IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

WENDY B. DOLIN Individually and as Independent Executor of the Estate of STEWART DOLIN, deceased,	No. 12 CV 6403
Plaintiff,	
vs.	Chicago, Illinois
SMITHKLINE BEECHAM CORPORATION D/B/A GLAXOSMITHKLINE, a Pennsylvania Corporation,	April 10, 2017
Defendant.	9:20 o'clock a.m.

VOLUME 16 A
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART

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(The following proceedings were had out of the presence of the jury in open court:)

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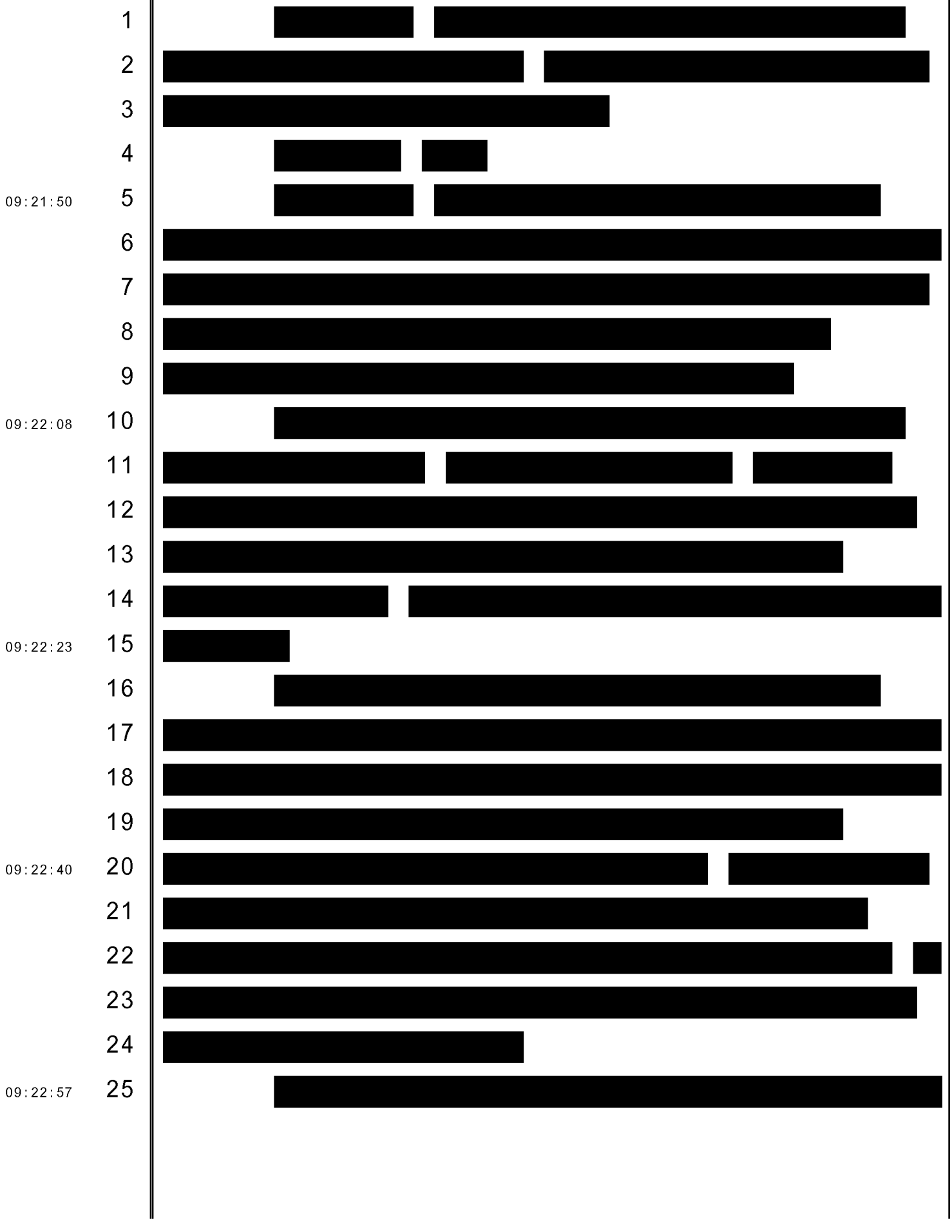
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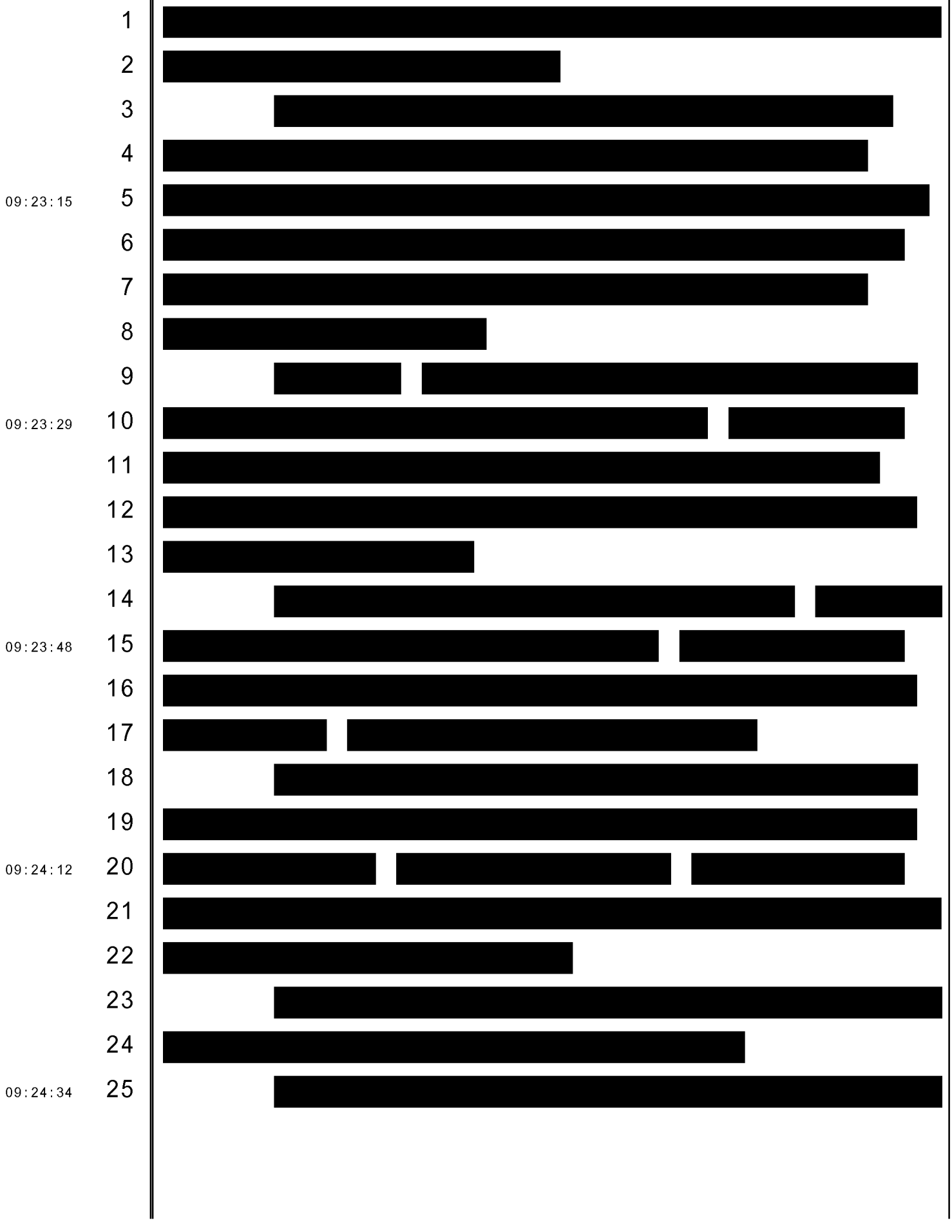
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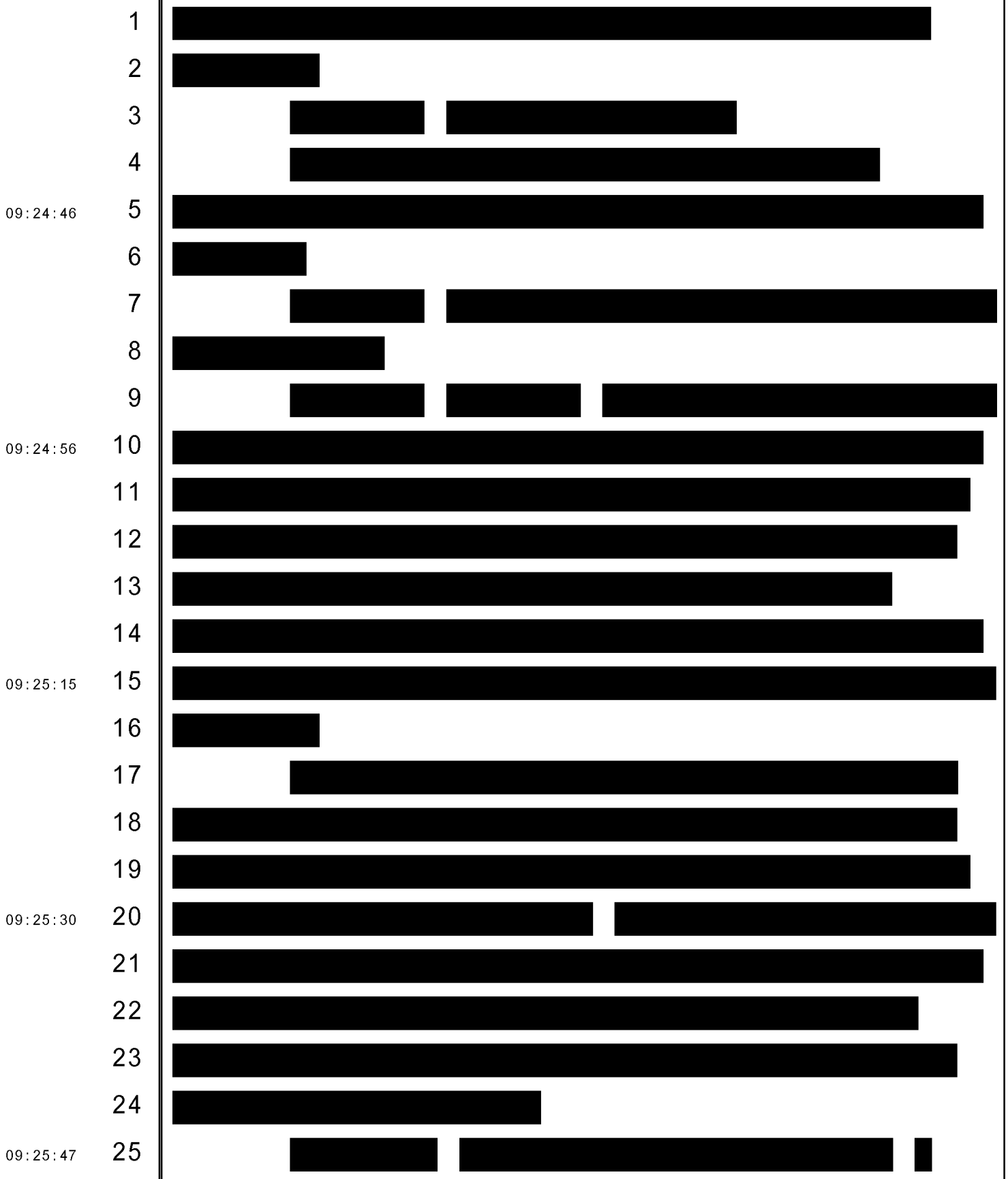
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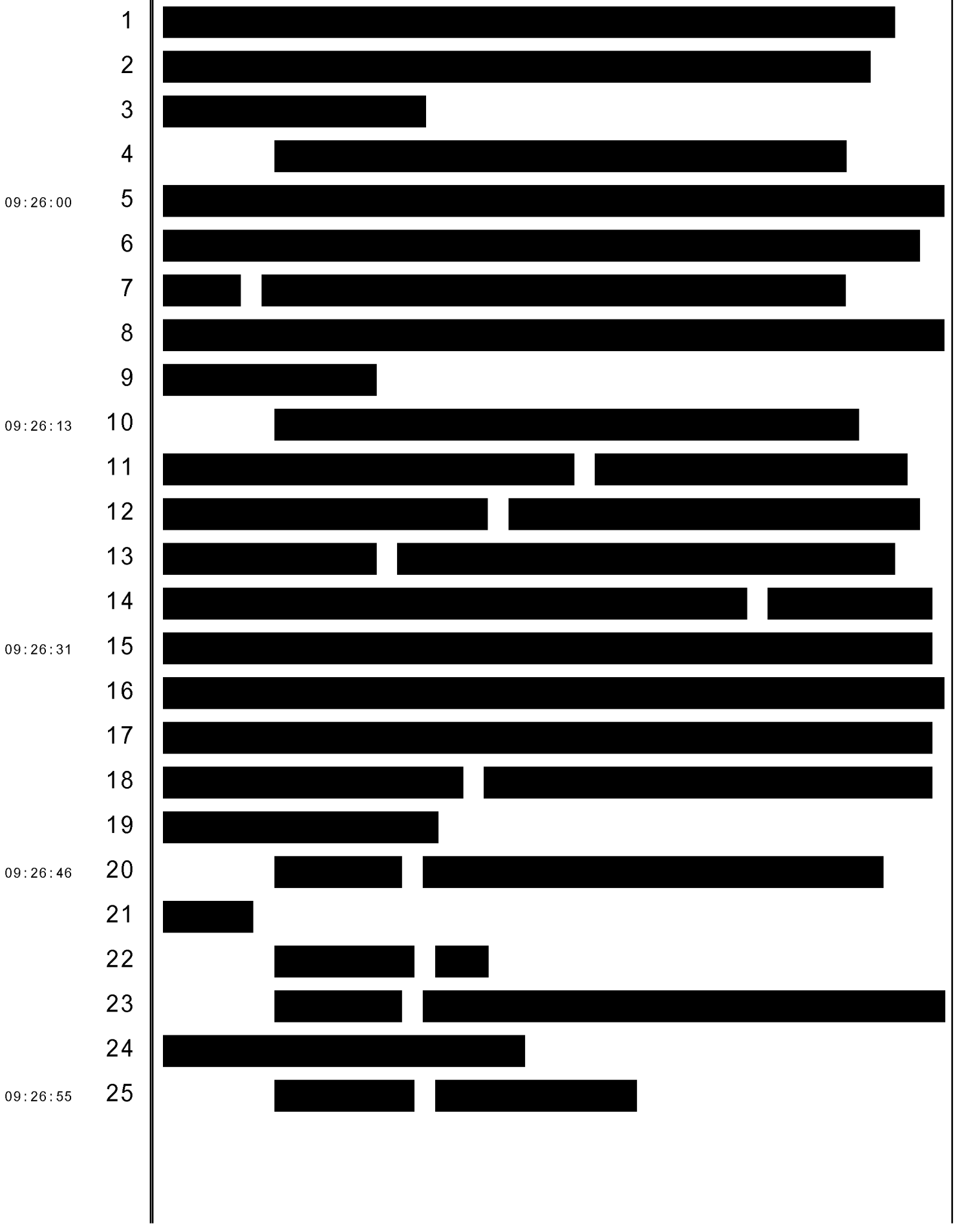
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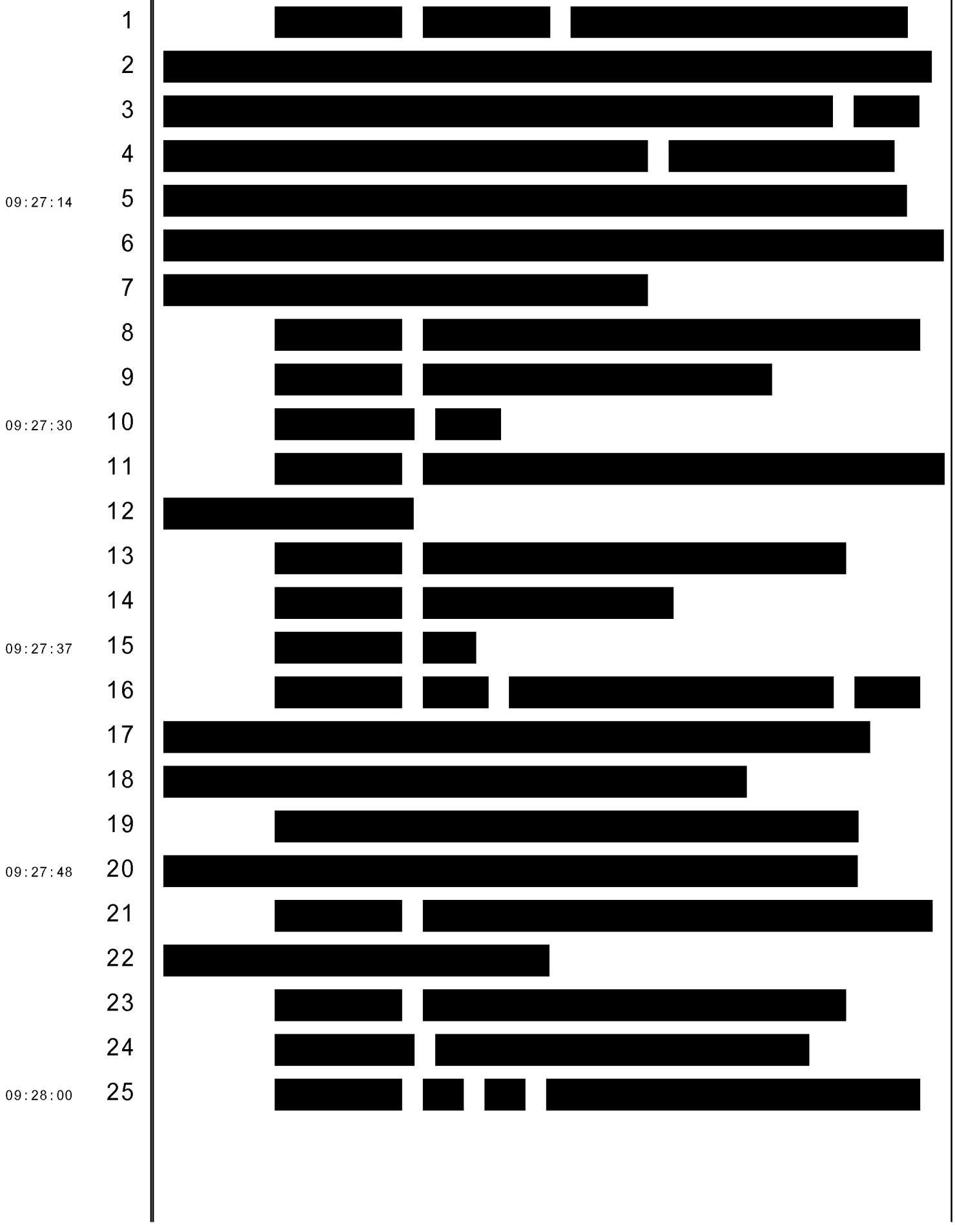
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(The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen. Please be seated.

We will resume.

Ladies and gentlemen, for your own schedules and planning, we have matters, legal matters, which we will have to take up outside the presence of the jury, which wouldn't be of interest to you in any event. And so we're going to do that on Wednesday afternoon.

So, you will know head of time that you will have Wednesday afternoon off. We'll go until noon on Wednesday, and you'll be excused Wednesday afternoon. We will resume on Thursday, however, and have court session all day Thursday. So, we'll have court today, Monday, Tuesday, Wednesday morning, Thursday all day. That's what I see the schedule at the moment.

All right. Sir, you may proceed.

MR. BAYMAN: Good morning, ladies and gentlemen. Your Honor; counsel.

JOHN KRAUS, DEFENDANT'S WITNESS, PREVIOUSLY SWORN

DIRECT EXAMINATION (resumed)

BY MR. BAYMAN:

Q. Dr. Kraus, when we left on Thursday we were talking about the 2006 GSK adult analyses of -- analysis of Paxil and suicidal in adult patients. We're going to talk a little bit more about that, but before we do, I just want to cut to the bottom line, looking at GSK's 2006 analysis as a whole, including the dozens of individual analyses that were done on

various subpopulations, does the overall data indicate an increased risk of suicidal ideation or behavior in adults over age 25?

A. No, it does not.

09:31:13 Q. In your opinion, did the 2006 analysis provide scientific evidence to support changing the paroxetine label to say that paroxetine increases the risk of suicidal thinking and behavior in patients over age 25?

A. No.

09:31:28 Q. What did GSK -- once GSK completed its analysis, what did GSK do in terms of disclosing the findings from that analysis?

A. As we discussed, we shared our results with FDA. We had a teleconference with FDA about the results. We informed them over our plan to update the labeling and to communicate the

09:31:50 findings with clinicians with Dear Healthcare Provider letter. And at the time we sent that letter we also posted all the results and analyses to our web page.

Q. And the revised labeling, which we're going to look at, did that describe the 6.7 odds ratio finding in MDD or major

09:32:15 depressive disorder patients?

A. The revised labeling did not mention that odds ratio, no.

Q. And we're going to look at that.

Did -- I want you to turn in your book to Tab 31-A, which is Plaintiff's Exhibit 285 which has already been

09:32:34 published to the jury previously in the case.

That is the -- the jury has heard the term the Carpenter Paper. Are you familiar with that paper?
A. Yes.
Q. Were you an authored of that paper?
09:32:48 A. Yes, I was one of the authors.
Q. Okay. And did GSK publish the results of the 2006 analysis in a peer-reviewed medical journal?
A. Yes, the Journal of Clinical psychiatry.
Q. Why did GSK publish this article if it had already put the
09:33:09 results on its website and sent them to the FDA?
A. It's -- it's important for any study that is done or any analysis that is done that the results be subject to something called peer-review. So, this is where the paper is submitted to the journal. Experts outside of the authors review it, make
09:33:31 suggestions for revisions, and then we publish it in the literature.

And it's also a way to share the information and begin a discussion with a group of individuals who would be most likely to be interested or affected. In this case
09:33:48 psychiatrists who treat patients, so that's the Journal of Clinical Psychiatry.
Q. Did you present, in this article, did you present the data on suicide risk based on something other than just the number of suicide-related events?
09:34:02 A. Yes; the paper reported on all the analyses that we did,

which included analyses of rating scales scores.

MR. BAYMAN: Could you pull page 6, Mr. Holtzen.

BY MR. BAYMAN:

Q. What did you and your colleagues report based on the rating scale measurements that you did.

09:34:22

A. So, one of the analyses was looking at what's called treatment-emergent suicidality by rating scales. So, starting that -- if you remember last week we were talking about a low number being a low risk, and then increasing during the study to a higher number.

09:34:40

So, we're able to take a look at the percentage patients with treatment emergent suicidality. And in this case, as you can see it was less for the paroxetine-treated patients than for the placebo-treated patients, 0.81 percent versus 1.2 percent in the overall population.

09:34:56

We also saw that in the major depressant patients as well, that same sort of trend.

Q. In the rating scales were some of the questions of patients that you described to the jury last week?

A. That's correct.

09:35:13

Q. Such as past 2 weeks, have you felt suicidal, felt like not wanting to wake up, those kind of questions?

A. That's correct. These are related to those items on those rating scales.

Q. Did you and your colleagues discuss the findings related to

09:35:25

the age ranges of patients?
A. Yes, that was reported here as well.
Q. I want to ask you about Table 6, which the jury has seen before in connection with testimony of Dr. Healy and Dr. Ross.
09:35:41 What is Table 6?
A. So Table 6 is looking at both the primary and secondary end points. So definitive suicidal behavior or ideation, that was the primary endpoint; and the suicidal behavior alone, the secondary end point; looking at it by age range as well as by
09:36:06 indication, meaning the disease state.
Q. Does the chart provide information for patients age 18 to 24 and patients 25 and up?
A. It does.
Q. How did the odds ratios for the 18 to 24 group compare to
09:36:20 the odds ratios for the 25 to 64 group?
A. So, across the comparisons, the younger age group 18 to 24 has a higher rate compared to placebo than the older age group 25 to 64.
Q. And of the 10 results here for the 25 to 64 age group, how
09:36:41 many indicated increased risk?
A. Our interpretation was that none of these showed increased risk per se, given that these were secondary end points, subgroups to subgroups, and we reported on the primary end points.
09:36:57 Q. Now, plaintiff's expert, Dr. Ross, drew the jury's

attention to the infinity symbols in these charts and indicated that suggested an extraordinarily high risk. Would that be a correct interpretation of the data?

A. No, it just suggests that when one of the groups has zero as the enumerator, the top number, when we divide by zero it's infinity. So it can be 1 versus zero or 1,000, versus zero and it would be similar. So it doesn't necessarily speak to the degree of risk, just the inability to calculate.

MR. BAYMAN: Mr. Holtzen, could you pull up page E8.

BY MR. BAYMAN:

Q. Dr. Kraus, what did you and your colleagues say about the risk in adults over age 25 in this paper?

A. As you can see highlighted here, we did not see an increase in risk in older age group 25 to 64 across all the indications. However, as we've discussed, the data suggested that the young adult group may be at increased risk for suicidal ideation or behavior following treatment.

MR. BAYMAN: Could you pull up page E8, second full paragraph.

BY MR. BAYMAN:

Q. What did you and your coauthors conclude about whether the data supported the conclusion that paroxetine causes suicidal behavior in the overall MDD population?

A. So, as we stated in the paper, and you can see here in the highlight, it's not possible to definitely conclude a casual

relationship between this increase in the major depressive population for several reasons: One is that the absolute number of events was very small. So, in this group of individuals, it's a total of 12 subjects. So, a change in even one subject could make a big difference in the risk.

09:39:00

And as they were so low, there still is a chance with many of these comparisons that it could have been a chance finding as well.

They were broad confidence intervals, which means that being able to estimate the actual risk was very difficult to do, and they weren't supported by other end points in the study. So, we only found one group of this increased risk, every other group we looked at showed no difference. And we just discussed, the rating scales showed an effective paroxetine being superior to placebo in terms of reducing emergent suicidality. So, none of the other analyses kind of were consistent with this one finding.

09:39:17

09:39:40

Also, it's important to understand that these were studies in which when those patients are randomized to placebo or drug, they weren't controlled for baseline suicidality. So, there could've been an imbalance in the groups as to who was at risk. And so this risk may have been unevenly distributed. We already talked about the differences in the rating scale items.

09:39:57

So, there were a lot of reasons why it was difficult to conclude a causal relationship here.

09:40:19

Q. You mentioned a secondary end point which was suicidal behavior, correct?
A. Yes.
Q. Okay. In the entire population of patients studied, was there an increased risk of suicidal behavior?
A. In the entire population all indications, no.
Q. In the all depression population, that is depressive disorders beyond MDD, was there an increased risk of suicidal behavior?
A. No.
Q. In the non-depression population, was there an increased risk of suicidal behavior?
A. No.
Q. In the non-depression population, would that include generalized anxiety disorder, JAD, or social anxiety disorder, or some of the other non-
THE COURT: Not so fast, Mr. Bayman.
MR. BAYMAN: Sorry.
BY THE WITNESS:
A. Yes, it includes all the different indications we looked at last week for all those different anxiety disorders.
BY MR. BAYMAN:
Q. In any of the 12 specific indication, was there an increase risk of suicidal behavior?
A. Yes.

Q. Which one?
A. This was in the major depression group.
Q. How many events were there in the major depressive disorder subgroup that supported the increased risk?
09:41:31 A. In the Paxil group there were 11 out of, I think, 34 - 55 subjects treated, so 3,455 for a rate of 0.32 percent. Placebo was one out of, I think, 1978 for a rate of .05 percent.
Q. What were these 11 events?
A. These were all suicide attempts.
09:41:57 Q. Were there any completed suicides?
A. There were no completed suicides, no.
Q. Were there any what are called preparatory acts --
A. No.
Q. -- or suicide suicidal acts.
09:42:08 Turn, if you would, in your book to Tab 30, which is Plaintiff's Exhibit 9 which is already admitted into evidence.
MR. BAYMAN: Permission to publish, Your Honor.
THE COURT: Proceed.
(Exhibit published to the jury.)
09:42:24 BY MR. BAYMAN:
Q. I want to talk about the suicide attempts with you. This is the April 2006 briefing document, and I want to take you to page 6 of that report.
A. Okay.
09:42:37 Q. Does this document -- in this document does GSK report to

the FDA of its analyses on suicide attempts in adults with major depressive disorder or MDD?
A. Yes, we did. This is the briefing document we sent to the FDA that included all of the indications, including major depressive disorder.
09:42:57
Q. And are these the results that you provided and just explained to the jury?
A. Yes, that's correct. That essentially is written what I just told you.
Q. And you informed the FDA of the 6.7 odds ratio?
09:43:06
A. Yes.
Q. And you mentioned that it was 11 suicide attempts out of 3455, which is .3 percent?
A. That's correct.
Q. Did any of these 3,455 adults with major depressive disorder exposed to Paxil actually commit suicide?
09:43:26
A. No, no major depression patients committed suicide.
Q. What was the rate in the placebo group?
A. 0.05 percent.
Q. Is that important to you?
09:43:44
A. It -- it -- it is important in light of the FDA's analysis where they were looking at placebo rates. Their placebo rate was 0.22 percent, I think. So, our rate is actually quite low compared to what was seen across all the FDA.
Q. And what does it mean when it says:
09:44:06

"As the absolute number in incidence of events are very small, these data should be interpreted with cause of action"?

A. It's similar to what i was talking about when we said we couldn't define the causality. Because the numbers are so small, one subject either way can have a big impact on the results. So, it's difficult to make definitive conclusions.

Q. Now, we see that the P-value is identified as .058. Based on your experience, are you familiar with P-values?

09:44:47 A. Yes.

Q. The jury has heard a lot about P-values in this case. What does a P-value of .058 mean for purposes of assessing statistical significance?

A. Typically, when you are using a P-value to assess for

09:45:00 statistical significance you are looking at a value of less than 0.05 to be able to say that it's less likely that the finding was due to chance. This is over that threshold.

Q. So based on this P-value, this finding on suicide attempts could be due solely to chance?

09:45:16 A. Based on the P-value, that's right.

Q. If that's the case, why then did GSK report on this finding?

A. We had as our analysis plan, if -- if you take a look at what we call the confidence interval, which comes after that

09:45:35 6.7, when a confidence interval crosses 1, which means that

there is a less than 1 of one side of it, the lower bound greater than one on the other side, it's likely not significant.

What we did for this secondary end point was to define if it didn't cross one, it would be statistically significant. So, since the lower bound was 1.1, despite the P-value we considered this statistically significant.

Q. If Dr. Gibbons, the statistician, said he doesn't find this statistically significant, would you disagree with him?

MR. WISNER: Objection; relevance.

THE COURT: Sustained as to what the other witness said.

BY MR. BAYMAN:

Q. Was this finding for suicide attempts unexpected?

A. Yes.

Q. Explain that.

A. As we've talked about a bit last week, we've done a number of analyses on socialities over the years and have not seen evidence of an increased risk until this finding.

And we have also obviously looked at many indications over time, including depression, and we find that Paxil is effective in treating those disorders. So as patients get better, you wouldn't expect to see this sort of ratio.

And then further, in terms of the history of looking at the rating scales and suicidality in rating scales, we've

seen the opposite. We've seen reduction in suicidality based on rating scales, as well as a reduction in that emergent suicidality. So this was unexpected, I can tell you that, having been there and seen these results that morning.

09:47:16 Q. I want you to assume that Dr. Healy has told the jury that his opinion, the mechanisms by which paroxetine can induce suicidal include akathisia, emotional blunting, and psychotic decompensation, and they affect people independent of whether they have MDD, anxiety, or other disorders, and that they even

09:47:37 affect healthy volunteers. How does this finding in the MDD subpopulation square up with Dr. Healy's opinion?

MR. WISNER: I would object to the characterization of Dr. Healy's opinion.

THE COURT: Your objection to what? The summary of

09:47:50 it?

MR. WISNER: Yes. I mean, that's Mr. Bayman's opinion. That's actually not Dr. Healy. I mean, whether or not it's accurate or not is a different question, but his summary of Dr. Healy's opinion is inappropriate.

09:48:00 COURT: Well --

MR. BAYMAN: I'd be happy to put up his graphic showing his --

THE COURT: I'm going to let him testify subject to cross-examination.

09:48:07 BY THE WITNESS:

MR. BAYMAN: Thank you, Your Honor.
BY THE WITNESS:
A. The finding are inconsistent with that result as we only saw it in one occasion, we didn't see it in any of the other several analyses that we did. I also looked at the cases and didn't see evidence of these sorts of behaviors in the subjects even seen in the MDD.
BY MR. BAYMAN:
Q. If Dr. Healy's opinion was correct, what would you have expected to see in the GSK analysis?
A. You would expect to see expect to see this sort of difference across every indication that you would look at.
Q. Now, did you and your colleagues at GSK draw any conclusions about whether the finding regarding suicide attempts in adults with major depressive disorder was a real finding?
A. No, we couldn't tell whether it was real. As I said, because of some of the limitations this could've been a chance finding, there could've been artificially low placebo, but we found these results and we thought it was important to communicate them.
Q. Did you -- did you and some of your colleagues think it might be a chance finding?
A. Well, yes, that was a possibility -- or is a possibility still.

Q. But did you nevertheless report the findings?
A. Yes; absolutely.
Q. Now, did GSK, and you personally, undertake any efforts to further study this finding regarding suicide attempts in adults
09:49:34 with major depressive disorder?
A. Yes. In particular what I did was take all of those cases, the 11 and the one placebo, and review those cases to try and understand if there was any common theme that might represent a reason why these patients may have been at risk to help us
09:49:58 understand what this effect may have been.
Q. How did you do that?
A. It's -- couple of different ways. One is, each of these patients, as we discussed before, had narratives created for them. So, a summary of their time in the clinical trials.
09:50:15 I also pulled for each of these subjects what's called their case report form. So the entire record of their time in the trial to review against the narrative as well.
Q. The jury has heard the term raw data. Did you look at raw data for these patients?
09:50:34 A. Yes, I looked at raw data. We kind of call these source documents. These are the documents from the investigator sites where they record the rating scale results, where they record adverse events. So that's raw data. That's what I looked at, and the narratives.
09:50:49 Q. Have you assisted us in preparing a series of graphics that

will help explain to the jury the results of your review and analysis of these patients?
A. Yes, I have.
Q. Are you familiar with, based on your work in this case, the opinion of the plaintiff's expert that suicide events allegedly caused by antidepressants occur with a --
THE COURT REPORTER: ".... suicide events ..."
THE COURT: You gotta slow down little bit.
MR. BAYMAN: Yes, sir.
BY MR. BAYMAN:
Q. Suicide events allegedly caused by antidepressants occur when a patient starts taking an SSRI or upon a dose change, are you familiar with that?
A. Yes, I'm familiar with that concept.
Q. Did you look at that issue when studying the patient files for these 11 patients?
A. Yes. One of the factors that we looked at was the relative timing of the event, the suicide attempt to when they started medicine or when they had a change in their dose. So looked at both of those things.
Q. Did you help us prepare a slide to help explain what you found?
A. Yes, I believe the slide is looking at time since first treatment.
MR. BAYMAN: Your Honor, at this point permission to

publish slide 7036-21.

THE COURT: You may.

MR. WISNER: Objection; lacks foundation and hearsay, as well as there's been no foundation laid as to why looking at these 11 suicide attempts as opposed to the hundreds that happened in the Paxil clinical trials is appropriate. This is scientifically illegitimate, so it's an improper opinion as well, Your Honor.

09:52:09

MR. BAYMAN: Your Honor, he personally went to look -- this is what drove the finding that they reported to the FDA, and he went and looked at these individual case files. This is not --

09:52:19

MR. WISNER: That's hearsay.

MR. BAYMAN: That is personal knowledge based on his review and analysis as an expert psychiatrist.

09:52:30

MR. WISNER: I mean he's literally relating information that he saw in these case files, that's hearsay.

MR. BAYMAN: It's factual information.

THE COURT: I'm inclined to let him present it, but subject to the objection it may be stricken if it is shown to it is an improper analysis for this case or for this purpose.

09:52:43

MR. WISNER: Yes, Your Honor.

THE COURT: All right. You may proceed.

MR. BAYMAN: Can we publish it.

(Exhibit published to the jury.)

09:52:56

BY MR. BAYMAN:
Q. All right. Explain what this graphic is and what you found.
A. Mr. Bayman, am I able to address a comment by Mr. Wisner?
09:53:11 THE COURT: No. No. Just answer the question, sir.
THE WITNESS: Okay. That's fine.
THE COURT: You'll get a chance. He's going to cross examine you in a few minutes.
THE WITNESS: Okay.
09:53:20 BY MR. BAYMAN:
Q. Explain to the jury what this graphic is.
A. This is looking at when the event occurred relative to the initiation of a start of study drug.
And what you see here is there was no common theme
09:53:37 related to time of event versus starting study drug. And also, quite a substantial time has passed for most patients since starting medicine and having the event.
And you see a range here of, I believe, 24 days to 66 days.
09:53:54 And when we looked at the dose change as well, we saw similar concept, that there wasn't a clustering around a specific time for the patients.
So no consistency in terms of time of onset versus treatment.
09:54:11 Q. When did the earliest event occur?

A. Day 24, I think. Yes.
Q. And when did most of the events occurred?
A. If you take a look at this, it would be around day 40 sort of thing.
09:54:23 Q. Did you also examine the length of time each patient had been depressed before starting Paxil?
A. That was part of their past medical history, that's correct.
MR. BAYMAN: Your Honor, at this point permission to
09:54:37 publish slide 7036-22.
MR. WISNER: Subject to our prior objections, Your Honor.
THE COURT: Yes. And subject to cross-examination as to the accuracy of the exhibit, you may proceed.
09:54:48 (Exhibit published to the jury.)
BY MR. BAYMAN:
Q. Explain to the jury what this chart means.
A. So, when we're studying patients in clinical trials we also obtain they're past medical history, and that includes the
09:55:01 duration of the episode that they're being treated for in the clinical trial, how long has it been going on.
And here you see quite a wide range, from 14 days. And actually, 14 days is interesting because the minimum period to diagnose major depressive disorder is 2 weeks. So, that's
09:55:21 the shortest really it can be. And it's all the way to

10 years. So, a large range indicating that at least in this group of patients the length of time of the depressive episode didn't appear to be related to risk for event.

Q. Why is that significant to the issue of whether Paxil causes or induces suicidality in adult patients?

09:55:41

A. Well, what we were trying to do is to see if there is a common theme for these 11 patients in placebo-controlled trials that we knew had an event, if they're truly at risk. And that could include past history and the acuity of the depression. So, patients earlier in their treatment may be at higher risk but we don't see that, we see a wide range.

09:56:02

Q. Did anything about this suggest that the drug, Paxil, playing a role in their suicide attempts?

A. No, there was no consistent history here that would suggest that.

09:56:19

Q. Okay. Did you prepare another graphic about the findings whether -- there were common findings consistent with suicide attempts among the 11 patients?

A. Yes. I spent a lot of time on that, yes.

09:56:38

MR. BAYMAN: Permission to publish 7036-23.

THE COURT: You may proceed.

MR. BAYMAN: Thank you.

(Exhibit published to the jury.)

BY MR. BAYMAN:

09:56:46

Q. Tell us what this is depicting.

A. So, these are -- this is just a simple graphic. These are the 11 subjects. You can see the images denote the genders. So they're both men and women there. And we looked at a series of characteristics that build in this slide.

09:57:07 Q. Did you look at whether these patients with suicide attempts had prior treatment for depression before they entered the clinical trial?

A. Yeah. Yes.

Q. How many of them?

09:57:18 A. The majority of patients had prior treatment for depression.

Q. Did you examine whether these patients had some stressful event in their life that precipitated their suicide event?

A. Yes. In the description of the adverse events, we're often 09:57:33 able to understand what's going on in the patient's life at the time. And for 9 of the 11 patients we were able to identify an acute stressor in their life.

MR. WISNER: Objection; lacks foundation. This witness hasn't explained what those stressors were and without 09:57:53 that context this is an improper opinion.

THE COURT: Yes. Sustained. I think you're going a little far now.

BY MR. BAYMAN:

Q. You personally reviewed the case reports forms and the 09:58:00 narratives?

A. That's right.
Q. What were the kind of stressors that you found in these 9 out of 11 patients?
A. So, in the manuscript that we wrote, we reported these, these included: Angry fight with spouse; alcohol use precipitating an external event; puppy died; roommate stole girlfriend; pending divorce; alcohol; fight with girlfriend; taken into police custody; just a quote "psychosocial stressors," unquote; fight with boyfriend; fight with husband; fight with boyfriend.
Q. Why is this again relevant to the question of whether Paxil or paroxetine can induce suicidality in adult patients?
A. Well, what we're seeing so far is that the types of factors that are shared in these patients are similar to what happens with suicide attempters in the general population. These are most often precipitated by psychosocial stressors in the context of mental illness.

So, there is nothing here that was surprising in that case. So it didn't suggest a drug-induced type of effect, but something consistent with what happens to people who have suicide attempts in the general population.
Q. In your experience treating hundreds if not thousands of patients with anxiety and depression, were these kind of stressors the kind that you've seen that cause people to commit suicide?

A. Yes.

MR. WISNER: Objection; lacks foundation.

THE COURT: He may answer.

BY THE WITNESS:

09:59:25 A. Yes. This is highly typical.

BY MR. BAYMAN:

Q. Did you analyze whether these patients had suicide thoughts before they started on Paxil?

A. Yes, we did. All patients before they begin treatment get

09:59:40 the rating scale analyses. And 8 of those 11 had at least to a greater on the rating scales for suicidality.

Q. And why is that significant?

A. As we've talked about before, risk of suicide attempt is associated with prior suicidal ideation. So again, it's not

10:00:05 surprising that patients who had attempts had some baseline suicidal thinking.

Q. Did you look at whether the patients had other psychiatric conditions other than MDD that increased their risk for suicide?

10:00:18 A. Yes. As we collect the information, past medical history, we know if they had what are called comorbid or coexisting conditions, usually these are anxiety or substance-abuse type disorders.

Q. And what were the results of that analysis?

10:00:33 A. So 5 of 11 had those comorbid type disorders.

Q. And when you say comorbid, what does that mean?
A. It means two diseases that are occurring at the same time.
Q. Did you examine whether the suicide attempts were particular violent?
10:00:49 A. We looked at the method, yes.
Q. And what did you -- what did that analysis reveal?
A. Most of the subjects, 8 of 11, had nonviolent means, mainly overdose as the method of suicide attempt. Again, this is fairly consistent with the general profile of suicide
10:01:09 attempters in the general population.
Q. I want you to assume Dr. Healy has said that SSRI induced suicides are in his opinion more likely to be violent. What does your analysis of these 11 attempts mean with respect to that opinion?
10:01:24 A. These were not, on the whole, violent attempts. So, it's inconsistent.
Q. While we're on that subject, is there any evidence from your review of the paroxetine or Paxil clinical trial data that suicides -- that suggest that suicides by patients taking Paxil
10:01:44 or paroxetine were of a more violent nature than suicide by patients not taking any medication at all?
A. No, that's not the case.
Q. What were the majority of suicides in the Paxil or paroxetine clinical trials?
10:01:56 A. These would be overdoses or nonviolent means as in the

general population.
Q. Did you look at and investigate the dose of Paxil that each of these 11 patients was taking?
A. Yes. So we had the doses for every one of these patients.
10:02:16 Q. And what was the results of that analysis?
A. All patients were taking at least 20 milligrams per day of paroxetine. Again, this isn't surprising because for the indications that we're looking at, 20 milligrams or greater is needed to get a good clinical effect. So in a clinical trial,
10:02:36 that's not surprising that we see this.
Q. Did you see any relationship to dosage or dose change with events occurring from 5 to 34 days following a dose change?
A. No, we didn't.
Q. Were any of these suicide attempts in patients taking a 10
10:02:53 milligram dose?
A. No.
Q. Was that surprising to you?
A. No, it wasn't surprising for the reason I stated, is that remember these patients had been on medicine for quite
10:03:04 sometime, they had reached a dose that would be considered therapeutic. For these indications, 10 milligrams is not a therapeutic dose.
Q. What do you mean by not a therapeutic dose?
A. Most patients would not have a clinical effect to 10
10:03:21 milligrams. That doesn't mean every patient wouldn't, but, in

our studies, the doses supported are typically 20 milligrams and higher for a chronic treatment.

Q. What is the recommended starting dose in the label for patients with depression or generally anxiety disorder?

10:03:38 A. It depends on the indication. So for depression, you can start at 20 milligrams. For anxiety disorders you often will start lower, you can start with 10, but you may even have to go higher. So sometimes with OCD, you're in 50 and 60 range, but you usually start slower.

10:03:57 Q. Now, I mentioned a minute ago Dr. Healy's opinion regarding akathisia and that he believes SSRIs, including Paxil, cause akathisia which cause suicide. Are you familiar with that theory?

A. Yes, I've heard that.

10:04:14 Q. Did you look at whether any of the patients, these 11 patients with suicide attempts were preceded by akathisia?

A. We did look to see if akathisia was listed as an adverse event, and we also looked at rating scale items that can be informative of the kind of behaviors you see around akathisia.

10:04:35 Q. What rating scale items did you look at to determine whether the patients had akathisia prior to their suicide attempts?

A. These include the psychomotor agitation aspects of agitation part of the scales, but we also looked at some other

10:04:50 things -- well, specifically akathisia mainly is agitation, but

we also looked at sleep anxiety, things of that nature.
Q. Have you prepared a slide that reflects the results of that analysis?
A. Yes, I have.
10:05:05 MR. WISNER: Sorry, before we show something to the jury, just tell me what document.
MR. BAYMAN: Sorry. 7036-30.
MR. WISNER: I would object. This is argument, Your Honor, as well as lacks foundation, and improper opinion, and
10:05:22 hearsay.
MR. BAYMAN: He just said that he personally looked at the indicators and symptoms --
THE COURT: He looked at the raw data?
MR. BAYMAN: Yes, sir.
10:05:27 THE COURT: To find out whether or not there was a diagnose of akathisia?
MR. BAYMAN: Or symptoms consistent with akathisia.
MR. WISNER: To be clear, Your Honor, he did not look at the medical records. He looked at the case report forms,
10:05:40 that is very different, that's what he testified to.
MR. BAYMAN: Well, that's what clinical investigator's report --
THE COURT: But he couldn't draw a conclusion of akathisia from the report itself?
10:05:48 MR. BAYMAN: He can, Your Honor, yes.

THE COURT: Is that what he's reporting to do?
MR. BAYMAN: What he's reporting to do, yes.
THE COURT: Although even though there is not a diagnosis in the case report?
10:05:55 MR. BAYMAN: That's right. But he was looking for symptoms that would be consistent with akathisia, such as agitation, pacing, things like that.
THE COURT: Okay. He may testify subject to cross-examination as to whether or not the diagnosis is
10:06:07 supported by the case report.
MR. BAYMAN: Permission to publish.
THE COURT: You may proceed.
(Exhibit published to the jury.)
BY MR. BAYMAN:
10:06:14 Q. What were the results of that analysis?
A. We had no adverse events of akathisia, nor did the rating scale items of agitation indicate an increase in patients.
Most patients decreased in their agitation item over time. There was one patient that went from zero to 1 on the
10:06:35 agitation score, which is going from none to just a little bit of fidgetiness .... it's hard to say, but ....
Q. Did you find any patient that you looked at had anything close to akathisia?
A. No.
10:06:51 Q. Now, does this finding have any significance to your

analysis of the suicide attempts data?
A. It does, in the sense that the data we reviewed on these patients was not supportive of this concept of this sort of drug-induced behavioral change.
10:07:12 Q. Finally, did you study the age of the patients who made suicide attempts?
A. Yes, we did.
Q. Have you prepared a slide to help you explain what you found?
10:07:25 A. Yes, I have.
MR. BAYMAN: Counsel, 7036-19.
MR. WISNER: No objection.
MR. BAYMAN: Permission to publish.
THE COURT: You may proceed.
10:07:41 (Exhibit published to the jury.)
BY MR. BAYMAN:
Q. All right. On information on this slide, could you just explain this to the jury and what this shows.
A. Right. So the bottom line, I'll tell you what our
10:07:49 interpretation of this is and then I'll explain the slide, is that despite the majority of patients being older adults with a mean age of 46, the majority of the cases we saw were in the younger group.
So, what this slide shows is we're plotting age, so 18
10:08:09 to 88, on the bottom there. And on the other axis we're

looking at the total number of subjects that were in that age group.

And what you see on kind of the left-hand side, and the blue versus the yellow is paroxetine versus placebo.

10:08:28 So, a couple of things is, one I said is that the average age was middle-age, around 46 years old. There was a lower proportion of subjects in the younger age group. So, if you look at the bars contributing there from 18 to 30, et cetera, you see it's lower than what we see in the ages of 40

10:08:49 and on.

And we were struck by the fact that the clustering of the suicide attempts occurred in the age group even though they represented less than 20 percent of the total subjects studied.

So, when we saw this, this appeared to us to be

10:09:08 related to age as a risk factor as well.

Q. Is this what you'd expected to see given this distribution of the number of patients who were taking paroxetine and placebo?

A. Well, we didn't expect to see a finding as I said earlier,

10:09:28 but a finding was related specifically just to drug treatment rather than to other risk factors such as age, you would expect to see a distribution that mirrors the population distribution; in other words, you'd see dots where the highest peaks are rather than where the lower peaks are.

10:09:46 Q. And is that because that's where the most patients were who

were taking the drug?
A. Yes, that's where the most patients were.
Q. Now, in patients over --
A. And sorry, Mr. Bayman, I didn't point out that those dots
10:09:57 at the bottom represent the age of the subjects who had suicide attempts. Apologies for interrupting, I wanted to explain that.
Q. And are the blue dots attempts on -- the ages -- attempts of ages of the people who attempted suicide on Paxil?
10:10:11 A. That's correct, the blue dots are.
Q. And the yellow dot, the one yellow dot is placebo?
A. Yes, that's a placebo subject who is 67, I believe.
Q. Now, in the patients over 35, there were only 2 paroxetine suicide attempts and one placebo suicide attempt. Is that what
10:10:27 you would expect?
A. That's what I would expect if this was, at least if you were looking at that side, if this was related to an occurrence just occurring as part of the disease.

There are twice as many paroxetine patients treated as
10:10:41 placebo. You can see that in the bars and you can see that in the total numbers. And we had twice the number in the older age group than placebo. So, it's not necessarily surprising to see that. It was surprising to see the clustering towards the young, because that is not explained by the distribution in the
10:11:00 population.

Q. And is that because there are fewer younger patients in the studies taking the medicine?
A. Right. I think it was something like less than 18 percent were 30 or less, and yet 8 of the 11 cases occurred in that group.
Q. In your opinion, what's the most important takeaway from this chart?
A. In our opinion, and this is how we wrote in the label, is that the risk appeared to be specifically for younger adults.
Q. Now, we do see and we mentioned the two paroxetine attempts -- patients who attempted suicide over age 40, does this mean that the medicine is associated with an increased risk of suicidal attempts of adults in all ages?
A. No, it doesn't. It seems to suggest that there's -- well, it doesn't seem, it does suggest that there is an increased risk in the younger adults.
Q. I want you to assume that Dr. Ross testified that GSK's statements that the majority of these attempts were in younger adults age 18 through 30 was misleading because you could just as well argue the majority of attempts occurred in people older than 25. What is your reaction to that?
A. I don't think it's misleading at all, actually. It's an interpretation of the data based on the distribution of the population age.
So, I see this as being informative to the prescriber

and not misleading. And FDA ultimately came to the same conclusion that we did from looking at these data by looking at a broader dataset.

Q. Was it accurate to say 8 of 11 suicide attempts were in patients under age 30?

10:12:48

A. Yes, that's accurate. Or 30 or less.

Q. And you mentioned the average age of the entire population in taking the medicine in the trials was 46, is that right?

A. That's correct.

Q. What was the average age of people who attempted suicide?

10:13:04

A. 30.2.

Q. And what does that tell you?

A. Again, if this were a risk related to simply treatment with medicine, we would expect the average age for these attempts to be around 46 as well, but it skewed towards younger. So, the increase risk exists for the young adults.

10:13:19

Q. Was there a pattern among the 11 patients who exhibited -- or made a suicide attempt during the clinical trials?

A. Yes, the pattern that we saw was that these were primarily younger age, that these were related to psychosocial stressors, that these were primarily overdose attempts in these subjects.

10:13:47

As I said before, it's similar to what you might expect for suicide attempters in the major depression population if you did epidemiological studies.

Q. Does that pattern lend you support to the theory that Paxil

10:14:10

or paroxetine is inducing the suicide attempts?
A. No, we couldn't find evidence here of causal association.
Q. I want to turn you back to the April 2006 GSK briefing document to the FDA.
10:14:27 A. Can you please remind me what tab that is?
Q. Sure. Tab 30. Plaintiff's Exhibit 9, which is already in evidence.
And have you turn to page 9.
A. Okay.
10:14:52 MR. BAYMAN: Can you pull up the fourth paragraph.
(Exhibit published to the jury.)
BY MR. BAYMAN:
Q. Do you see that, Doctor?
A. Yes, I do.
10:14:59 Q. Did GSK, you and your colleagues, reach any conclusions about whether a causal relationship existed between Paxil use and suicidality in adult patients?
A. We stated that it was difficult to conclude a causal relationship for some of the reasons I described earlier:
10:15:18 The small incidents and absolute number of events. The retrospective, meaning going back in time and looking at studies that weren't necessarily designed to access this issue. And importantly, we talked about this a lot last week is, there is a potential for confounding or confusing by the fact that
10:15:40 the events of interest are actually a symptom of the diseases

themselves.

So suicidal thinking and behavior is a symptom of major depressive disorder, so it does make it difficult to assess causal relationship in that situation.

10:15:54 Q. Turn, if you would, to Tab 31 in your notebook which is Defense Exhibit 1197.

(Exhibit published to the jury.)

Q. What is that document?

A. This is the paper or the article that we wrote summarizing

10:16:14 the case that I just described, the 11 and the 1 placebo case.

Q. And when was that paper published?

A. It was available online in May of 2009 and was on paper, I think, early 2010.

Q. And were you an author on that paper?

10:16:34 A. Yes.

Q. And what journal was that in?

A. This is the Journal of Effective Disorders. Effective disorders is just another name for mood disorders.

Q. In your experience, is that a reliable authority for

10:16:48 experts in the field?

A. Yes; particularly for disease like major depressive disorder.

MR. BAYMAN: Your Honor, at this point we would move for permission to publish Dr. Kraus's Article.

10:17:01 THE COURT: You may proceed.

(Exhibit published to the jury.)

BY MR. BAYMAN:

Q. That lists -- the graphic, the blowup lists the authors of the publication?

10:17:19 A. Yes.

Q. And you are what's happened called the lead author?

A. Yes, that's correct, first author.

Q. And there's another name on there, John Davies. Can you remind the jury who John Davies is?

10:17:30 A. John Davies is the statistician that led the analyses who I've worked with for many years.

Q. Did he do the re-analyses of the MDA clinical trial data for suicide and suicide attempts that was submitted to the FDA in 2002 and 2003 that we saw earlier?

10:17:47 A. Yes, John Davies did those.

Q. Let's look at the conclusion section of the abstract on the first page.

What was you and your coauthors conclusion about the analysis of the suicide attempt data?

10:18:02 A. So, this paper is describing the definitive suicidal behavior, so without the ideation.

And if we look overall in the entire population study, the rate was similar between paroxetine and placebo, but as we've just reviewed we did see a higher frequency in those

10:18:22 major depressive disorders.

And as I showed you in that graphic of the population ages, this was driven, this finding was driven by young adults age less than or equal to 30 years.

Then I talked about most of the patients improved prior to the attempt, and that there was a psychosocial stressor. And we reinforced the guidance in the labeling that the patient should receive careful monitoring for suicidality during treatment.

Q. Turning to page 42, if you would, and look at the result section.

A. Okay.

Q. How -- how do these numbers relate to what you said about the age distribution of the suicide attempts?

A. Right. This is what I had stated earlier is that although 8 of 11 or about 73 percent of those who had a suicide attempt age 18 to 30, they only represented about 18 percent of the total population. So, it was striking to see that clustering given their representation in the total population.

Q. Now, in the paper do you describe your efforts to see if agitation or akathisia played a role?

A. Yes, we did.

MR. BAYMAN: Pull up the last sentence of page 43.

(Exhibit published to the jury.)

BY MR. BAYMAN:

Q. And what did you report here?

A. So again --

MR. WISNER: Your Honor, I'm going to object. This is cumulative. He's actually literally testified to all this already.

10:19:53 THE COURT: I think we've already covered this, haven't we?

MR. BAYMAN: Well, this is what he reported to the scientific community, Your Honor.

MR. WISNER: And for the record, this is a journal

10:20:02 that's published --

THE COURT: Sustained. Same information that you previously described.

MR. BAYMAN: Well, it also --

THE COURT: It's contained in the journal. You can

10:20:09 prove up what's contained in the journal.

BY MR. BAYMAN:

Q. You provided the information that some of the information we talked about earlier in the journal article that went out to physicians?

10:20:19 MR. WISNER: Objection; lacks foundation. Dr. Sachman did not get this journal article. This is irrelevant.

THE COURT: Overruled.

MR. BAYMAN: Thank you.

BY THE WITNESS:

10:20:28 A. So can you repeat the last question, please.

THE COURT: Read it back.

(Question read.)

BY THE WITNESS:

A. Yes. So, when speaking specifically about the rating scales and agitation and insomnia and anxiety, we did look at those scores, and I described this earlier, you see that item scores relating to a sleep disruption, to agitation, or to anxiety were either unchanged or improved during the treatment period, except for the one patient who had their item go from zero, to none, to one fidgetiness.

Q. What conclusions did you and your colleagues take with respect to whether causality can be inferred from any of these findings?

A. We cannot establish causality, as I've described before, for a number of reasons. We've talked about that this is a relatively small number of events, .32 percent versus .05 percent, and that the confidence intervals are the precision of the estimate was fairly broad.

The other analyses that we did did not support this finding. So, on the primary end point we saw no difference across all populations.

In the secondary end point, we saw no difference except in this group, and in the rating scales we saw a different finding as well with improvement in paroxetine versus the placebo.

We talked about how the studies weren't stratified or controlled for baseline suicidality to see who got paroxetine or placebo. So, there could've been an imbalance in the groups. And that, I mentioned this before, that the rating scale findings were inconsistent with this finding.

Q. Nevertheless, did you believe it was important to provide this data to the medical community?

A. Yes. Regardless of the ability to establish causality, we saw this finding, it met our predefined analysis plan for a significance, so it was important that we report that.

Q. What did you and your colleagues state in this article about whether the cases of suicide attempts support the theory that akathisia precedes suicide attempts in paroxetine-treated patients?

A. It does not support that.

Q. And what did you --

A. I said it right here (indicating).

Q. What did you and your colleagues report about the relatedness assessments made by study investigators?

A. So, we did assess in the narratives whether or not the investigator made an attribution or made a judgment as to whether he or she believed that the adverse event or suicide attempt was related to drug.

And we were able to in 9 of the cases find that attribution. 7 of these 9 listed medication treatment as

unrelated to the suicide attempt; one of 9 is probably unrelated; and 1 of 9 is possibly related.

Q. After you completed the 2006 adult suicidality analysis, and identified the finding with respect to suicide attempts, did you and your colleagues at GSK take any action with the FDA?

A. Yes; we created a briefing document which we sent to the FDA and established a meeting with them to discuss our proposed next steps.

Q. Did you propose new labeling for Paxil with respect to adult suicidality?

A. Yes. In a call with the FDA, in addition to describing the results, we also presented revised labeling in the precautions or warnings -- or the warnings and precaution to them as well for comment or opinion.

Q. And did you actually send draft labeling to the FDA?

A. Yes, we did.

Q. Had FDA requested that labeling change?

A. No, they did not.

Q. Did FDA request that you send out a Dear Healthcare Provider letter?

A. No, they did not.

Q. Why did you do it, anyways?

A. For the reason I described, when we undertook to do the analysis, when we defined what we would consider significant,

and when we saw this finding in the major depressive group, we thought it was important to notify physicians.

You know, part of the reason for this is that even though it was difficult to -- to determine whether or not the drug is causal, suicide and suicide attempts are a fairly significant adverse event. So, it's important, since we saw this, to actually be able to inform clinicians to ensure that their vigilance remain strong during treatment.

Q. Turn, if you would, to Tab 32 in your notebook.

10:25:43 This is Defense Exhibit 107, and I'm going to ask you if you're familiar with this document.

A. Yes, I am.

Q. What is this document?

A. This is our communication to FDA. The first page is the 10:26:03 cover letter detailing our updating and labeling for paroxetine to reflect this finding.

Q. Are you at Tab 32?

A. No, I'm at Tab 33 (laughing).

Q. You're a little bit ahead of me. All right, turn to 10:26:21 Tab 32.

A. Tab 32 is the minutes of the teleconference we had with the FDA.

Q. Okay. And what is this -- did you receive these minutes of the teleconference with FDA? Are you a recipient?

10:26:34 A. Yes, I am.

Q. Okay. Did you participate in that teleconference with FDA?
A. Yes, I did.
Q. And that was the document Thursday, April 20, 2006?
A. Yes.
10:26:49 Q. And then is it a practice of GSK for someone to record minutes of any meetings or telephonic meetings with individuals at FDA?
A. Yes, we do.
Q. Is that something you do in the ordinary -- that GSK does
10:27:08 in the ordinary course of business?
A. Yes, we do.
Q. And the records of teleconferences and meetings with FDA are regularly prepared and maintained in the ordinary course of business at GSK?
10:27:25 A. Yes, they are.
Q. And has this been maintained in GSK's ordinary course of business?
A. Yes, it has.
Q. And you're familiar with this document?
10:27:35 A. Yes.
Q. And you rely upon it for purposes of your testimony in this case?
A. That's correct. I also have personal recollection, but yes.
10:27:45 Q. And do you have personal recollection because you were

involved in the telephone conference?
A. That's correct.
MR. BAYMAN: Your Honor, I'd move at this point for admission of Defense Exhibit 107 as a business record and for
10:27:57 permission to publish it to the jury.
MR. WISNER: Objection; hearsay. They have not properly laid the foundation, nor has the author of this document been called to the stand to be cross-examined.
MR. BAYMAN: Your Honor, in their case they admitted
10:28:11 FDA conversation records for GSK witnesses who they didn't call to the stand.
MR. WISNER: Those were admissions by party opponent, it doesn't apply for GSK, Your Honor. Additionally, I point out that the witness has just testified that he recalls the
10:28:26 conversations, so this would be cumulative as well as hearsay.
MR. BAYMAN: It can help him refresh his recollection of the conversation, and I believe foundation has been laid for admission as a business record.
THE COURT: I don't think it's a business record for
10:28:38 the reasons I previously indicated to you, and it does contain hearsay statements of people from the FDA who have not been called. There's no way to cross-examine the statements made in the document, which are attributed to somebody at the FDA.
On the other hand, there has been some evidence about
10:29:00 approval. I don't think the door has been opened by the

plaintiffs, however, as to this document. The doctor may use it to refresh his recollection as to what was going on, but it's not received in evidence.

BY MR. BAYMAN:

10:29:17 Q. Take a look at that document.

A. Yes.

Q. And you recall the telephone meeting with the FDA on April 20th?

A. Yes, I do.

10:29:26 Q. And at this point in time, had you submitted your briefing document and the proposed labeling to the FDA?

A. Yes, we had submitted that.

Q. At this point in time had the FDA had an opportunity to complete its review of the GSK data submission?

10:29:44 A. No, the FDA had not completed their suicidality review.

Q. Did FDA voice any objections to GSK's plan to go ahead and change the Paxil labeling?

A. No, they did not.

Q. Did FDA indicate whether they had made a final

10:30:03 determination about whether they would accept or reject GSK's proposed labeling change at this point in time?

A. No, they had not.

Q. Did you in the telephone conference, did you inform the FDA that GSK intended to send out a Dear Healthcare Provider letter

10:30:23 and new labeling to physicians?

A. Yes, we did. And we provided a draft language for that as well.
Q. Did FDA make any objection to your proposal to send out a Dear Healthcare Provider letter with labeling?
10:30:37 A. They didn't object to our sending out the letter.
Q. Now, at this point in time was FDA still conducting its own analyses of the adult suicide data from GSK and other antidepressant manufacturers?
A. Yes. They told us that was still ongoing.
10:30:57 Q. After this telephone conference with the FDA, did GSK take any steps to implement the labeling change that we discussed a minute ago?
A. Yes, we did.
Q. Turn in your book to Tab 33, which is Defense Exhibit 114.
10:31:19 What is this document?
A. This is the submission to FDA. The cover letter and the updated labeling with our label change that we had described in that telephone conference with FDA.
Q. Are you familiar with this type of correspondence to FDA
10:31:38 submitting labeling changes based on your experience working at GSK?
A. Yes, I am.
Q. Are you familiar with this letter?
A. Yes; absolutely.
10:31:55 Q. Did you participate?

A. Yes. And was also involved in the updated labeling.
Q. So did you actually help draft the labeling?
A. Yes, I did. I think I actually wrote the first draft of it.
10:32:03 Q. And are letters -- when GSK attempts to make labeling changes by way of what the jury has heard the term CB or changes being effected, is this the way that GSK does it?
A. That's one of the ways GSK can do it, yes.
Q. And is this letter draft, was this letter prepared and sent
10:32:27 in the ordinary course of GSK's business?
A. Yes.
Q. Has this correspondence been maintained in the ordinary course of GSK's business?
A. Yes, it has.
10:32:38 MR. BAYMAN: Your Honor, I would move for -- move into evidence Defense Exhibit 114 and ask for permission to publish.
MR. WISNER: Again, Your Honor, objection; hearsay. This is GSK's statement. Additionally, this is cumulative. I don't think there's any dispute that they attempted to change
10:32:54 the label in 2006. So, I don't know why this needs to go into evidence.
THE COURT: Don't we already have this label in evidence?
MR. WISNER: Yes.
10:33:05 MR. BAYMAN: That's the draft labeling, Your Honor.

THE COURT: It's not in evidence?

MR. BAYMAN: No, sir. This is what was sent to the FDA that Mr. Kraus drafted and --

THE COURT: Okay.

10:33:14 MR. WISNER: Your Honor, to be clear, this label is in evidence. It's Joint Exhibit 5. So this is just a draft version which is identical to the label as Joint Exhibit 5.

THE COURT: I thought it was Joint Exhibit 5.

MR. BAYMAN: Well, it's -- this is them sending --

10:33:27 THE COURT: Well, we'll receive the letter, forwarding letter if you want.

MR. BAYMAN: Okay.

THE COURT: The forwarding letter document, Defendant's Exhibit 114 may be received in evidence.

10:33:41 MR. BAYMAN: Thank you, Your Honor.

THE COURT: The other document is already in evidence as Joint Exhibit 5.

(Defendant's Exhibit 114 was received in evidence.)

10:33:48 BY MR. BAYMAN:

Q. By the mere fact that GSK submitted this letter with the proposed labeling change that it later implemented, does that mean that the FDA had approved it?

A. No, it doesn't.

10:34:00 Q. Please explain that.

A. So under "changes being effected," we update the label, it is sent to FDA. At some point in time FDA makes a judgment as to whether or not the labeling is appropriate to stand.

So, when you submit this, you're waiting for an FDA reply to changes being effected to understand whether they ultimately approve.

Q. Now, in the labeling that you drafted, do you inform the FDA that in adults with MDD there was a statistically significant increase in the frequency of suicidal behaviors in patients treated with paroxetine compared to placebo?

A. Yes, we did.

Q. And did you give them the numbers that we looked at earlier of the 11, over 3,455?

A. Yes, we did. That number and the percentage.

Q. And are those the findings that we looked at earlier from the 11 suicide attempts from the MDD population?

A. Yes, that's correct.

Q. And that was -- again, this was the labeling that -- that you -- you did the first draft?

A. That's correct. Yes.

Q. And is the information, the letter and the proposed labeling sent to the FDA, was that true and accurate?

A. Yes, it was.

Q. Now, did GSK go ahead and implement this labeling change by way of changes being effected?

A. We did.
Q. Were those -- was that labeling still subject to FDA's review and approval?
A. Yes. As I've described, when it's the CBE it's still under review until FDA responds to your changes being effected.
Q. Turn in your book to Tab 34, which is Joint Exhibit 4 and admitted into evidence.
MR. BAYMAN: Pull that up please, Mr. Holtzen.
(Exhibit published to the jury.)
Q. What is this document?
A. So, this document is the Dear Healthcare Provider letter that was distributed to treating clinicians advising them of the update in the label and the findings.
Q. Are you familiar with this letter?
A. Yes. I'm the signatory of the letter.
Q. That's your name? You signed it?
A. Yes, that's correct.
Q. Let's look at the first paragraph. What did GSK tell doctors about this subject?
A. Advising them that we are making changes to the warning section of the clinical worsening and suicidal risk.
Q. Did GSK indicate that these warnings were limited to just young adults?
A. We said these labeling changes relate to your adult patients, particularly those who are younger.

Q. Let's look down at the fifth paragraph.

Is that -- did GSK provide the findings that we've been talking about with respect to the 2006 analyses with respect to suicide attempts?

10:37:07 A. Yes, we did.

Q. Again, did GSK limit this finding communicated to doctors from its 2006 analysis to only young adults?

A. No, we did not.

Q. And look at the second page, the second full paragraph,

10:37:33 what did GSK tell doctors about what patients should be monitored?

A. So, we say that all patients need to be monitored during paroxetine treatment.

Q. Did the GSK, your letter of May 2006, and the revised

10:37:54 labeling put any limit, age limit on the adult patients who should be monitored?

A. No, it did not.

Q. Did you put the revised labeling in the Dear Healthcare Provider letter on your website for anyone to come look at?

10:38:09 A. Yes, we did. In addition to mailing it out, it was also posted to the website.

Q. Now, did FDA take any action themselves to publicize GSK's 2006 label change?

A. Yes; they posted this on, I think, their GSK's MedWatch

10:38:27 website as well.

Q. And remind the jury what that is.
A. It's a FDA website for providing updates on different medications. So they posted our letter and provided the summary as well.
10:38:41 Q. And did the FDA include that same information that you provided?
A. Yes, I believe the letter was posted as well.
Q. Based on your experience working with and interacting with the FDA and your review of the Paxil regulatory history, did
10:39:04 FDA typically tell GSK if it thought some aspects of GSK's proposed label was false and misleading?
A. Yes, they would do that if they came to that opinion.
Q. And based on your review of the regulatory file and the discussions that you participated in with FDA and those your
10:39:22 colleagues participated in, did FDA ever tell GSK that GSK's description in the label of the 8 out of 11 patients that we've talked about was false and misleading?
A. No.
Q. After GSK submitted the April 27, 2006, labeling change,
10:39:40 did FDA make any statement to GSK in 2006 about whether it had accepted those proposed changes?
A. No, they did not.
Q. And as of the time of your letter in May, the posting on the website, posting on FDA's website, was FDA still
10:40:05 considering the label change?

A. Yes. During that time they would still be considering the label change, that's correct.

MR. WISNER: Objection. Move to strike as speculation. He wasn't there.

10:40:16 THE COURT: Sustained.

BY MR. BAYMAN:

Q. Did the FDA inform you in May of 2006, inform the company, in April or May of 2006 that they were still considering the label change?

10:40:29 A. They had not made a decision as to whether they would accept the label change at that time. So they were still considering it, yes.

MR. WISNER: Objection. Move to strike.

THE COURT: That may stand. Let's get on with it.

10:40:44 That may stand.

BY MR. BAYMAN:

Q. Following GSK's publication of the results of its analysis, did FDA later announce the results of its own analysis of the data on Paxil and other antidepressants in adult suicidality?

10:40:59 A. They did.

Q. Do you remember when that is?

A. I want to say December of 2006. November, December, something like that.

Q. Let's turn to Tab 35 which is Joint Exhibit 13.

10:41:11 You are you familiar with this document?

A. Yes, I am.
Q. What is this document?
A. This is the FDA's analysis of suicidality across all antidepressants, and this is the clinical review by the
10:41:28 physician reviewers.
Q. Would that be Dr. Stone and Dr. Jones of the FDA?
A. Yes, that's correct.
Q. Did you and your colleagues at GSK review this report when it came out?
10:41:37 A. Yes, we did.
Q. Why did you do that?
A. As we had contributed information to the FDA report, and as also we had our own analyses, we were, of course, very interested in how FDA's assessment across the entire
10:41:56 antidepressant field would correspond to what we had seen for paroxetine.
Q. The jury has seen this many times and I'm not going into the details, I just want to do this very high-level. Turn to page 24, Table 15.
10:42:17 A. Okay.
Q. What is this table?
A. This is looking at the suicidality risk for a drug versus placebo for that primary end point of suicidal ideation or worse.
10:42:30 Q. What are the results for paroxetine or Paxil?

A. The odds ratio for paroxetine is 0.93.
Q. Does that suggest an increased risk of suicide, suicidal ideation or worse?
A. No, it -- it -- it does not. There's no difference between
10:42:52 drug and placebo, and that was true in all drugs pulled as well.
Q. Was that consistent or inconsistent with GSK's own findings in your 2006 analyses?
A. That was consistent with our finding.
10:43:05 Q. Does FDA's analysis show reasonable evidence of an association between Paxil and suicidal thoughts or behavior for patients?
A. No.
Q. Let's turn to page 26, Table 16.
10:43:19 What data is reflected in this table?
A. So, this table represents what was the secondary end point looking at preparation or worse. So this is looking at suicidal behavior by drug and drug class.
Q. And what's the result for Paxil or paroxetine?
10:43:37 A. So, for paroxetine an odds ratio of 2.76 is reported.
Q. Now, when you saw this at the time, -- when the report came out, how did you interpret the finding of the 2.76 odds ratio?
A. This was probably consistent with what we had seen in our own analysis. Again, the FDA had additional information. So,
10:44:03 additional high rate of placebo, but in general, this is

consent with what we had seen.
Q. Did the FDA -- do you recall the FDA indicating that were any limitations as to how to interpret this finding?
A. Yes. FDA specifically said when looking at drugs on their own, despite the P-value being statistically significant or less that .05, that that had to be discounted because there were many, many comparisons being made, and if that isn't in control some of these comparisons can be due to chance.
Q. Explain to the jury what you mean by many comparisons being made.
A. So, if you look at this table and the table before, there are literally several dozen comparisons that are being made, and further here to look at age as well. With -- with -- just generally, when you think about that P-value of 0.5, there could be one in 20 chance that the finding could be by chance even if the P-value is statistically significant.

So, typically you do something called controlling for multiple comparisons. There are tests that you can use to do that to make sure that the finding is solid. However, that was not done in this analysis, and the FDA pointed out that, therefore, the individual P-values should be discounted.
Q. Turn, if you would, to Tab 35A which is Defense Exhibit 447.

Are you familiar with this document?
A. Yes.

Q. What is it?
A. This is FDA news release posted on their site where they are describing their intent to update the class labeling for antidepressants based on the results of that analysis you just saw.
Q. And does this press release set out the FDA's official position?
A. Yes, it does.
Q. Do you and your colleagues at GSK regularly monitor the FDA's website for press releases such as this?
A. Yes, we do.
Q. Did you and your colleagues at GSK rely on the information contained in FDA press releases such as this?
A. Yes, we do.
Q. Did you and your colleagues rely upon this particular press release by FDA in your ongoing assessment of the paroxetine label as it related to suicidal thinking and behavior in adults?
A. Yes, we did, in addition to direct correspondence of FDA to us.

MR. BAYMAN: At this point, Your Honor, I move for admission of this press release under federal Rule 803(8) and permission to publish it to the jury.

MR. WISNER: Your Honor, this is hearsay. It's not a business record. They have not laid that foundation since this

witness is not an employee of the FDA. To the extent that it is not being offered for the truth of the matter asserted but merely GSK's understanding the document should not be admitted, but we have no objection to it being published.

10:47:04 THE COURT: All right. You may publish.

MR. BAYMAN: I think I laid the foundation for permission, Your Honor.

(Defendant's Exhibit 447 was received in evidence.)

10:47:09 (Exhibit published to the jury.)

BY MR. BAYMAN:

Q. Let's look at the first paragraph, what's happened the subject of this labeling change?

A. So, as I said, it was proposing new warnings about suicidal

10:47:19 thinking behavior in young adults taking antidepressant medicines. And specifically, they were letting the manufacturers --

THE COURT: Doctor, let's just stay with the question, please.

10:47:32 THE WITNESS: Okay.

BY MR. BAYMAN:

Q. What were -- was the FDA informing manufacturers and -- was this just for manufacturers or was this also informing prescribers and the public?

10:47:41 MR. WISNER: Your Honor, I would object to this line

of questioning about what the FDA was doing or not doing. I have no opposition to him testifying to what GSK understood from this press release, but speculating about the FDA's intent, motives, objectives is really outside the purview of this witness.

10:47:59

THE COURT: The objection is sustained. This document relates only to young adults, as I understand it, is that right?

THE WITNESS: Is it a question for me?

10:48:09

It's an updated warning to the --

THE COURT: No. No. My question is does the document relate only to young adults or is it as to all patients.

THE WITNESS: It does also describe in the updated warnings what should occur with all patients, but this document

10:48:29

itself is primarily about the increased risk from the analysis in young adults.

THE COURT: Okay. Go ahead.

BY MR. BAYMAN:

Q. Look at the second paragraph. How does the FDA summarize

10:48:40

the results of its 2006 analyses in this press release?

A. Yes, they -- in their analysis, they found that the scientific data did not show this increased risk, meaning the risk seen in young adults, in adults older than 24, and that adults age 65 and older actually had a decrease risk in the

10:49:04

drug versus the placebo.

And then further, they say that the warning statements emphasize that depression itself and other disorders are also important causes of suicide, and that goes across all ages.

Q. And when you saw this at the time, what was your takeaway from this press release?

A. Our takeaway was that the findings identified by FDA were similar to what we had seen in our paroxetine analysis.

Q. I ask you to turn, if you would, to Tab 36, which is Defense Exhibit 122.

What is this? What is this letter?

A. This is correspondence from FDA to our regulatory lead for Paxil telling us, based on their analysis, that they were updating the labeling for antidepressants.

So, in essence, this is in response to that changes being effected we had submitted approximately a year before, so ....

Q. Are you familiar with this correspondence?

A. Yes.

Q. Did you review it at the time it came in?

A. , yes.

Q. And this would be now about a year later after GSK had changed the Paxil labeling and sent your Dear Healthcare Provider letter?

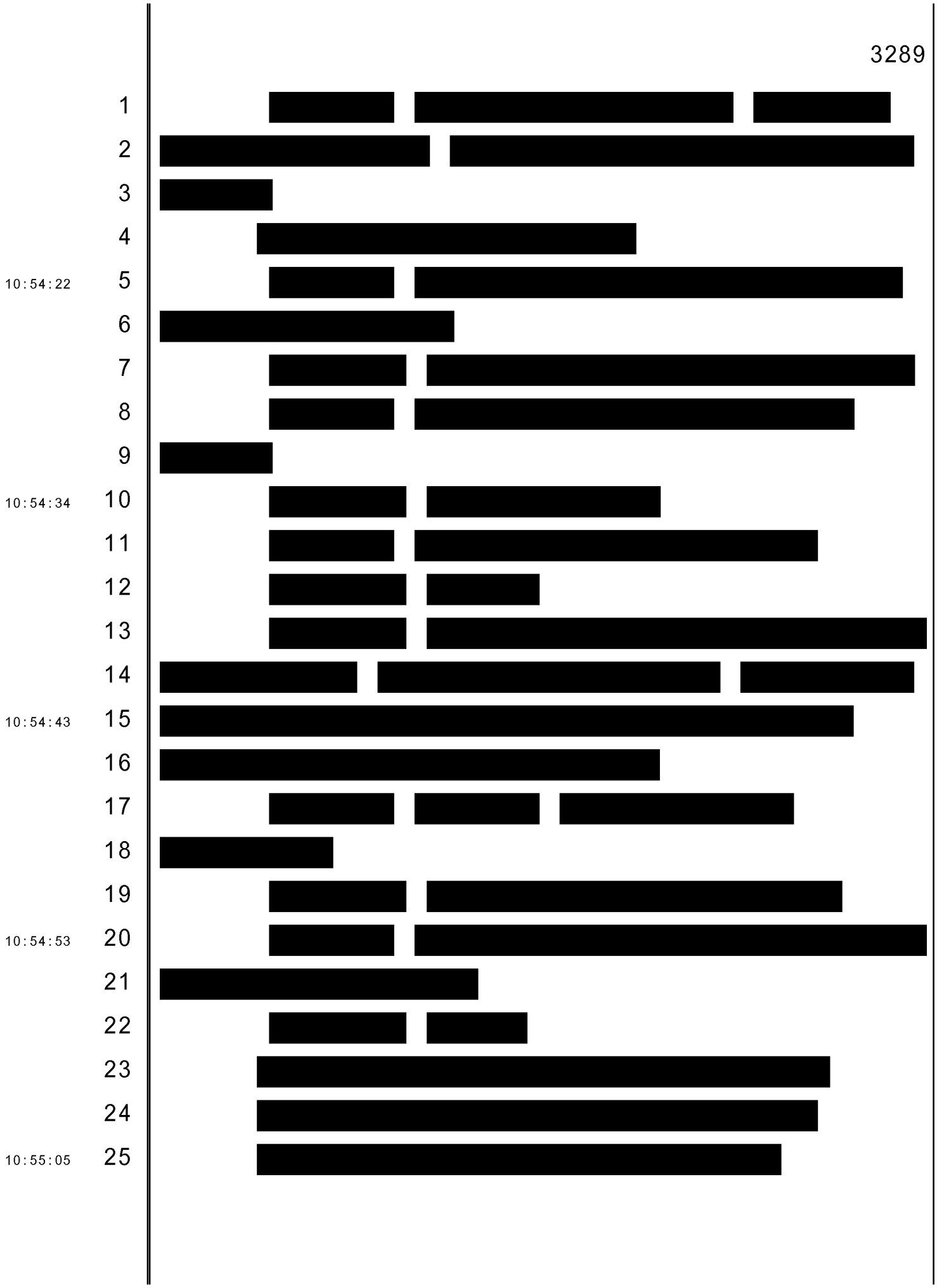
A. Yes. That's right.

Q. And did FDA attach to this correspondence new proposed

labeling?
A. Yes, they did.
Q. And was that labeling drafted by the FDA?
A. Yes, it was.
10:50:46 Q. And is this the kind of correspondence, based on your experience at GSK, that you've seen from the FDA with respect to labeling changes?
A. Yes, I have.
Q. Is this maintained in the ordinary course of business at
10:51:05 GSK?
A. Yes, it is.
MR. BAYMAN: Your Honor, at this point I move for permission to admit Defense Exhibit 122 and to publish it to the jury.
10:51:13 MR. WISNER: Your Honor, we have no objection to publication. We do object to admission under hearsay as illustrated by the question of whether or not this document was regularly maintained in the course of business at GSK, that is not the standard. The standard is did the FDA -- because this
10:51:28 is an FDA document regularly maintained and they haven't laid that foundation. So, it's not an admissible document, we have no problem showing it to the jury.
THE COURT: Well, as far as it's a documentary from the FDA, we don't have to apply a business test to GSK in order
10:51:44 the receive this document.

MR. BAYMAN: Well, GSK maintains correspondence --
THE COURT: That doesn't matter, sir. This document was issued by the FDA, but it's not in dispute it's a correct document.
10:51:56 MR. WISNER: That's correct. That's correct, Your Honor.
THE COURT: It may be received on that basis.
MR. BAYMAN: Thank you.
(Defendant's Exhibit No. 122 was received in evidence.)
10:52:01 (Exhibit published to the jury.)
BY MR. BAYMAN:
Q. Who drafted and prepared this letter?
THE COURT: No, sir, it's not his letter. It's the letter from the FDA. And it is received in evidence but is not basis for commentary.
10:52:10 MR. BAYMAN: I was just asking him if this is a letter from the FDA.
THE COURT: We've already established that.
10:52:24 MR. BAYMAN: Okay.
BY MR. BAYMAN:
Q. Does this letter respond to GSK's April 27, 2006, changes being effected label change?
A. Yes, it does.
10:52:32 Q. What does the letter say about GSK's changes being effected

label change from April of 2006?
A. It states that they have completed their review and before our label is approved we would have to make the revisions to the labeling as outlined in the letter and in the labeling that
10:52:52 FDA sent to maintain standardization in the labeling.
Q. What is that "ensure standardized labeling pertaining to adult suicidality with all of the drugs" mean to you?
A. So this is called class language, such that all the antidepressants would have the same information across them.
10:53:14 So standard for all of the drugs used to treat major depression.
Q. This by letter was FDA rejecting GSK's April 2006 CB labeling change?
MR. WISNER: Objection; speculation.
10:53:29 BY THE WITNESS:
A. The answer is yes.
MR. WISNER: I'm sorry. I have a pending objection.
THE COURT: You got ahead of me. All right, we'll take a recess at this time.
10:53:38 Ladies and gentlemen, we'll recess.
THE WITNESS: Sorry about that, Judge.
THE COURT: That's all right. You're faster than I am.
(The following proceedings were had out of the
10:54:07 presence of the jury in open court:)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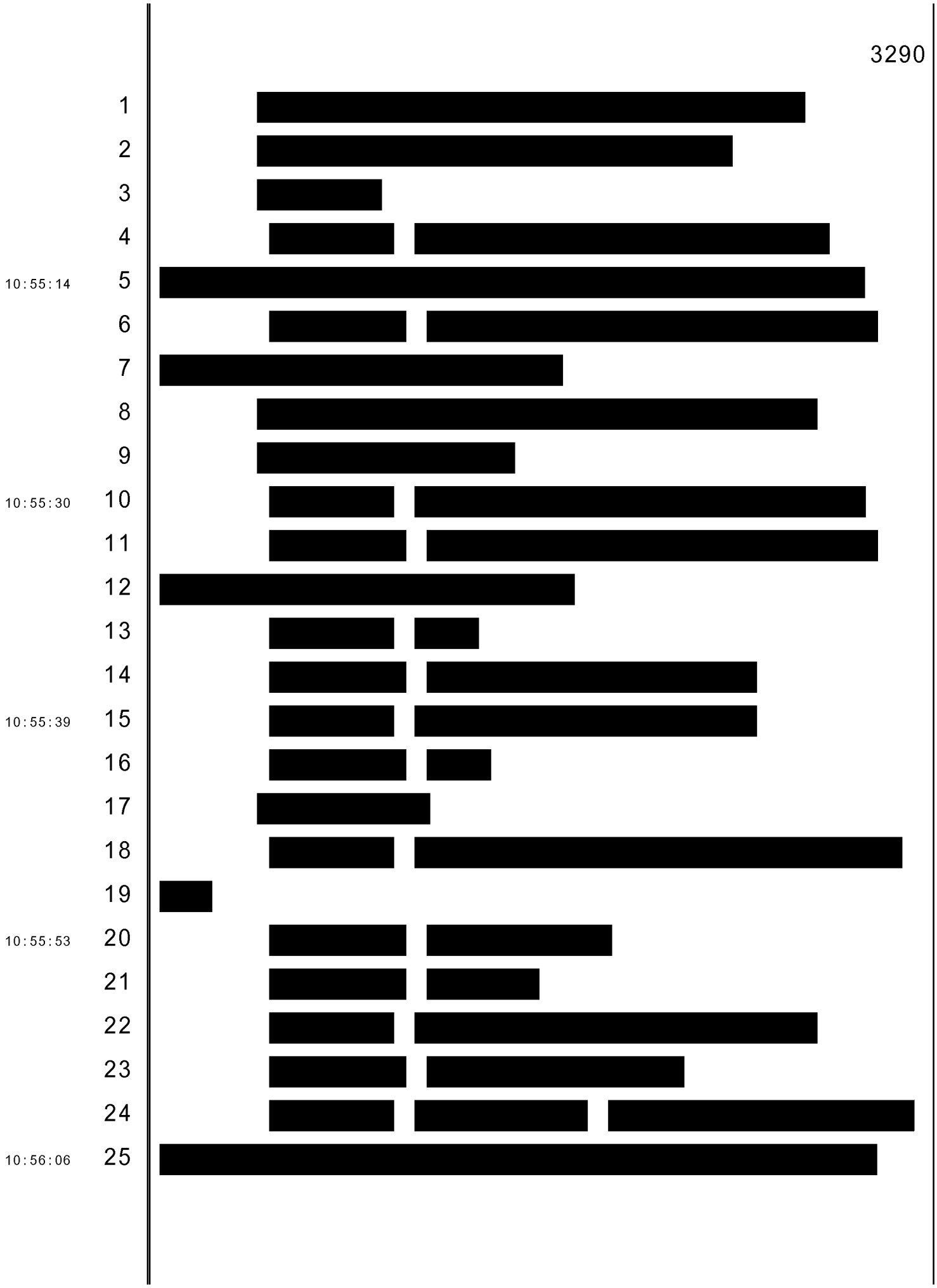
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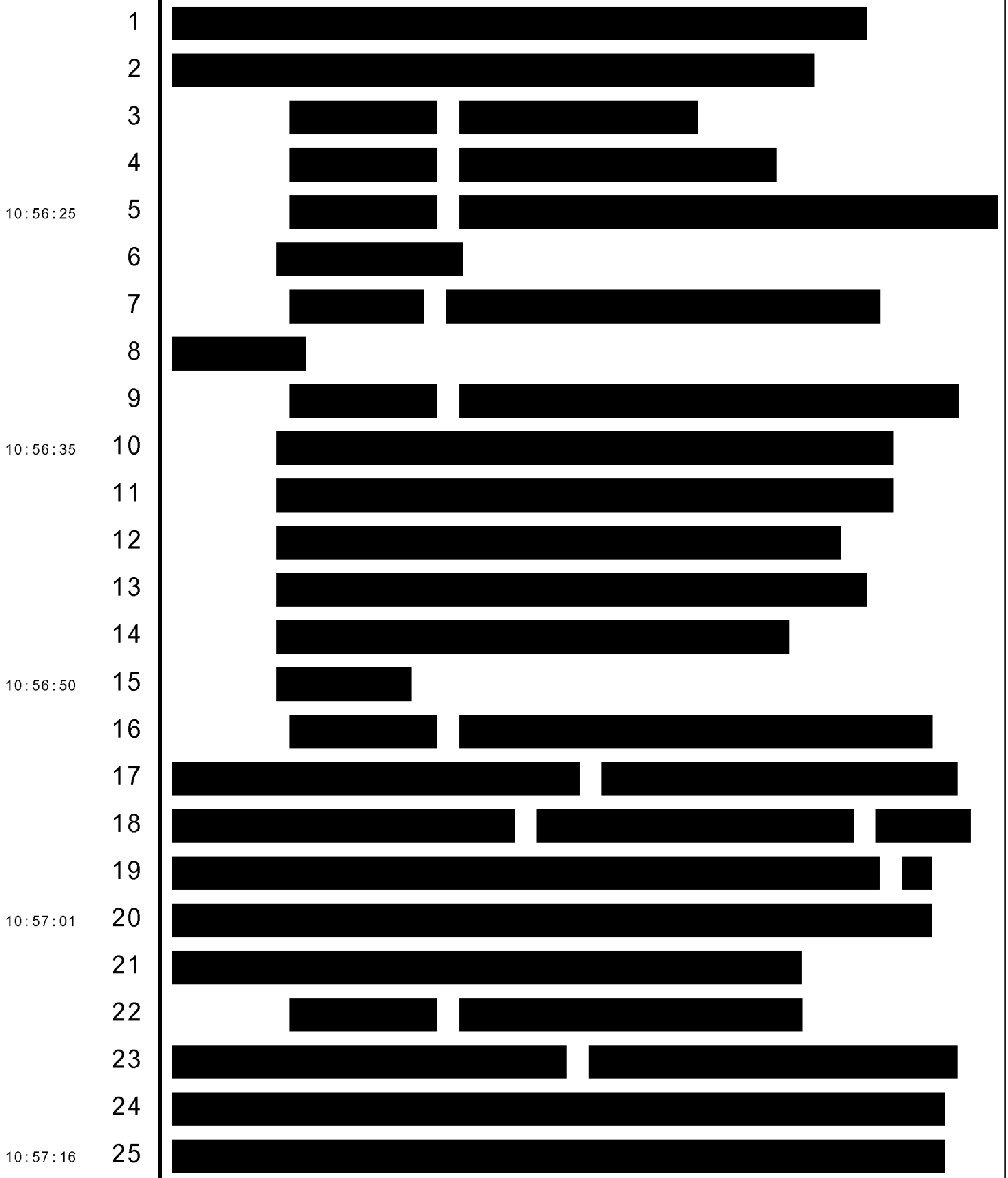
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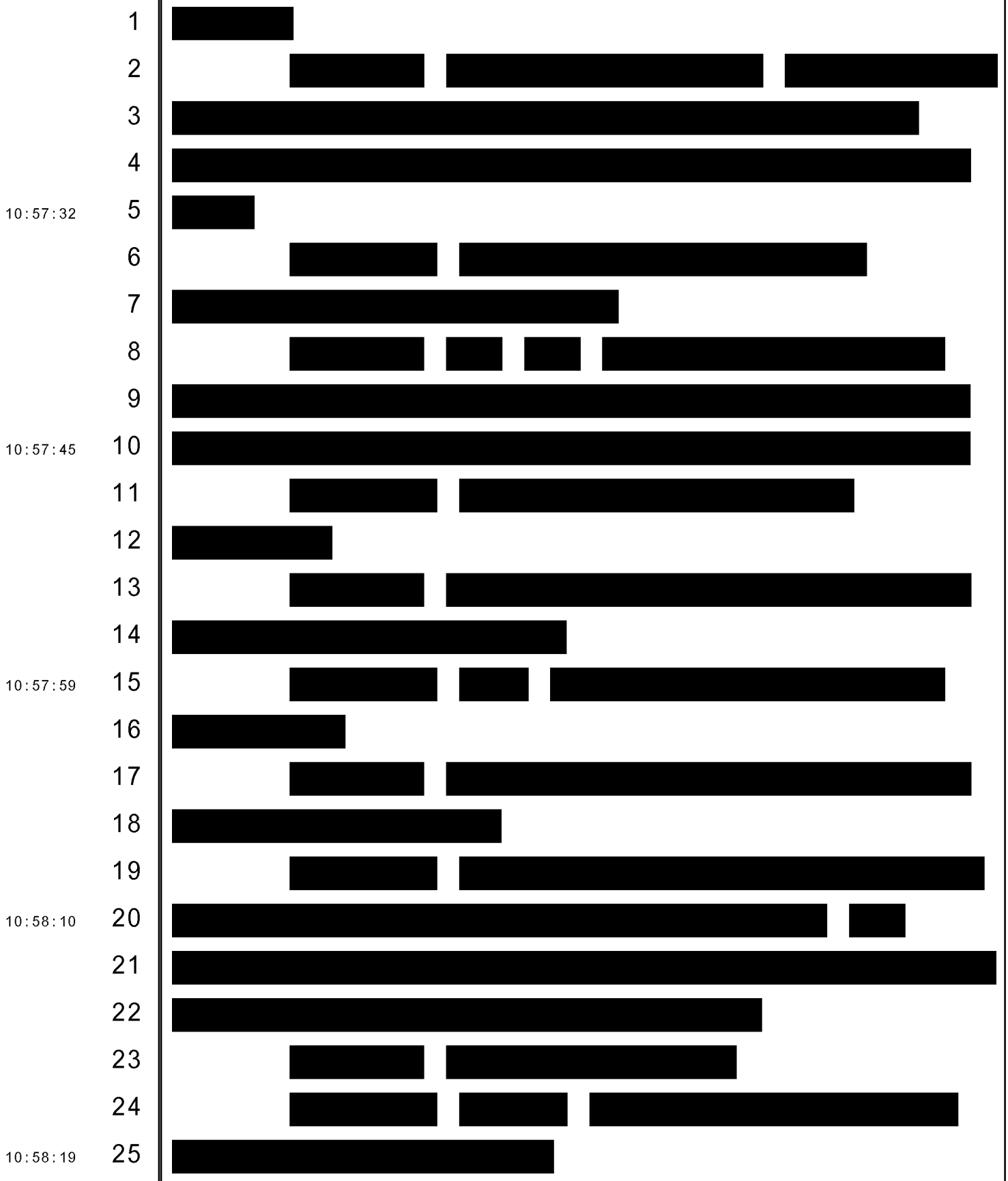
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[redacted]

(The following proceedings were had in the presence of the jury in open court:)

THE COURT: All right. Thank you very much, ladies and gentlemen. Please be seated. We will resume.

You may proceed, sir.

MR. BAYMAN: Thank you, Your Honor.

Could we put that letter back up that we were looking at just before the break. The paragraph "before these applications may be approved."

(Exhibit published to the jury.)

BY MR. BAYMAN:

Q. Doctor, taking you back to the letter of May 1, 2006.

A. Yes.

11:19:17 Q. Prior to receiving this letter, had FDA acted on GSK's 2006 changes being effected labeling change with respect to adult suicidality?

A. Prior to receiving this letter, no.

Q. Okay. And the FDA says:

11:19:37 "We have completed our review of your supplemental applications and they are approvable. Before these applications may be approved, you will need to make revisions to your labeling as outlined below so as to ensure

11:19:52 standardized labeling pertaining to adult suicidality with all the drugs treating major depressive disorder."

When you got this letter, what did this mean to you?

11:20:02 A. What they're --

THE COURT: No. No. He can testify to his understanding of the letter.

BY MR. BAYMAN:

Q. Okay. What was your understanding of what this meant?

11:20:11 A. Well, what the FDA is telling us is they would approve our label if we removed the paroxetine language that we had before and replaced it with the class language that the FDA is providing us now.

Q. Did you understand this letter to be an approval of the

11:20:31 2006 CBE supplement that you proposed?

A. Assuming that we make the changes, which is removing the paroxetine-specific data and replacing it with the class language, then it's approvable, yes.

Q. Did you understand this to be FDA accepting the language in

11:20:53 the April 2006 CB that GSK proposed with respect to adult suicidality?

A. No, this is FDA rejecting that language in favor of the class language that they had in their labeling.

Q. Let's look at the fifth paragraph.

11:21:13 Just briefly tell the jury what the FDA was telling you here.

MR. WISNER: Objection.

THE COURT: Sustained. The letter speaks for itself. Again, he may testify to his understanding only.

11:21:26 BY MR. BAYMAN:

Q. What is your understanding of what the FDA was indicating needed to be done in the labeling with respect to adult suicidality?

MR. WISNER: Again, Your Honor, renew my objection.

11:21:45 THE COURT: Well, he may testify to his understanding.

BY THE WITNESS:

A. Yes, our understanding was that this is -- the results of their analysis would go into the antidepressant labeling in what's called the medication guide, that's sort of the

11:21:59 information that's specific or used for the patients to understand the drug.

And it's really to talk about alerting the clinicians, patients, family members about this increased risk found in the FDA analysis in young adults with major depressive disorder and

11:22:22 other that psychiatric illnesses who are taking these medicines.

They also changed the label to inform practitioners about the possibly beneficial effect seen in the older adults, and to again remind them that these disorders that are being

11:22:36 treated with these medicines are themselves at high risk of suicidality, suicide attempts, and suicide.

So, to remind clinicians and caregivers and family members that these diseases themselves are a big risk for these behaviors.

11:22:57 Q. Go to the second page of the letter.

Was this the language, the revised black box warning that FDA proposed?

A. Yes. This is the updated box warning that presents the results of FDA's complete analysis.

11:23:21 Q. Is the FDA's label restricted to adult patients of a certain age?

A. No, this references information across all ages.

Q. And does the -- what does it say with respect to patients of all ages?

11:23:39 A. It states:

> "Patients of all ages who are starting on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in

11:23:52 behavior, and also families, caregivers, should be advised for the need for close observation and communication with the prescriber."

Q. In your opinion, is that disease state management?

A. No, this is specific to antidepressant therapy.

11:24:10 Q. Earlier we looked at one finding from the FDA's 2006 analysis concerning not only significant increased risk for Paxil on the secondary end point of suicidal behavior and MDD. Did FDA require GSK to add any language to the Paxil labeling at this time reflecting that finding?

11:24:32 A. No.

Q. Did that surprise you?
A. No, because they said in this letter to us there is an attempt to standardize across antidepressants. So, there is no specific antidepressant data in any of the class labeling.
11:24:48 Q. Did this May 1, 2007, letter from FDA have any practical effect on GSK's ability to continue to include the language in the Paxil labeling that it had added in April 2006 with respect to Paxil in adult suicidality?
A. Yes. Based on this response, we could no longer have that
11:25:12 language in the label.
Q. Now, did GSK actually follow up with FDA to discuss whether GSK can continue to include the Paxil-specific language in its label?
A. Yes, we did.
11:25:26 Q. Before we get to that, I want to ask you a few questions about the structure of the label.
A. Okay.
Q. First, for medications that were approved in the timeframe that Paxil was first approved, are there specific defined
11:25:42 sections of a label that a company must prepare and maintain?
A. Yes, there are.
Q. And are you familiar with those seconds?
A. Yes, I am.
Q. How have you become familiar with the various sections of
11:25:56 the label?

A. The sections of the label are defined in the federal regulations and provide the different sections of the label and what should go under those sections.

Q. Now, as a medical doctor who prescribes medications, do you have to be knowledgeable about the contents of the various sections of the label?

A. Yes, you do.

Q. And in your role at GSK, have you had to draft prescription labeling?

A. Yes, I have.

Q. And have you had to draft labeling for Paxil or paroxetine?

A. Yes, I have.

Q. Have you prepared, helped us prepare a graphic that lays out the sections of a prescription medicine labeling?

A. Yes, I have.

MR. BAYMAN: Your Honor, at this point I would ask for permission to publish for demonstrative purposes slide 7036-31, the sections of the label.

THE COURT: You may proceed.

(Exhibit published to the jury.)

BY MR. BAYMAN:

Q. Dr. Kraus, can you briefly describe what we're seeing on this graphic?

A. Yes, these are the headings that are defined in the federal regulations as to what constitutes the appropriate labeling for

a marketed drug.
Q. Okay. And are these the various headings or sections in a prescription drug label such as Paxil and other drugs at the time?
11:27:21 A. Yes, these are the headings.
Q. Tell us about it. What's the description?
A. So the description is simply that usually you see the chemical structure of the medicine, and sometimes some of the biological activity that the medicine may result in.
11:27:36 Q. And what's "clinical pharmacology"?
A. Clinical pharmacology is kind of--we talked a little bit about this on Thursday--how the drug is metabolized, excreted, removed from the body in different areas that it may interact within the body. So, it gives subscriptions of what happens to
11:27:59 the medicine once it goes into the body.
Q. How about "indications and usage"?
A. Indication and usage is all the various diseases that we talked about. Each time a new one was approved based on the efficacy and safety data, they get listed the different disease
11:28:18 states and the evidence for them in that section of the label.
Q. How about "contraindications"?
A. Contraindications are things that you must not use with the drug. So, it's a particularly dangerous combination or treatment with a particular medicine.
11:28:34 Q. And what's contained in the warning section?

A. The warning section highlights potentially serious events, usually events that can have either significant harm to the patients or change the way their disease is managed.

Q. How about "precautions," what goes into the precautions section?

A. Precautions is similar to warnings, but typically it's also informative in terms of what a practitioner or a caregiver might do in the event of seeing these sorts of adverse events.

Q. How about "adverse reactions"?

A. Adverse reactions are kind of the side effects that are seen in the different studies over time with the medicine. They're usually listed in tables.

Q. What's in "drug abuse and dependence"?

A. This is whether or not there's been evidence of the possibility of either physical or psychological abuse of the medicine. So, kind of the need to have higher doses to get the same effect over time, a craving for the medicine, things of that nature.

Q. What's in the "overdoses" section?

A. Overdoses, experience and overdose, so in clinical trials you sometimes have overdose, you can report what occurred in those instances. If there are recommendations of how to treat in the event of an overdose, that's in this part of the label as well.

Q. "Dosage and administration"?

A. That simply states how the drug should be dosed for the different indications or diseases, and then also how it is supplied. Is it a tablet, oral suspension, is it an injection, those sorts of things.

11:30:24 Q. Now, based on your experience, of all of these sections of the label, and they are set out -- did you say they are set out in code of federal regulations?

A. Yes.

Q. Based on your experience, of all these sections, how many

11:30:37 are places where one would discuss a possible association or risk with suicide?

A. Primarily the warnings but also the precautions.

Q. Any other sections?

A. No, they aren't relevant.

11:30:48 Q. And for which sections of the label did FDA implement class labeling for suicide in 2007?

A. In the warnings and precautions.

Q. I want you to turn in your notebook to Tab 37 which is Defense Exhibit 124.

11:31:11 A. Okay.

Q. That's -- it's already admitted.

What's that document?

A. This is an e-mail correspondence detailing a question from our regulatory lead, Barbara Arning, about clarification on the

11:31:29 Paxil-specific language and FDA's view as to whether it should

remain.
Q. Could you go to page 3. Let's go to the first e-mail in the chain. We're going to go in chronological order. This is the oldest e-mail in the chain.
11:31:48 A. Yes.
Q. At the end. Okay.
What is this e-mail?
A. This is basically informing our regulatory person that the FDA has decided upon the final language for the labeling and
11:32:02 for the medication guide, and attached is the request letter with that new language. And they wanted us to submit our revised label, verbatim, meaning exactly as FDA outlined, within 30 days of our receipt of the note.
Q. And the sender is Renmeet Grewal, do you understand who
11:32:22 that is?
A. Yes, she was, I think, the project manager that we were working with at the FDA. She was at FDA but I think her role is project director.
Q. Are you familiar with this e-mail chain?
11:32:43 A. Yes.
Q. How did you understand FDA's -- did you -- were you familiar with the e-mail chain at the time that this happened?
A. Yes. At the time I was still project physician but I was also project leader as well.
11:32:54 Q. How did you understand FDA's request that GSK submit

revised labeling verbatim to what FDA had outlined?
A. This is what I said before, they had rejected the paroxetine-specific label in favor of being replaced with the class language from FDA.
11:33:12 Q. And did you believe that upon receiving this e-mail, that GSK would be permitted to include its own Paxil-specific warning?
A. No. We would not be permitted, but we did seek additional clarity.
11:33:25 Q. Let's look at -- did GSK respond to Dr. Grewal's e-mail?
A. Yes, we did.
Q. Look at the first page of the exhibit, the bottom of the page.
What is that?
11:33:43 A. That is us asking for the clarification that I described where we asked if FDA intended for us to keep the Paxil-specific paragraph on the young adults that we had added in April 2006 in addition to the class labeling they provided, or do you ask us to replace the complete warning section on
11:34:10 this topic by the new labeling. So we're specifically, explicitly asking the question here.
Q. Who is Dr. Barbara Arning?
A. Barbara Arning was the regulatory lead on the Paxil team at that time.
11:34:21 Q. Now, did Dr. Arning actually cut and paste the 2006 Paxil

adult suicidality labeling language and put it in the e-mail?
A. Yes, she did.
Q. And did she ask whether that could be included or whether FDA wanted that language replaced entirely with class labeling?
11:34:40 A. Yes, that's what she's asking in this note.
Q. Now, look at the top of the document, it's the last e-mail in the chain. What is that e-mail?
A. That's the response to Barbara saying:

> "Please replace the previous warning section
11:34:58 with the new language we provided to in the class labeling letter signed on May 9th."

Q. And Rimmy, that's Dr. Grewal from the FDA?
A. Yes.
Q. Okay. What was your understanding of what the FDA meant
11:35:13 when it made this response?
A. That the warnings and precaution section around suicidality must be replaced entirely with the class language and the paroxetine-specific language should be removed.
Q. And you were familiar with these communications at the
11:35:28 time?
A. Yes, I was.
Q. Were there any further communications between GSK and FDA on the issue of whether GSK can retain the Paxil-specific language in the labeling after this e-mail chain?
11:35:42 A. Yes, I was.

Q. Let's turn to Tab 38 which is Defense Exhibit 126. It's already in evidence.

(Exhibit published to the jury.)

BY MR. BAYMAN:

11:35:55 Q. What is this document?

A. This is a note from Barbara Arning to the FDA where we are proposing inclusion of the Paxil-specific language within the warnings and paroxetine section of the label.

Q. Is this a formal request letter?

11:36:18 A. Yes, it is.

Q. Okay. And were you familiar with this letter at the time it was sent?

A. Yes.

Q. Were you involved in actually preparing this submission to

11:36:33 FDA?

A. Yes, I was, in terms of the labeling and leading the project at the time.

Q. Okay. What was the Paxil-specific language that GSK was asking to include in the Paxil labeling?

11:36:45 A. That's shown on the next page. We revised our language in the label slightly to fit within the FDA class language. And it fairly similarly shows some of the findings from our analysis, and again, our conclusion that this was still driven by the young adults without seeing such an effect in the older

11:37:16 age groups 25 to 64 or greater than 65.

So, basically it gives similar information within the context of what FDA provided.

Q. So did you actually take the FDA's black proposed label, proposed class labeling and attempt to edit it as is shown on the screen?

11:37:37

A. We did not edit FDA's language. What we did was edit what our language had been to being included within the warnings and precaution. So the class language, we didn't change anything that they had suggested.

Q. You changed the language that you had proposed in the April 2000 CBE to make it complimentary to the class language?

11:37:52

A. That's correct.

THE COURT: I'm confused by the exhibit. That first line that's in lighter type, what is that? Is that in or out?

MR. BAYMAN: That is -- well, I'll let Dr. Kraus explain.

11:38:13

THE COURT: Yeah. Yeah. Let him testify.

MR. BAYMAN: Sure.

BY THE WITNESS:

A. Those light lines would be things that -- you see strikethroughs are things that would be --

11:38:19

THE COURT: That's intended to be strike-throughs?

THE WITNESS: I think that --

THE COURT: Why would it be light -- I see some other strike-throughs.

11:38:31

THE WITNESS: I think this is a copy issue, myself.
BY MR. BAYMAN:
Q. But the first --
THE COURT: I've seen it before and that's why --
11:38:40 MR. BAYMAN: The first --
THE COURT: Just a minute. Just a minute. We're having a little conversation here.
Can you tell me, sir, that light line, is that intended to be in or out?
11:38:51 THE WITNESS: Yes, I can tell you. Just a minute here.
(Brief pause).
THE COURT: I'm only interested in the exhibit, not the content. I just want to know what you're purporting to
11:39:06 show here.
THE WITNESS: I think it's -- I know it is, so I'm looking right now, sir, at the label we submitted, and I think that's just a copying --
THE COURT: That's a copying problem.
11:39:15 THE WITNESS: -- issue.
THE COURT: That's supposed to be in there, though?
THE WITNESS: Yes.
THE COURT: In your proposal?
THE WITNESS: That's correct.
11:39:23 THE COURT: Okay. And the strikeover is what you

would take out, is that right?

THE WITNESS: That's correct.

THE COURT: Okay.

MR. WISNER: Your Honor, I think if we ask Dr. Kraus if that light portion was what GSK intended to add to the label.

11:39:28

THE COURT: All right. I'm creating confusion. I should let the lawyers do this, but I'm not -- it's not clear in my mind what's shown here.

11:39:41

MR. BAYMAN: No problem, Your Honor.

BY MR. BAYMAN:

Q. Dr. Kraus, why don't you -- and it may be easier for you to read on your screen, read that -- what the first sentence in light that His Honor pointed out to.

11:39:47

A. So this indicates that:

"... GlaxoSmithKline sponsored analysis of the placebo-controlled trials paroxetine found that ... "

and then the rest. And that is language introduced

11:39:59

to clarify that this was our analysis, not --

THE COURT: That's your proposal?

THE WITNESS: That's correct.

THE COURT: Okay. And that's the same with the other light language.

11:40:05

THE WITNESS: That's right.

BY MR. BAYMAN:
Q. And were you proposing to add the GSK-specific data to the class language?
A. Yes, that's correct.
11:40:17 THE COURT: And what is that specific data? Is that shown?
THE WITNESS: Yes, sir. This is the data showing a higher frequency of suicidal behavior in young adults --
THE COURT: Is it all the type that that's of a
11:40:32 different character?
THE WITNESS: It's all the type that follows, that's correct. That's all specific for our Paxil analysis.
THE COURT: I'll be grateful, counsel, if you give me a copy of this in due course.
11:40:43 MR. BAYMAN: Yes, sir. I think there is one in your notebook.
THE COURT: It may be there, yeah.
MR. BAYMAN: We'll see if we can get you a better copy. That actually shows it better on the screen there.
11:40:51 THE COURT: Okay. All right.
BY MR. BAYMAN:
Q. So, you took -- is it fair to say you took -- or did you take the language that was proposed in the April 2006 CBE regarding Paxil in suicidality in adult patients and try to
11:41:14 edit that to make it complimentary or harmonize it with the

class labeling that had been proposed?
A. Yes, that's correct. That's why there's some modifications here.
Q. Okay. Let's turn to the next which is Tab 39, Defense
11:41:28 Exhibit 127, that's also admitted in evidence.
Are you familiar with these e-mails?
A. Yes, I am.
Q. And what are these e-mails?
A. Excuse me (coughing). This is our writing to the FDA
11:41:48 project manager about the proposal to include the Paxil-specific labeling into the warnings and precaution section, and the response is to submit that CBE. And FDA says:
"...we will be discussing all sponsor's proposals during the last week of May. After we
11:42:11 discuss everyone's proposal, I will have a response to your questions."
Q. So did GSK at this time, May 15th, were you still attempting to submit a label that contained Paxil-specific information with respect to adult suicidality?
11:42:29 A. We did, yes.
Q. And what did FDA tell you to do?
A. They said submit it, they'll review it with the other sponsor's submissions.
Q. Okay. Let's look at Tab 40 in your book, Defense
11:42:49 Exhibit 133 which is also already in evidence.

Are you familiar with this document?
A. Yes, I am.
Q. What is it?
A. This is the actual submission to FDA, which provided our updated label with the edited changes that you had seen in that e-mail.
Q. Did GSK actually include Paxil-specific language in this labeling submission?
A. Yes, we did.
Q. Let's look at some of that.
What is GSK submitting here?
A. So, this highlights the language that we just looked at that was being added by us in the label, that's what the underlines indicate.
Q. And is this the same language that GSK, in the May 11, 2007 letter to the FDA requested FDA add to the Paxil prescribing information?
A. Yes.
Q. And did you say this is the formal submission?
A. Yes, that's right.
Q. To FDA.
Let's turn, if you would, to Tab 41.
THE COURT: And this document is what?
MR. BAYMAN: This document, Your Honor --
THE COURT: You've been looking at?

MR. BAYMAN: Defense Exhibit 133, Tab 40 of your book.

THE COURT: Okay. Go ahead.

BY MR. BAYMAN:

Q. Let's turn to Tab 41, which is defense exhibit 128. It's already been admitted into evidence.

Are you familiar with this document?

A. Yes, I am.

Q. Okay. What is this?

A. This is the response from the FDA project manager to us again providing their class labeling which has to be revised for all drugs.

Q. And this, again, is Dr. Grewal from the FDA sending the e-mail?

A. That's correct.

Q. And the subject is adult suicidality class labeling changes?

A. Yes.

Q. And you recall when this e-mail came in at the time?

A. Yes, I do.

Q. Back in 2007?

A. Yes.

Q. What does the FDA say in this document?

A. Here they said they have completed their review of responses. Based upon these responses they edited the language from their original language and they detail what they did

there, just kind of small changes in the language. And they gave some other clarification about some sponsored-omitted class labeling paragraph starting with "consideration should," so they're ensuring that the sponsors understand exactly what they need to do.

11:45:57

They also noted that some sponsors have taken the opportunity to include other revisions to the labeling but they were related to the class labeling, so they didn't rule on those.

Q. What did they say with respect to whether they were requiring manufacturers to put in class labeling with respect to the suicidality warnings and precautions?

11:46:05

A. Yes, it still is that the class labeling revisions for all drugs has to occur with the language they submitted to us.

Q. And did the FDA in this letter provide new language?

11:46:28

A. Yes, they did.

Q. And were they requiring that all SSRIs antidepressants include that in their label?

A. Yes.

Q. Did FDA's proposed language include any of the Paxil-specific language that GSK had asked to be included?

11:46:37

A. No, it did not.

Q. Did FDA comment in the letter on whether they wanted the labeling to be consistent for all antidepressants?

A. Yes, they actually said:

11:46:58

"Please be reminded that it is critical that the labeling is consistent for all these products."

Q. Now, at this time after some back and forth with the FDA, did GSK abandon its efforts to include the Paxil-specific language in the label?

A. Yes, we accepted the label per this last note.

Q. Okay. Well, let's look at Tab 42, which is Defense Exhibit 129. It's an e-mail. It's already in evidence.

Are you familiar with this e-mail exchange?

A. Yes.

Q. What's the subject of this e-mail exchange?

A. (Reading:)

"Subject: Adult suicidality e-mail."

But what they were talking about was, we had just called to ensure that this, indeed, reflected their rejection of the Paxil language, and she says it does.

Q. So even after the prior e-mail from Dr. Grewal, did GSK call to say they wanted to make sure that the Paxil-specific language could not be included in the label?

A. Yes. Dr. Arning left a voicemail, that's correct.

Q. And Dr. Grewal says:

"FDA is not going to include the Paxil-specific language in the class labeling."

A. Right. And again, because it's targeted at a class of

drugs and they had highlighted their opinion to be consistent among the medicines.

Q. So GSK, through Dr. Arning's voicemail, did attempt one more time to include the Paxil-specific language?

11:48:42 A. To make sure we clarify, yes.

Q. Did FDA in this e-mail from Dr. Grewal suggest putting any Paxil-specific language in some other portion of the label?

A. No.

Q. So at this point in time, was this the second CB submission

11:49:06 GSK submitted to FDA to have Paxil-specific data on adult suicidality in the Paxil labeling?

A. Yes, that's right.

Q. And was the first submission in April of 2006?

A. Yes. With our first results, yes.

11:49:21 Q. And the second submission to include the Paxil-specific data with respect to adult suicidality was in May of 2007?

A. Right. Within updated class language, that's correct.

Q. Were either of those CB changes being effected labeling submissions accepted by the FDA?

11:49:40 A. No, they were not.

Q. Now, at this stage how many times had GSK gone back to FDA requesting that the FDA keep the Paxil-specific data on adult suicidality in the Paxil labeling?

A. I didn't keep track as we're talking, but it looked like

11:50:02 about four times or so.

Q. What did you and your colleagues at GSK conclude after these exchanges of e-mails and correspondence with the FDA about whether you could include Paxil-specific language with respect to suicidality in adult patients in the Paxil label?

11:50:21 MR. WISNER: Objection. Speculation as to what FDA would or would not do.

MR. BAYMAN: I asked him what they concluded from the exchange.

THE COURT: He may testify.

11:50:29 BY THE WITNESS:

A. We concluded, obviously, that FDA wanted consistent class language across the medicines and would not consider Paxil-specific language for this topic.

MR. BAYMAN: Could we, Mr. Holtzen, pull that last

11:50:47 e-mail from Dr. Grewal.

BY MR. BAYMAN:

Q. Now, Dr. Kraus, at the end of the second paragraph, Dr. Grewal says:

> "If you would like to discuss this matter
>
> 11:50:56 further, please submit a formal meeting
>
> request."

A. Yes.

Q. Why didn't you and your colleagues at GSK formally request a meeting?

11:51:04 A. There's a couple of reasons:

One, as we've gone through, it's quite clear FDA's intent for the class language within the label. We had attempted several times to clarify and each time they were clear in their answer.

11:51:20 Additionally, when proposing a new meaning with FDA, typically what you would bring in hand also is new data that they haven't seen to support any argument you may have. We didn't have any new data in this regard.

Q. Didn't you think you believed there was a chance you could

11:51:39 change FDA's position if you requested a meeting?

A. No. Not based on the exchanges we had to date, no.

Q. What would be the harm of asking for a meeting?

A. Well, the harm is, again we didn't have justification to ask for a meeting based on having new data or insights, so

11:51:58 we're taking the time of FDA.

The harm also is, the potential for ignoring the -- the appearance of ignoring the advice they had and affecting the relationship we would have with the FDA as well.

Q. Did you believe that the FDA had made its position clear

11:52:15 that it wanted the language to be class language with respect to Paxil and adult suicidality?

MR. WISNER: Objection; leading, asked and answered, and speculation.

THE COURT: It's been covered, but it is quite

11:52:32 leading.

BY MR. BAYMAN:
Q. Well, what was your view about whether the FDA had made its position clear about it wanted class labeling as opposed to Paxil-specific specific?
11:52:41 MR. WISNER: Objection; asked and answered.
THE COURT: Covered.
BY MR. BAYMAN:
Q. Did you and your colleagues, did you conclude that a meeting with the FDA would've been futile?
11:52:51 A. Yes.
MR. WISNER: Objection. Asked and answered; speculation.
THE COURT: It may stand.
BY THE WITNESS:
11:52:55 A. Yes, I was the project leader at the time --
THE COURT: Just answered, sir.
BY THE WITNESS:
A. It would've been futile, yes.
THE COURT: Just a "yes." Let's get on with it.
11:53:05 BY MR. BAYMAN:
Q. Okay. Following that conclusion that it would have been futile, what did GSK do?
A. We accepted the FDA class labeling, incorporated that into the label, and updated our label appropriately.
11:53:16 Q. Why didn't GSK submit a CB labeling supplement to the FDA

to include the 2.76 odds ratio finding from the FDA's adult suicidality analysis after that finding came out in December of 2006?

A. Again, it gets to the same point about our specific data. The class language is class, so it's across all drugs, did not specifically call out any individual medicine. So the same concept was at hand.

11:53:39

Q. And why didn't you submit a CB labeling supplement to the FDA to include that 2.7 odds ratio finding from the FSDZ adult suicidality analysis after you received the FDA's May 1, 2007, letter?

11:54:00

A. Again, this was FDA's data analysis, what we were proposing to do was include our own data analysis. So, that would be their decision as to whether or not they would include those sorts of items. And again, they did not because they were looking for a consistency across the class.

11:54:19

Q. Turn in your book, if you would, to Tab 51. This is Plaintiff's Exhibit 70.

MR. WISNER: Objection, Your Honor. This is the document that Dr. Ross marked up, which is Joint Exhibit 1, and his opinions and testimony. Defense counsel objected when we tried to use this exact same document with Dr. Glenmullen. They cannot then use it with their expert; it's inappropriate.

11:54:35

MR. BAYMAN: Well, he's here to talk about the labeling and I think he should comment on --

11:54:53

THE COURT: It's 70?

MR. BAYMAN: Yes, sir.

THE COURT: It's the one he marked up?

MR. BAYMAN: Dr. Ross, yes, sir.

11:54:59 MR. WISNER: Your Honor, you wouldn't let us enter it into evidence, and then you wouldn't let us use it with Dr. Glenmullen. This is entirely unfair. If they want to use a brand new label and mark it up, that's fine, but having them use a document that you prohibited us from doing is entirely

11:55:16 prejudicial.

THE COURT: Well, let's go to sidebar.

(Proceedings heard at sidebar on the record.)

[redacted]

11:55:57 [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11:56:07 [redacted]

[redacted]

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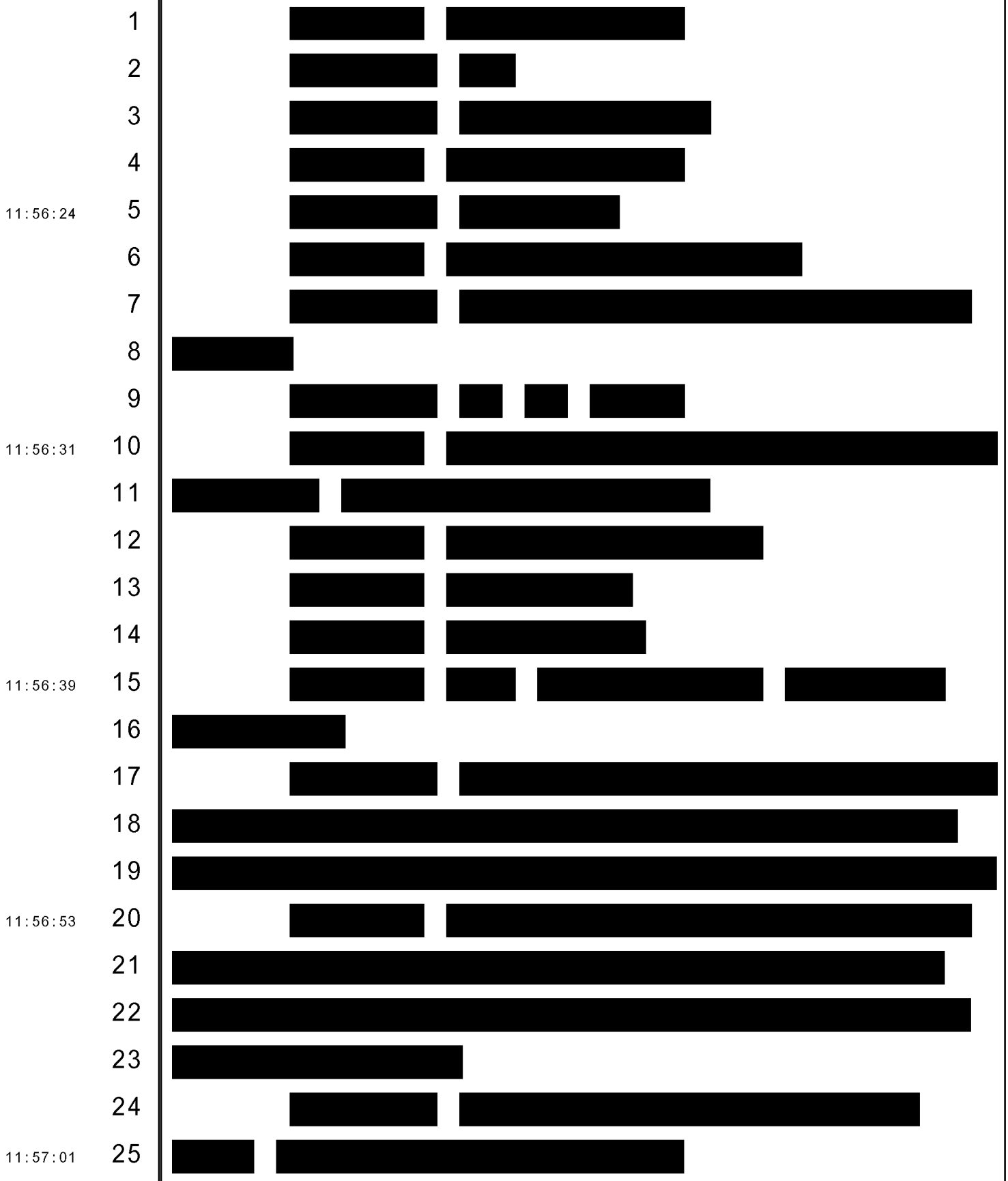
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(Proceedings resumed within the hearing of the jury).

BY MR. BAYMAN:

Q. Dr. Kraus --

A. Yes.

Q. -- I want you to assume that the jury has heard from Dr. Ross, plaintiff's expert, about various places where he believes GSK could have included Paxil-specific information about a risk of suicidality in adult patients.

A. Okay.

Q. There is --

(Exhibit published to the jury.)

BY MR. BAYMAN:
Q. I want you to -- and I'm not going to go through them all, but I want you to assume that Dr. Ross said that GSK could have included Paxil-specific information in the area of number 1 where the arrow is inside the black box warning (indicating).
11:59:43
MR. WISNER: Your Honor, this misstates Dr. Ross's testimony. His testimony was that GSK could've proposed putting Paxil-specific language in the black box warning. If Mr. Bayman is going to start paraphrasing Dr. Ross's testimony, I'd ask that he do it correctly.
12:00:00
MR. BAYMAN: I object again to the speaking objections, Your Honor.
BY MR. BAYMAN:
Q. Could GSK have proposed Paxil-specific language regarding adult suicidality in the black box label?
12:00:13
A. We would never propose to put language in a boxed warning which is mandated by FDA. That's just something that would not be done.
MR. WISNER: Objection. Move to strike. The question was "could they," not "would they." He's not responding to the question asked by counsel. I believe he should answer.
12:00:29
THE COURT: They couldn't change the black box.
THE WITNESS: That's correct.
THE COURT: That's, as I understand his testimony, but let's get on with it. You can cover some of this with
12:00:43

cross-examination if necessary.
BY MR. BAYMAN:
Q. Well, I'd ask you to assume that Dr. Ross has indicated in number 2, where the arrow is pointing, in your opinion would it
12:01:09 have been appropriate for GSK to have put Paxil-specific language with respect to a risk of suicidality in adult patients in that place in the label (indicating)?
A. No. Again, there's no defined as federal regulations, and nothing goes there.
12:01:28 Q. All right. Turn, if you would, to page 4 of the label, Clinical Trials.
Do you see that?
A. Yes.
Q. Would it have been appropriate for GSK to put
12:02:07 Paxil-specific language about a risk of suicidality in adult patients where arrow number 3 is pointing but right below the clinical trials, pharmacology section?
A. No, again this is the indication and usage section, it's note appropriate to have a warning and precaution.
12:02:33 Q. How would a the end of the paragraph, number 4?
A. The same answer, it does not fit in this section. It's not appropriate in this section.
Q. I'm not going to go through all the other places Dr. Ross has indicated, but have you had an opportunity to look at the
12:02:49 other places Dr. Ross identified in this document?

A. I did see the document itself, yes.
Q. What is your opinion about whether it would have been appropriate for GSK to request that Paxil-specific language be inserted in any of the other locations Dr. Ross has identified?
12:03:08 A. The opinion is, we inserted in the warnings and precaution section because that's the appropriate area. I think some of his recommendations were within the warnings and precaution section, which we had done before and had been rejected by the FDA.
12:03:25 Q. Would it have been appropriate, in your opinion, to include Paxil-specific language about a risk of suicidality in adult patients taking Paxil in any of the other sections outside warnings and precautions?
A. No, it's not appropriate. And as we discussed before,
12:03:43 clinicians searching for information wouldn't be able to find it if it were not in the right place.
Q. All right. Turn, if you would, in you book to Tab 43, which is Defense Exhibit 130.
A. Okay.
12:04:12 Q. Are you familiar with this document?
A. Yes.
Q. What is it?
A. This is our sending the correspondence with the updated label with the FDA class language saying we will comply with
12:04:34 their request.

Q. And were you familiar with this document at the time, back in June of 2007?
A. Yes, I was.
Q. And were you involved in this submission?
12:04:43 A. Yes, I was.
Q. And was this document created in the ordinary course of GSK's business?
A. Yes.
Q. Was it maintained in the ordinary course of business?
12:04:53 A. Yes, it was.
Q. Does it reflect the type of correspondence that GSK had with the FDA about this issue?
A. Yes, it does.
MR. BAYMAN: I would at this point, Your Honor, move
12:05:06 for the admission of Defense Exhibit 130 and for permission to publish to the jury.
MR. WISNER: Your Honor, at this time we'd move to exclude it under hearsay grounds. The author of this document has not been presented by GSK for cross-examination, so
12:05:19 therefore, it is inadmissible hearsay. I believe the Court previously ruled on this document pretrial and excluded it.
MR. BAYMAN: This is the same Dr. Arning, Your Honor, who's been involved in all the other e-mail communications that have been admitted into evidence.
12:05:32 MR. WISNER: And that doctor is not here today, and I

don't believe GSK has agreed to produce her.

MS. HENNINGER: That's not true.

MR. BAYMAN: Well, that's not accurate, but the fact of the matter is, she's been in all these communications back and forth with the FDA. This is just one more in a series of communications at the time, and it is a business record and admissible.

12:05:45

MR. WISNER: And, Your Honor, this does not qualify as a business record. This is hearsay and they haven't laid the proper foundation to get this particular document into evidence.

12:06:00

THE COURT: This is the final edition of the label?

MR. BAYMAN: This is GSK sending --

THE COURT: Sending the label to --

MR. BAYMAN: With the class labeling language.

12:06:21

THE COURT: With the class labeling language.

MR. BAYMAN: Yes, sir. It's part of the chain that we've seen already, all of which has been admitted into evidence.

MR. WISNER: Your Honor, there's no evidence or testimony from anyone that FDA considered this or thought about it. There's no testimony from Ms. Arning as to how this document was prepared. It reads like an exhibit to be used at trial.

12:06:32

THE COURT: I'm going reserve ruling on it.

12:06:48

MR. BAYMAN: Okay. May I publish it?

THE COURT: No.

BY MR. BAYMAN:

Q. In June of 2007, did GSK send the Paxil label with the class language for adult suicidality to the FDA?

A. Yes, we did.

Q. When GSK did that, did GSK indicate that it still believed that the Paxil-specific language that had been in effect since 2006 would be useful for prescribers?

A. Yes.

Q. But did GSK say that, nonetheless, it would implement the class labeling required by the FDA?

A. Yes, we did.

Q. And did GSK indicate that it understood the FDA's reasons for keeping the language as class labeling?

A. Yes, we did.

THE COURT: That sort of gets the letter in, doesn't it?

MR. BAYMAN: Yes, sir.

MR. WISNER: It was actually all hearsay, Your Honor, but we don't want admission of the document, but if that testimony stands, I think it's a good compromise.

THE COURT: It gets the content of the letter in, and has received attitude.

MR. BAYMAN: Thank you, Your Honor.

THE COURT: So you sort of slid it in.
MR. BAYMAN: May I publish it to the jury?
THE COURT: Yes.
MR. BAYMAN: Thank you.
12:08:07 (Exhibit published to the jury.)
MR. BAYMAN: Just, Mr. Holtzen, if you highlight the "GSK still believes."
MR. WISNER: I do believe this is now actually the definition of cumulative.
12:08:19 MR. BAYMAN: I'm just showing him the language.
THE COURT: Yes, we've had that definition shown to us several times in this case.
BY MR. BAYMAN:
Q. Is that the language you talked about?
12:08:28 A. Yes, it is.
Q. Okay. Great.
Let's go to Tab 44, Defense Exhibit 344, which is admitted in evidence.
What is that document?
12:08:44 A. This is FDA's note back to us acknowledging their receipt of our submission.
Q. Is this what's called the FDA's approval letter for the Paxil labeling implemented in August of 2007?
A. Yes, this is the letter where they approved the warnings
12:09:03 and precaution section on suicidality.

Q. What does the FDA say in the letter about GSK's July 3, 2007, letter and the resubmission of the labeling that GSK submitted?
A. They stated that the July 3rd, 2007, letter constituted a
12:09:23 complete response to our action letter dated May 1st, 2007. And basically what they mean is, we have satisfied their requirements for their recommendations for labeling.
Q. Did GSK comply with the labeling language, the class labeling language set out in FDA's May 1, 2007 letter and the
12:09:41 attached labeling that FDA had sent?
A. Yes, we did.
Q. What does the letter indicate would've been the consequences had GSK failed to make FDA's labeling changes?
A. Again:
12:09:52 "Failure to make these changes within the specified period could make your product misbranded."
And they cite the federal regulations around misbranding.
12:10:02 Q. Was the use of FDA's class labeling with respect to Paxil and the risk of suicidality in August 2007 optional for GSK?
A. No.
Q. By approving the label, the final attached labeling, what determination did FDA make about the statements in Paxil's
12:10:29 labeling in order for FDA approve the final labeling?

MR. WISNER: Objection; hearsay, lacks foundation. He is not an FDA expert.

THE COURT: Sustained.

BY MR. BAYMAN:

12:10:37 Q. Let's turn to page 3.

A. Okay.

Q. What does that labeling say with respect to suicidality in adults beyond age 24?

A. So, this is the updated boxed warning, it says that:

12:11:03 "Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond 24."

Q. And what else did it say about what patients -- what prescribers should do with respect to patients, to all adult

12:11:23 patients?

A. Right:

"Despite the findings of the analysis they still indicate in the boxed warning that patients of all ages who are started on antidepressant

12:11:32 therapy should be monitored appropriately and observed closely for clinical worsening, suicidality or unusual changes in behavior."

Q. Is this disease state management?

A. No, because it's related to initiation of antidepressant

12:11:48 treatment.

Q. And did FDA approve that language as part of the Paxil labeling?
A. Yes, they did.
Q. And based on your experience and interacting with the FDA and working in the industry, drafting labeling yourself, does the FDA's approval over labeling mean that FDA is determined that the labeling is not false and misleading?
MR. WISNER: Objection. Speculation and improper opinion.
THE COURT: Overruled.
BY THE WITNESS:
A. Yes, that's correct, the label stands for those reasons.
BY MR. BAYMAN:
Q. Did GSK and FDA take any steps of their own to communicate the new labeling to the public and to the medical community?
A. We would have indicated in the website, but there was no letter sent out or anything in that regard.
Q. All right. I want you to turn now to Tab 45, Joint Exhibit 1, which is the June 10th Paxil-prescribing information.
Are you familiar with this?
A. Yes.
Q. Let's just look at a couple of things. Let's look at the box warning. Is that the same language we just looked at?
A. Yes.

Q. And is that language consistent with what the FDA required GSK to place in the labeling in 2007?
A. Yes.
Q. And it has language -- does it have language about
12:13:14 depression and other psychiatric disorders being --
THE COURT: All right. Sir, we've covered this now several times. Please, move along.
BY MR. BAYMAN:
Q. Doctor, based on -- and I don't want to go through every
12:13:25 section of the label, but is the language in the 2010 label the same language with respect to the warnings and precautions about suicide and suicide risk in adult patients?
A. Yes, it's the same.
Q. So all of the things we went through with respect to the
12:13:43 2007 label would be in the 2010 label?
A. Yes, it's been maintained.
Q. And was this information in the 2010 label available to prescribing doctors?
A. Yes.
12:13:58 Q. And was some of this language that was in the 2010 label in the label as a far back as 2004?
A. Yes.
Q. Including the language with respect to certain symptoms such as agitation and akathisia, and some other symptoms, that
12:14:35 have been associated with an increase -- or the emergence of

suicidality, was that in the label as far back as 2004?

MR. WISNER: Objection as to leading and vague.

THE COURT: Yes. We're covering an area that's been covered thoroughly in the case so far.

12:14:54 BY MR. BAYMAN:

Q. Did the Paxil prescribing information in 2010 continue to have a precaution with respect to akathisia?

A. Yes, it did.

Q. And has that precaution been in the label since 2005?

12:15:12 A. Yes.

Q. And was that information available to doctors in 2010?

A. Yes.

Q. I want to show just one last thing.

MR. BAYMAN: Mr. Holtzen, at the very end, "patients, their families and caregivers."

12:15:26 (Exhibit published to the jury.)

BY MR. BAYMAN:

Q. Do you see that?

A. Yes.

12:15:33 Q. And you see where it says -- it lists the symptoms that we've talked about before and it says at the end, does it not -- or does it say at the end:

"Symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close

12:15:52

monitoring and possibly changes in the medication"?

A. Yes, it does.

Q. Is there anything in this paragraph from the 2010 label that limits the warning information to patients under age 24?

A. No.

Q. And is the paroxetine label, the language with respect to the warnings and precautions for suicidality in the 2010 label, is that still in the label today?

A. Yes, it is.

MR. BAYMAN: Take that down, please.

(Brief pause).

BY MR. BAYMAN:

Q. From the paroxetine clinical trial data, is there an association between paroxetine and completed suicide in adult patients of any age?

A. No.

Q. From the paroxetine clinical trial data is there an association between paroxetine or Paxil in definitive suicidal behavior or ideation in adult patients of any age?

A. No.

Q. From the paroxetine clinical trial data is there an association between paroxetine or Paxil in suicide attempts in adult patients over age 24?

A. No.

Q. In 2007 when GSK asked FDA for permission to include the Paxil-specific warning about a possible risk of suicide attempts in young patients, what was FDA's response?
A. FDA did not allow us to use Paxil-specific language; so, no.
Q. We talked on Thursday about GSK's reanalysis of the NDA clinical suicide attempts and suicides that was done in 2002, do you recall that?
A. Yes.
Q. Was that the apples to apples analyses?
A. That's correct. The placebo-controlled portions.
Q. I meant to ask you, and I think I neglected, were these analysis submitted to FDA?
A. Yes.
Q. Please turn to Tab 52, which is Defense Exhibit 40.
Are you familiar with that document?
A. Yes.
Q. Is that a document drafted by GSK in the ordinary course of business?
A. Yes, it was.
Q. Has it been maintained by GSK in the ordinary course of business?
A. Yes.
Q. Is that part of the GSK regulatory Paxil -- regulatory file for Paxil that you reviewed as part of your job

responsibilities?
A. Yes, it is.
Q. Does this document indicate that GSK did, in fact, submit the reanalysis to the FDA in February of 2003?
12:18:27 A. Yes. That's the topic of this note, is to submit that data and describe that we're doing it.
MR. BAYMAN: At this point, Your Honor, I would move for admission of Defense Exhibit 40.
MR. WISNER: Object again, your Honor; hearsay. I
12:18:43 don't think there's any dispute as to whether or not they submitted that analysis to the FDA. This includes a much regulatory material, and, in fact, duplicates those reports which are already in evidence as Plaintiff's Exhibit 122 and 129.
12:18:55 THE COURT: You dispute that that was submitted?
MR. WISNER: No, we don't.
THE COURT: Okay. That covers it. It need not be received in evidence.
BY MR. BAYMAN:
12:19:04 Q. 6 months later, in August of 2003, what correspondence took place between GSK and FDA with respect to a new indication for Paxil or paroxetine?
A. It was an approval. I can't remember the indication actually, but --
12:19:24 Q. Do you recall it was PMDD?

A. Yes, premenstrual dysphoric disorder. This was an approval for acute treatment of that.
Q. To be approved to be used for -- for Paxil to be used for PMDD --
12:19:45 THE COURT: Why do we have to look into PMDD?
MR. BAYMAN: I'm not going into PMDD. I'm just going to ask him one question.
BY MR. BAYMAN:
Q. To be approved for that indication 6 months after GSK had
12:19:54 submitted the reanalysis of the adult suicidality data that we've looked at, did GSK have to demonstrate that Paxil was safe and effective?
A. Yes.
Q. And did GSK approve Paxil for safe and effective for PMDD
12:20:10 in August of 2003 after it had received the reanalysis of the adult suicidality data?
MR. WISNER: Objection. GSK doesn't approve anything.
THE WITNESS: I would clarify FDA-approved.
THE COURT: Objection is sustained.
12:20:23 MR. BAYMAN: Sorry.
BY MR. BAYMAN:
Q. Did FDA approve Paxil for the PMDD?
A. FDA approved, yes.
Q. 6 months after GSK submitted the re-analyses of the Paxil
12:20:35 adult suicidality data?

A. That's correct.
Q. Now, Doctor, one topic that the jury has heard about is clinical trials. And I want to ask you, they've heard the phrase central or centrally funded studies and local or locally
12:20:50 funded studies. Are you familiar with those terms?
A. Yes.
Q. Can you explain the difference?
A. Yes. It's a fairly simple concept. The centrally funded trials are those studies that are supported by global GSK in
12:21:09 its legacy companies. These are studies that are typically done for the registration or approval of a medicine for a specific indication.

So, these are usually the larger placebo-controlled studies, as well as the safety studies. And we call them
12:21:27 central because they support filings and submissions throughout the world.

Locally, LOC, or local operating company studies are studies that are specifically done in a country sometimes for a specific reason, a question of locally or something important
12:21:45 for understanding in that regulatory environment, usually smaller studies and not necessarily a part of the support for registration and approval of the drug in terms of those pivotal studies I discussed earlier.
Q. Has the difference between central studies and local
12:22:06 studies come into play when analyzing data from different types

of studies?
A. Yes. The thing about the central studies is we use a consistent set of data standards, such that they -- do you remember we talked about the integrated summary of safety and
12:22:21 efficacy, so you can combine that information in order to make collusions about the compound. Local operating companies may use distinct data standards, making it difficult to pool.
Q. Does GSK collect adverse information from both central and local studies?
12:22:40 A. Yes.
Q. Now, isn't it a problem that you don't have every bit of data collected centrally?
A. No, not necessarily.
Q. Does GSK make information about both central and local
12:22:52 studies public?
A. Yes, we do, on our clinical trial register.
Q. Does GSK post both results of both central and local studies on the clinical trial register on the website?
MR. WISNER: Objection; relevance.
12:23:06 MR. BAYMAN: Dr. Ross got into this, Your Honor, about why certain studies were included or not included.
MR. WISNER: They're talking about posting it on the Internet, I'm not entirely sure that has any relevance to this case.
12:23:18 THE COURT: Sustained as to posting.

BY MR. BAYMAN:
Q. Are there other -- still other categories of clinical trials that GSK has some relation to?
A. Yes.
12:23:28 Q. Tell the jury about those.
A. These can include investigator-initiated studies, they can include database type studies where we look at observational data, things like that.
Q. Are there studies where GSK provides the medicine for the
12:23:48 study?
A. Yes. At times we have request for supply of medicine usually from investigators, but it can be a wide number of people, including, for example, different -- hospital labs for standards so they can look into overdose, things of that
12:24:08 nature, and we get requests for drug supply.
Q. And what rights does GSK have to the data when it just provides the product but doesn't conduct the study?
A. We don't own that data. That's the accountability of the investigator, the person using the compound.
12:24:24 Q. The jury has heard the term investigator-initiated study. How does the fact that a studies investigator initiated affect the data that GSK is able to collect?
A. So investigator-initiated study, and I've done some of these when I was an investigator was, it's your idea, your
12:24:42 concept, your protocol. You might ask for drug supply or other

support to do those studies, but you are the sponsor, you are accountable for the study, you are accountable for the conduct, the safety of the patients in those studies, and for the ethics review, all of that.

12:25:01 Q. Does GSK get adverse-event data from these investigator-initiated studies?

A. Yes, for these studies we ask if there's a serious adverse event that would be reported to us.

Q. Does it get all the rest of the data, such as the data on

12:25:17 efficacy or effectiveness?

A. No, we typically do not get the raw data files or what you would call the statistical analysis datasets. We usually require a summary report or a publication.

Q. You said you did, as an investigator, you did some of these

12:25:34 investigator-initiated studies?

A. Yeah.

Q. Just tell the jury about how one goes about doing it and what kinds of things you were looking to study.

A. So, the one I worked on was actually a GSK supported one

12:25:47 where I was examining something called post-psychotic depression and schizophrenia. In the first episode, the first time a patient has a psychotic break in schizophrenia, they have a high risk of depression. And we had a question as to whether the metrogene, which has had efficacy in bipolar

12:26:11 depression, may help prevent that. So, we conducted a study to

look at that.
Q. And did you ask the company to provide medicine?
A. Yes.
Q. Does GSK consider investigator-initiated studies to be GSK
12:26:23 studies?
A. No, they're the responsibility of the investigator.
Q. And why is that?
A. Again, it's the investigator's protocol, the investigator site patients, it's the investigator's data analysis. It's in
12:26:38 their control.
Q. Does GSK maintain a clinical trial registry of all the clinical trials that it has conducted, the company has conducted on Paxil?
A. That the company has conducted, yes.
12:26:50 Q. Are investigator studies on that clinical trial registry?
A. No.
Q. Why not?
A. Again, we don't own that data. That is the data of the investigator.
12:27:04 Q. I want to ask you about two particular studies the jury has heard about. Are you familiar with studies 513 and 559?
A. Yes, those are investigator-initiated studies.
Q. Are either of those studies on GSK's clinical trial register?
12:27:16 A. No, they are not.

Q. Did any of GSK employee participate in any aspect of conducting these studies?
A. No.
Q. Did GSK provide any money so that the studies could be done?
A. No, not that I'm aware.
Q. Did GSK completely ignore these studies?
A. No. Again, serious adverse events, if they were to occur in the studies, would be reported to the company.
Q. Are you aware that a suicide occurred in each of these studies?
A. Yes, I believe that's true.
Q. Did GSK report each of these suicides to the FDA?
A. Yes, they would be reported as serious adverse events and that's why we know about them.
Q. Were these studies part of GSK's 2006 analysis?
A. No, they were not.
Q. Why not?
A. For the reason that they were out of scope. They were not sponsored-initiated studies. We did not have the datasets and they were not in our data format. So, they did not meet the criteria for inclusion.
Q. Were these suicides part of the FDA's analysis in 2006?
A. No.
Q. Why not?

A. For the same reason, the FDA requested sponsor studies, meaning GSK and other company studies. So it wouldn't fall under that requirement.

Q. Did GSK make the FDA aware that these type of studies were not included in GSK's submission of data to the FDA?

A. Yes.

Q. Now, do you have any concern that not including investigator-initiated studies somehow makes the results of the GSK and the FDA 2006 adult suicidality analyses any less reliable?

A. No.

Q. Has GSK ever done an analysis of deaths in clinical trials that included both central and local studies?

A. Yes, I believe so.

Q. Do you recall when that was done?

A. I want to say 1999.

Q. Did you review that data as part of your work in assuming responsibility for the Paxil program?

A. I did.

Q. Can you tell us how that analysis in 1999 came about?

A. This was a request by FDA to look at all deaths occurring in clinical trials for certain conditions, and depression was one of them. Looking at both placebo-controlled studies and active-controlled studies to ascertain, in part, whether patients on placebo for diseases that could have significant

outcomes as part of their disease--for example, suicidality--whether they could be at an increased risk of going on placebo and not receiving treatment.

THE COURT: Are you about finished?

12:29:56 MR. BAYMAN: No, sir. I got a little bit more to do. You want to take a break?

THE COURT: Okay. We'll take the luncheon break, ladies and gentlemen.

(The following proceedings were had out of the presence of the jury in open court:)

12:30:23 [redacted]

(Luncheon recess taken from 12:30 o'clock p.m. to 1:30 o'clock p.m.)

* * * * * * * *

I CERTIFY THAT THE FOREGOING IS A CORRECT TRANSCRIPT FROM THE RECORD OF PROCEEDINGS IN THE ABOVE-ENTITLED MATTER

/s/Blanca I. Lara April 10, 2017