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,	March 23, 2017
Defendant.	9:20 o'clock a.m.

VOLUME 7 A
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART

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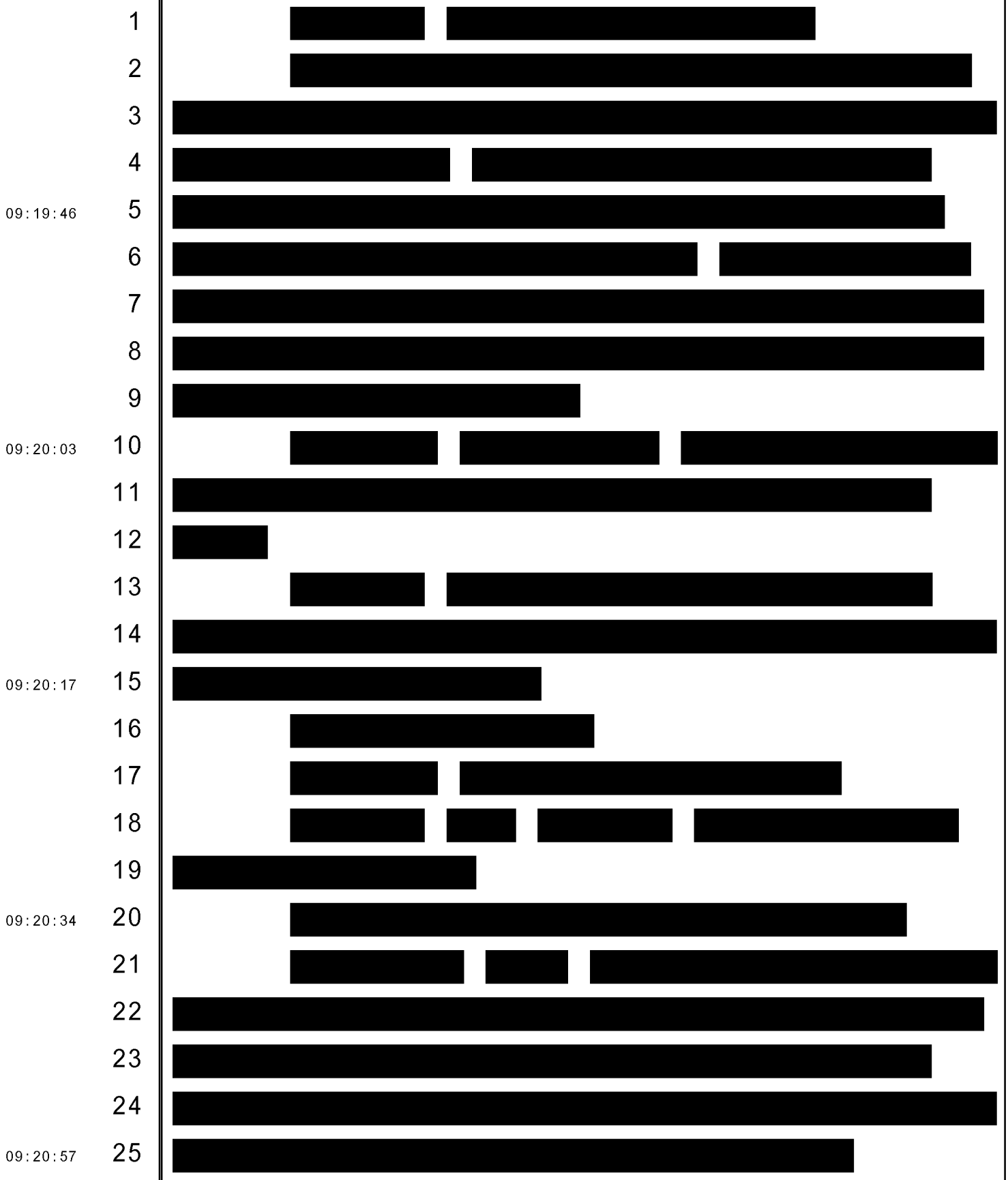
(The following proceedings were had out of the presence of the jury in open court:)

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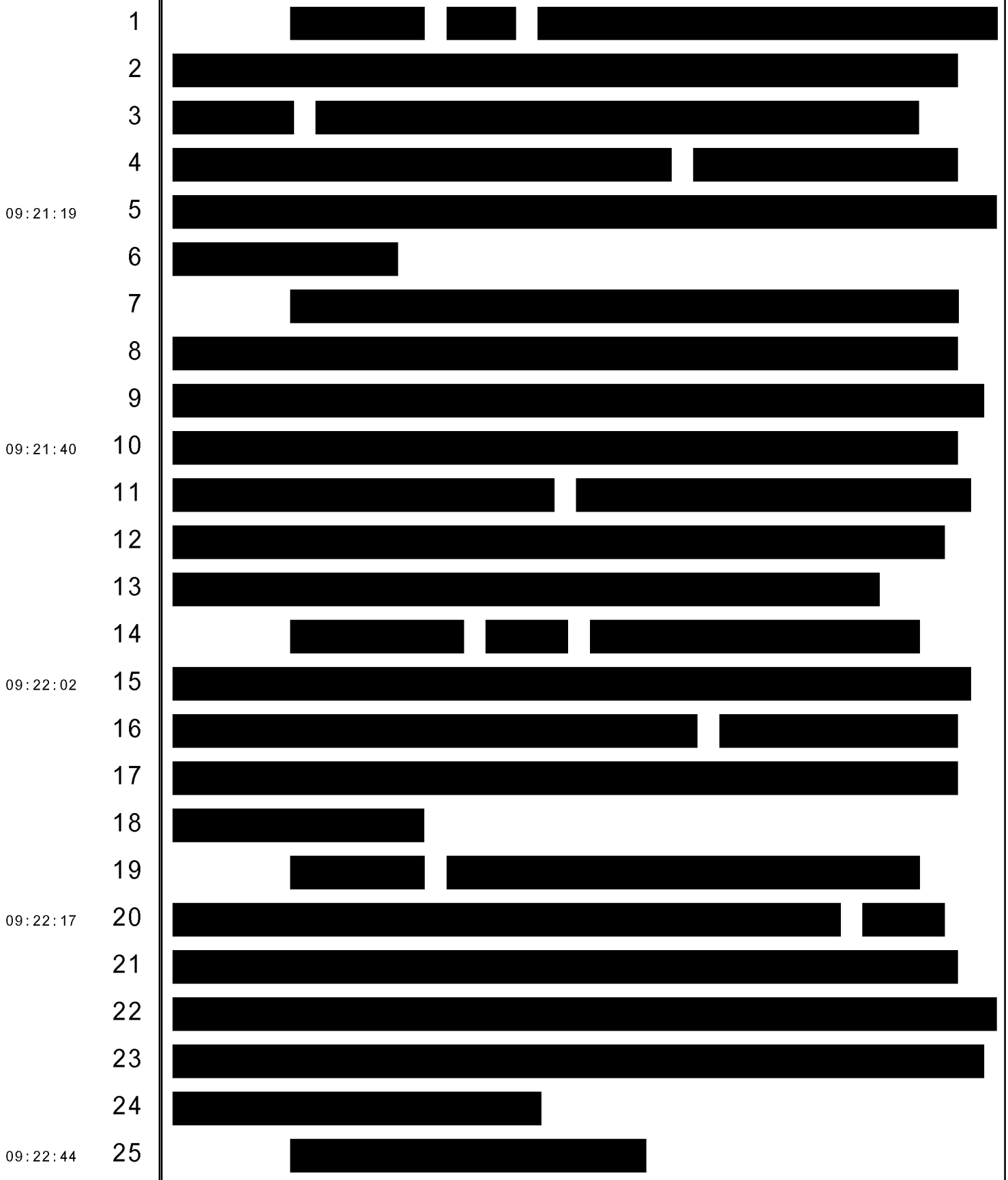
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(The following proceedings were had in the presence of the jury in open court:)

09:26:24 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.

09:26:31

DAVID ROSS, PLAINTIFF'S WITNESS, PREVIOUSLY SWORN

CROSS EXAMINATION

BY MR. BAYMAN:

Q. Good morning, Dr. Ross.

09:26:36 A. Good morning.

Q. When we finished up yesterday, we were talking about the January 2005 label, which is Joint Exhibit 6. And we had talked --

MR. BAYMAN: Let's go ahead and put that up, please.

09:26:46 BY MR. BAYMAN:

Q. We had talked about the warning section and the clinical worsening and suicide risk section, do you recall that?

A. Let me just turn to that tab.

Q. Sure.

09:27:03 A. Thank you.

(Brief pause).

BY MR. BAYMAN:

Q. That's Tab 9 in your notebook.

(Brief pause).

09:27:17 BY THE WITNESS:

A. Yes.

BY MR. BAYMAN:

Q. Can you look at the second page, second full paragraph.

A. I'm sorry, were you talking about the letter or the label?

09:27:31 Q. Label.

A. Okay.

(Brief pause).

BY THE WITNESS:

A. Under "precaution section" -- oh, okay.

09:27:47 BY MR. BAYMAN:

Q. You got it?

A. Yes.

Q. We had talked about yesterday the list of symptoms that were listed and I want to call your attention to this

09:28:06 paragraph, at the end of the warning that says:

"Adults with MDD or comorbid depression in the setting of other psychiatric illness being treated with antidepressants should be observed similarly for clinical worsening and

09:28:22 suicidality, especially during the initial few months of a course of drug therapy, or a times of dose changes, either increases or decreases."

Do you see that?

A. I do.

09:28:33 Q. Is it your testimony that this language added on the other suicide-related language does not alert doctors to the risk of suicidality especially during the early few months of taking Paroxetine?

A. It doesn't do so for Paxil. It simply says it for all

09:28:52 antidepressants. And it does not aid prescribers in saying,

how do I treat this with a patient with depression. Again, this is not like, "I've seized on Paxil or some other drug, now I want to know how to use it."

Q. Well, Doctor --

09:29:09 A. Adequate directions for use, this is what it's all about for the drug, not disease management, which is what we've got here.

Q. Doctor, when a physician goes to look at the Paxil label, the label clearly tells them the drug is Paxil, correct?

09:29:25 A. It does.

Q. Right?

I mean, it says it right there on the label, right?

So a doctor presumably reading the Paxil label will know this is about Paxil, correct?

09:29:36 A. Oh, you mean it doesn't say on the -- I'm sorry, I misunderstood. You mean it doesn't say on the label "antidepressant."

Q. No, it says at the top of the label "Paxil," correct?

MR. BAYMAN: Could we have the top of the label. Blow

09:29:52 it up, please, up at the top.

(Brief pause).

BY MR. BAYMAN:

Q. Right?

A. It doesn't just say, generically, "antidepressant."

09:30:00 Q. Right.

A. Okay.
Q. So a doctor would know that this warning applies to Paxil, correct?
A. But it's actually not -- does not include information about Paxil that was known to GSK at the time of this label. It does not apply.
09:30:13
If you're going to say, we're going to have a generic warning in here, then you need -- "generic" not in the sense of generic drugs but just kind of a general warning here, then we should change this to "antidepressant manufactured by GSK." Right? You've got specific language here, you need to have, if you have the information, specific language there, including the data.
09:30:32
Q. Despite the fact that this section is class labeling, it's the same language for every SSRI and antidepressant, correct?
09:30:49
A. As I've said earlier, and as I put in my report, there's no bar to putting product-specific information in a label outside the class labeling section.
And if somebody can point me to a section of either the Food, Drug and Cosmetic Act or the regulations that says you can't, I would be very happy to reconsider my opinion.
09:31:10
Is that in one of the future exhibits?
THE COURT: Don't ask questions, doctor. You get to answer them, he gets to ask them.
THE WITNESS: I'm sorry, Your Honor.
09:31:27

BY MR. BAYMAN:
Q. Did you have a chance to talk to plaintiff's counsel after your testify yesterday?
A. Did I have a chance -- we discussed the fact that I needed
09:31:35 to stay an additional day, that was the extent of our conversation.
Q. You didn't talk about your testimony?
A. Not at all. Not at all.
Q. All right. There is another section I want to show you in
09:31:45 this same label and it's the precaution section.
So could you please turn to page 6 of that document.
A. Yes.
(Brief pause).
BY MR. BAYMAN:
09:32:00 Q. You see the section entitled Clinical Worsening and Suicide Risk?
A. Yes.
MR. BAYMAN: Could you blow that up, please.
BY MR. BAYMAN:
09:32:10 Q. It says:
"Patients, their families and their caregivers should be encouraged to be alert to the emergence ..."
and it gives a list of symptoms that talked about
09:32:21 yesterday, correct?

A. Yes.
Q. Including agitation and akathisia, correct?
A. Yes.
Q. And it says:
09:32:27 "... they should be alert for unusual changes in behavior, worsening of depression, and suicidal ideation."
Correct?
A. Yes.
09:32:35 Q. And then starting in the middle of the bottom line on the page continued to the top of the next page it says:
"... symptoms such as these may be associated with an increased risk for suicidal thinking and behavior and indicate a need for very close
09:32:53 monitoring and possibly changes in the medication."
Did I read that correctly?
MR. WISNER: Objection; argumentative. He's shouting at the witness.
09:33:03 THE COURT: Overruled.
He may answer.
Don't shout.
MR. BAYMAN: Yes, sir.
(Brief pause)
09:33:38 THE WITNESS: Your Honor, I apologize. Could I have

the last question?

THE COURT: Question back?

THE WITNESS: Please.

THE COURT: Yes.

09:33:43 Read it back.

(Question read.

BY THE WITNESS:

A. Yes, you did.

BY MR. BAYMAN:

09:34:07 Q. Okay. Do you maintain the opinion you gave yesterday that this label, with the language that says "symptoms like akathisia may be associated with increased risk for suicidal thinking," does not adequately warn doctors of the risk of suicidality?

09:34:25 A. Well, I would say it's not just physician, but it's also patients. Let me support that --

Q. No, I just asked -- I said doctors. It's a very simple question.

A. I apologize. I'm maintaining that testimony, yes, sir.

09:34:38 Q. That this doesn't adequately warn of the risk of suicidality?

A. Correct.

Q. Okay. All right, I want to move you forward to 2006.

You know in 2006 GSK analyzed the available clinical

09:34:55 trial data on adults and suicidality regarding Paxil, correct?

A. Yes.
Q. And the FDA did an analysis of the Paxil adult suicidality data, as well as suicidality data for other antidepressants, correct?
09:35:12 A. From those sponsors who did submit it to the FDA.
Q. Turn, if you will, to -- well, turn to tab -- Tab 10.
MR. BAYMAN: Which is DX101, Your Honor.
(Brief pause).
BY MR. BAYMAN:
09:35:39 Q. This is GSK's March 8, 2006, submission to the FDA, correct?
A. Yes.
Q. And the jury has seen this before with Dr. Healy.
MR. BAYMAN: May I have permission to publish?
09:35:51 THE COURT: Yes.
MR. BAYMAN: Thank you.
(Exhibit published to the jury.)
BY MR. BAYMAN:
Q. And you're familiar with this submission, correct?
09:36:00 A. I have -- excuse me. I'm sorry.
I have reviewed the analysis that the company provided to the FDA.
Q. Okay. Let's go to the cover letter for the submission.
Do you see it's dated March 8, 2006?
09:36:16 A. Yes.

Q. All right. Can you look at the first paragraph, second sentence.

MR. BAYMAN: Blow that up, please.

BY MR. BAYMAN:

09:36:27 Q. This just says that GSK is responding to the FDA's request and providing the clinical trial data from double-blind randomized placebo-controlled studies in adults with major depressive disorder, correct?

A. Yes.

09:36:46 Q. Okay. And if we go down to the second paragraph, it says:

"GSK has recently completed the first portion of a comprehensive meta-analysis to evaluate the risk of suicidality in adult patients treated with Paroxetine in placebo-controlled trials and

09:37:07 in this submission we're providing the results of the first portion of this meta-analysis which is of trials of patients with MDD."

Do you see that?

A. Yes.

09:37:14 Q. And GSK's analysis reflected in the report mirrored what FDA asked of it, which was to look at randomized, double blind placebo-controlled trials, correct?

A. I would say that -- say that the analysis was performed on the data set, as far as FDA could tell, that it had requested.

09:37:51 Q. And in response to Mr. Wisner's questions on direct

examination, you focused on one specific outcome from this 2006 analysis, that is, the analysis related for suicide attempts in adults with major depressive disorder, correct?

A. I focused on the most important outcome.

09:38:14 Q. That is the -- and, in fact, that's the only finding that you considered to be a positive finding concerning GSK's 2006 adult suicidality analysis, the 6.7 odds ratio that you told the jury about, correct?

A. The 6.7 that was the confidence interval that didn't cross

09:38:43 1, meaning that it was real.

Q. My question was, that's the only positive finding, correct?

A. Yes, sir.

Q. Okay. Other than the 6.7 finding with respect to the secondary analysis of definitive suicidal behavior, you're not

09:39:05 aware of anything in GSK's 2006 adult suicidality analysis that would meet the definition of reasonable evidence of an association between the use of Paxil and suicidality that would warrant a label change, correct?

THE WITNESS: Your Honor, could I have that question

09:39:24 read back.

THE COURT: Yes, read it back, please.

(Question read.)

BY THE WITNESS:

A. Well, the answer to that is yes, I am, but more

09:39:59 importantly, as I said to your colleague 2 years ago, that's a

little bit like saying, "aside from that, Mrs. Lincoln, how did you enjoy the play."
BY MR. BAYMAN:
Q. Okay. I just -- simple question: Is there anything else
09:40:12 in this analysis that, in your opinion as a regulatory expert, would meet the definition of a reasonable evidence of an association between the use of Paxil and suicidality that would warrant a label change?
A. Yes.
09:40:25 Q. Okay. Can you turn to your deposition, page 275, Line 7.
A. I'm not sure if I have it, but --
Q. You don't have it?
A. I apologize. I don't think I have it here.
Q. Sure. I have a copy.
09:41:01 (Binder tendered to the witness).
BY THE WITNESS:
A. Thank you, sir.
(Brief pause).
BY MR. BAYMAN:
09:41:13 Q. Can you turn to page 275, Line 7.
A. Yes.
Q. You were asked:
"And other than the 6.7 finding with respect to the secondary analysis of definitive suicidal
09:41:32 behavior, you're not aware of anything in GSK's

2006 adult suicidality analysis that would meet the definition of a reasonable evidence of an association between use of Paxil and suicidality that would warrant a labeling change."

09:41:48 And your enhance was:

"... with the caveat that it's a little misleading to talk about primary and secondary end points, because these are all analyses that have been conducted after the trials were

09:41:58 completed and were not part of the original perspectively planned end points, yes, I agree with that."

Did I read that correctly?

A. Ah, hang on one second here.

09:42:22 (Brief pause).

BY MR. BAYMAN:

Q. I just asked if I read it correctly.

A. No. No, I understand. I actually want to make a point that --

09:42:32 THE COURT: No, Doctor, at this point your lawyer will get a chance to ask you further questions.

THE WITNESS: I understand Your Honor, yes.

THE COURT: But at this point you have to answer whether he did or did not correctly read the deposition.

09:42:43 BY THE WITNESS:

A. Yes, you did.
BY MR. BAYMAN:
Q. And on the primary endpoint of definitive suicidal behavior and ideation, there was no statistically significant difference between adults with MDD treated with Paroxetine compared to placebo, correct?
09:42:55
A. There was a 30 percent increase, statistical significance is not required, and that's the additional evidence that I'm talking about, now that I've got that first bullet on this cover letter in front of me, which you, I'm sorry, you are not displaying right now.
09:43:11
MR. BAYMAN: All right. Let's put up first paragraph.
(Brief pause).
BY MR. BAYMAN:
Q. That's the bullet you're talking about?
09:43:24
A. That is the one that says there was no statistically significant difference. It does not say there was not reasonable evidence of association.
Q. All right. I want to turn you, if you would, to Tab 11.
09:43:49
MR. BAYMAN: Which is Defense Exhibit 103, Your Honor. That's the cover letter and briefing document that GSK sent to FDA.
(Brief pause)
MR. BAYMAN: Your Honor, that's in evidence. May I
09:44:10
publish?

THE COURT: You may.

MR. BAYMAN: Thank you.

(Exhibit published to the jury.)

BY MR. BAYMAN:

09:44:25 Q. You're familiar with that document, correct?

A. I believe this is the analysis referred to in the cover letter that we were just discussing, if I'm not mistaken.

Q. Well, actually this is the updated.

A. I apologize. Yes.

09:44:38 Q. Which included trials beyond MDD, correct?

A. That is correct.

Q. If you turn to page 6 of the briefing document, which is attached to the letter.

MR. BAYMAN: Let's go ahead and put that up.

09:44:56 (Brief pause).

BY MR. BAYMAN:

Q. Let's pull up the first bullet, please.

(Brief pause).

BY MR. BAYMAN:

09:45:18 Q. That's the same finding that was reported on previously, correct?

A. That was the --

Q. The MDD.

A. The one that we were just discussing and the cover letter.

09:45:31 Q. Right.

Turn to page 7, if you would. The footnote at the bottom of the page.

Do you see that?

A. Yes.

09:45:43 Q. There was not a single completed suicide in any of the clinical trials that made up this analysis, correct?

A. I disagree with that statement.

Q. You disagree with that statement?

A. I do.

09:45:56 Q. What suicide and from what trial are you referring to?

A. Study 83, which was a randomized placebo-controlled study, which I believe -- I can't remember which defense exhibit it's in, but I believe it's Defense Exhibit 25. There was a death attributed to suicide by hanging in a 58-year old woman that

09:46:23 was fatal.

Q. Was that a -- did that happen during the controlled portion of the placebo-controlled trial?

A. I believe so.

Q. Well, we'll talk about that later.

09:46:36 Turn to page 8, if you would.

A. Okay.

Q. Do you see that GSK also examined the same primary outcome, definitive suicidal behavior ideation with patients other than major depressive disorder, right?

09:47:02 A. Yes.

Q. And GSK reported:

"... in placebo-controlled trials and psychiatric disorders other than MDD, there was no evidence of an increased risk of suicidal behavior or ideation ..." and then it says "primary endpoint" in parenthesis "... in patients treated with Paroxetine."

Correct.

A. That's what the text says. I don't agree with it.

09:47:29 Q. Let's look at table 2.08, which is page number 214 and 215.

Do you see that?

A. Yes.

Q. This is a presentation of the data on the primary endpoint suicidal behavior and ideation by age group, among other

09:47:59 factors, correct?

A. No. No, I'm sorry. As I made the point to your colleague 2 years ago, this was not a perspectively planned clinical trial.

The term "endpoint" and "primary endpoint" is not

09:48:14 correct here. This is a look at the data that have already been collected. The term "endpoint" should not be applied here. And as I said in my deposition, these studies were not designed to assess safety.

Q. Well, it's not the endpoint of the study, it's the endpoint

09:48:31 of the analysis, correct?

A. Sir, I am -- don't need to get into a debate over semantics, but calling it an endpoint says this is -- there's no prespecified hypothesis here. This does not meet the requirements to call something an endpoint and draw those kind of conclusions from it.

Q. So you disagree with the FDA when they used the term "primary endpoint," I take it?

A. Sir, I'm not responsible for what they did.

Q. Do you disagree with them when they use that term, then?

A. I am just disagreeing with your use of it.

Q. Okay. This is the presentation of the data looking at suicidal behavior and ideation by age group, among other factors, correct?

A. Yes.

MR. BAYMAN: Can you blow that up further. Blow up the first one, please, at the top.

(Brief pause).

BY MR. BAYMAN:

Q. So there are two different, slightly different analyses. This one is for all indications, correct?

A. Yes.

Q. Okay. And the other one --

A. I'm sorry, this appears to be "for all," I apologize. For all depression.

Q. I'm sorry, all depression.

And the other one is for all indications, correct?
A. Yes.
Q. And for adults ages 25 to 64 in the chart, there was no association between Paroxetine and definitive suicidal behavior and ideation for all indications, correct?
09:50:13
A. With the caveat that this is completely different result than the company published in 2011, I agree that's what that text there says.
Q. And, in fact, there was a protective effect with an odds ratio of .7 for Paroxetine, albeit not quite statistically
09:50:31
significant, correct?
A. No, sir, that does not meet the criteria for protective effect. You're getting into causation here. This does not in no way, shape, or form qualify as a protective effect. No ifs, no ands, no buts.
09:50:51
Q. And we can see that there were 59 events out of 7543 Paroxetine patients, correct?
A. If you could just show me where you are getting that number, that would be helpful.
Q. We're going to get it right now.
09:51:10
(Brief pause)
MR. BAYMAN: Blowing it up right now.
BY MR. BAYMAN:
Q. See that 59 over 7543?
A. Yes.
09:51:35

Q. And there were on placebo, right next to it, there were 57 events out of 5,000 placebo patients. So basically the same number of events, even though there were 2500 more patients in the Paroxetine group, correct?

09:51:53 A. Just to be clear, that 59, does that include the woman in study 83 who killed herself? I just want to clarify.

MR. BAYMAN: Your Honor, I move to strike that. That was a gratuitous comment.

THE COURT: Sir, if you can't answer the question, you

09:52:10 say I can't answer.

THE WITNESS: I'm sorry, Your Honor.

THE COURT: You can't ask questions of the examiner.

THE WITNESS: I apologize and I will try and refrain from doing so.

09:52:17 BY THE WITNESS:

A. I apologize, Mr. Bayman. That is what the text says.

BY MR. BAYMAN:

Q. And similarly, in the other chart, which is for all depression for adults ages 25 to 64, the odds ratio was also

09:52:37 .7?

A. That's what the text here says.

Q. And that's not significant, is it?

A. (No response.)

Q. It's not statistically significant, is it?

09:52:52 A. Well, to answer your question, in terms of those -- you

want to say this is a comparative safety claim, that did not represent substantial evidence.
Q. Is it statistically significant?
A. It's not powered to be statistically significant, no.
09:53:07 Q. But it is a -- it shows a protective effect, does it not?
A. No, I disagree. Protection implies causation, and there's no evidence here for that.
Q. Now, you're not here criticizing using statistical significance, are you?
09:53:25 A. In what context are you -- I'm sorry for asking a question. I'm just trying to clarify. That's a very broad term.
Q. Looking at statistical significance when analyzing clinical trial is an appropriate methodology, is it not?
A. In some instances, yes; in other instances, it's not
09:53:45 necessary; in other instances where you use the wrong techniques, it can actually obscure things or give you a false positive.
Q. In GSK's analysis, in 2006, it did not show -- neither GSK's analysis nor FDA's analysis did not show a statistically
09:54:07 significant in increase risk of completed suicides following the use of Paxil or Paroxetine, correct?
A. With the caveat that these underlined studies were not designed or powered to do so and could not have unless you have a very big effect, I'd say yes.
09:54:26 Q. You didn't show the jury, during your direct examination,

the results on the primary outcome measure, did you?
A. Well, I didn't show anything. It was Mr. Wisner who was putting up exhibits.
Q. Okay. You agree that looking at the primary outcome of
09:54:48 definitive suicidal ideation or behavior in this analysis, that that is not reasonable evidence of an association, correct?
THE WITNESS: Your Honor, could I ask that that be read back?
THE COURT: Yes.
09:55:00 Read it back.
(Question read.)
BY THE WITNESS:
A. The conclusion about reasonable evidence and association is it not based on any one issue. I would say this is actually
09:55:35 consistent with reasonable evidence of an association. And again, this gets to the power issues that we've been discussing.
BY MR. BAYMAN:
Q. Okay. Can you turn in your deposition to page 274,
09:56:03 Line 14.
A. Yes.
Q. You were asked:
"... well, did you agree that looking at the primary endpoint of definitive suicidal ideation
09:56:18 or behavior in this GSK's analysis, that is not

reasonable evidence of an association."

Do you see that?

A. Yes, sir.

Q. There was an objection. And then you said:

09:56:32 "That is not reasonable evidence."

A. No, sir, that is not what I said.

Q. I'm going to keep reading.

A. Please. Actually, first off, I said that is not reasonable evidence. I was actually attempting to get clarification.

09:56:46 Q. Okay. I'm going to keep reading.

A. Please. Go ahead.

Q. (Reading:)

"I'm sorry, Mr. Davis, I'm really not trying to make your life more difficult here, I'm just --

09:56:57 I'm thinking about the -- the parsing of that. What I would say is that it does not represent by itself reasonable evidence of an association, fair."

Did I read that correctly?

09:57:08 A. You did.

Q. Okay. All right. Now, when the FDA did its analysis of the suicidality data for Paxil and other antidepressants, that was later in 2006. It released the results in November of 2006, correct?

09:57:23 A. I believe that's correct.

Q. Okay. Turn in your book to Tab 7.

MR. BAYMAN: Which is Joint Exhibit 13, Your Honor, already in evidence.

(Exhibit published to the jury.)

09:57:36 BY MR. BAYMAN:

Q. You're familiar with this analysis, correct?

A. This is the Stone/Jones analysis, yes.

Q. And Dr. Stone and Dr. Jones were with the FDA, correct?

A. Yes.

09:57:48 Q. All right. And if we look at the first page, we see that the FDA analyzed data involving 11 different antidepressants, correct?

A. Data on 11 different antidepressants.

Q. And turn to page 6, that Section 1.2. It's called Review Content.

09:58:07 A. Yes.

Q. The FDA stated the following about its methodology for undertaking the analysis:

"This review examines the relationship between antidepressant drugs and suicidality in adult subjects, as assessed within randomized, placebo-controlled trials for various indications."

09:58:21 Did I read that correctly?

09:58:32 A. You did.

Q. So the FDA was looking only at randomized placebo-controlled trials, correct?
A. For purposes of this analysis, yes, that's correct.
Q. Look at page 24, table 15.
09:58:50 MR. BAYMAN: Blow that up, please. Could we get the top of the heading of the table.
(Brief pause)
BY MR. BAYMAN:
Q. See that FDA:
09:59:07 "... in looking at suicide risk for active drugs relative to placebo, ideation or worse, adults with psychiatric disorders by drug and drug class."
Did I read that correctly?
09:59:20 A. Yes.
Q. And that is the primary outcome measure of this analysis, correct?
A. That is what FDA, I guess, said was, the quote, the primary endpoint for this analysis.
09:59:31 Q. And we see, in this table, FDA found there was no increased risk for suicidal ideation or behavior when the data from all the SSRIs or antidepressants was analyzed, correct?
MR. WISNER: Objection, Your Honor, misstates the document. This is not FDA, this is Stone and Jones.
09:59:50 MR. BAYMAN: They work for the FDA, Your Honor.

Sorry.

THE COURT: Proceed.

BY THE WITNESS:

A. So you're correct, compared to the following table where it shows an odds ratio of 2.76, this particular analysis does not show an increased risk.

BY MR. BAYMAN:

Q. And FDA did a subgroup analysis for each SSRI or antidepressant on the primary outcome, correct?

A. Again, I'm going to -- well, never mind. Go ahead, please. They did do a subgroup analysis, yes.

Q. And in the fifth line we see Paroxetine, which is Paxil, correct?

A. Yes.

Q. So you would agree with me that on the primary endpoint for this analysis, that there was no increased risk of suicidal thoughts or behavior for patients taking Paxil or Paroxetine, correct?

A. Actually, what I would say is, a subgroup analysis of Paroxetine, or any other of the SSRIs, was not a primary endpoint.

This is a secondary subgroup analysis. So this is not a primary endpoint with respect to Paxil. They were only looking at a class effect. So you cannot draw any conclusions and say, "well, if they only looked at Paxil alone," perhaps

you could say that, but this was not -- this was a across all antidepressants.

Q. But the primary endpoint was the question they were asking, was suicidality risk for active drugs relative to placebo, ideation or worse, in adults with psychiatric disorders, correct?

10:01:32

A. This is a subgroup analysis. And I published on this topic. This is a great way, a classic technique for either finding something you want to demonstrate by inflating the false positive rate or obscuring something by considering it in isolation. So no, I do not agree with that.

10:01:54

Q. Okay. Turn in your deposition, if you would, to page 284, Line 23.

(Brief pause).

BY MR. BAYMAN:

10:02:33

Q. Are you with me?

(Brief pause).

BY THE WITNESS:

A. Yes, I'm there.

BY MR. BAYMAN:

10:02:42

Q. The question was:

> "... you are agree that on the primary endpoint for the analysis, that there was no increased risk of suicidal thoughts or behavior for patients taking Paxil or Paroxetine, correct?"

10:02:54

And then it says:

"Look at table 15, Doctor."

And your answer was:

"That's what I was going to do, I was looking for."

And then:

"That is correct."

Did I read that accurately?

A. Yeah. I mean, I would agree, that is what it says here, that's the text. I agree with you.

But you asked me a different --

I'm sorry, Your Honor.

BY MR. BAYMAN:

Q. And GSK's analysis and the FDA -- GSK's analysis didn't show -- strike that.

The FDA's analysis did not show a statistically significant increased risk of completed suicides following the use of Paxil or Paroxetine, correct?

A. With the caveat -- with the caveat that it was not designed to, and, in fact, it would've been almost impossible to show that given the design of the trials, yes.

Q. And FDA's analysis found there was an age-related effect when it came to SSRIs and other antidepressants, correct?

A. There was a table in which they analyzed showed analyses for individuals 18 through 24, I believe, if that's what you're

referring to.
Q. Well, what I'm referring to is for adults -- in the FDA's analysis for adults age 25 to 64, FDA actually found a statistically significant protective effect for suicidality
10:04:32 from the use of antidepressants, correct?
A. Could you point me to that point? That'll would be helpful in terms of answering your question.
MR. BAYMAN: Pull that up, please.
(Brief pause).
10:04:45 BY MR. BAYMAN:
Q. You recall saying, in your direct examination, the FDA didn't look at the data by age, correct?
A. I -- if I -- if you could point me to my deposition, I'll concede that.
10:05:03 Q. No, in your direct examination here in the courtroom.
MR. WISNER: Objection; misstates his testimony.
BY THE WITNESS:
A. I would need to look at the question and answer to answer your question.
10:05:09 THE COURT: You don't recall?
THE WITNESS: I don't recall. I'm sorry, Your Honor.
THE COURT: He answered that.
Proceed, please.
BY MR. BAYMAN:
10:05:14 Q. For adults, age 25 to 64, the FDA actually found a

statistically significant protective effect for suicidality from the use of antidepressants, correct?
A. Can you -- to answer that question, could you point me to text in the report that says -- that uses the word "protective"?
Q. I'm just asking you isn't that what it shows.
A. "Protective effect"? No, I disagree that that is a protective effect. Again, I'm -- your question to me --
THE WITNESS: I'm sorry, Your Honor, may I have the last two questions read back. I apologize.
(Record read back.)
BY THE WITNESS:
A. So I just wanted to be clear, because the first time you asked you said did the FDA find it and then the question was did I agree. So I have not answered your question, I guess about the FDA, did the FDA find it, and that's what I was getting at. Do I see that? No.
Q. You don't think this shows a protective effect?
A. Again, in order to show a protective effect, you need to start out in advance. This is a classic, classic, classic example of using a subgroup analyses to try and show that something is happening by slicing up the data.
And again, I published on this. This is a little bit like shooting an arrow and then drawing a bull's-eye around it afterwards, frankly.

Q. So you don't agree with the FDA when they said they found a protective effect for adults 24 to 64?
A. And I'm just -- if you could help me here.
Q. We'll get to it.
10:07:50 A. No, just -- I can't answer that question --
THE COURT: All right. That's it, then you can't answer.
Let's go on.
BY MR. BAYMAN:
10:07:55 Q. You agree that the odds ratio is less than 1, correct?
A. In this analysis, yes.
Q. And the confidence interval does not include 1, correct?
A. That is correct.
Q. And the feed value is .03, which indicates -- it's below
10:08:10 .05, it indicates a statistical significance, correct?
A. No, I disagree with that statement.
Q. Okay. Look, if you would -- you recall that in your direct examination you talked about the data on Paxil and suicidal behavior. There are actually subgroup analyses done, correct?
10:08:46 We can agree with that, right?
A. Yes.
Q. Look at page 23 of the Stone and Jones of the FDA report, a paragraph under the table.
A. Yes.
10:09:07 Q. Dr. Stones and Jones of the FDA write:

"That although the values for some individual drugs are statistically significant at the .05 level, the significance of those findings must be discounted for the large number of comparisons being made."

Did I read that correctly?

A. You did.

Q. And what FDA is saying is that with respect to any drug that's in those tables that have a statistically significant showing at the .05 level, such as the Paxil finding you discussed with Mr. Wisner, the 2.76, that you have to exercise caution in terms of interpreting whether there's a real finding versus a finding that generated by chance because of multiple comparisons, correct?

A. With the caveat, the very strong caveat that this is different from doing multiple comparisons to show efficacy, and that that does not discuss the difference between doing these analyses for efficacy versus safety, in that safety analyses need to be more sensitive, and you, therefore, will not normally be concerned about multiple comparisons.

And that there is nothing magic about the .05 level. You can, for regulatory purposes, set a P value that is higher than that. For example, .10 or.15, if you want to make sure you're not missing something. Yes, that is what they're saying.

Q. So the answer to my question is yes, that's what they're saying?
A. With the caveat that I provided.
Q. It's a very straightforward principle of statistically
10:11:10 analysis that, when you multiple comparisons, you increase the likelihood of having a false positive, correct?
A. It is not a straightforward principle. And as I was just trying to explain, basically as you want to be sure that you're not getting a false positive or do you want to avoid missing
10:11:32 true positives.

We accept the latter as a consideration for efficacy, but in safety we do not think that just ignoring an event, because of arbitrary P value, is something we should take the risk for.
10:11:48 Q. Well, you would agree with me under some circumstances, when you do multiple comparisons, you increase the likelihood of having a false positive, correct?
A. That's correct.
Q. In your direct examination you focused on some of the
10:12:05 analyses that FDA did on suicidal behavior, correct?
A. Yes.
Q. Turn, if you would, still to the FDA Stone and Jones review, Joint Exhibit 13. Look at table 7 -- I mean, sorry, it's Tab 7.
10:12:28 A. Uh-huh.

Q. You got it.
A. Yeah.
Q. Now, you testified that while the FDA review found that antidepressants, as a whole, were not associated with an
10:12:39 increased risk of suicidal behavior, Paxil or Paroxetine showed a statistically significant increased risk, do you recall that testimony on direct examination?
A. I believe so.
Q. Now, again, the primary objective of the FDA's analysis was
10:12:55 to look at suicidal thinking or behavior for patients taking all SSRIs and antidepressants, correct?
A. That's correct.
Q. And looking at page, in that same report, page 44, Section 5.2.
10:13:30 A. Yes.
Q. FDA summarized the results of its analysis as follows:
> "...in contrast with the previous FDA review of pediatric studies, the pool estimates of studies of the adult population support the null
10:13:46 hypothesis of no treatment effect on suicidality."

Did I read that correctly?
A. That's correct.
Q. The FDA goes on to say:
10:14:03 > "The most obvious explanation for this

difference in results is that the effect may be age related. When the results are analyzed by, age it becomes clear that there is an elevated risk for suicidality and suicidal behavior among adults younger than 25 years of age that approaches that's seen in the pediatric population. The net effect appears to be neutral on suicidal behavior but possibly protective for suicidality for adults between the ages of 25 and 64 and to reduce the risk of both suicidality and suicidal behavior in subjects aged 65 years and older."

Did I read that correctly?

A. You did. That's what the text says.

Q. And 25 to 64 is Stewart Dolin's age group, correct?

A. I'm sorry, I just want to make sure. I'm going to read this back:

"... the net effect appears to be neutral ..."

"appears" not "is."

"... neutral on suicidal behavior but possibly, possibly protective for suicidality for adults between the ages of 25 and 64 and to reduce the risk of both suicidality and suicidal behavior in people 65 and older."

I'm sorry, I'm confused because that actually

directly contradicts what they said earlier in the first sentence that it supports the null hypothesis.

The null hypothesis means the treatment doesn't make any difference on suicidality, but here they're saying, well, it does. So I'm -- I'm just -- anyway, to answer your question, yes.

Q. The null hypothesis they were looking at here is, do these drugs increase the risk of suicidality, correct?

A. No, I don't know that that's true. A null hypothesis is saying that an exposure to something doesn't affect anything. That's literally what it says here, the null hypothesis of no treatment effect on suicidality. If your study is designed to properly -- properly designed to test that and you do show an effect, then you say that you reject the null hypothesis. If you say that you've excluded a treatment effect, then you would accept the null hypothesis.

They actually don't say either. They don't say "accept," "reject," they say support, which means, in some ways, they didn't even reached a very good.

But having said that, the null hypothesis is that antidepressants don't affect suicidality, and then they go on to say, but it does.

So I'm -- I'm just saying that I'm looking at it again, I know that I've looked at it before, but somehow I realize, you know, is it that it doesn't have an effect, that's

the null hypothesis, or it does. And so I'm -- I'm just noting that. Sorry that that's a long answer.
Q. Yeah, I just wanted to get an answer to my question.
A. Okay.
10:17:16 Q. Can I get an answer to that?
A. Mr. Dolin fell in that age group, yes.
Q. Thank you.
Turn to the next page, page 45, Section 5.2.3 where it says "differences among drug and drug classes."
10:17:34 A. Yes.
Q. And you see that the FDA said:
"The observed effects wither generally similar among drugs and drug classes."
Did I read that correctly?
10:17:45 A. Yes.
Q. Thank you, Doctor. You can put that down.
A. Okay.
Q. Now, Dr. Ross, you said yesterday that when you had a very unusual event, like unfortunately suicide is, to detect one
10:18:02 event I need to study a lot of patients, do you remember that?
A. That's, in essence, what I said. It was a little more technical than that. But specifically, yes.
Q. And you told the jury that the suicidality data that GSK submitted in the New Drug Application did not properly reports
10:18:32 suicides and suicide attempts that occurred during the run-in

phase of clinical trials, do you recall that?
A. I do.
Q. Those submissions that you told the jury about were in 1989 and 1991, correct?
10:18:40 A. Correct.
Q. That was 15 years or more before GSK and the FDA separately analyzed the Paroxetine clinical trial data from randomized placebo-controlled trials in 2006 to evaluate the risk of suicide in adult patients, correct?
10:19:02 A. At least that. Probably more than 15 years. You're talking from '89 to 2006.
Q. And during the 15 years, from '91 to 2006, you know, based on your review of the regulatory file, that GSK applied for and approved numerous additional indications for Paxil in adults,
10:19:23 correct?
A. Supplemental NDA's.
Q. Now, in order to support new indications, such as GAD, generalized anxiety disorder, or OCD, obsessive compulsive disorder, GSK had to submit clinical trial evidence showing
10:19:44 efficacy in safety in treating those conditions, correct?
A. Correct.
Q. So you know that many more clinical trials in adults were conducted by GSK after Paxil was first approved for major depressive disorder in 1992, correct?
10:19:58 A. Yes.

Q. All right. I want to show you a graph.

MR. BAYMAN: Your Honor, I conferred with plaintiff's counsel. I just want to show the graph that we put set up with Dr. Healy.

10:20:18 (Brief pause).

(Exhibit published to the jury.)

BY MR. BAYMAN:

Q. The jury has seen this before. You see there that in the 1991 suicidality report, the GSK reported 2963 patients who

10:20:46 were taking Paxil. Do you remember that, from looking at the '91 report?

A. Yes.

Q. And that included all kinds of clinical trials, correct?

A. Yes.

10:20:56 Q. Placebo-controlled, correct?

A. I believe it included trials that were placebo-controlled.

Q. It included active-controlled trials, meaning one arm the study patients were taking Paxil, and another arm they were taking another antidepressant, correct?

10:21:15 A. Yes.

Q. It included what's called uncontrolled, meaning there was no other -- no other medication in the study, correct?

A. Let me give the clarification for that, that when we say "uncontrolled" there's always the potential to have a

10:21:41 historical control. But you're correct, there was no what we

call concurrent control, something given at the same time.
Q. And then there were patients in studies that are called open label, that means the patient knows they're taking the study medication like Paxil, correct?
10:21:54 A. Correct.
Q. So it's not blinded?
A. Correct.
Q. And so -- and then we have the second line, which is in 2002 the reanalyses that Mr. Wisner and you discussed yesterday
10:22:20 which was looking only at the controlled portions of placebo-controlled trials, GSK in that analysis, there were 921 patients on Paroxetine and 554 on placebo, do you recall that?
A. I do.
Q. And then when we go to 2006, GSK's analysis of, again
10:22:48 patients in the controlled phase of placebo-controlled trials, there were 8958 patients on Paroxetine and 5953 on placebo, correct?
A. Correct.
Q. And then when the FDA analysis done by Dr. Stone and Dr.
10:23:08 Jones, again only the patients in the controlled phase of placebo-controlled trials, they had 8728 on Paroxetine and 7005 on placebo, correct?
A. Yes.
Q. Okay.
10:23:27 A. Or I'm seeing this table for the first time.

Q. Okay. You don't dispute these number, correct?
A. No, not per se. Just wanted to be clear about that.
Q. Thank you. I'm just trying to move along.
A. Sure.
10:23:39 Q. You would agree with me that the GSK and the FDA analyses in 2006 contained about ten times more patients on Paxil than were in the placebo-controlled studies in the '91 submission?
A. With the caveat that in a safety database of 9,000 patients, in the general population you would be unlikely to
10:24:04 see even a single suicide, yes, I would agree with that.
Q. So you would agree with me, based that comment, that more data is better, correct? You'd rather have more patients, more studies to do an analysis, correct?
A. I would agree more high quality data is better.
10:24:23 Q. And in looking at these, there were three times more patients on Paxil in the 2006 analyses, both by GSK and FDA, than there were on all of the studies in the 1991 submission, correct?
A. Yes.
10:24:51 Q. So the 2006 analyses by FDA and GSK were much bigger data sets than were in the 1991 submission, you would agree with that?
A. With the caveat that they're severely under, yes, I would agree.
10:25:06 Q. And all things being equal, the bigger a sample size, the

more reliable the analysis, correct?

THE COURT: Let's go back to that last answer.

Read it back, the caveat.

(Answer read.)

10:25:38 THE COURT: I don't think we got that answer.

BY THE WITNESS:

A. I'm sorry. With the caveat that these data sets, even though they're larger, are still under-powered, severely under-powered. In other words, way too small to reliably

10:25:58 detect where events such as suicide, yes, I would agree that they're larger.

BY MR. BAYMAN:

Q. So you would hope there would be more patients and more data, correct?

10:26:09 A. It's not a matter of hoping. It's a question of simple math.

Q. And to get back to that, my further question, all things being equal, the bigger a sample size, the more reliable the analysis, correct?

10:26:25 A. I would say the stronger -- the conclusion -- you can draw stronger conclusions when you have more data, all other things being equal.

Q. Thank you, Doctor.

The jury has heard a lot about run-ins from Dr. Healy,

10:26:43 and I know you've given some testimony about that. I'm going

to try and shortcut that.

MR. WISNER: Your Honor, the demonstrative that was just shown to the jury, it hasn't been marked in any way. We'd ask that it be marked so that there's a record of it.

10:26:58 MR. BAYMAN: Sure. We'll mark it.

THE COURT: At a later time take care of it.

MR. WISNER: Sure.

THE COURT: You're responsible for marking, not the court reporter.

10:27:05 MR. BAYMAN: Yes, sir. We'll be happy to do that.

BY MR. BAYMAN:

Q. Tab 16.

MR. BAYMAN: Your Honor, that's Defendant's Exhibit 305. That's Dr. Brecher 1992 safety review which is in

10:27:18 evidence. May I publish that?

THE COURT: Yes.

(Exhibit published to the jury)

BY MR. BAYMAN:

Q. You're familiar --

10:27:32 MR. WISNER: Objection, Your Honor, this document is actually not in evidence.

MR. BAYMAN: I'm sorry. It's my fault. That's the wrong exhibit.

(Brief pause).

10:27:54 MR. BAYMAN: Your Honor, we've gone over this with

Dr. Healy and I thought it was in evidence. I apologize.

(Brief pause)

MR. WISNER: Your Honor, just to clarify, there might be a Plaintiff's Exhibit number that this might refer to, but this definitely, Defendant's Exhibit 305, is not in evidence. So they were running into the problem you asked us to avoid.

THE COURT: It's a problem I wanted to avoid. Do you see how it works, if you don't avoid it?

MR. BAYMAN: We'll clear it up.

BY MR. BAYMAN:

Q. You're familiar with Dr. Brecher's safety review, correct?

A. I've reviewed it.

Q. And that's an official FDA report, correct?

A. Yes.

Q. Reflecting the FDA's official activities in reviewing the Paxil New Drug Application?

A. It documents the primary medical reviewer's review.

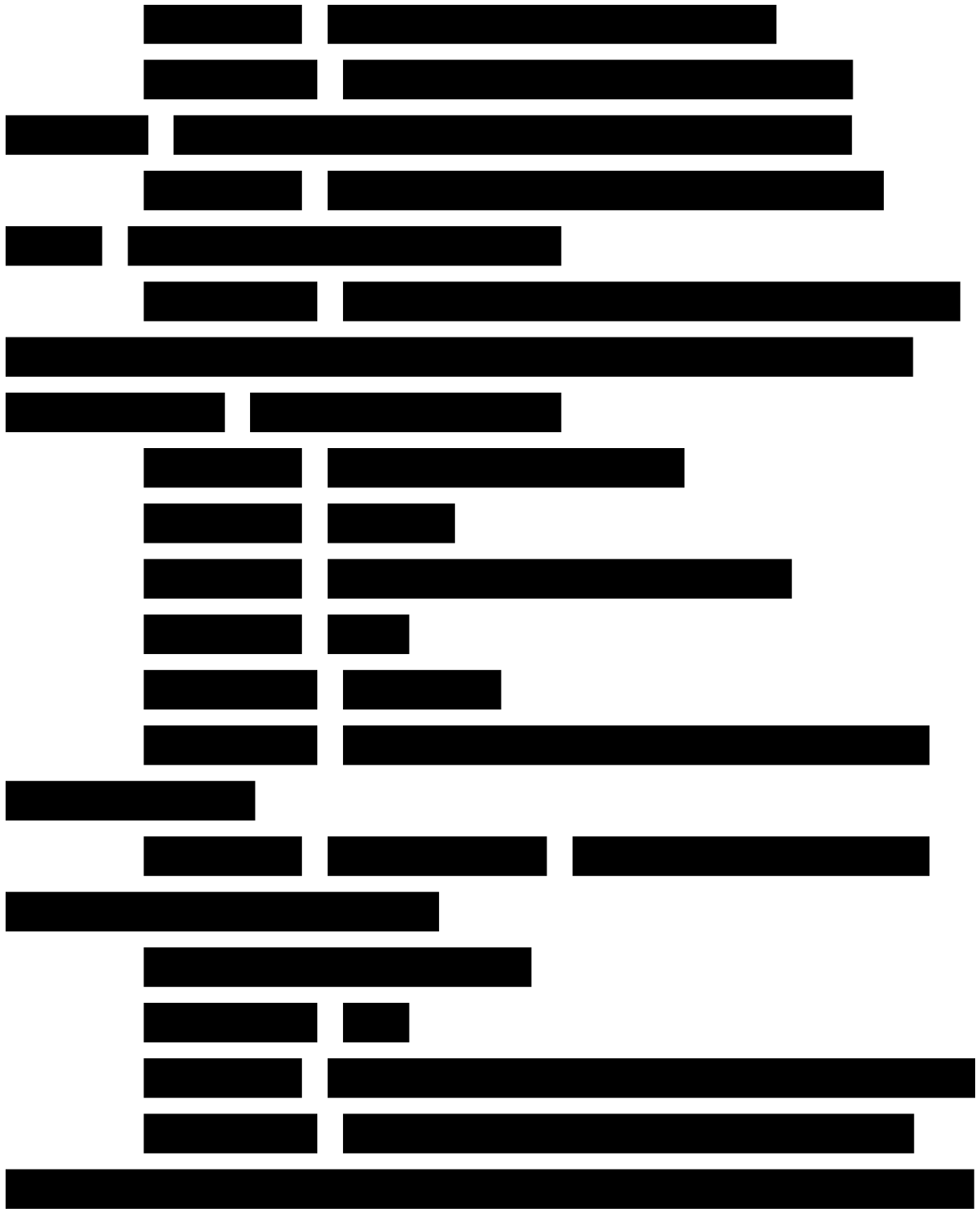
MR. BAYMAN: At this time, Your Honor, I move for admission of Dr. Brecher's safety report, Defendant's Exhibit 305.

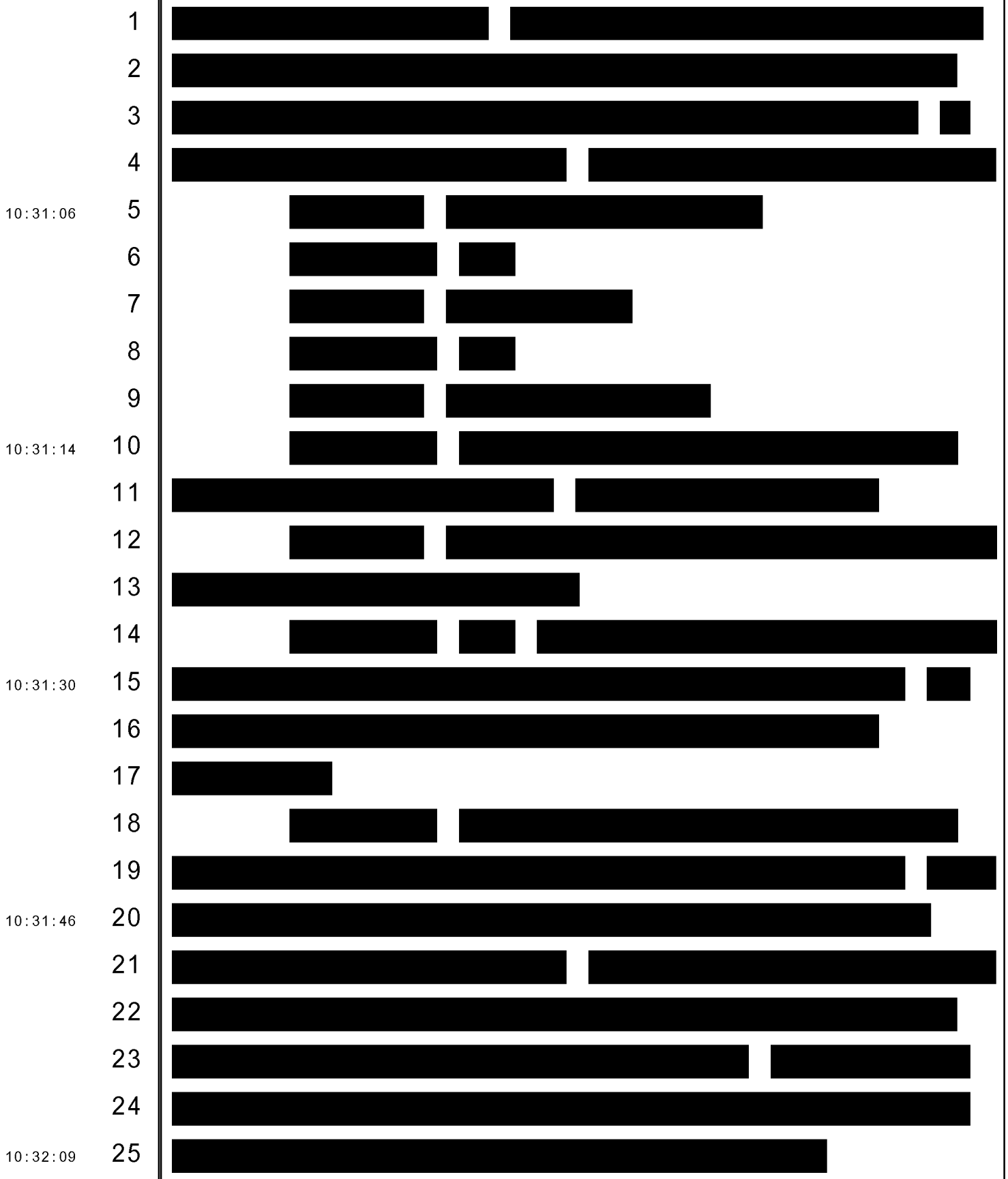
MR. WISNER: Your Honor, I object to hearsay. This document is not admissible. And Dr. Brecher has not admitted into evidence. We don't object to publishing portions of it for purposes of cross-examination, but the document itself should not be admitted into evidence.

MR. BAYMAN: I think under Rule 803(a).

THE COURT: Let me see it. We'll go to sidebar.

(Proceedings heard at sidebar on the record.)

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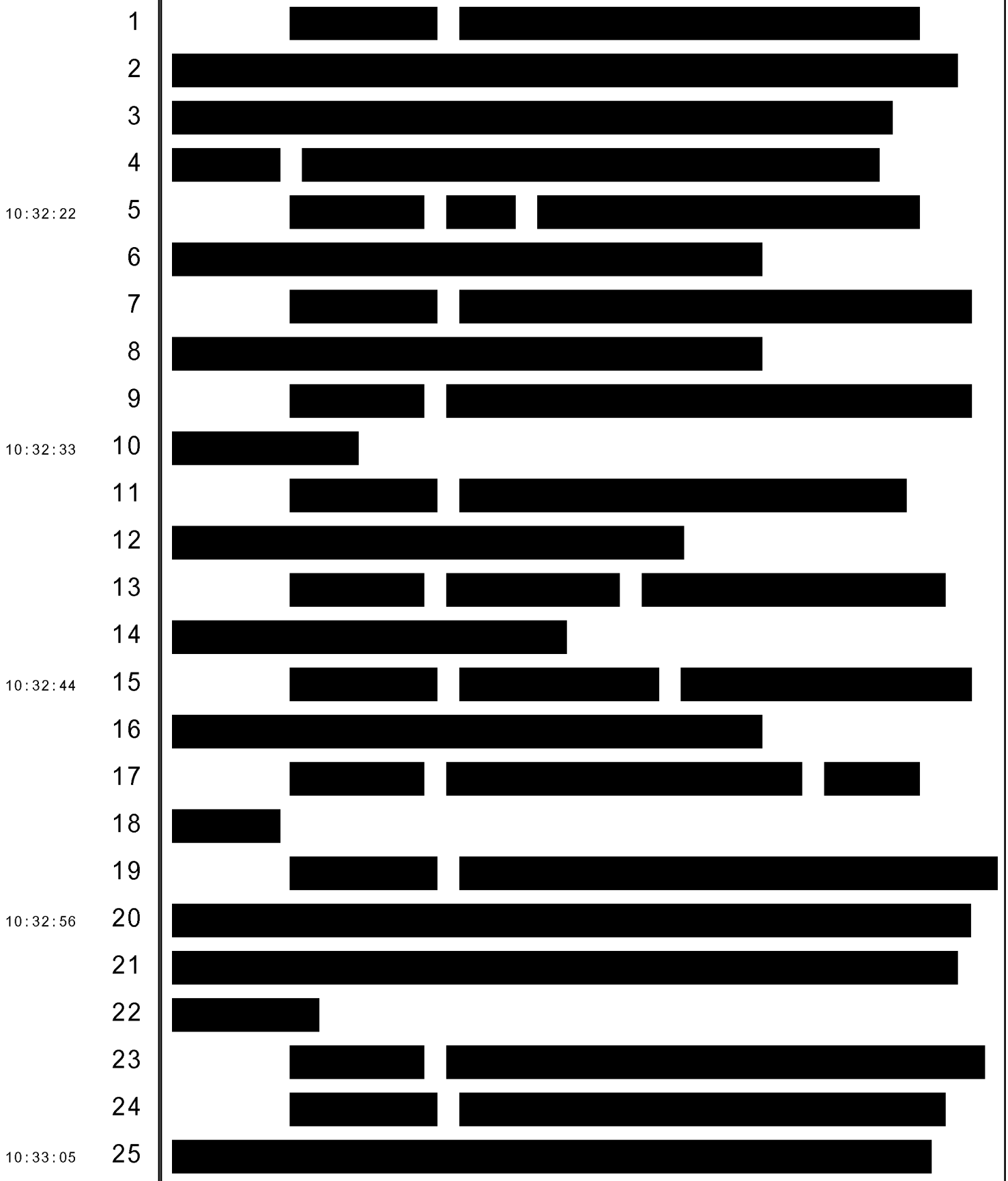
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[redacted]

(Proceedings resumed within the hearing of the jury.)

BY MR. BAYMAN:

Q. All right. I want you to -- you've reviewed Dr. Brecher's deposition, correct?

A. Yes.

Q. I want you to turn to page 23 of his report, which is actually page 28 of the exhibit, if that's easier.

A. Yes.

MR. BAYMAN: Let's put that up, please.

BY MR. BAYMAN:

Q. Look, if you would, at the first full paragraph at the top, the last sentence.

It says:

"2 of the 5 placebo suicide occurred during the run-in."

Correct?

A. That's correct.

Q. So you see where Dr. Brecher is stating this in his report?

A. Actually, one thing that I observed in reviewing Dr. Brecher's report and submissions from the sponsor is, similar type phase font and formatting. So I'm not sure if this is Dr. Brecher stating this or if this is something that was cut and paste from a document provided by the sponsor.

MR. BAYMAN: Put the first page up, please.

(Exhibit published to the jury)

BY MR. BAYMAN:

Q. It's Dr. Brecher's name on there as the reviewer, correct?

A. That's correct.

Q. Okay. And if we go back to the previous page.

At the very bottom of that page it states that:

"A 43-year old man who committed suicide during the placebo run-in of the study DFG119."

Do you see that?
A. Yes.
Q. You agree there's no doubt that the FDA knew about these two suicides occurring during the placebo run-in phase, correct?
A. No, I don't agree. As I just said, I know that Dr. Brecher's name is on this, but there are other portions of, for example, the summary basis of approval that were actually written by the company. And as I said, it looks very similar. I'm not -- I don't claim to be a document expert, but, in that era, people would frequently cut and paste things.

I mean, if this was in a different font or something like that, I'd say, well, yes. But A, I don't know that they knew. B, you know, there's no discussion, actually, of whether that's appropriate or not.

And given Dr. Brecher's deposition where he said, "well, that's not appropriate," it's not clear to me that he, in fact, recognize -- did he know it or recognize the significance of it, I don't know. So I actually can't agree with your statement.
Q. Okay. Turn to your deposition, page 230, Line 25. The question is:

"And then you agree there's no doubt that Dr. Brecher knew about these two suicides occurring during the placebo run-in phase?"

And your answer was:

"Yes."

Did I read that correctly?

A. You did.

10:38:02 Q. Okay. Look at -- you're not aware of any other suicides that occurred during the placebo run-in, are you?

A. Besides these two?

Q. Yeah.

A. I've not identified any.

10:38:15 Q. Then turn again to Dr. Brecher's report, page 25, which I think is page 30 of the exhibit, in the middle of the page.

A. Yes.

Q. The report with the analysis of the suicidality data says:

"There is no signal in this large database that Paroxetine exposes a subset of depressed patients to additional risk for suicide, suicide attempts, or suicidal ideation."

10:38:39 Did I read that correctly, Doctor?

A. You did.

10:38:53 Q. Thank you.

Now, your report -- you did some analysis of the data from the 1991 report, correct, that you shared with the jury?

A. That's correct.

Q. In fact, you showed a table. You have your report there?

10:39:19 I think it's tab --

A. Tab 1?
Q. Tab 1, yes.
A. Give me a second here. I'm going to pull that out for reference.
10:39:29 (Brief pause).
BY THE WITNESS:
A. I cannot seem to find that report. I apologize.
BY MR. BAYMAN:
Q. Sure. Not in there?
10:39:44 A. No, apparently not.
THE COURT: Give him a copy of it.
THE WITNESS: Yes, sir.
MR. WISNER: I have a copy right here, Your Honor.
THE COURT: Give him a copy of it.
10:39:53 MR. WISNER: May I approach?
THE COURT: Yes.
(Document tendered to the witness).
THE WITNESS: Thank you. I'm sorry. Go ahead.
BY MR. BAYMAN:
10:40:03 Q. I wanted you to turn to table 3. It's a table that you showed the jury yesterday, do you recall that?
A. Yes.
Q. Now, it's entitled "incidence of events consisting of suicide attempts or worse in adult MDD patients in original Paxil NDA," correct?
10:40:31

A. Yes.
Q. And by "suicide attempts or worse," you mean you combined suicide attempts and completed suicides, correct?
A. Correct.
10:40:42 Q. Okay. And this is not anything you generated, Doctor. You copied this from Dr. Glenmullen's report, correct?
A. No, sir, I did not copy it from Dr. Glenmullen's report. I absolutely reject that.
I saw this, I obtained the same numbers, I did the
10:41:01 calculations myself, and I got the same result as he did, but I absolutely and totally did not copy that.
Q. The data was not taken from Dr. Glenmullen's report?
A. There were 42 suicide attempts, the enumerators and the denominators were taken from the data that I had from the
10:41:28 documents that I reviewed.
Q. Look in your deposition on page 33.
A. Uh-huh.
Q. Line 4. You were asked:
"... where do they come from?"
10:41:47 Your answer was:
"... the data was -- I'm sorry, taken from Dr. Glenmullen's expert report."
A. Right, but also verified through. I mean, I didn't just take what he said for granted, sir, okay. If you want to get
10:41:59 into discussion about my methodology, I would be very willing

do that, but I read his report, I saw that, and then I went to the actual documents, but I didn't simply copy it from his report.

Q. But he did these calculations, correct?

10:42:12 A. He also did them.

Q. You did them too?

A. I independently did them. I have not ever met or had any discussions with Dr. Glenmullen.

Q. Okay. And you told the jury, in response to Mr. Wisner's

10:42:24 questions, that when one properly analyses the Paxil NDA clinical trial data from late '80s, for events of suicide attempts or worse, there were 47 suicide attempts and suicides -- or the 5 suicides over 2963, correct?

A. Based on the data at that time, as we've discussed, there

10:42:55 were 2 suicide attempts and the company simply submitted another data that just went away, but yes.

Q. And then down below, you have one suicide attempt for placebo out of 554, is that right?

A. That is correct.

10:43:16 Q. And it's from this analysis that you told the jury that the original Paxil New Drug Application is associated with an increased risk of suicide attempts or worse in adults patients with depression?

A. Yes.

10:43:34 Q. That's the basis of your conclusion, is this data, correct?

A. With the regulatory conclusion that this represents reasonable evidence of an association.
Q. And as we discussed earlier, the Paxil or Paroxetine New Drug Application included data from all kinds of different
10:43:58 trials, correct?
A. That's correct.
Q. And so then you would agree with me that not every patient who received Paxil or Paroxetine in a clinical trial that made up this original NDA data set received it during a randomized
10:44:24 placebo-controlled trial, correct?
A. That is correct.
Q. So, in fact, your analysis of the NDA suicidality data includes data for Paroxetine attempts, the Paxil, the left column, that occurred in open label trials, extension phase
10:44:43 trials, active controlled studies, correct?
A. That's correct.
Q. But in contrast, for placebo, the second column, you included only in your analysis data from double blind, placebo-controlled clinical trials, correct?
10:45:05 A. You can't have a placebo in any other kind of -- there were no other placebo patients in any other kind of trial.
Q. So that's correct?
A. That is correct.
Q. Okay. And that second column excludes events that occurred
10:45:23 during the placebo run-in, correct?

A. Yes.
Q. But it does -- for Paxil, it includes events that happened, say, for example, in the extension phase, after the controlled phase of the trial was over, and some patients were taking
10:45:44 Paxil and there was no placebo arm to compare against, correct?
A. No, that is not correct.
Q. Really?
A. Really.
Q. You don't agree that the 2963 includes patients from
10:46:00 extension studies?
A. No, I agree with that.
Q. Okay. And in the -- in some of those trials, in the extension phase, there was no placebo arm, correct?
A. Oh, you're asking was there what we call a concurrent
10:46:16 placebo arm?
Q. Okay. Thank you. Appreciate that clarification.
A. Okay. There was not a concurrent placebo arm, but that does not make use of placebos from earlier in the trial, in the same population use and the same methodology, wrong.
10:46:34 Q. No, I just want to make it clear that some of those -- in fact, a lot of those Paxil events occurred in studies where there was no head-to-head comparison with placebo, correct?
A. No, again I would disagree with that. Head-to-head means everything is happening at the same -- I'm sorry, there's an
10:46:52 assumption that you can only compare if you're doing things

exactly at the same time. In fact, if you have a good estimate of the placebo rate, you can do a comparison with placebo patients who were treated earlier.

The key issue here is that those run-ins were before 10:47:16 patients actually got randomized to any treatment. The Paxil deaths were after patients got randomized. So that is a key statistical distinction between pre-randomization and post-randomization, but it is not correct to say that there was no placebo arm to compare it to. There was the prior placebo 10:47:41 experience.

So again, this is an incredibly complicated technical area, but the assumption that you have of placebo has to be run at the same time to have a good estimate effect, is just wrong. There are trials where we compare two drugs to see how similar 10:47:58 they are, and there's always an implicit understanding of what the placebo rate would be from other trials, and that's completely valid.

Q. Dr. Ross, I'm just trying to simplify it for the jury that there were events that occurred on Paxil in trials in which at 10:48:18 the same time patients were not taking placebo, you'll agree with that, correct?

A. I would agree with that.

Q. And, for example, in an open label trial, the patients are taking Paxil and they know it, and there may not even be a 10:48:32 placebo arm in any point in that trial, correct?

A. Well, if there is -- I'm sorry, open label certainly can have a placebo control. Open label does not mean on control, it just means you know what you're taking. If there is no concurrent control, then, by definition, that's open label.

10:48:53 So I just wanted to make that clarification. But again, I don't -- I really can't accept the idea that there was no placebo arm to compare this to.

And I think the idea that there's one right analysis is one that I need to put out there, but if you are saying 10:49:06 there was not a concurrent placebo control with the caveat that Dr. Brecher did the same thing, I would agree.

Q. Well, when the FDA asks manufactures to submit data for a New Drug Application from the control phase of randomized placebo-controlled trials, it compares events that happened on 10:49:27 the drug being studied and placebo when patients are in the controlled phases, meaning they're taking them at the same time, correct?

A. Yes.

Q. And it measures events on the drugs versus events on 10:49:39 placebo because we know the placebo can't be causing a side effect, correct?

A. In general, that's correct.

Q. Because it's a sugar pill, right?

A. First, it usually is.

10:49:54 Q. Okay. So --

THE COURT: All right. We'll take a recess now. A morning recess.

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

10:50:24 [redacted]

11:04:50 [redacted]

11:05:36 (The following proceedings were had in the presence of the jury in open court:)

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

We'll resume. You may proceed, sir.

11:06:05 BY MR. BAYMAN:

Q. Thank you, Your Honor.

BY MR. BAYMAN:

Q. If we can put that table back up.

(Brief pause).

11:06:14 BY MR. BAYMAN:

Q. All right, Doctor, back to where were with the table.

So that we're clear, the Paxil event, the 2963, there were patients among the 2963 in trials where there was no placebo in the study at all, correct?

11:06:53 A. Where there was no concurrent placebo control.

Q. There were some where there was none at all, correct?

A. Again, I -- the reason I'm saying that, I understand what you're -- the study -- sorry, the application as a whole, had placebos. And this is a well recognized principle not just by

11:07:18 the statistical community, but by FDA that it's issued -- this is just gets to what I was saying before in what's called the E10 guidance choice for comparator group for clinical trials.

Placebos used as comparators do not have to be run in the same exact trial as the people getting it, the active drug,

11:07:47 your study drug. What's important is that they're in the same population studied under the same conditions to make for a valid comparison.

So if you want to say some of them were in studies where there was no concurrent placebo control, that is correct.

11:08:02 There was, however, a really, really good set of external placebo controls but contained within the data set for the NDA.

Q. Well, let me try to simplify this. There were studies where patients were given Paxil and they were given no concurrent medications at all, correct?

11:08:27 A. There was no concurrent comparator, is what you are saying?

Q. Right.
A. Yes, that is correct.
Q. Okay. And there were patients in trials where instead of being compared to placebo, they were compared to another
11:08:42 medication, correct?
A. I don't recall if there were any that were just active control and there was no simultaneous placebo control, I just don't remember off the top of my head.
Q. Fair enough. And then there were some patients who were
11:09:02 taking Paxil after the controlled phase of the trial ended, they stayed on Paxil but the placebo patients stopped taking anything, correct?
A. As part of the trial, they may have been taking other drugs or they may have crossed over.
11:09:20 Q. Or they may have left the study, right?
A. That could happen at any time.
Q. Well, what I'm saying is, just so it's clear to the jury, when we talk about extension phases, there were trials where people stayed on Paxil and the comparator group, whether it be
11:09:36 placebo or another medicine, those patients stopped, they were done with the trial, they weren't taking any medicine, correct?
A. As part of the trial, yes.
Q. Okay. I just want --
A. They --
11:09:49 Q. I think you've answered it.

A. Sorry. Go ahead, please.
Q. So with respect to the methodology that you utilized to calculate the differences that are shown in this chart --
A. Uh-huh.
11:10:02 Q. -- are you aware of any instance in which the FDA utilized that same methodology for the purposes of assessing suicidal risk with any SSRI, any antidepressant, or any psychiatric medication after 2004?
A. In terms of what's publicly available and what I've seen, I
11:10:23 can't say that I've seen anything.
Q. And you would agree with me that given what the FDA said in terms of its guidance in the Stone and Jones report, that we just saw a few minutes ago, about what data it wanted for purposes of assessing suicidality risk in medications, it did
11:10:42 not want uncontrolled data, or open label data, or extension phase data, or active controlled studies with another medication, but rather, it wanted only data from randomized double blind placebo-controlled trials?
A. For the very -- with the caveat that that was for the
11:11:03 narrow purpose of that analysis, and they did not say, we're not going to even consider such data if it comes from case reports, or uncontrolled studies, or extension phase studies, which, by the way, some active medication patients who are on Paxil could also have dropped out.
11:11:29 But anyway, with this caveat, yes, for the Stone/Jones

analysis, which was not intended to answer a labeling question, it was an epidemiology question, yes, you're correct.

Q. You're saying that the Stones and Jones -- the reason the FDA did that review was not for purposes of considering whether there needed to be changes in labeling, is that your testimony?

A. I would say that the direct reason was to determine, and they talked about a null hypothesis of a no treatment effect, to say what do the data show us about the relative risk of various events in patients taking antidepressants.

Q. And the events we're talking about are suicidal events, correct?

A. Yes.

Q. That's the question being studied, do these drugs increase the risk of suicide in adult patients?

A. Do they affect the rate or the risk of suicide.

Q. Do they increase the risk, correct?

A. You know, my understanding is that the testing, statistical testing that was done on this, was done in such a way as to answer the question either way, doing what are called two-tailed tests rather than one-tail tests.

Q. You don't agree that the question they were assessing was whether these medications increased the risk of suicide in adult patients?

A. I would just go back to the words in the Stone/Jones report, which is that they were looking at a null hypothesis

that these drugs -- that's -- that's kind of like we're going to assume that's the situation, there's no effect.

If it was just an increase, then the null hypothesis would be different. It would be we're going to assume that these drugs don't increase suicide risk, but that's not what they said in their report, was the question. It said, is it true that these drugs have no effect. They didn't specify increase decrease, and that was the test.

Q. I want to talk to talk to you about a document that Mr. Wisner discussed with you yesterday, the deaths report that GSK submitted in 1999. That's Defense Exhibit 24 from your notebook.

A. I'm sorry, what tab is that?

Q. I'm sorry. It's in this notebook (indicating).

Do you have the plaintiff's notebook?

A. I apologize. I had it here but I do not have it now.

Q. I'll bring you a copy.

A. Thank you.

(Binder tendered to the witness).

BY THE WITNESS:

A. Thank you, Mr. Bayman.

BY MR. BAYMAN:

Q. You're welcome.

MR. BAYMAN: Permission to publish, Your Honor.

(Exhibit published to the jury.)

BY MR. BAYMAN:
Q. This is the July 13th, 1991 FDA submission to -- the submission of the FDA regarding deaths in Paroxetine clinical trials that you discussed yesterday with Mr. Wisner.
11:15:03 A. Yes.
Q. Okay. Turn, if you would, to page 5. There's a chart that you showed the jury yesterday that I want to ask you about.
(Brief pause).
BY MR. BAYMAN:
11:15:23 Q. Do you see that?
A. So you're talking about this spreadsheet.
Q. I'm talking about this chart right here that you showed the jury yesterday (indicating)?
A. Oh, I'm sorry.
11:15:36 Q. The 12 suicides on Paroxetine and 1 in placebo, do you remember that?
A. Yes.
Q. Okay. You we asked yesterday if this was for -- this chart was reflecting placebo-controlled randomized clinical trials
11:15:51 and you said yes, correct?
A. I believe so, yes.
Q. Okay. But you know that's not, correct, right? The FDA requested an analysis of all randomized controlled trials, not just placebo-controlled, randomized controlled trials, correct?
11:16:14 A. That's -- that's correct.

Q. These 12 suicides come from both placebo-controlled and active-controlled studies, correct?
A. Come from both placebo-controlled and active-controlled studies?
11:16:50 (Brief pause.
BY THE WITNESS:
A. I would just note that it says treatment was with active comparator. So in terms of the second paragraph up above, that those cases were eliminated. I'm sorry, the paragraph up above
11:17:47 -- the one that you're --
BY MR. BAYMAN:
Q. Hold on, please.
(Brief pause).
BY MR. BAYMAN:
11:18:05 Q. Not all -- active controlled studies do not all have a placebo group, correct?
A. That is correct.
Q. Okay. Look at the letter, back to the cover page, page 1. It says:
11:18:24 "Please refer to attachment 1 for review of the data from deaths occurring in randomized controlled trials with Paroxetine."
Do you see that?
A. Yes.
11:18:32 Q. It doesn't say placebo-controlled anywhere, does it?

A. No.
Q. And so you know that these 12 deaths reported are coming from both placebo-controlled and active-controlled clinical trials?
11:18:50 A. Well, again, you need to go back to that paragraph, and if we could highlight the text, talking about the second paragraph where it says "attachment 1."
(Brief pause.
BY THE WITNESS:
11:19:11 A. Okay:
"... those cases were eliminated where the trial evaluated a primary condition other than depression, treatment was with activity comparator or run-in placebo or the death
11:19:24 occurred in the open label portion of the randomized trial."
Frankly, from that language, I'm not clear if they eliminated -- if this involved active comparator trials or just portions of active comparator trials where the -- the suicide
11:19:42 occurred in a patient who had been randomized active. So that's -- and, frankly, by doing that, you know, there's nothing like, you know, no line here saying "active comparators excluded." Okay.
Q. Okay.
11:20:01 A. So that's -- that's what -- what it says. Now, if you say

these are from active comparator, okay.
Q. Okay. Let's walk through this a little bit. You showed -- look at -- you showed -- and I'll get it for you --
This is an e-mail, do you recall an e-mail from Daniel Burnham of SmithKline Beecham that Mr. Wisner and you talked about yesterday?
MR. WISNER: Your Honor, I actually have a copy of the binder.
MR. BAYMAN: Oh, sure. That would be great. Thank you.
MR. WISNER: May I approach, Your Honor?
THE COURT: You may.
(Binder tendered to the witness).
THE WITNESS: Thank you.
BY MR. BAYMAN:
Q. All right. I don't think that one is tabbed, that binder, but it's DX136.
A. Okay. Yes.
Q. You showed the jury this document yesterday, do you remember?
A. Well, I responded to questions from Mr. Wisner.
Q. Yes. Right.
And if turn, if you would, to page 6, the chart that you showed the jury yesterday.
A. I just want to make sure I'm on the right page here.

Q. Page 6.
A. Page 6. Okay.
Q. (Reading:)
"Deaths occurring on drug within 3 days ... double blind Paroxetine and placebo depression trials."
A. Yes.
Q. And you pointed out yesterday that study 04 is on this list, do you remember?
11:22:23 A. Yes.
Q. And you told the jury that in this chart GSK was listing study 04 as a placebo-controlled trial?
A. I don't recall if I said that. That was an extension phase of study 03 which had a concurrent placebo.
11:22:43 Q. You don't -- you don't recall saying that that was a placebo-controlled trial?
A. I -- I would have to see -- I don't recall. I would have to see the question and my answer to be sure.
Q. We'll get that in a second. A question about --
11:23:15 (Brief pause).
BY MR. BAYMAN:
Q. I'm going to hand you the trial transcript.
(Transcript tendered to the witness).
MR. BAYMAN: Counsel, that's trial transcript page 1067, Line 24.
11:23:35

BY MR. BAYMAN:
Q. The question was:
"So in this report from 1999, GSK ..."
MR. WISNER: Your Honor, there's a refreshing of recollection.
11:23:46
MR. BAYMAN: I'm actually impeaching him.
MR. WISNER: He says he doesn't recall.
THE COURT: You got to find out first whether he remembers it.
11:23:55
Go ahead.
BY MR. BAYMAN:
Q. I thought you said that you don't -- that you said yesterday that --
THE COURT: Wait a minute.
11:24:03
Did you read it, Doctor?
THE WITNESS: I did.
THE COURT: Now put your question, sir.
BY MR. BAYMAN:
Q. You said yesterday that PAR 04 is a placebo-controlled
11:24:10
trial?
A. Yes.
Q. Okay. I've got a simple question about the document, the Burnham e-mail with the attachment that you're looking at.
Are the cover letter and the chart attached, are they
11:24:28
preliminary or are they final?

A. I'm saying I believe they -- I'm sorry, there are so many papers here. I'm in trouble.

I believe they said it was -- actually, I don't want to speculate. Let's go back to this.

11:25:09 (Brief pause)

BY THE WITNESS:

A. So we are talking about the letter dated -- this is Defense Exhibit 24, July 13th, 1999?

BY MR. BAYMAN:

11:25:19 Q. Yeah.

A. Okay.

Q. And the chart.

A. And the chart.

Q. The e-mail attaches a letter and a chart, correct?

11:25:31 MR. WISNER: Just to clear up the record, he's referred to Defendant's Exhibit 24, I believe Mr. Bayman is referring to Defense Exhibit 136, which is the e-mail from Mr. Burnham with the attachment.

THE WITNESS: Got it.

11:25:47 MR. WISNER: That's also in the plaintiff's binder, if you'd like to look it up that way.

THE WITNESS: My apologies. I don't mean to delay the proceedings here.

(Brief pause).

11:26:04 BY THE WITNESS:

A. This is the final response, that is what it says in the letter.
BY MR. BAYMAN:
Q. So you weren't told by plaintiff's counsel that you were looking at a draft and that the final version that was actually submitted to the FDA was substantially revised 28 days later?
A. I'm -- I'm sorry. I'm completely lost. When you say I wasn't told about --
Q. You were told that what you were looking at there was a draft, correct?
MR. WISNER: Objection. Could we just clarify what he is looking at?
THE COURT: What exhibit number are you referring to, sir?
MR. BAYMAN: It's Defense Exhibit 136.
BY THE WITNESS:
A. Ah yes. I was aware that this was a draft.
BY MR. BAYMAN:
Q. You were aware that it was a draft, okay.
A. I mean, there's no date filled in there.
Q. Okay.
A. There's no signature, there's no time stamp.
Q. So when you were testifying to the jury, you didn't tell them that it was a draft, did you?
A. No.

Q. And you know it was substantially revised 28 days later, don't you?
A. Substantially revised 28 days later? I'm not -- I honestly don't understand what you mean.
11:27:33 Q. Well, in fact, in the notebook, the plaintiff's notebook of exhibits, you had the final version in the notebook and you've had it in there the whole time, DX 25, correct?
A. Ah, DX25. Thank you for clarifying that.
(Brief pause).
11:27:57 BY THE WITNESS:
A. Yes, that is correct.
BY MR. BAYMAN:
Q. That's a notebook that Mr. Wisner gave you with exhibits, correct?
11:28:09 A. Yes.
MR. BAYMAN: May I publish that, Your Honor.
THE COURT: Yes.
(Exhibit published to the jury.)
BY MR. BAYMAN:
11:28:15 Q. Unlike the version you showed to the jury yesterday, this one has a stamp on it that says "U.S. regulatory affairs archive," correct?
A. Yes.
Q. And unlike the version you showed the jury yesterday, this
11:28:25 one is signed by Mr. Kline?

A. Yes.

MR. WISNER: Objection. Dr. Ross didn't show the jury anything.

MR. BAYMAN: No, I said unlike the version he showed the jury yesterday sorry you and plaintiff's counsel.

BY THE WITNESS:

A. I haven't shown anybody anything.

BY MR. BAYMAN:

Q. Sorry, you and plaintiff's counsel.

A. No, I answer questions. I'm not -- I don't have any control over these things.

Q. Okay. Unlike the version that Mr. Wisner displayed yesterday that you were questioned about and you answered questions about, this one has a signature on it, right?

A. That is correct.

Q. Okay. Let's look at the letter.

A. Uh-huh.

Q. In the first paragraph it says:

"Reference is also made to the FDA letter of April 2, 1999 requesting information on deaths and suicide in randomized controlled clinical trials for Paroxetine and depression."

Correct?

A. Yes.

Q. So he's referring to FDA's request for all kinds of

randomized clinical trial information and deaths from those trials and he's not noting any limitation to placebo-controlled trials, correct?

A. Correct.

11:29:24 Q. And in the second paragraph of the letter, first sentence, he refers to:

> "... my telephone conversation of December 8, 1999, with Dr. Michael Seoka in which we discussed updated and additional information

11:29:40 > regarding the aforementioned request."

Do you see that?

A. I do.

Q. Okay. And then in the third paragraph, first sentence he says:

11:29:49 > "As you know, SmithKline Beecham responded to this request on July 13, 1999, with a preliminary assessment of the incidence of deaths and suicides in Paroxetine clinical trials and depression."

11:30:02 Do you see that?

A. That's what the text says.

Q. So it says that the July report with the 12 deaths listed was a preliminary assessment, correct?

A. Okay.

11:30:14 Q. And then he goes on to say:

"However, at that time, there are were several cases that remained minded to double-blind treatment, thus a conservative approach was chosen and all deaths were reported that occurred in double-blind trials and trials where the design was not known. These cases have now been unblinded and open-label studies identified and removed from consideration,."

Did I read that correctly?

11:30:43 A. You did.

Q. And what that means, Dr. Ross, is that for some of the patients that were identified back in the July report that were shown to the jury yesterday, GSK had not yet been able to determine whether these patients were on Paroxetine, placebo, 11:30:57 or the active control comparator drug, correct?

A. That's what they state.

Q. And it says in the letter in the time since GSK has made those determinations and some studies were removed from the analysis because they didn't meet FDA's criteria for inclusion 11:31:20 in the analysis of the randomized controlled trials, correct?

A. No. As I explained earlier, open label does not mean uncontrolled, it means unblinded. It's perfectly possible to have an open-label randomized control trial. It does happen on indication.

11:31:44 Q. And there are a lot of label trials where they're just

taking the medication. There's no comparator, right?
A. No, sir, I'm sorry, these are two different concepts. Open label means people know what drug they're getting. If it is uncontrolled or no there's no concurrent control, you're just
11:32:07 taking drug A, that is both uncontrolled, and, by definition, open label, unblinded. Everyone knows what the patient is getting unless somebody says, well, we're going to get a drug but we're not going to tell you what it is. It's uncontrolled and unblinded.
11:32:26 You can also have, and people frequently do this, unblinded, that is open label, and controlled. And so I'm -- I think this raises more questions because if you have open label controlled studies, then this would not be what the FDA asked for.
11:32:47 Q. But you can have open label uncontrolled studies, can't you?
A. That's redundant. Open label -- I'm sorry, uncontrolled is automatically. But it doesn't say open label uncontrolled studies, it says open label.
11:32:59 Q. In any event, the FDA was looking for randomized controlled trials, correct? And GSK said, we've gone back and looked and we realized in our earlier submission there were some submitted from trials that were not randomized controlled trials, correct? You'd agree with that?
11:33:17 A. No, it does not say that here. It actually, frankly, makes

no sense. Double blind or open label is independent, really, of randomization. So I'm -- I'm -- or -- or controls. As I said, an uncontrolled -- a controlled trial can easily be open label.

11:33:40 So actually what this says to me is, they may have taken out some randomized controlled trials because they were open label, which would be completely inappropriate.

Q. And it also says that there may have been open label trials where there was no randomization, correct? Patients were

11:34:03 taking just Paxil, there was no other arm, there was no randomization, correct?

A. It doesn't state. It is silent on that.

Q. Turn to Defense Exhibit 25, which was in that notebook, page 7. That's the final submission that we've been looking

11:34:20 at, Section 2.

A. Yes.

Q. It's entitled "Incidence of Deaths and Depression Trials in the Paroxetine Central Database," is that what it says?

A. Yes.

11:34:35 Q. It starts:

> "The 18 post-randomization deaths in the 88 depression RCTs in the central database are organized by treatment as follows ..."

and then there's a chart, correct?

11:34:47 A. Yes.

Q. Looking at the chart, let's start at the right-hand column, there's 17 for Paroxetine and there's 1 for placebo for a total of 18, correct?
A. Yes.
11:35:00 Q. And the 17 deaths on Paroxetine, 11 are non-suicides and 6 are suicides, right?
A. Yes.
Q. And the 1 placebo death is a non-suicide, right?
A. This is the classification that GSK submitted to the FDA, 11:35:19 that is correct.
Q. And below the chart it reads:
"Thus, 17 out of the 5981 ..." and there's parenthesis .28 percent "... patients died after randomization to Paroxetine IR or within 30 days 11:35:36 of last dose."
A. Yes.
Q. (Reading:)
"... 6 of those cases are identified as suicides, 1.0 percent."
11:35:43 That's what it says, right?
A. That is what it says.
Q. Now jump down two paragraphs, it says:
"All but 2 of these 18 cases came from RCTs ..." that's randomized controlled trials, right?
11:35:58 A. Yes.

Q. (Reading:)
"... with an active comparator but no placebo."
Do you see that?
A. Yes.
11:36:02 Q. So 16 of the 18 deaths were not in placebo-controlled trials, but rather, were in active controlled studies according to this final analysis, correct?
A. That is what it states.
Q. Which means there are only two deaths in placebo-controlled
11:36:18 trials, correct?
A. "All but 2 of these 18 cases came from RCTs with an active comparator but no placebo ...."
Yes.
Q. And then we get more information from these two deaths. It
11:36:41 says:
"These 2 cases came from study 083 where one patient taking Paroxetine committed suicide, that's 1 over 172.6 percent, and one patient taking placebo died from cardiac arrest."
11:36:58 Do you see that?
A. Yes.
Q. And you mentioned 083 earlier today in response to my question, you said you didn't think a suicide from 083 was counted in the 2006 analysis, do you recall that?
11:37:16 A. I believe what I said was that it wasn't counted in the

Carpenter paper. In terms of the 2006 analysis, you know, I don't recall saying that.
Q. I asked you -- I said, "there was not a single completed suicide in any of the clinical trials that made up this
11:37:35 analysis, correct?" And you said, "I disagree with that statement." And I said, "what suicide and what trial are you referring to." And you said, "study 083."
A. Ah, okay.
Q. And I said, "did it happen during the controlled portion of
11:37:52 the placebo-controlled trial," and you said, "I believe so."
A. Okay.
Q. All right. So of the 18 deaths identified in this document, only one death occurred in the placebo-controlled trial, which is 083, correct?
11:38:08 A. Right.
Q. Okay. But you've looked at study 083, correct?
A. Not just -- just selected -- I've only had access to selected data from it.
Q. Your lawyers didn't give you study 083?
11:38:23 A. Ah, that data is proprietary. If it's available, I'm -- I would have requested it, but to the best of my knowledge it was not available to anybody, except people selected by GSK.
Q. You know it was made available to the plaintiff's experts in this case, correct?
11:38:42 A. We're talking about the raw data here?

Q. I'm talking about the study report.
A. No, I refer -- I referred to the data, okay. I wasn't asking about the study report. I'm referring to the data. I don't believe anybody has access to that.
11:38:58 Q. You've seen the final study report for study 083?
A. You know, off the top of my head, I honestly don't remember.
Q. You don't remember seeing it, yet you told the jury earlier today that a suicide from that trial was not included in the
11:39:15 2006 analysis?
A. Well, I was responding to your question.
Q. Okay. How did you know that?
A. So I'd be happy to walk you through how I know that.

So your question to me was, there were no completed
11:39:25 suicides in the 2006 analysis. The 2006 analysis was restricted to, I believe, placebo-controlled trials, we're agreed on that.
Q. Okay.
A. Okay. In Defense Exhibit 25 lists double blind Paroxetine
11:39:48 Paxil depression trials in the SmithKline, which is GSK central database, as of June 17, 1999.

In row 83, it shows that there were 172 patients randomized to Paxil and 67 randomized to placebo. So that is a placebo-controlled trial. This is in attachment 4. And then
11:40:20 looking at attachment 2, I believe, in the same exhibit --

MR. WISNER: Your Honor, I think for clarity for the jury, if we could get to show this up to them.

THE COURT: Well, let him go through. He hasn't his answer.

11:40:46 THE WITNESS: Thank you, Your Honor.

BY THE WITNESS:

A. So this is the same exhibit -- sorry. My eyes are not what they used to be.

Okay, so case ID1988902624 -- I'm sorry. 1989901176-1, 58-year old female randomized to Paroxetine committed suicide in study 83. So this would've been a study included or should've been included in the 2006 data. So that is why I answered your question, when you said there were no completed suicides, I said, no, I disagree.

11:41:40 BY MR. BAYMAN:

Q. Okay.

A. That is at least one completed suicide. So that's why I disagreed.

Q. That's a serious charge that I want to explore.

11:41:48 A. Sir, I'm not making a charge. I'm simply stating facts provided, based on GSK's own data.

Q. Let's talk about 083.

A. Please.

Q. You're aware that study 083 was known as a depression

11:42:03 relapse study where it starts with:

"... all patients taking Paroxetine for 8 weeks, then the patients who did well on Paroxetine were put into a second phase where they're either randomized to either Paroxetine or placebo to see if the ones who go off Paroxetine and on to placebo experienced a relapse of their depressive symptoms."

THE COURT: Is that a question?

MR. BAYMAN: Yes. I'm just asking him if he is aware --

BY THE WITNESS:

A. To the best of my understanding, that's true.

BY MR. BAYMAN:

Q. Okay. And so study 083 had what they called an acute phase at the start where everyone was on Paxil or Paroxetine and no placebo patients, correct?

A. I believe so.

Q. And do you know whether the suicide that you were just talking about occurred in the acute phase or the Paxil-only phase or later in the placebo-controlled phase?

A. I honestly don't know. I -- I -- well, this is a partial answer to your question: You know, the information that I relied on, again from -- this is GSK's line listing as line listing of deaths occurring on drug or within 30 days of last dose of double blind Paroxetine or placebo in depression -- I'm

sorry, in depression trials. So that's what I relied on, depression trial, randomized Paroxetine, occurring within this window, that's -- that's all I'm saying.

Q. Would it surprise you to learn that that suicide occurred in the Paroxetine- or Paxil-only phase where there was no placebo arm?

11:44:12

A. There was no -- excuse me, again, this was a randomized placebo -- that's not a selection criteria that was used here, okay. It said within 30 days of the last dose of double blind Paroxetine or placebo.

11:44:37

Q. And my question to you, knowing what you know about 083, that it had an acute phase in the beginning where everyone was on Paroxetine and no one was on placebo and then later there were two arms, there was Paroxetine and placebo to see if people relapsed, would it surprise you to learn that that suicide was in the acute phase when patients were taking only Paroxetine and there was no placebo arm?

11:44:54

A. I would need to -- I don't think "surprise" is the issue. I do not have access to the raw data. And so I honestly don't -- and the only thing I will say, if I understand correctly as you're saying, "well, there's a reason to exclude that," fine, then that needs to be mentioned up-front.

11:45:12

Typically, when you're dealing with a clinical trial, there's a set of guidelines that the FDA uses, research use it called consort statement where you go through and you account

11:45:30

for what happened in every patient in detail. So I don't see that here in this analysis. I don't know what happened.
Q. You know, though, because we went at great length yesterday and we're going to talk about it today, that when GSK
11:45:45 reanalyzed the data from the original NDA in 2002, that study 083 would not -- that suicide from study 083 would not meet the criteria for inclusion because it was not in the placebo-controlled portion of 083, correct?
A. All I -- actually, I don't know. All I -- I -- I have data
11:46:16 from the sponsor with a spreadsheet that says line listing of deaths occurring on drug or within 30 days of last dose of double blind Paroxetine, that's the data that I rely on and that is from the sponsor, the GSK.
Q. You're aware that in this lawsuit documents were produced
11:46:39 by GSK to the plaintiff's expert, including Dr. Healy, Dr. Glenmullen, yourself, that included the final study report for study 083, correct?
A. Yes.
Q. Okay. And you didn't review that final study report,
11:46:57 correct?
A. I may have reviewed it, but that was produced by the sponsor. I'm talking about line listings here. These are not narrative explanations of the data. These are actual data.
Q. Would it help you to see the final study report?
11:47:14 A. It might. Again, I don't know if there -- you know,

there's not been -- unless, however, there's an independent verification of the data and an analyses in that report, I would have no way of accessing its accuracy and reliability.

Q. So it wouldn't help you to see that?

11:47:40 A. That's not what I said, sir. I am just telling you that the report alone, without knowing were there mistakes made, were there things that were wrongly attributed, were there coding problems, the sorts of things that we do at the FDA, but that's what would be needed. And I think what I'm saying is,

11:48:05 at the FDA we used to have a saying "in God we trust, all others must show data."

MR. BAYMAN: I'm move to strike that statement, Your Honor.

THE COURT: That may go out.

11:48:16 BY MR. BAYMAN:

Q. You are not disagreeing with me that the suicide that occurred in that study was in the acute phase where patients were only on Paroxetine and --

THE COURT: I think you've asked that question. It's

11:48:28 covered. Let's go on to something else.

MR. BAYMAN: Thank you, Your Honor.

BY MR. BAYMAN:

Q. Well, we talked about the 2002 reanalyses, and Mr. Wisner went over those with you yesterday, so let's talk about those.

11:48:48 In your notebook there's Tab 20, which is Plaintiff's

Exhibit 129, which is the April 2, 2002 results for review of data about suicides in the 2001 FDA death report submitted to the FDA.

A. Yes, sir.

11:49:23 (Exhibit published to the jury.)

BY MR. BAYMAN:

Q. Do you recall giving testimony about this yesterday?

A. Yes.

Q. That was submitted to the FDA on February 6, 2003?

11:49:39 A. The -- I'm sorry. Yes. You said 2003, okay.

Q. That's -- that's an analysis that GSK conducted on suicide and Paxil that was submitted to the FDA that you had never seen before reaching your opinions in this case, correct?

A. To the best of my recollection, and again there were

11:50:02 multiple reports that -- same appearance basically. There were some involved in pediatric suicides. And so I am not clear -- I don't -- I don't -- and I wanted to be clear in my depression that while I wasn't sure, I rather err on the side of not saying well, yeah, I've seen this, if I haven't, okay.

11:50:28 Q. Speaking of your deposition, could you turn to it at page 242, Line 13.

A. Yes.

MR. WISNER: Objection, Your Honor, improper impeachment. There's been no inconsistent statement.

11:51:09 MR. BAYMAN: He said.

THE COURT: Wait. Wait. Excuse me.

Have you read it, sir?

THE WITNESS: Certainly since the deposition I have, sir.

11:51:17 THE COURT: All right. Now, have you read it this morning. Just calling your attention to it. Have you seen it? Do you have it in front of you?

THE WITNESS: I'm sorry --

THE COURT: Page 242.

11:51:29 THE WITNESS: I have seen it.

THE COURT: All right. What's the question, sir?

BY MR. BAYMAN:

Q. My question was, prior to formulating your opinions in your expert report, which was March 6, 2015, you had never reviewed

11:51:43 this reanalysis of the suicide data that GSK did and submitted to the FDA regarding the randomized placebo-controlled portions of the New Drug Application or NDA clinical trial data?

A. I -- in -- given the fact that I couldn't recall at the deposition formulating my expert report as opposed to going

11:52:14 back, which I have done, did afterwards, and said "would this change my opinions," no.

Q. So you had not seen the results of this until they were shown to you at your deposition?

A. I don't recall having seen them.

11:52:27 Q. You said no, though, didn't you, in your deposition?

A. You know, there was a section later on in this deposition where I made clear I couldn't -- I wasn't really sure. But I did answer "no" there.
Q. All right. You're testifying in this case as an expert on
11:52:45 FDA labeling and regulations, correct?
A. Yes.
Q. And part of -- as part of your testimony and review, you' agree that you should be familiar with GSK's submissions that pertain to its labeling, correct?
11:53:01 A. I would say that I should review them and take them into account in formulating my opinion.
Q. And you never asked Mr. Wisner to give you all the analyses that GSK had submitted to FDA concerning suicidality and the use of Paxil, correct?
11:53:21 A. Ah, I actually had thought that he -- that that was what I asked him. I believe and I think he pleased that he had as well.
Q. Is it your testimony that you asked Mr. Wisner to give you all the analyses that GSK had submitted to FDA concerning any
11:53:43 suicidality issue and Paroxetine?
A. Yes.
Q. Turn your deposition to page 248.
A. Uh-huh.
Q. Line 5.
11:54:09 A. Ah .... you mean did I put it in those exact words?

Q. No, I'm going to ask you the question.
A. I apologize. I apologize, Mr. Bayman.
THE WITNESS: I apologize Your Honor.
THE COURT: What's the question.
11:54:18 BY MR. BAYMAN:
Q. Okay:
"... did you ask counsel to give you all of the analyses that GSK had submitted to FDA concerning any suicidality issue and use of
11:54:30 Paroxetine?"
And your answer was "no."
MR. WISNER: Objection. I mean, the next question.
THE COURT: Read the rest of the page.
MR. WISNER: It reads, Your Honor --
11:54:43 THE COURT: No. No. It doesn't work that way.
Mr. Bayman, read the rest of it.
MR. BAYMAN: Yes, sir, I will.
(Brief pause).
BY MR. BAYMAN:
11:54:55 Q. (Reading:)
"Question: You didn't ask him to do that?
"Answer: I asked him to supply documents that I thought would address questions that I had.
"Question: You didn't ask him, do I have every
11:55:10 submission that GSK has made about Paxil and

suicidality that was submitted to the FDA.

"Answer: No."

And then it goes on, "all right, let me hand you" and a new exhibit.

11:55:22 THE COURT: All right. Proceed.

MR. BAYMAN: Thank you.

BY MR. BAYMAN:

Q. But yesterday you gave an opinion about those reanalyses, correct?

11:55:36 A. Yes.

Q. When did you form that opinion?

A. Ah, let me -- again, I want to clarify the use of the word "opinion." I say in my report that I reserve the right to amend or modify language to that effect if new information

11:55:59 comes in. Believe me, after this I thought, did I look at this, did I not look at this.

So believe me, I went back and I looked at it. And I thought, does this change the opinions that I've rendered in my report. If anything, it made me more confident in my opinions,

11:56:19 but it didn't leave me to change my opinions in the sense like, "well, no, I'm wrong that the labeling is okay."

So I would say, you know, when you say opinion about that study, I would say the language I would use is, "what do I --" And, I'm sorry, I don't know if this answers your

11:56:41 question, but I'm not using the word "opinion" in the sense of

opinions on questions I've been asked to render. This is a piece of data that I certainly have reviewed since the deposition multiple times and said, "does this change my opinions," and the answer to that is "no."

11:56:58 Q. You didn't amend or supplement your report then, correct?

A. That's correct.

Q. All right. Let's look at the analysis.

A. Okay.

Q. Page 2 of the exhibit.

11:57:08 A. Uh-huh.

Q. And this is -- what GSK is doing here is looking at the randomized double-blind placebo-controlled data from GlaxoSmithKline clinical trials in the NDA, correct?

A. Yes.

11:57:26 Q. And this analysis excluded adverse events of suicidality that occurred in uncontrolled phases of the trial, correct?

A. Again, I am going to say specifically with PAR 04, very specifically, that referring to that as not placebo-controlled is not correct.

11:57:57 And although I don't have the exact location of it, the citation at the top of my head, there are instances in which GSK employees referred to it as placebo-controlled.

So I just want to be clear about what I mean by "placebo," because I don't see the word "concurrent here. And

11:58:21 it is certainly of extremely valid trial design in, for

example, on cancer trials, to say, "we're going to have a crossover after the double blind finishes," but those are not considered to be not placebo-controlled. There is a preexisting placebo arm consisting of patients randomized from
11:58:43 the same group at entry, and, therefore, I would just say, referring to PAR 04, as uncontrolled is not correct.
Q. Well, we're going to get to PAR 04, I promise you.
A. I look forward to it.
Q. PAR 04, what you know about it, would not be included in
11:59:03 the criteria for the FDA's analysis in 2006, correct?
A. I can't say one way or the other, at this point.
Q. And you would agree that the criteria that GSK used back in 2002, the inclusion criteria of what trials would be analyzed, was the same criteria that the FDA used in 2006, correct?
11:59:31 THE WITNESS: I'm sorry, Your Honor, could I ask that that be read back to me.
THE COURT: Read it back.
(Question read.)
BY THE WITNESS:
12:00:03 A. I'm not clear -- I'm not sure off the top of my head. I'd have to go back and do a side-by-side comparison of these.
BY MR. BAYMAN:
Q. All right. Let me ask it more simply: This analysis, like the FDA's analysis in 2006, excluded adverse events that
12:00:18 happened in open label or, extension phases, or uncontrolled

data, correct?
A. I don't think that's -- well, I think my answer would be to the extent that one is willing to accept that excluding something like PAR 04 and throwing out any events that happened there because it's suddenly called "uncontrolled," yes, I'd agree with you.
Q. All right. Let's look at the table at the bottom of the page.
You got 5 suicide attempts in patients taking Paxil out of 921, correct?
A. That's correct.
Q. Hang on. Wrong table.
(Brief pause).
BY MR. BAYMAN:
Q. This is the attempts.
A. Okay.
Q. This is Tab 15, suicide attempts.
A. I'm sorry, in which binder?
Q. The big one; ours. Tab 15. Plaintiff's Exhibit 122, which is what you were shown yesterday.
(Brief pause).
BY THE WITNESS:
A. Okay.
BY MR. BAYMAN:
Q. Okay. This is --

MR. BAYMAN: Okay; got it, Roger?

(Exhibit published to the jury)

BY MR. BAYMAN:

Q. While he's pulling that up, this is the report that you looked at with Mr. Wisner yesterday that contained GSK's reanalysis of the suicide attempt data that was part of the NDA and analyzed in the 1991 report, correct?

A. I believe so, yes.

Q. And you were shown a document yesterday involving a conversation between Dr. David Wheadon of the FDA and Dr. Laughren -- I mean, Dr. David Wheadon of GSK and Dr. Laughren of the FDA, correct?

A. I believe so.

Q. Okay. Just turn to the analysis. It's page 2 of the exhibit.

A. Yes.

Q. And this analysis, it says looked at randomized placebo-controlled double-blind portion of the studies, correct?

A. Yes.

Q. And it excluded adverse events that occurred in uncontrolled phases of the trials, correct?

A. Yes.

Q. And if you look down at the bottom, it shows 5 suicide attempts in patients taking Paxil out of 921, correct?

A. Yes.
Q. And that's -- that's .5 percent, correct?
A. Yes.
Q. And it shows one suicide attempt in patient taking placebo
12:03:54 out of 554 or .2 percent, correct?
A. Yes.
Q. You would agree with me that GSK's analysis submitted to FDA in May of 2002 did not reflect a statistically significant increased risk for suicide attempts for patients who had taken
12:04:16 Paxil, correct?
A. With the caveat that the study was not powered to show that. It was never set up to do that in the first place. I'd agree with you that it doesn't show a statistically significant association.
12:04:31 Q. Okay. Thank you.

Now, let's go back and look at 129, which is Tab 20 in your book.
A. Yes.
Q. You see here that GSK submitted a reanalysis of the data on
12:05:00 completed suicides from the NDA clinical trials, correct?
A. The page that I have in front of me says --

MR. BAYMAN: Blow that up, Roger.

(Brief pause)

BY THE WITNESS:
12:05:13 A. It says -- I'm sorry, maybe I'm in the wrong tab here. I'm

looking at Defendant's Exhibit 40. Are we taking about Tab 20 in plaintiff's binder?
BY MR. BAYMAN:
Q. No, Tab 20 in our binder.
12:05:24 A. Tab 20 in your binder.
Q. Plaintiff's Exhibit 129, which I think is already in evidence.
A. I'm sorry, what I'm seeing here is Defendant's Exhibit 40.
MR. WISNER: Mr. Bayman, Tab 20 has Defendant's
12:05:38 Exhibit 40 in it.
MR. BAYMAN: May I approach?
MR. WISNER: He has it in our binder. Saves some paper.
MR. BAYMAN: Okay.
12:05:52 (Binder tendered to the witness).
THE WITNESS: Thank you, sir.
BY MR. BAYMAN:
Q. Plaintiff's Exhibit 129, the results-reviewed data about suicides in the FDA death report submitted to the FDA.
12:06:06 A. Okay.
Q. Got it?
A. I do.
Q. And these -- this is also an analysis that GSK conducted on suicidality in Paxil that was submitted to the FDA that you
12:06:18 never seen before reaching your opinions in this case, correct?

A. I don't believe so.
Q. Okay. And if we look at -- this analysis also looked at completed suicides from randomized placebo-controlled clinical trials that were part of the New Drug Application in 1989 and
12:06:48 part of the 1991 suicidality report that we talked about earlier, correct?
A. Yes, I believe so.
Q. And this analysis also went back and looked at the suicide data from the clinical trials that were included in the '91
12:07:03 report and excluded adverse events that were included in uncontrolled phases of the trial, correct?
A. Again, I'm going to say you keep saying "uncontrolled" and I'm going to disagree with you on that.

For example, PAR 04 had a placebo-control and that is
12:07:23 a well recognized statistical and regulatory principle or design that that is not suddenly uncontrolled. So I'm not going to agree with the question in that form.
Q. Okay. We're going to talk about 04 in a minute.
A. Sure.
12:07:40 Q. Look at the table at the bottom of page 2.
A. Uh-huh.
Q. You see that this is the number of suicides on Paroxetine against the number of suicides on placebo during randomized placebo-controlled clinical trials, correct?
12:07:57 A. Yes.

Q. And there were zero suicides for Paroxetine patients, correct?
A. That's what's listed there.
Q. And zero for placebo, correct?
12:08:11 A. Yes.
Q. And it mentions, down below, that 2 patients have been excluded from this analysis because their suicides occurred during pretreatment, correct?
A. That is what the text states.
12:08:27 Q. Those are the run-in suicides that we saw reflected in Dr. Brecher's report, correct?
A. Ah, so you -- just so I make sure I understand before I answer. These are patients who previously had been listed as placebo suicides. This does not indicate what arm they were on
12:08:48 here, but these are two -- you are saying, in essence, it's two placebo patients.
Okay, I actually don't recall the patient ID's, but if you say those are placebo suicides that occurred were attributed to placebo even though they were pre-randomization,
12:09:06 sure.
Q. Now, on Tuesday, I think it was, and today, you've told the jury that study 04 should've been included in this analysis because it was placebo-controlled, correct?
A. That is correct.
12:09:25 Q. Okay. Let's look at --

(Brief pause).
BY MR. BAYMAN:
Q. Do you have -- if you go back and look at Plaintiff's Exhibit 129. Do you have it there?
12:10:23 A. If you could just direct me to a binder and a tab.
Q. The document I handed you.
A. Oh. Sorry.
Okay. I apologize.
(Brief pause).
12:10:45 BY MR. BAYMAN:
Q. And let's go and look at now in the plaintiff's binder that Exhibit 25, which we've looked at earlier. That was the final version of that 1999 submission that we were talking about.
MR. WISNER: Defendant's Exhibit 25.
12:11:15 BY MR. BAYMAN:
Q. Yes.
A. Okay. That's defendant's exhibit.
Q. Yeah, in the binder that Mr. Wisner gave you.
A. Uh-huh. Okay. Yes.
12:11:21 Q. Okay. You see the chart there, attachment 4?
A. Attachment 4, yes.
Q. And you see the fourth study listed is study 004.
A. Yes.
Q. And right above is study 003?
12:11:53 A. Yes.

Q. And you know that's 003 is related to 004, correct?
A. I do.
Q. Because in the far right column it says, for study 004, it says extension of study 003?
12:12:10 A. Right.
Q. Okay. So let's see what we have for study 003. Do you see there's a column for Paroxetine, placebo, and active comparator that gives us the number of patients in each group, do you see that?
12:12:24 A. Yeah.
Q. And for study 003, we see 240 on Paroxetine, 240 on placebo, 237 on active comparator?
A. Yeah.
Q. That's what's called a three-arm study, right?
12:12:41 A. Actually, if there's only -- normally if there's 3 different kinds of pills the patients are taking, that would be a three-arm study. In this instance I'll agree, study 004 would be a three-arm study.
Q. No, 003.
12:13:04 A. Oh, yes. 003, sure.
Q. Now, look at the line for 004.
A. Uh-huh.
Q. It's got 219 for Paroxetine and 79 for active comparator --
A. Hmm.
12:13:15 Q. -- but it has zero for placebo?

A. Uh-huh.
Q. So if a study has zero placebo patients, that means it's not placebo-controlled, correct?
A. In this instance I wouldn't agree with you for the reasons
12:13:27 that we've been debating back and forth, okay.
It is very common in studies -- this is not -- again, science is science. This is not something that is unique to neuropharm drugs. This happens in oncology, this happens in HIV, this happens in HCV. And an original placebo group
12:13:54 represents a placebo-controlled group. And that is something certainly that I'd be happy to point you to FDA guidances. I mention the E10 guidance that is accepted internationally, not just by FDA but by others.
But, I mean, if you say there's not a concurrent
12:14:18 placebo-controlled group, with the caveat that that is creating a distinction that doesn't make a difference, I would agree with you.
Q. You know, Doctor, that what happened in these two studies, 03 and 04, is that patients who met certain criteria at the end
12:14:37 of 03 were then enrolled in 04 where they took either Paroxetine or an active comparator but not placebo, correct?
A. Well, not all of them. It's obvious there were fewer patients than in the original study, but please go ahead for the sake of argument.
12:14:59 Q. Well, no, my point is, they're in 003 and they meet the

criteria, but when they go to 04 they either take Paroxetine or an active comparator but there were no patients in 04 on placebo, correct?

A. Sir, this is an extension study. It is not a completely new study with new trial cites, new protocol, new investigators, new monitoring methods. It is the same -- drawing from the same population that went into study 3.

So, again, if your point is that there weren't controls, placebo controls matched with them, I would agree and say, so what? Because the placebo arm in 03 is your comparator for 04, and that is why I said it was inappropriate to exclude those 3 suicides and make them go away.

Q. You said it's the comparator, 04 is the comparator for 03?

A. No, that is not what I said, sir.

Q. I'm sorry.

A. I said the placebo patients in 03 represent an external comparator for 04.

And again, this principle is widely applied in cancer trials where you don't want to continue people on a placebo or no added drug trial, but you do want to know things like what happens with later events. This is something that happened a lot with our analysis with the stimulating agents.

So I'm just not going to agree with you, I'm sorry, that PAR 04 is, quote, doesn't have a placebo control group.

And again, I don't recall the exact citation, but I've

certainly seen it in documents, where GSK itself referred to PAR 04 as placebo-controlled.

Q. But in PAR 04 there were no patients on placebo, correct?

A. There were no concurrent patients on placebo.

12:17:20 Q. Not concurrent, not at all, correct?

A. Sir, I -- I said there were no concurrent placebo patients. I think we're saying the same thing. I think you want me to stay it differently, if I understand. I don't mean to impute anything to you, but I'm not going to agree that this was not a

12:17:42 placebo-controlled trial.

Q. So you would not agree that suicides -- or suicide attempts from that study should not have met the criteria for inclusion in the 2002 analysis, is that right?

THE WITNESS: Your Honor, I'm sorry, could I ask that

12:17:59 that be read back.

THE COURT: Yes.

(Question read.)

BY THE WITNESS:

A. I'm trying to take out double negatives here. So what I

12:18:24 would say is that based on my description of the issues, and these are not sort of like -- these are fundamental statistical issues, is a study controlled or not, I would say these events should be -- should've been included in 2002 trial -- 2002 analysis, I'm sorry.

12:18:49 BY MR. BAYMAN:

Q. Okay. Even though no one in study 04 was on placebo?
A. They were not -- there was no -- sir --
THE COURT: We're getting into an argument now. I think we understand your point.
12:19:03 MR. BAYMAN: Yeah. I'll move on.
THE COURT: Move on.
MR. BAYMAN: Yup.
BY MR. BAYMAN:
Q. I want to briefly ask you, because Mr. Wisner brought it
12:19:10 up, about emotional lability.
A. Yes.
Q. You testified in response to Mr. Wisner's questions that GSK had not provided information to FDA on the adverse event known as emotional lability, do you recall that testimony?
12:19:28 A. I believe what I said was they did not indicate that the actual event or the actual adverse event was suicide or suicide attempts. And I'm referring to, I believe, the original NDA.
Q. Fair enough. Let's go back to the original NDA. Let's put up -- look at Tab 21, which is Plaintiff's Exhibit 75.
12:20:04 (Exhibit published to the jury.)
MR. BAYMAN: I believe that is in evidence, Your Honor.
BY THE WITNESS:
A. Okay.
12:20:17 THE COURT: What's the question?

BY MR. BAYMAN:
Q. The question is, that's what's called the integrated summary of safety Paroxetine from November of -- November 10, 1989, correct?
12:20:32 A. I believe so.
Q. And that was submitted to the FDA, right?
A. To the best of my knowledge, yes.
Q. I mean, to get an NDA approved, you've got to submit an integrated safety summary, correct?
12:20:45 A. Integrated efficacy summary and safety summary.
Q. All right. Turn, if you would, to page -- the page with 301 in the lower right corner. It's the start of a section entitled "Summaries of Suicide Attempts In U.S. Clinical Trials."
12:21:04 A. Uh-huh.
Q. And turn to page 208A.
A. Okay.
Q. Look at the second listing on the page.
A. Uh-huh.
12:21:19 MR. BAYMAN: Roger, can you bring the columns down from the top.
(Brief pause).
BY MR. BAYMAN:
Q. Got that?
12:21:35 A. I do.

Q. This is a report of a suicide attempt. And below the column "adverse experience" it says "suicide attempt," right?
A. Yeah.
Q. Okay. And in the column then, on the far right, is headed "PT," that stands for preferred term, correct?
12:21:59
A. Uh-huh.
Q. That's a term used for a coding, what is -- you talked about a coding dictionary. Coding dictionaries have preferred terms, correct?
A. Yes.
12:22:22
Q. And I think what you explained to the jury, and correct me if I'm wrong, that if someone has stomach distress, someone might call it upset stomach, someone might call it indigestion, someone might call it upset stomach, and it might code to a preferred term of nauseous, for example?
12:22:39
A. Okay.
Q. Right? I mean, that's an example.
A. Yes.
Q. In those -- in terms like upset stomach or indigestion, those would be called verbatim terms and they would code to a preferred term called like nauseous, correct? Just a simple example.
12:22:52
A. Yes.
Q. Okay. So here, the preferred term in the column is "emotional lability," correct?
12:23:04

A. That is the term that the sponsor decided was the preferred term.
Q. Based on the coding dictionary, correct?
A. No, sir. This was -- there are thousands of preferred
12:23:21 terms, and "suicide attempt," if I remember correctly, also could've been chosen as a preferred term.
Q. Do you know what coding dictionary SmithKline Beecham was using in the 1980's?
A. In the 1980's? The only one that might be familiar to me
12:23:43 at the FDA at that point would be COSTART.
Q. But you don't know which one SmithKline Beecham was using, correct?
A. I only know that from the FDA, COSTART had emotional -- I'm sorry, "suicide attempt" is a preferred term.
12:23:59 Q. Okay. Let's look at the next page, 208B.
(Brief pause).
BY MR. BAYMAN:
Q. Do you see that?
A. Uh-huh.
12:24:27 Q. There, again, we have an adverse experience suicide attempt, we have a preferred term "emotional lability," right?
A. That's the term the sponsor chose.
Q. And this indicates that that suicide attempt was coded to the preferred term "emotional lability," correct?
12:24:45 A. With the caveat that in its guidance developed after these

kind of things on premarket and post-market safety assessment, the FDA said clearly that code manipulation and inappropriate coding leads to huge problems, I agree with you that that's what that says.

12:25:06 Q. And on the previous one I showed you, which was an overdose, that was coded to the preferred term -- it was a suicide attempt that was coded to the preferred term "emotional lability," correct?

A. I agree that they were coding it to an inappropriate term, 12:25:23 if that's what you mean, which was emotional lability.

Q. You would agree with me, though, that this document shows, and this was was submitted to the FDA, this document discloses suicide attempts that are clearly coded to the preferred term "emotional lability," correct?

12:25:40 A. No, I wouldn't agree with that. These are buried in the tens of thousands of pages. They are not the basis for the summary tables, of adverse event experiences, that typically reviewers rely on.

This is a common practice by sponsors who say, "well, 12:26:01 there's something that's not so good in here, I'm going to bury it." And that's not my random opinion, that is stuff that I had to deal with directly at FDA. So this was buried.

And I've talked about the size of NDA's. It's almost impossible for a reviewer to find this unless the sponsor calls 12:26:24 it out in some way. For example, puts it in a table. But this

is what, I would say, is the equivalent of extremely fine print.

MR. BAYMAN: I move to strike that as nonresponsive, Your Honor.

12:26:40 THE COURT: That may go out.

MR. BAYMAN: Thank you.

BY MR. BAYMAN:

Q. Tab 22, quickly, and we'll wrap this up, this line of questioning.

12:26:53 And that's Plaintiff's Exhibit 263.

A. Yes.

Q. The jury saw this last week. Look at the page where there's numbers called PAR numbers, and it's 347126.

THE COURT: I'm going to have to break now, ladies and

12:27:17 gentlemen. 12:30, and we will break for lunch for an hour.

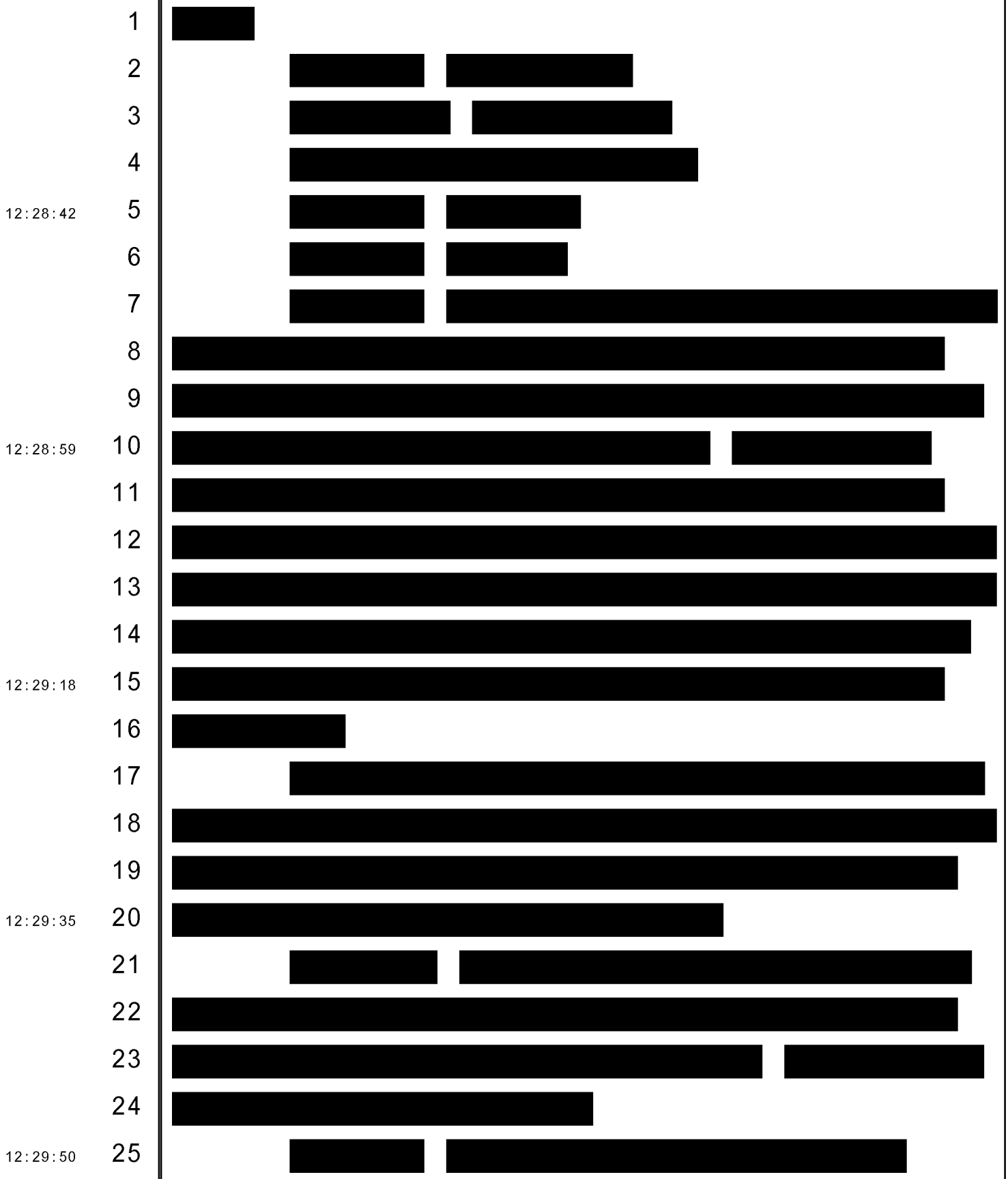
(The following proceedings were had out of the presence of the jury in open court:)

[redacted]

12:27:54

[redacted]

12:28:07


12:28:42
12:28:59
12:29:18
12:29:35
12:29:50

[redacted]

12:30:10

[redacted]

12:30:31

[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 March 23, 2017