilly was encouraging Lilly to develop some materials to help doctors deal with the issue of weight gain; is that correct?
A. Absolutely right.
Q. And that was something that your wife was particularly interested in as you were, as well?
A. Yeah. Precisely. Donna's had a long-abiding interest in that.
Q. And some of that was translated into, I think, what it was called the Solutions for Wellness program. Do you remember that?
A. Oh, yeah. I think -- I think that there was a good deal of our ideas that were put forth

in that, yes, sir.
Q. And Lilly prepared extensive materials for doctors on how they may intervene with patients to help them manage their weight gain; is that right?
A. They did, provided CME lectures, outreach, and additional mailings and that kind of stuff.
Q. And much of that was based on the information that you and Donna had provided to Lilly in terms of how to deal with weight gain, given your extensive experience in that; is that right?
A. I think much would be a bit narcissistic, but I think some of it, yes.
Q. Very modest. Thank you very much, Dr. Wirshing.
But you were very involved in communicating with Lilly how they could develop this material; is that right?
A. Yeah. I mean, my primary -- my primary goal was to -- was to prevent patients from having so many problems with -- with the drug. I considered these, as most problems with antipsychotics, I considered these manageable,

understandable, treatable. If you paid attention to them.
Q. Let's go back up to that article for a minute. If we can go to the fifth page in, I wanted to ask you another question about this article.
And you see the part there in the article that begins, novel antipsychotic drugs have superiority over haloperidol?
A. Not yet. Where is it?
Q. It's in the second -- in the right-hand column. Although -- there we are.
A. Yeah, I got it.
Q. Although novel antipsychotic drugs have superiority over haloperidol both in increased effectiveness and reduced side effects.
A. Yes, sir.
Q. That's the conclusion that you all reached when you were doing this study; is that correct, back in 2000 -- 1999?
A. Yes. That's correct.
Q. And you really haven't changed your opinion about that over time; is that correct?
A. No. Clozapine in particular continues to be clearly demonstrably better than

haloperidol.
Q. And you were including when you wrote about the novel antipsychotic drugs, Zyprexa as well, olanzapine; is that right?
A. Olanzapine and risperidone both have efficacy above haloperidol and control drugs.
Q. Right.
And you heard Dr. Hopson here yesterday, I think, or Wednesday, you were in the courtroom when he testified that they no longer use first-generation antipsychotics at the Alaska psychiatric institute; isn't that correctly?
A. I did hear him say that, yes.
Q. And you heard him say that they, in fact, use Zyprexa as a first-line treatment and some of the physicians actually prescribe it as a first-line treatment; is that correct?
A. Yes, I did.
Q. And you don't have any qualms with that, do you? You don't think they're doing anything wrong at the API, do you?
A. No.
Q. Thank you very much.
A. I think that that's defensible.
Q. In fact, you -- when you were practicing

at the VA, up until what, late 19 -- 2006, you would prescribe Zyprexa as a first-line treatment; isn't that correct?
A. I -- I continue to provide -- to prescribe olanzapine. I -- if by first line treatment you -- you refer to patients who have never been diagnosed before, it's the first time they've ever been on antipsychotic, that's a patient even somebody with my experience virtually never sees. But I do start people on -- on olanzapine but I have a drug history. I did that as we talked about in direct, I did that twice on Monday.
Q. Gave a -- gave a patient olanzapine --
A. Two patients.
Q. Two patients. First time they'd been prescribed an antipsychotic?
A. No. That's -- schizophrenia is --
Q. You started them on Zyprexa?
A. I started them on Zyprexa. They had been on other compounds previously and I reviewed their medication response profile and decided that that was the most reasonable strategy to choose at that time.
Q. You were weighing what potential

benefits may accrue from giving them Zyprexa at that time versus the risks that you know are associated with the drug and you decided to start them on Zyprexa; is that correct?
A. Of course. I -- I have -- I have respect for, knowledge about and I think I know what to do with the toxicities of all these compounds.
Q. Now, and one of the reasons I think you told me that you will stick with a compound that you find is working with somebody is because that's really the hardest thing to treat, the psychosis that may be associated with that disease; is that correct?
A. Amen. Absolutely.
Q. And you'll deal with whatever toxicity if the drug is working; is that right?
A. With the exception of a few really, really bad, ugly things I'll fight the devil himself to keep a person on a drug -- if it's working for him. Schizophrenia is the hardest thing to treat. You luck out and you find something that works, you hang onto it like a pit bull with lockjaw.
Q. And, Doctor, that's really one of the

reasons -- when we were talking in your deposition, again, that you said to me that you thought these drugs, including Zyprexa at the time, were a godsend; isn't that right?
A. As -- as I think I said, and I believe that your co-counsel presented it in opening arguments, I -- I continue to be just staggered when you -- you know, you put your money on the table, you guess right, and it fixes somebody, at least in a good portion of their illness. I mean, it's -- it almost brings tears to my eyes every time it happens.
Q. I mean, I think the words you used were it's the closest thing to magic you've ever experienced; isn't that correct?
A. In my medical career. It's like you're curing a rock.
Q. And that happens when you use Zyprexa, that happens when you use any of these second-generation antipsychotics; is that correct?
A. It happens with all of the antipsychotic compounds, and the dramatic thing is when you -- you know, you find the one that works for that particular patient. I mean, it -- you can't

always find it -- you frequently can't, for all patients, but when you do, it is -- it is a profound emotional and professionally gratifying experience.
Q. I mean, these are the kinds of drugs that can, I think as you said, sort of free people from a -- really just a horrible hell of a life; isn't that true?
A. Potentially so. Now, the life they continue to live even with effective treatment is hellacious. The way they are treated by society is awful. This is not to minimize the burden that they have to experience, but the subjective torture that they have to go through is potentially dramatically released by these compounds. These -- this is not cosmetic psychiatry, I mean, this is real stuff we're talking about.
Q. Real life-changing kind of thing?
A. Indeed. Family changing.
Q. Pardon?
A. Family changing.
Q. Family changing. Allows people to kind of integrate back into society on occasion; is that correct?

A. Absolutely. When they -- when they work, I mean, it's -- as I say, I -- superlative.
Q. And your decision to decide -- and the kind of calculus that you go through, the decision-making process that you go through, tell me a little bit about that. How do you decide --
A. Well, I can tell you. For the last 50 years the selection of antipsychotic drugs, because there's very little to guide you in terms of, this drug clearly works better, that drug clearly works better. Efficacy, you can't make book on anything with the exception of clozapine. Excepting that very unusual molecule. The rest of them, they're all approximately the same, they're within shouting distance of one another. So it becomes a selection of side effects. That is what has been for the last half a century's time, selection of side effects. Once you go through that, because the illness lasts 50 years, you have lots of -- usually lots of history guiding you as to what gets better and what doesn't get better.
Q. And you know that some of these other antipsychotics have very serious side effects. We'll talk about Zyprexa and we've been talking

about Zyprexa but we've seen some of the more very serious side effects associated with Risperdal. We've seen some of the very serious side effects associated with Seroquel, we looked at the label. You're familiar with some of the very serious side effects associated with those drugs; is that correct?

A. Yeah, it's -- it's my belief that the -- the atypicals in general, with a couple little exceptions, but we're talking spectrum. I mean, everything we've talked about you can talk about with risperidone, you can talk about with quetiapine, you can certainly talk about with clozapine. It's just one of -- one of a magnitude along a continuum.

Q. And probably the most important thing I suspect is your clinical experience. You've seen patients that look like a patient who might be in your office and you say, you know, the patient worked on this; is that correct? I mean, your own information that you develop from actually looking at a patient and calculating what do I know about this patient compared to what I've done?

A. It would -- it would -- it would be cool

if I could -- if I could tell you a person could walk in and I go you're a quetiapine guy, you're an olanzapine guy. That -- I would love to have that ability and love to pretend that I could do that. I can't.

The most important thing that you have is the person themselves. That -- that brain has been exposed to various treatments and so that history and how you derive that history from a person is the most critical factor. What was their toxic experience, what were their positive experiences. So it's not really what they look like at this moment. That's part of the gemish, that's part of the mix, but it's really what's worked for you before, what hasn't worked for you before, what's hurt you before, what hasn't hurt you before.

Q. And that's what you're listening to a patient telling you, right?

A. A patient, the chart, family members, what you beg borrow or steal, whatever data source you can get, you take it.

Q. Doctor, let me ask you a question about, again, conversations that you've had with Lilly over the years.

A. Yes, sir.

Q. You've talked about that you had a lot of contact with people at Lilly and you've mentioned a number of the physicians and I think you mentioned Dr. Gary Tollefson and Dr. Charles Beasley, and you mentioned some others, as well.

A. Yes, sir.

Q. And you've certainly been at a number of meetings where you've met Lilly scientists and I'm sure you've met Lilly executives over the years; is that correct?

A. I'm not the kind of person that usually people introduce to executives, I'll be quite honest with you.

Q. Well, Gary Tollefson was a senior executive at Lilly.

A. Well, then it counts. I did meet him on occasion.

Q. And Charles Beasley was the chief medical officer and chief scientist at Lilly. You met him on many occasions; is that correct?

A. Oh, yeah. I didn't really consider them executives, but if that's what they were, that's great.

Q. And your wife Donna was on several

advisory boards at Lilly consulting with Lilly on a number of different topics; is that correct?

A. Mostly about this topic, but yeah.

Q. And you -- as we've said, are very knowledgeable about labeling and what should be in labels and what shouldn't be in labels and you mentioned your familiarity with the regulations that you were shown that the FDA has.

A. Yes, sir.

Q. And in light of all that, you never went to Lilly with any specific recommendation as to how Lilly might change its label for Zyprexa concerning either weight gain or any of the other issues that you were concerned with; isn't that correct?

A. I've never done that with anybody.

MR. LEHNER: Thank you very much, Doctor.

Can I have a minute, Your Honor?

THE COURT: You may.

(Discussion off the record.)

MR. LEHNER: That's all, Your Honor.

THE COURT: Thank you. Mr. Suggs?

FURTHER EXAMINATION

MR. SUGGS: A few questions, Dr. First of all, would you regard Zyprexa as an everyday agent for primary care use?

THE WITNESS: By primary care, you mean primary care practitioners?

Q. Yes.

MR. LEHNER: Objection, Your Honor. He hasn't been offered as an expert on primary care.

MR. SUGGS: He talked about how safe the drug is.

THE COURT: I'll allow the question.

THE WITNESS: It's my belief that antipsychotics should not be prescribed by anybody except those with significant familiarity with them. Zyprexa included.

Q. (BY MR. SUGGS) Okay.

And fair to say that Zyprexa should be used only for very severe psychiatric disturbances?

A. Of course.

Q. Okay.

And I believe you testified when Mr. Lehner was asked you questions that for the

last decades, at least, the choice of which antipsychotic you're going to use in a person who needs an antipsychotic drug is looking at side effects, the side effect profile of the drug, correct?

A. That is correct.

Q. Okay.

Now, in order for a -- for a doctor to consider the side effect profile, would it be fair to say that the doctor has to have adequate warnings about the adverse effects of the drug?

A. Among many other things, but yes.

Q. Okay.

And did Lilly adequately warn about the risks of Zyprexa?

A. No, I don't believe so.

Q. Okay.

By the way, Mr. Lehner showed you some medical letters. Do you happen to have the one that was numbered 2996?

A. Yes, sir.

Q. If you could turn to Page 4.

A. Yes, sir.

Q. About the middle of the paragraph there's a sentence that starts off about midway

through the line, data conclude. Do you see where I'm at?

A. Yes, sir.

Q. That sentence says, Data conclude that nonfasting serum glucose levels are not significantly associated with weight gain experienced with long-term Zyprexa treatment. Do you see that language, sir?

A. I do.

Q. Do you believe that's an accurate statement, sir?

A. I -- it's such a tortured English statement, it's hard to know exactly what it means, so -- do I -- do I believe it as I understand it? No. Of course not. I mean, if you gain weight it's going to -- it's going to cause a perturbation in the average person's glucose. It just is.

Q. And so if it -- if Lilly sent this letter to doctors, supposedly informing them about the properties of Zyprexa, and it stated data conclude that nonfasting serum glucose levels are not significantly associated with weight gain experienced with long-term Zyprexa treatment, would that be a misleading statement?

A. Yes. I mean, this is -- this is from the same data that we talked about in the -- in that article, the same article which -- which concluded that -- that olanzapine was not associated with increased impaired glucose tolerance compared to haloperidol placebo.

Q. By the way, this particular document that we were talking about, in fact, all of them, do any of them bear your -- your address on here?

A. No, sir.

Q. Do any of them have your name on here?

A. No, sir.

Q. Do any of them have a date on here?

A. None that I see.

Q. Did anybody sign any of these things?

A. Not in these one, two, three, four, five, six documents I see.

Q. Is there a Lilly logo on any of these things?

A. There's Zyprexa with a --

Q. Little copyright sign?

A. Little copyright law.

Q. Do you see a Lilly logo at all?

A. Not -- not in my brief perusal. I can't guarantee that -- I don't think so.

Q. Okay.
Mr. Lehner was asking you some questions about whether there was evidence in 2004 to determine whether there was a differential risk of diabetes, I think, and between the various antipsychotics. Do you remember that discussion you had with him?
A. That's correct.
Q. And was he talking about whether or not there was evidence to determine whether there was a differential risk in terms of a drug's specific effects on the pancreas?
A. Well, the answer is, I don't know. I was having a little trouble with -- with the entire line there. It is my belief that -- that people in the FDA and the folks at that meeting were focused on the specific impact on a person's glucose regulation of the drug, irrespective of the impact on weight. That question is open to the present day, and my response to the question as I sit here today, as I sat there 10 years ago, is no. I don't believe these drugs have a direct impact on glucose regulation apart from their impact on weight.
Q. Okay.

A. So I -- I agree with the FDA if they're talking about the impact on glucose regulation directly.
Q. Okay.
And so what you're saying is -- correct me if I'm wrong. Your opinion is that, yes, Zyprexa can cause diabetes by first causing the weight gain; is that correct?
A. That -- in susceptible people who gain weight in a certain way.
Q. Okay.
A. Absolutely.
Q. But you're not aware of scientific evidence demonstrating to your satisfaction that Zyprexa causes diabetes by some mechanism other than that; is that a fair statement?
A. That is correct. There have been little bits of data here and there, little controlled experiments, some suggestion in certain animal models, but no, I don't believe they do. And I've done a good deal of work in this regard. I don't think that olanzapine does, I don't know if risperidone does. I don't think any of these do.
Q. And for the patient who develops diabetes as a result of taking Zyprexa because of

the impact on weight gain leading to diabetes, does that patient care when it came directly or whether there was some more direct effect that was not mediated or influenced by weight gain?
A. I think -- I think -- I think you do. And here's why, because the -- when it's due to weight gain, that's going to be the focus of your treatment, but if you've got a toxic effect on the pancreas, I mean, that's a different game.
Also, if you have a direct toxic effect on the pancreas there are medications that do that, that quickly leads to insulin dependence. It's a much different condition than glucose resistance. So yeah, you do -- you do care about it, because there's -- you got a different treatment for it.
From the patient's perspective, yeah, you got to take meds, you got to watch your diet, you got to take care of yourself. But if a -- if a drug has a toxic effect on the pancreas that's a potentially much more irremediable, untreatable circumstance than a drug that just causes you to gain weight.
Q. Okay.
Do you recall Mr. Lehner asking you

some questions about a letter to the editor that FDA -- well, do you recall Mr. Lehner asking you about a question that certain representatives of the FDA sent to the editor of diabetes care after the consensus statement --
A. Yes, sir, I do.
Q. -- in which the FDA indicated that they didn't know if there was enough evidence to make a conclusion as to whether there were differences in the rates of diabetes with various second-generation antipsychotics?
A. That is correct.
Q. And do you know whether or not FDA has changed its position on that?
A. I do.
Q. And did they change their position on that?
A. They have.
Q. May I approach the bench, Your Honor?
THE COURT: You may.
(Bench discussion.)
MR. SUGGS: When he asked him the questions about that FDA letter, I think he opened up the door to the 2007 --
THE COURT: The consensus statement

comes out, the letter to the editors -- the consensus statement says differential rates, the letter to the editor says we don't think there's enough evidence.

MR. LEHNER: Your Honor, that is -- we went through this the other day. That is bootstrapping of the -- this is what the FDA knew in 2004.

MR. SUGGS: He's raised the implication that the FDA still till this day doesn't think there's enough evidence when this man has already testified he believes that the FDA --

THE COURT: I don't think the implication was raised by the question. The letter that was done. You'll have your Lilly people arm and you can ask to your heart's content what's gone on then.

MR. SUGGS: May I have a moment, Your Honor?

THE COURT: You may.

(Discussion off the record.)

MR. SUGGS: Another line of questioning I wanted to ask you about. Sorry, Dr. Wirshing. It will be very brief.

Q (BY MR. SUGGS) Mr. Lehner asked you about whether the 1996 label and the 2000 label and the 2003 label, whether they were erroneous or inaccurate. Do you recall that line of questioning.

THE WITNESS: Yes, sir.

Q. Did those labels tell the whole truth?

A. No, sir.

Q. Did those labels adequately warn about the risk of diabetes?

A. It is my opinion the warning labels to the present moment are not adequate.

Q. Okay.

So your testimony is that the lag -- the words that are -- that were in the labels back at those time, you can't point to anything that was erroneous or inaccurate about those particular words, but you don't believe that those labels appropriately warned about the risk of diabetes?

A. That's absolutely true. And in particular, they didn't adequately warn about the weight gain. The single most defining characteristic of olanzapine is that it causes you to gain weight. Second, third and fourth

places are weight gain, weight gain and weight gain. The fact that it's not highlighted in aggressive fashion from the outset is -- is inexplicable to me.

Q. You talked about the utility of the second-generation antipsychotics can have. Does the fact that they have such great utility and can be so effective in relieving misery, does that relieve a drug manufacturer from adequately warning physicians about the risks that those drugs can also pose?

A. No. Of course, not.

Q. Thank you. I have no further questions.

THE COURT: Mr. Lehner?

FURTHER CROSS-EXAMINATION

Q (BY MR. LEHNER) I just wanted to ask you one question, Dr. Wirshing. We've heard a lot, and I think we were reminded indeed the other day that we're here talking not about numbers but really about individuals at the end of the day.

A. Yes, sir.

Q. And you would agree with me that in any one individual who's prescribed Zyprexa and then developed diabetes, we really wouldn't know

whether it was just a coincidence whether Zyprexa caused their diabetes, would we?

A. No. With certainty, no, sir, you would not.

MR. LEHNER: Okay.

FURTHER EXAMINATION

Q. BY MR. SUGGS: Does the use of Zyprexa increase the risk of diabetes in a population of people who are using the drug?

A. Demonstrably, reliably and predictably.

Q. And in the state of Alaska, when a population of Alaska was subjected to and used the drug Zyprexa, do you have an opinion as to whether with certainty any individuals within the state developed diabetes as a result of their use of Zyprexa?

A. A Predictable and definable number did.

Q. Okay. Thank you.

THE COURT: Do any members of the jury have any questions for the doctor?

I think you're done.

THE WITNESS: Thank you, Your Honor.

Thank you, jury.

THE COURT: Mr. Allen, I think we

can get, as I see the length of your first deposition, we certainly can get in one by 1:30. Dr. Kinon, and if we go 15 minutes late we can probably get two in?

MR. ALLEN: Yes, sir. As -- whatever you wish. I can play Dr. Kinon right now.

THE COURT: Let's play Dr. Kinon and then we'll see, because I want to talk to the lawyers a little bit after the day is over about a few things, so maybe we'll just play one and then -- it appears, ladies and gentlemen, just so that you know, that this first deposition is going to be about 17 and a half minutes long, and then the rest that we have is about an hour and 40 minutes, that we'll probably take up on Monday, and then the State will be done with its case, as I understand it from them. So we're not going to finish with their case today. There are, one, two, three, four, five more witnesses by -- all of whom are by video deposition that you're going to see. We'll do one today and then we'll break for the weekend.

MR. ALLEN: Okay, Your Honor. The State of Alaska -- can you hit the lights for me,

please.

The State of Alaska would call Dr. Bruce Kinon, a Zyprexa physician, you'll see, to the stand, by oral videotape deposition.

VIDEOTAPE DEPOSITION OF DR. BRUCE KINON

Q. (BY MR. SUGGS) Sir, would you please state your full name for the record.

A. Bruce Jerome Kinon.

Q. And what's your occupation?

A. Physician.

Q. And you're a physician employed by Eli Lilly; is that correct?

A. That's correct.

Q. Okay.

And what's your job title?

A. Medical Fellow II.

Q. You've been with Eli Lilly ever since 1996; is that correct?

A. Yes, that's correct.

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, sir?

A. Yes.

Q. And it also makes reference to the core

team. Do you see that reference?

A. I'll need a minute to review this document, please.

Q. Do you recall being a member of this core team of the hyperglycemia/diabetes project back in 2000?

A. When this team was initially developed, I was a member of the medical component of this team.

My recollection of the -- the role of this group was to understand from a medical point of view the hyperglycemia and diabetes issues involved with Zyprexa and try to deliver that information to clinicians in a way that they would have the answers they needed to the questions that they were posing.

Q. Let me hand you what's been previously marked as Exhibit 8905. For the record, this is a two-page e-mail from Paula Trzepacz, am I pronouncing her name correct?

A. Trzepacz.

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. Okay.

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. Dr. Trzepacz says that, quote, "the primary person respon -- 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. Hayes being the number twos and number threes, correct?

A. Yes.

Q. And her plan also entailed you -- pardon me -- Dr. Baker being the number one 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. Okay.
So you were the number one guy dealing with 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?
A. That's correct.
Q. Let me show you what's been previously marked as Exhibit 1213.
As I mentioned -- 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?
A. I have no basis to deny or not. I just have never seen this document before.

Q. 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.
As far as I can recollect, these were never key messages in terms of our interpretation of the data.
Q. Did the data that the company have 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 80, 90 pounds of weight while they were using the drug; isn't 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 -- might have been that.
Q. And 22 pounds of weight gain is a lot of weight gain, isn't it?
A. That would be considered a significant amount of weight.
Q. Clinically significant, correct?
A. Depends upon the -- the amount of time.
Q. Well, and also depends on the weight of the individual, right?
A. That's correct.
Q. Because don't doctors typically think that if you have weight gain more than seven percent of your body weight, that that is clinically significant?
A. That's correct.
Q. Okay.
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.
Q. Right.
So bottom line, what your studies were showing, that, you know, on average people

were going to have clinically significant weight gain with Zyprexa, correct?
A. That's correct.
Q. Now, if you can 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, language, sir?
A. Yes, I do.
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. 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 2 diabetes. Were you aware of that, sir?
A. I was not aware of that.
Q. Okay.
Let me show you what's been previously marked as Exhibit 1586.

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.

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 months -- pardon me -- at the end of the 12 months. Did I read that correctly?

A. Yes.

Q. And so is it your testimony as you -- 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.

Q. Did anybody tell that you back in 1995 analysis was done which showed a statistically significant increased incidence of high glucose in Lilly's own clinical trials? Yes or no?

A. I'm not aware that anyone specifically

told me of that analysis that you're referring to.

Q. Okay.

I'm going to show you what's been previously marked as Exhibit 1605.

For the record, this is a computer printout dated June 19, 1995; and it's titled Treatment-Emergent Abnormal High or Low Laboratory 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 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.

Q. I'm going to show you what's been previously marked as Exhibit 1215.

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 Schmidt on December 1, 1998.

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. Richards, with copies to Jeffrey Ramsey and Robert Schmidt 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, in the product team.

Q. Okay.

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 with statistics.

Q. And Robert Schmidt, who was he with?

A. Marketing on the product team.

Q. Okay.

So you're the only medical guy, apparently, who is being copied on this e-mail.

A. Apparently.

Q. Okay.

And the reference is to articles by Wishing and Goldstein, do you see that reference, sir?

A. Yes.

Q. If you just read on into 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 article. Do you see that language, sir?

A. I see that language, sir.

Q. Any, in any event, the marketing department was concerned about these reports that were being published and wanted to know what their response was going to be, correct?

A. As reflected by Peter Clark's e-mail, I would say yes.
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. Okay.
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, correct? That if you gain weight, that can lead to ultimately diabetes, correct?
A. I don't know specifically what Peter Clark was referring to, but in general medical knowledge, weight gain can lead in some patients to insulin resistance, which in some patients may eventually go on to be diabetes.

Q. Okay.
And 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 of 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. Sir, let me show you what's been previously marked as Exhibit 4532.
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.
Do you recall seeing this document before, 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. If I can direct your attention to Page 3.
There's a heading on Page 3, Zyprexa -- 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. Okay.
And from who did you -- did you hear that?
A. We -- we've heard that through market research.
Q. Sir, my question was when did you first learn that Lilly was perceived as minimizing

weight gain by physicians?
A. I -- I don't know exactly, but certainly around the time of 1999, perhaps 2000.
MR. ALLEN: Your Honor, that concludes our offer of the deposition of Dr. Kinon, but we'd also like to have admitted and published various exhibits.
THE COURT: Well, --
MR. ALLEN: What would you like me to do?
THE COURT: I don't want to take the jury's time at the end of the day to circulate this document so why don't you make that application on Monday morning.
MR. ALLEN: Yes, sir. Yes, sir.
THE COURT: And then we can --
MR. ALLEN: I gotcha.
THE COURT: Do that.
MR. ALLEN: Okay. What do you want --
THE COURT: Can you turn the lights on, Mark?
MR. ALLEN: Do you want me to go home or --
THE COURT: I'm going to let the

jury go.
Ladies and gentlemen of the jury, we've reached the end of our trial day and end of our trial week. As I've indicated, I believe we've got about an hour and 40 minutes of deposition testimony on the State's case and then we'll begin the presentation of Lilly's defense. Again, I would remind you, please do not discuss this case with anyone or let anyone discuss it with you. Please try to keep an open mind until you've heard all of the evidence in this case, and please do not read or watch or listen to any newspaper articles, TV articles, radio or Internet materials related to the subject matter of this litigation.
I'll see you on Monday at the usual time, and have a nice weekend.
(Jury out.)
THE COURT: We're -- please be seated.
We're outside the presence of the jury. I had four things that I just wanted to raise briefly with the parties. One, I've been meaning to but keep on forgetting to compliment the people on both sides who have been -- the

technical people who have been dealing with putting the documents up on the screen and the videotape transitions and stuff, and it's been some of the best, least technological problems that I've had in a trial, and I just compliment both of the -- both sides for the people that are doing that.
The -- we have hanging, from my recollection, AK3645, which is the document that was the article prepared by the doctors who work for Lilly that was submitted for publication that Dr. Wirshing indicated he peer-reviewed and it was rejected for publication. As I recall, Lilly wanted to look it over before they told me whether they had any objections. I don't know whether you're prepared to do that now or whether to take it up on Monday, but I just want to remind -- just note that it's a hanging exhibit.
MR. LEHNER: We made a note of it, and maybe we can take it up when I guess we're going to introduce some other exhibits, if you don't mind, Your Honor.
THE COURT: That's fine.
Two things. I think a couple of days ago I mentioned a question that occurred to

me about who decides certain issues in this case, and then provided briefing on that. I thought I said Monday, and so I just wanted to remind everybody about that.
The other thing is I started last night to start taking a look at the jury instructions that have been submitted, and we're going to have to start taking that up sometime towards the end of next week at some point, whether we need to shorten our trial day to do it or how we're going to do it, I don't know. One of the things I noted was that while Lilly submitted a proposed special verdict form, the State indicated that it thought that we needed to wait to see how the evidence was developing to submit the special verdict form, and so they didn't really submit one.
I'd like the parties to start reviewing jury instructions and special verdict forms because I don't have any doubt we'll have a few discussions about that, and particularly the special verdict form. I'd like to at least start being able to think about it sooner rather than later rather than have to -- I just want to get prepared, and I certainly expect that I'm going

to devote a good portion of next weekend to thinking about jury instructions, and so I just am putting everybody on notice that the sooner you can start taking a look at -- now, almost -- at this point, since you know what the next four witnesses are going to say completely, I think this is a time for people to start reviewing the jury instructions that have been submitted to me and seeing if you can agree on some more or certainly give me revisions and the special verdict form, and the two issues may tie in together as to who decides certain things, as well. So if you could start doing that and if I can start getting your new proposals or additional proposals towards the end of next week, Thursday or -- as soon as I can get them, I'd appreciate that, so that we don't have to take this up as a last minute matter.
Those were the things that I wanted to raise. I assume that after we hear the last four video depositions we'll send the jury out and there will be some applications, but we'll take those up as they come.
MR. ALLEN: Would you mind, Your Honor, just because -- so I don't forget, I mean,

I've got so much paper, and I have the Kinon exhibits, if I can get -- ask to get them admitted now and get it over with?

THE COURT: Certainly if you don't care that we're not admitting them in front of the jury, or if you want me -- that's fine with me.

MR. ALLEN: Can I -- I'll admit them and then I'll publish them on Monday, just to save time.

THE COURT: That's fine.

MR. ALLEN: Paper's not my strong suit.

Your Honor, the State of Alaska offers the following exhibits --

THE COURT: Just let me get to the right page in my notes.

MR. ALLEN: And I actually believe -- I want to -- here we go. It's AK1110, which I believe has already been admitted but I just -- this came from Dr. Kinon's.

THE CLERK: It might have been admitted today, Judge. I'm not seeing it.

THE COURT: Go on with the rest of them.

MR. ALLEN: Yes, sir.

THE CLERK: Yes, it is admitted.

MR. ALLEN: I provided all these to opposing counsel already.

Alaska asked to be admitted AK1215. We also ask to be admitted A -- State of Alaska AK8905. We also ask to be admitted AK4517. We also ask to be admitted AK1213. We also ask to be admitted AK4532. We also ask to be admitted AK7668. And finally, Your Honor, we ask -- no, not finally.

Yes, finally, we ask to be admitted AK5522.

George, I don't know where that -- I don't know -- it's my paralegal's.

MR. LEHNER: Which is that number?

MR. ALLEN: 5522.

THE CLERK: Didn't we have --

THE COURT: That's hanging. It still is hanging.

MR. LEHNER: Your Honor, with respect to your previous honor. With respect with certainly this last one you had a note that we need to discuss that the objections were overruled but the witness -- but is this witness

able to authenticate, and I don't think there was any authentication of this document during that testimony. And the same thing with 4532.

THE COURT: Let me just start. I'm going to admit AK -- AK1110 was previously admitted. I'm going to admit AK1215, 8905, 4517, 1213 and 7668, subject, with all previously made objections by Eli Lilly preserved as to those. Exhibits -- what about 4532 and 5522, as to authentication?

MR. ALLEN: Your Honor, they're self-authenticating. They were produced as documents from the custodial files of the Defendant Eli Lilly. Self-authenticating.

MR. LEHNER: I think, Your Honor, just because something comes from a file doesn't make it self-authenticating. There's a lot of -- there's other procedures for making documents come from files and I don't think this one, the requisite foundation, is a business record or whatever ground that you want to admit it.

MR. ALLEN: Okay. Your Honor, they are -- do you want to say anything else?

MR. LEHNER: Go ahead.

MR. ALLEN: Your Honor, they are

authenticated when they are produced by the defendant as coming from their files. Now, if they want to claim they're not a business record, at least it's a record that came from their files that would put them at the very least on notice. So -- and if they want to get a limiting instruction at this time and claim that they're not their documents, they're fine. I'm not suggesting that Mr. Lehner or Ms. Gussack would do this, but I think it's relatively clear these are Eli Lilly documents. But --

THE COURT: Is there any dispute that they came from the Lilly files?

MR. LEHNER: No, Your Honor. They were produced by us.

THE COURT: Then I'll admit them at least for the purposes of notice.

MR. ALLEN: Thank you, Your Honor. And I'll tender these to Mr. Borneman. Mr. Borneman, did I do okay for your numbers?

THE CLERK: Beautiful. Yes.

MR. ALLEN: Okay.

THE COURT: So 4532 and 5522 were produced at least for the purposes of notice.

MR. SUGGS: Your Honor, can I bring

up one point?
THE COURT: And again, the objections to those exhibits are preserved, as well.
Mr. Suggs?
MR. SUGGS: At the beginning of our case, Your Honor directed us to tell defendants the order of our witnesses. We did that. We'd appreciate a similar instruction and direction from the Court.
THE COURT: I think there has been a similar instruction, but to the extent that there's any question about that, Lilly needs to do the same thing that the plaintiffs have been doing is giving them --
MR. ALLEN: Who are y'all calling Monday?
THE COURT: -- 24 hours notice of who you're going to call.
MR. SUGGS: It went beyond that, Your Honor. We were directed to give them the order of our witnesses --
THE COURT: That's right.
MR. SUGGS: And we have not received that yet, Your Honor.

THE COURT: At this point -- how soon can you do that?
MR. LEHNER: Your Honor, we are dealing with some travel plans in light of a change of schedule here and there but as soon as we have --
THE COURT: Everybody understands that, I think, and so to the extent -- as soon as you can do it, please do it, but certainly no later than -- is noon Sunday fine for this?
MR. SUGGS: Yes.
THE COURT: Noon Sunday.
MR. FIBICH: Your Honor, they've already indicated they're calling one witness out of order for Monday, so I presume that the State is not going to rest until such time as that person's been put on the stand and we've had the opportunity to --
THE COURT: Let me just ask about that. Is -- are we able to do an hour and -- what's left, 40 minutes of --
MR. FIBICH: Representation has been made to me that this is the only day --
THE COURT: Just -- let me just finish, Mr. Fibich. We've got an hour and 40

minutes of deposition testimony, then we will have to do applications while the --
MR. ALLEN: They have -- admit documents.
THE COURT: Jury's outside. And we've got to deal with the publishing of documents and that sort of stuff, so I'm figuring --
MR. ALLEN: Two and a half hours.
THE COURT: Yeah, two and a half hours is probably safe, so that -- if we actually got started at 8:30, which so far we haven't done, but if we start started at 8:30, that would put us at about 11 o'clock. Would I be correct that if we start at 11 o'clock with this witness we're not likely to finish with this witness?
MR. LEHNER: No, I think we started at 8:30 with him and take him out of turn as we've talked earlier on and we can finish with him and we may be able to get all the depositions. It's going to depend on the cross-examination.
THE COURT: We'll see if you rest on Monday or not, I guess, depended on how long this witness takes.

MR. ALLEN: Yes, sir. And we're going to obviously be working on the weekend, although you've complimented my staff. We worked till 4:00 a.m. last night so I'm giving them most of the day off tomorrow. So when we rest, I may rest, Your Honor, subject to the right to then go back through the documents and make sure I have everything admitted. I hope that's permissible with the Court.
THE COURT: Yeah, that's fine, although if you want to take a little time -- I don't know if you can right now, but if you could and wanted to take some time with Mr. Borneman as to what's in or isn't in, that would -- I know he's been eager, and I don't know -- we don't have anything till 3:00, I think.
THE CLERK: Yeah, right.
THE COURT: So if you or your paralegals or whoever it is from both sides want to make sure where we are with exhibits and clear that up, the sooner we do that, the better I'd like it.
MR. ALLEN: We will, but -- we will, and I know that Mary Beth Rivers, who is back here -- I mean, we were up till 4:00 last

night. My team's a little tired, I think they're a little mad at me too, so we're going to give them a little time off on Saturday, but I just want I to know we're going to rest subject to that and we're going to work with him, but I really don't want to make them work any more today if that's all right with the Court.

THE COURT: That's okay with me. I just want you to be -- what I'm concerned about is that we find a time where the people that are going to go over with Mr. Borneman his list and their lists have an ability -- have some time to do that.

MR. ALLEN: They will.

THE COURT: And we might have time on Monday because I have a settlement conference I think at 2:30, but they could be going over that stuff while I'm trying to settle whatever case.

MS. RIVERS: Your Honor, I talked with your clerk earlier, and I'm going to work this weekend so that I can be completely organized and take up just as little time as possible with him and provide that --

THE COURT: I don't know if Lilly

is designating who is in charge of their stuff, but maybe -- maybe after the trial day on Monday both sides can sit down and go through all the exhibits. We may actually have all the evidence in. It may not quite be done until Tuesday, depending on how long the next witness goes.

And I take it that the State is aware of who this out-of-order witness is, so you're all set for who they're going to call on Monday?

MR. ALLEN: Yes.

THE COURT: Anything else before we break for the weekend?

Then have a nice weekend.

REPORTER'S CERTIFICATE

I, RONALD L. COOK, Certified Realtime Reporter, do hereby certify:

That the proceedings were taken before me at the time and place herein set forth; that the proceedings were reported stenographically by me and later transcribed under my direction by computer transcription; 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 subscribed my hand and affixed my seal this 14th day of March, 2008.

_____

RONALD L. COOK, CRR, RMR, CCP
Notary Public