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 22, 2017
Defendant.	9:20 o'clock a.m.

VOLUME 6 A
TRANSCRIPT OF PROCEEDINGS
BEFORE THE HONORABLE WILLIAM T. HART

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

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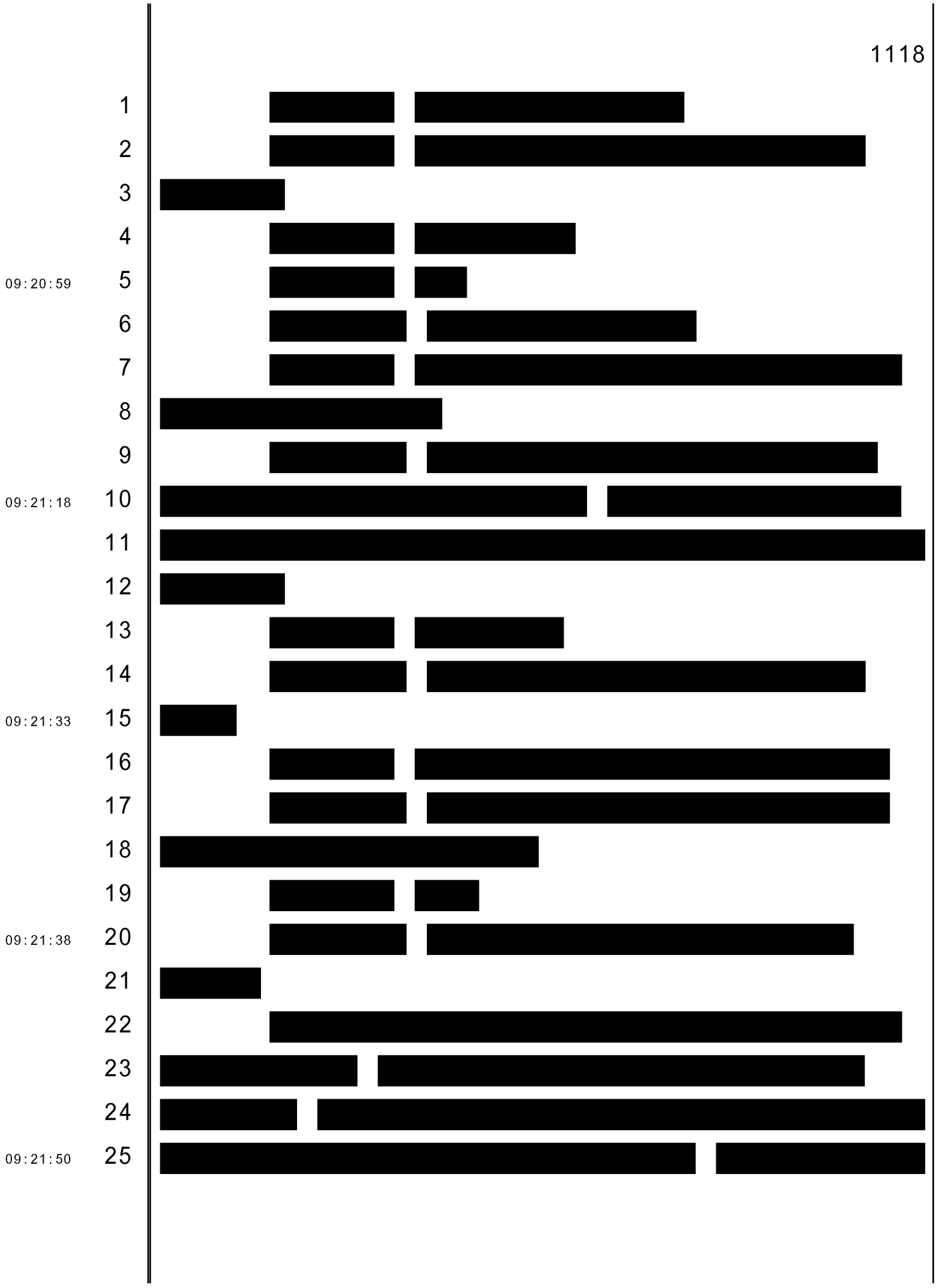
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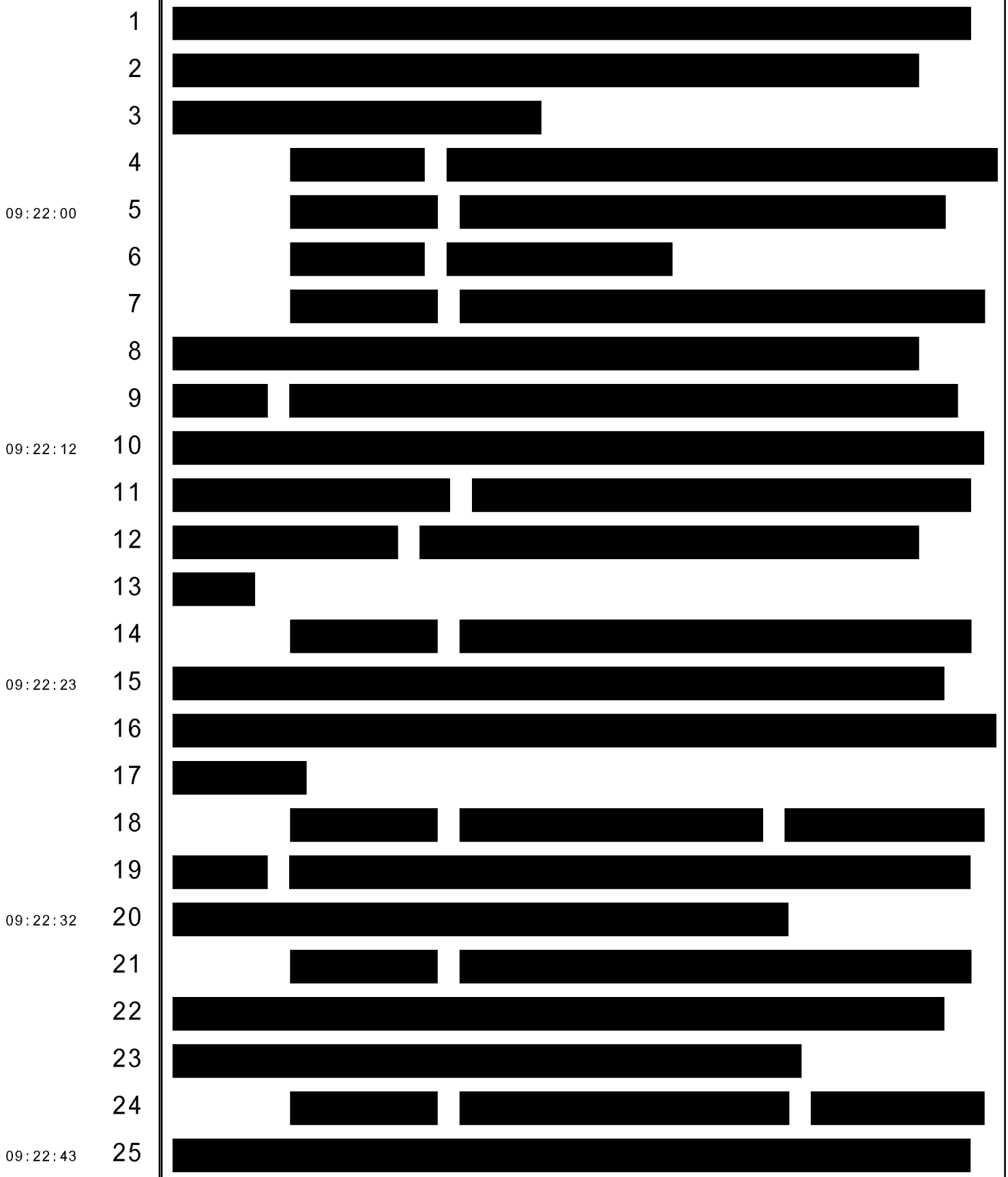
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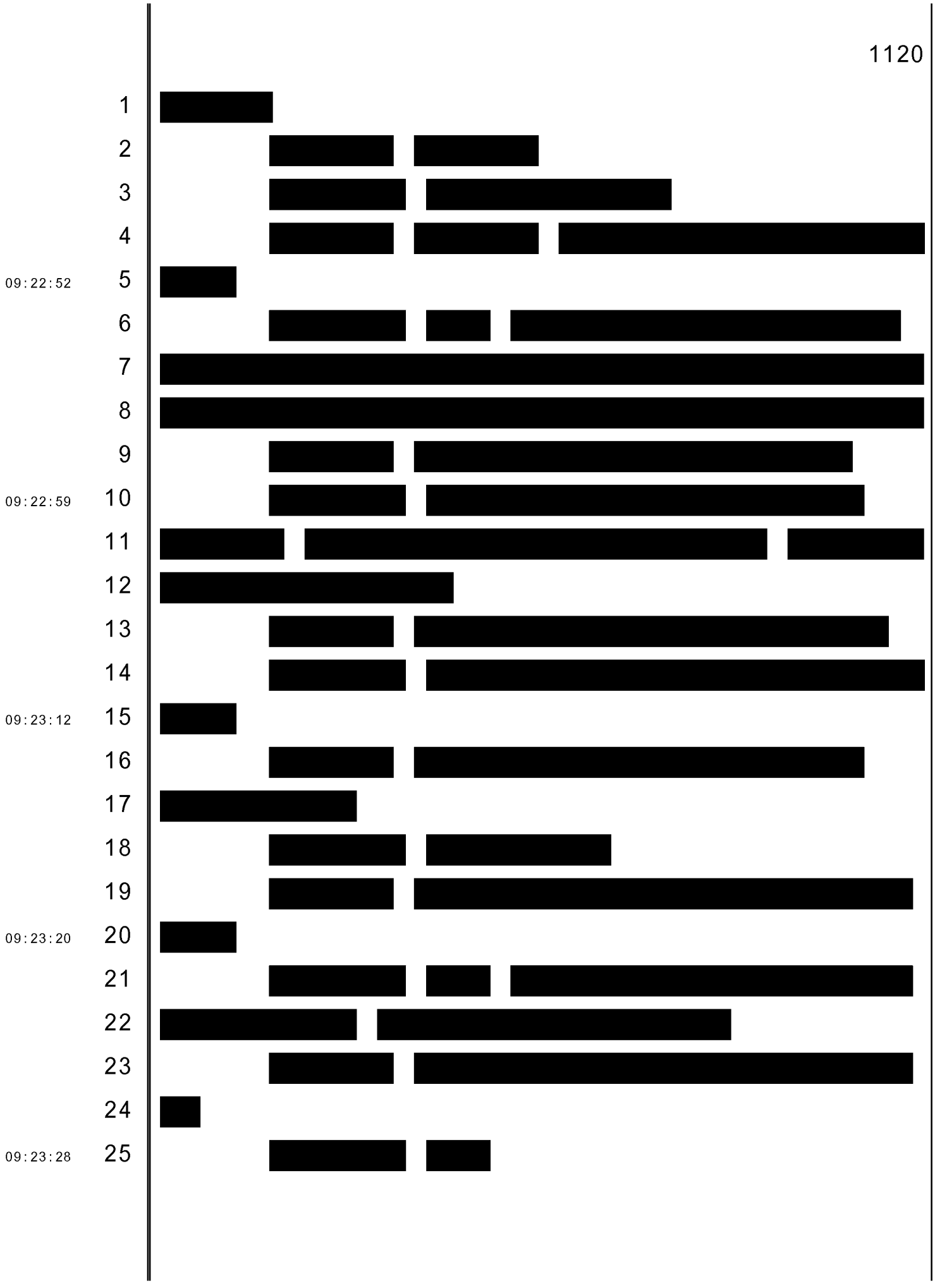
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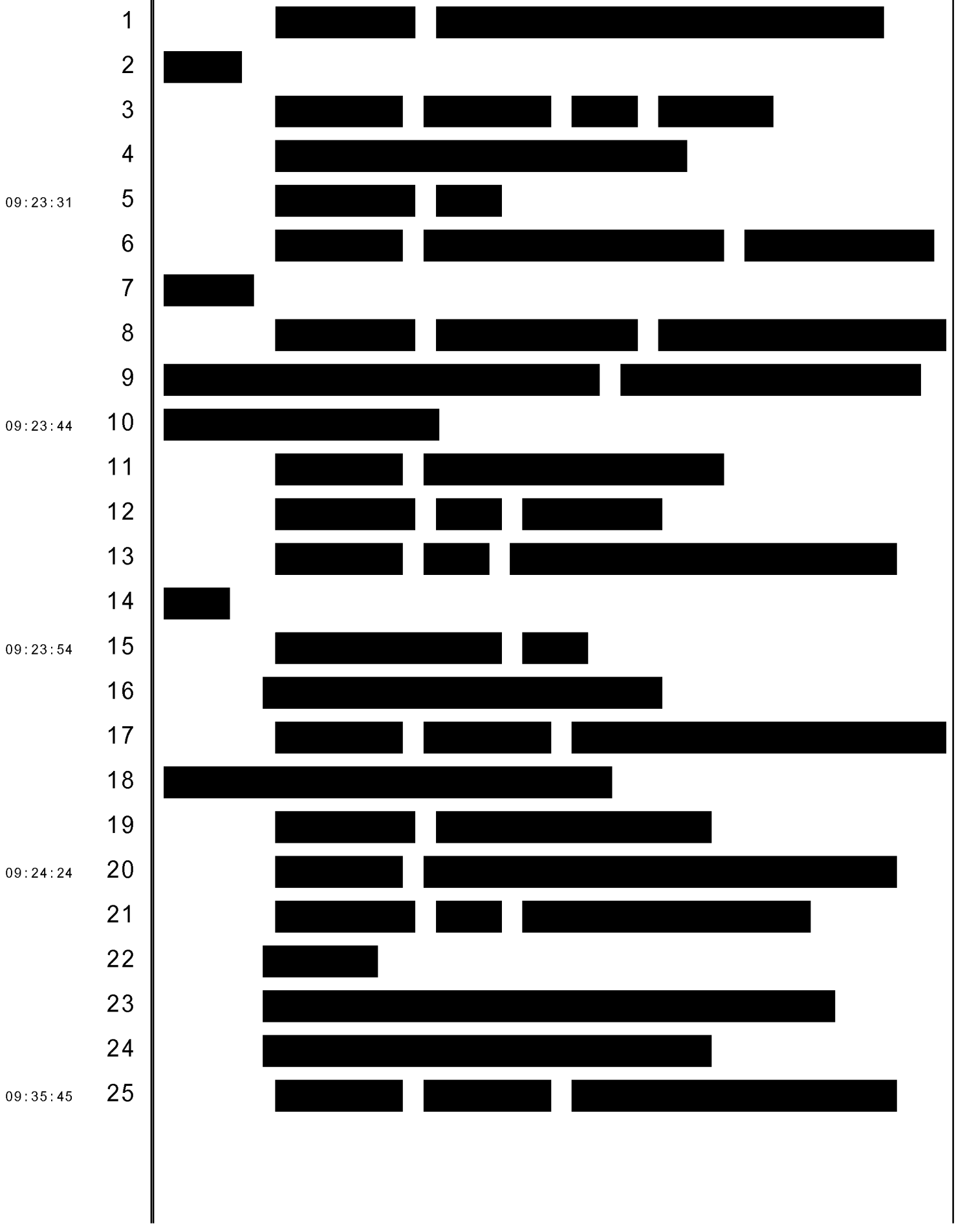
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09:36:20

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

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

09:37:21 You may proceed, sir.

MR. WISNER: Thank you, Your Honor.

DAVID ROSS, PLAINTIFF'S WITNESS, PREVIOUSLY SWORN

DIRECT EXAMINATION (resumed)

BY MR. WISNER:

09:37:27 Q. Good morning, Doctor.

A. Good morning.

Q. Let's get that mike on you.

(Brief pause).

BY MR. WISNER:

09:37:34 Q. All right.

MR. WISNER: Your Honor, permission to publish. We were in the middle of that before we ended for the day.

THE COURT: You may procedure.

(Exhibit published to the jury.)

09:37:48 BY MR. WISNER:

Q. Doctor, we were looking at Plaintiff's Exhibit 9. What document is this?
A. So this is a 2006 letter from GlaxoSmithKline to the FDA, specifically to the division director of psychiatry products at
09:38:17 CDER division that regulates Paxil. And I believe this is the results of GSK's analysis of suicidal behavior and other events occurring in Paxil.
Q. Okay. We were discussing this document yesterday, do you recall?
09:38:47 A. Yes.
Q. Okay. And in this letter there is a paragraph that we were talking about. And I'll pop it up right here. It says:

> "... in adults with MDD all ages, there was a statistically significant increase in the
09:39:03 frequency of suicidal behavior in patients treated with Paroxetine compared with placebo. However, the majority of these attempts for Paroxetine, 8 of 11, were in younger adults age 18 through 30 years. These MDD data suggest
09:39:21 that the higher frequency observed in the younger adult population across psychiatric disorders may extend beyond the age of 24."

Now, Doctor, is that discussion of the majority of the suicide attempts occurring in younger adults age 18
09:39:40 through 30 an accurate statement?

A. No.
Q. How so?
A. The words -- if you could just highlight these for me?
Q. Sure.
09:39:49 A. Or highlight not for me but for the Court.
(Short interruption by the court reporter.
BY THE WITNESS:
A. If you could highlight the words, and this is on the third line, "the majority of these attempts for Paroxetine."
09:40:21 Q. Okay. What's wrong with that, Doctor?
A. Well, it's, at best, misleading, and at worse, false. You could say that 8 of 11 were younger adults age 18 to 30 and that will be a correct statement; however, you could also say, as I pointed out yesterday, that 8 of the 11 were in adults
09:40:46 aged 25 and up, and that would also be correct.
Q. Well, then, Doctor, if this paragraph or something similar to it with that the majority-of-attempts language were to be put into the Paxil label, would that make the Paxil label adequate or no longer misleading?
09:41:11 A. So just so I'm clear, this statement -- what you are saying is the statement saying the majority of these attempts for Paroxetine?
Q. Correct. If they put something like that in the label, would that have made the label no longer misleading?
09:41:26 A. No.

Q. So --
A. It would've been more misleading, actually.
Q. In fact, did GSK put this language in the label in 2006?
A. It did.
09:41:37 Q. And did it do so without prior approval from the FDA?
A. That is correct.
Q. How can a drug manufacturer just put something in the label without getting approval from the FDA first?
A. So the regulations allow a manufacturer to add or
09:41:56 strengthen a warning on its own with the proviso that the FDA can review it, and based on the review, ask it to change the language.

And, in fact, if any recall correctly, there was quite a period of time between GlaxoSmithKline adding this language
09:42:18 and the FDA completing its review. It's not like -- at the FDA I conducted and supervised, I would say, hundreds of these reviews. These are called Changes Being Affected where the manufacturer tells the FDA, hey, we think there's information that is important here for a warning, we want to get it out
09:42:45 there as soon as possible, we're letting you know because we know you're eventually going to have to approve it, but we want to get it out there.

And so they basically give them 30 days notice and then they can start printing it up and sending it out, and they
09:43:03 do. And in my experience, it's extremely unusual for changes

being affected supplement to get reviewed by the FDA in less than 30 days. If the FDA comes back and says, no, we think you need to change this, it's not like the manufacturer suddenly has to immediately pull back what it's done, it works with the FDA to come up with new language and then it prints new labeling. But the idea is that to add or strengthen a warning the sponsor can -- when I say "sponsor," I'm sorry, more jargon there, but the manufacturer can do that on its own. Has to let the FDA know, but it can do it on its own.

09:43:44 Q. So GSK specifically uses this regulation to add this regulation to the label in 2006?

A. That is correct.

Q. Do you believe that by adding this language it made the label sufficient?

09:43:56 A. I think it made the label worse.

Q. All right. Now, I want to get closer in time to the present. In 2007 what happened with the labeling for Paxil?

A. So on the basis of analyses that pharmaceutical companies, manufacturers of SSRIs had done and that the FDA had done, the

09:44:26 FDA requested manufactures of SSRIs to add what I talked yesterday, class labeling, labeling that applies to a particular class of drugs, and in this case it was SSRIs. And that involved the potential for suicidal behavior to emerge in connection with people getting started on those drugs.

09:44:54 Q. Was it limited to a certain age group?

A. It was.
Q. What was that age group limitation for the class labeling?
A. For just looking at the class of all antidepressants and all SSRIs, it was that class labeling across all drugs was 18 to 24.
Q. Did that class labeling warn that Paxil could induce suicidal behavior in adults over 24?
A. No, it did not.
Q. Do you believe that GSK had an obligation to put that in the label after the class labeling?
A. Yes.
Q. All right. I want to talk about the label that existed in 2010 for Paxil when Stewart Dolin passed away.

Have you reviewed that label, Doctor?

A. I have.
Q. And have you gone through it in detail and figured out what was the problem or what needed to be added to it?
A. I did exactly the same thing I did when I was a medical reviewer and a medical team leader at FDA in terms of analyzing the label and saying, we're going into labeling negotiations with the manufacturer, what do we think should be put in and where.
Q. And did you -- did you mark up the label, different color pens and everything?
A. I did.

Q. Okay. I'm going to go through that label with you in just one second, but before I do that let me just ask you a simple question: What is wrong with the 2010 Paxil label as it relates to adult suicidal behavior over the age of 24?

09:46:54 A. So it does not say anything about Paxil in particular. It just talks about all antidepressants, all SSRIs. It doesn't mention anywhere in there that the data that we discussed yesterday show that the risk of inducing suicidal behavior in patients getting Paxil is not just for people under 24, 24 and

09:47:29 under, it extends to older ages.

So basically by being silent on that, it leads people, prescribers specifically, to think what applies to those antidepressants--that is, risk is restricted to people 24 and under--must be true for Paxil, even though that is really not

09:47:55 true. It is silent on that. And so it's almost like Paxil is getting a free ride on the other antidepressants.

Q. Have you seen any analysis done by the FDA that shows that Paxil is, in fact, worse than the other SSRIs?

A. Yes.

09:48:16 Q. And what analysis is that, Doctor?

A. So two reviewers at FDA analyzed the data that all these pharmaceutical manufactures had brought in in 2006. And the names of these reviewers were Dr. Stone and Dr. Jones, and so I'll refer to that as the Stone/Jones report.

09:48:39 MR. WISNER: Your Honor, permission to publish Joint

Exhibit 13. It's in evidence.

THE COURT: You may proceed.

(Exhibit published to the jury.)

BY MR. WISNER:

09:48:46 Q. Doctor, I'm putting it up on the screen. Is that the Stone/Jones report?

A. Yes.

Q. All right. And in this report did the authors from the FDA break down the drugs for all ages, all SSRIs for all ages in

09:49:03 the risk of suicidal behavior?

A. Yes, they did.

Q. I'm going to get to it right now.

I'm looking at table 16, Doctor. Is this the table you're referring to?

09:49:20 A. Yes.

Q. It says "all drugs" and it has an odds ratio of 1.1, do you see that?

A. Yes.

Q. And that's referring to not just SSRIs but every other

09:49:31 conceivably antidepressant?

A. All the antidepressants that were analyzed in this report, yes.

Q. Thank you. I guess you can see this.

A. Yes.

09:49:38 Q. All right. Then we have the SSRIs, risk ratio for all

SSRIs, and what is that, Doctor?
A. So this is basically the ratio of -- the relative -- it's not the relative risk, but it's how manyfold -- what's the increase in the chances that a patient is going to show
09:50:03 suicidal behavior on this particular drug that's listed here, the 6 drugs, compared to patients who just get placebo.
Q. And it has 1.23. Does that mean the best estimate of this analysis is that SSRIs increase suicidal behavior by approximately 23 percent?
09:50:23 A. That is correct.
Q. Okay. Now, the list of SSRIs here, do you see the one related to Paxil?
A. I do.
Q. And what is the point estimate for that one?
09:50:34 A. So it's 2.76. In other words, the risk is increased over -- the placebo -- if you had the placebo listed here, that would be 1.0.
Q. Now, if you look over on the right there's a confidence interval, do you see that?
09:50:52 A. Yes.
Q. And you also see the P value, do you see that?
A. Yes.
Q. All right. What -- which drugs have a confidence interval that actually is above 1?
09:51:04 A. So what -- if I can take a second and say, and

Dr. Healy may have covered this yesterday, but the confidence interval is where we think -- this 2.76 is just an estimate. You say, well, is that really what the value is? The true value, if you were to do this an infinite number of times would likely fall between in the confidence interval.

09:51:29

So if the confidence interval does not include 1--remember, 1 is where a placebo is-- then that is -- makes it very likely that this is not just some chance finding, but, in fact, is very real.

09:51:52 Q. Is there any significance to the fact that among all the SSRIs for which there was that class-wide label, only Paxil has a confidence interval of above 1?

A. From a regulatory standpoint, and I would also say from a clinical standpoint, I would draw the conclusion from this that

09:52:17 Paxil has a higher risk -- we're sure it has a higher risk, perhaps I should put it that way, compared to the other SSRIs of inducing suicidal behavior.

Q. Doctor, to clear it up, I want to make sure the record is clear, because we're concerned about the transcript. So if the

09:52:46 confidence interval is above 1 --

A. Yes.

Q. -- is that what shows that you have a particularly bad problem?

MR. BAYMAN: Objection, Your Honor.

09:52:56 THE COURT: Overruled.

BY THE WITNESS:
A. Yes, you're -- you're much more certain that you have a bad problem.
BY MR. WISNER:
09:53:04 Q. Now, if the confidence interval falls below 1, does that mean you don't have a problem?
A. No; it may just mean that you haven't looked at enough patients. If it doesn't cross 1, you can be very sure.
Q. And if the confidence interval, let's say, goes below 1, 09:53:20 could it also be that the studies that you're using the data from weren't designed to pick up the risk?
A. That's exactly right. And -- I'm sorry. Please go ahead.
Q. Okay. If you want to complete your answer, you're welcomed to. Did you want to say something else?
09:53:37 A. Yeah. These studies were all designed to show that the drug -- or test that the drug works. If you want to set out to see what the risk is for a drug, you need to study enough patients to do so.

There's a rule of thumb that says if you have a side 09:53:57 effect that occurs 1 percent of the time, that is 1 out of 100, in order to detect it reliably you need to study 3 times as much patients, in other words, 300 patients.

So if I have a very unusual event--like fortunately suicide is unusual--to detect one event, I need to study a lot 09:54:21 of patients. If I want to see -- and if there's a background

rate to see if a drug is associated with that, I need to study even more patients.

So the Paxil studies were never designed to look at that. The fact that they happened to find 5 suicides in the original NDA compared to none for placebo is amazing. The fact that they had a huge increase in the odds ratio -- remember yesterday we were talking about suicide attempts and there was a statistically significant difference between Paxil and placebo, when the study was not designed to do that really means there's a huge effect.

Q. And does this -- so let's look at another table. This is for all adults for all ages, is that right, Doctor?

A. That's correct.

Q. And it also is for all types of psychiatric disorders, is that right?

A. Yes.

Q. Okay. The FDA also did -- let me just find it really quickly.

Did the FDA also do an analysis of the risk under 25?

A. It did.

Q. All right. Let's --

A. Just to clarify, that is -- that analysis across all ages was for all drugs.

Q. Yeah. And the Paxil-specific number, that relates to Paxil, right?

A. Correct.
Q. So let's look at the table for just the under 25, okay Doctor.
A. Yes.
09:55:58 Q. Do you see that?
A. Yes.
Q. Is that this is?
A. Yes.
Q. All right. And again -- now, this is limiting it to just
09:56:04 25, but does Paxil in any way stand out when it comes to the confidence interval?
A. Yes.
Q. How so?
A. The confidence interval, again, is greater than -- or what
09:56:16 we call the lower bound.
Q. And what is the odds ratio here?
A. 2.23.
Q. Now, the previous one was 2.76?
A. Correct.
09:56:28 Q. So looking just at, you know, 18 to 25 year olds or under 25, right, we have 2.33, is that what this saying?
A. Correct.
Q. Okay. And then when we expand it to the entire age group, the odds ratio actually increases to 2.76?
09:56:47 A. Right.

MR. BAYMAN: Leading, Your Honor, objection.
BY THE WITNESS:
A. So if I can explain this --
THE COURT: Overruled. You may proceed.
09:56:56 THE WITNESS: I'm sorry, Your Honor.
THE COURT: Go ahead.
BY MR. WISNER:
Q. Is that right? I'm going to ask you why in a second.
A. Yes.
09:57:02 Q. What does that indicate to you?
A. That there's an increased risk for older patients as well. And let me -- this is -- let me walk through this.
If for all patients altogether the risk is increased and it's increased 176 percent. So that's how you get 2.76.
09:57:24 100 percent of the risk would be placebo, an additional 176 percent would be what is added, and that gives you 276 or 2.76. So that's all ages.
For younger individuals, that's actually -- their risk is 2.33, lower than 2.76. They actually have, compared to all
09:57:57 age group, they have an increased risk. And so this is all ages, 2.76.
This is younger adults, 2.33. Therefore, people who are older than -- to bring this up when you add in those older patients, that risk must be actually higher than 2.76. The
09:58:19 younger adults actually have a lower risk than the older

adults, and then when you combine everything that brings the older adults -- the risk that you see in older adults down.

I'm probably not explaining this as clearly as I might be, but I hope people get the idea. If the risk in older adults was normal, wasn't increased, and it's -- let's suppose that this is placebo and this is younger adults (indicating), and older adults are just the same as placebo. When you add those older adults risk to the younger adults risk, the total risk should come down.

09:58:42

Just like if you're adding hot water, cold water into hot water, the temperature should go down, but that didn't happen here. You have as you go from younger adults to let's say a certain temperature and then you add in the older adults, the temperature actually goes up.

09:59:05

Q. And is it a reasonable inference from there that the risk actually might be greater in adults over 25 than for adults or people under 25?

09:59:26

A. That's the conclusion I would draw. Again, if it were actually no risk or restricted, then the total risk should go down. You'd be, in essence, adding that cold water and bringing that temperature down.

09:59:44

Q. Did the FDA do an analysis just of 25 year olds to older?

A. In this document -- you're talking about for all drugs altogether?

Q. Yeah. All drugs, all indications, but they just looked at

10:00:06

above 25, not all ages. Did they do an analysis like that?
A. I believe they did. I believe they did, but I don't remember seeing it in here.
Q. Okay.
10:00:17 A. Which means -- I mean, when I say -- I mean that was not included in here, so --
Q. Oh, I see.
A. I mean, there's a lot of times you'll do preliminary analyses and that sort of thing, but this is the final document
10:00:31 that is publicly available.
Q. But you haven't seen --
A. And, no, I have not seen any such analysis. There are such analyses.
Q. Well, did GSK actually do an analysis of suicidality or
10:00:43 suicidal behavior from people 25 and older?
A. It did.
Q. And did it publish those results in a journal?
A. It did.
Q. And what did they show?
10:00:52 A. They showed that the risk for Paxil compared to placebo in individuals older than 24, that is those aged 25 to 64, was actually increased, just as I was saying. It was not lower.
Q. Was it higher than 2.76?
A. Yes, it was.
10:01:13 Q. All right.

Let's get to the label, Doctor. I have your marked up one and I have a blank one here. So what we're going to do is, I'm going to go through the label and I'm going to ask you questions about it and you're going to tell me what to do with the markups, okay?

10:01:27

A. Okay.

MR. WISNER: Your Honor, permission to publish Joint Exhibit 1. It's in evidence.

THE COURT: Yes.

10:01:39 (Exhibit published to the jury.)

BY MR. WISNER:

Q. Okay, Doctor, let's start off with what are we looking at here and what is this document?

A. So I believe this is the label that was for Paxil that was

10:02:02 approved by the FDA on the basis of what GSK submitted at the time of Mr. Dolin's death.

Q. All right. Let's just confirm that. Let's take a look at the last page here --

MR. BAYMAN: Excuse me. Could I see what he has?

10:02:19 MR. WISNER: Sorry, what?

MR. BAYMAN: What he has in front of him. I just want to find out what he has in front of him.

MR. WISNER: He doesn't have anything in front of him. He's got his binder.

10:02:25 MR. BAYMAN: I thought you have him a document.

MR. WISNER: No; it's right here.
MR. BAYMAN: All right. I thought you gave him the document.
MR. WISNER: It's right here. I didn't teleport it up there.
10:02:31
BY MR. WISNER:
Q. All right. So you see the data here, Doctor?
A. Yes.
Q. And that tells you what?
10:02:36
A. That tells me that this is a label that is current as of June 2010.
Q. And do you see also that it has "GSK" right there on the logo, do you see that?
A. Yes.
10:02:48
Q. Does that tell you that this is GSK's label?
A. Yes.
Q. All right. So a minute ago I asked you what's wrong with this label and you gave me two reasons basically why. What were those two reasons?
10:03:02
A. So first off, it restricts -- it does not include any information about Paxil inducing suicidal behavior, or worse, in adults 25 and older.
Secondly, it talks about the risk for antidepressants, in general, being restricted to the age of 24 and under,
10:03:36
implying that that is true for Paxil as well.

Q. Okay, Doctor, in this label anywhere -- we're going to talk about what is in the label in a second, but I want to talk about what is not in the label.

In this label is does it anywhere ever state in plain
10:03:56 English that Paxil can induce or can increase the risk of adult suicidal behavior in patients over the age of 24?

A. No, it does not.

Q. Okay. And if GSK had plainly said that somewhere in this label, do you believe they would have fulfilled the regulatory
10:04:16 obligations of warning physicians about a known safety risk?

A. I'm sorry, if you can -- repeat the question.

THE COURT: Read it back.

(Question read.)

BY THE WITNESS:

10:04:39 A. When you said "this information," the fact that it includes -- that it can induce suicidal behavior in adults older than 24?

BY MR. WISNER:

Q. Yeah.

10:04:51 A. I'm going to qualify my answer in the sense that the language in the label would have to be such that that information was not diluted or minimized by something else. In other words, it's not individual statements, it's the whole context that one has to look at.

10:05:17 Q. All right, Doctor, we're sitting here staring at the label

and the first thing we see is this black box; do you see that?
A. Yes.
Q. What is a black box?
A. So the regulations actually -- this is not a random
10:05:33 document. There's actually a structure to it. And the
structure -- it's like a book. It's like a story: How do I
use this drug. You describe the drug, you say what happens
when it goes in the body, how does it get absorbed, what can it
be used for, what sort of things you have to worry about when
10:05:55 you give it to patients, who should you never, ever, ever give
it to, who do you have to be careful about giving it to.
And so there's sections like description, precautions,
indications and usage, dosage. There's a section called
"warnings." And sometimes the warnings are so important that
10:06:17 the regs allow for them to be put at the very top in what's
called a black box warning.
Q. In your opinion and as regulatory expert, is the placement
of a warning in the black box make it the most prominent piece
of information on the label?
10:06:37 A. Yes.
Q. All right. Now, let's start off with the black box
warning.
Is there anything in this black box warning that, in
your opinion, is misleading as it applies specifically to
10:06:50 Paxil?

A. Yes.
Q. Please read to the jury, I'll zoom a little bit so we can walk through this, please tell me the part, Doctor, that you believe is.
10:07:02 A. So the most misleading part, if we can begin on the fifth line. If you could just highlight that.
Q. Sure. Is red ink okay?
A. Yes.
Q. So tell me what to underline.
10:07:24 A. So beginning with "short-term studies."
Q. Just tell me what they are.
A. (Reading:)
"Short-term studies did not show an increase in the risk of suicidality" which means suicidal
10:07:35 behavior and worse "... with antidepressants compared to placebo in adults beyond age 24."
Q. Okay, Doctor, is that an accurate statement as it relates to Paxil?
A. No.
10:07:52 Q. How so?
A. The increased risk in -- the increase in risk in suicidal behavior for Paxil goes to all ages. Across all ages, as we're talking about a few minutes ago, it's 2.76.
Q. And it goes on to say:
10:08:18 ".. there was a reduction in risk with

antidepressants compared to placebo in adults aged 65 and older."

What does that suggest to a physician reading it?

A. If --

10:08:32 MR. BAYMAN: Objection, Your Honor, what is suggest to a physician reading it.

THE COURT: Overruled. As an expert he can express his opinion on that subject.

BY THE WITNESS:

10:08:41 A. If you're saying the risk is here for young people and it gets lower for older individuals, the suggestion is going to be, well the risk goes down as you get older, and that's not true for Paxil.

BY MR. WISNER:

10:08:55 Q. In fact, if we look at the sentence before that, Doctor, what does that say?

A. It's saying:

"... anyone considering the use of Paxil or any other antidepressant in a child, adolescent or

10:09:10 young adult must balance this risk with the clinical need."

Q. What is your understanding of what this black box warning is telling physicians to be careful of?

A. Use of any antidepressant. And just to be clear, this is a

10:09:24 template. If you were to go to another SSRI, for example,

let's take, I don't know, Prozac, it would simply substitute in the word "Prozac."
Q. You mean right here with "Paxil"?
A. Correct. So that is not specific information that is
10:09:45 unique to Paxil. You would see that in any other SSRI.
Q. All right. So I'm going to stop right there. In your expert opinion, is this false or misleading?
A. Yes.
Q. Would it be okay if I wrote "false" right here?
10:10:01 A. Yes.
Q. All right.
And I'll say for Paxil.
A. Actually if I could, I would say false and misleading, but in the interest of time ....
10:10:16 Q. Okay. All right. So it goes on to say:
"... depression and certain our psychiatric disorders are themselves associated with increases in the risk of suicide."
Now, Doctor, is that a warning at all?
10:10:30 A. No.
Q. What would you call that?
A. That is what I'd call advise in taking care of patients, what we call disease management.
Q. I'm going to add "misleading" here because I don't want to
10:10:44 make it seem like I'm saying anything.

(Brief pause).
BY MR. WISNER:
Q. All right. So you said disease management. What is disease management, Doctor?
10:10:56 A. So that's basically the details of how we take care of patients. Depression can get worse and lead to suicide, that's one -- depression by itself, even if it doesn't get worse, is an extremely serious condition. Can lead to all sorts of problems besides suicide, but suicide, as I said in my report, 10:11:20 is the most extreme consequence of depression.
So you that's something you'd see in a medical textbook. It has nothing to do with drug risks, per se.
Q. By focusing in the label on how the underlying disease can cause a risk, does that take away from the potential additional 10:11:43 risk potentially caused by the drug?
A. Yes.
Q. And, in your opinion, with a statement like depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide, does that create any 10:11:58 obligation on GSK to focus specifically on the risks associated with Paxil?
A. Could I hear the question one more time?
THE COURT: Read it back.
(Question read.)
10:12:27 BY THE WITNESS:

A. Well, it doesn't -- I would say that it doesn't address the responsibility. It doesn't talk about the risk associated with Paxil. It's talking about the risk associated with the disease.

10:12:41 BY MR. WISNER:

Q. And you characterize that as disease management?

A. Yes.

Q. Do you believe statements in a label that relate to disease management qualify as a warning about a risk for a drug?

10:12:52 A. No.

Q. All right. So we're in the black box still. And it says:

> "... patients of all ages who are treated on an antidepressant therapy should be monitored appropriately and observed closely for clinical
10:13:07 worsening, suicidal, or unusual changes in behavior."

That sentence which follows a statement that depression itself increases the risk of suicidality, how would you characterize that?

10:13:18 A. That is disease management.

Q. All right. Keep going:

> ".. families and caregivers should be advised of the need for close observation and communication with the prescriber. Paxil is not approved for
10:13:28 use in pediatric patients."

Other than that last sentence, Paxil is not approved for pediatric patients, what is that sentence with families and caregivers, what is that?

A. It's good advise, but it has no connection with informing prescribers or patients about the risk of a drug.

Q. Does this black box anywhere state, in simple and bolded language, that Paxil increases the risk of adult suicidal behavior over the age of 24?

A. No.

Q. What does it say?

A. About that particular risk?

Q. Yes.

A. Nothing.

Q. What does it say about underage, beyond the age of 24?

A. It's silent on that with respect to Paxil. It just says, as a group, antidepressants -- the risk of suicidality associated with antidepressants is just 24 and under.

Q. So that statement about Paxil-specific language, reading this does this suggest that the risk for Paxil and suicidality does not extend beyond the age of 24?

A. It does.

Q. And this is in the first paragraph of the label?

A. Not just the first paragraph; the most prominent portion of the label.

Q. All right. Could GSK have added or could have requested to

add that statement, that Paxil could increase the risk of adult suicide or behavior over 24?

A. Yes.

Q. All right. Where could they have requested to put it?

10:15:10 MR. BAYMAN: Your Honor, objection. This is a totally new opinion. He was asked this question at the depression and he said he didn't have an opinion about where else it should go in the label. It's not in his report and we object that this is outside the scope and this is a violation of the Rule 26(e) 10:15:27 of the duty to supplement the expert report with new opinions.

MR. WISNER: Your Honor, he clearly stated in his report, as well as during his depression, that they could've put it anywhere outside of the class labeling, and that's exactly what he's testifying to right now.

10:15:39 THE COURT: He may testify.

BY THE WITNESS:

A. Thank you, Your Honor.

So the regulations are pretty general about what should go in. And it says, for example, under 10:15:58 "contraindications," these are population of patients who should not get the drug, but it doesn't go into a whole lot more detail.

So this give both manufactures and the FDA a lot of flexibility. And there's a whole part of FDA that's concerned 10:16:18 with risk communication. How do we best inform prescribers and

patients about what the risks are.

So having said that, there's a large number of areas in the label, in different sections, where this information not only could go but should go. The only one, I just want to address this up front, that the FDA said "we don't want it in this section" is in the exact middle of the class labeling, but that's the only thing they said "no" to. They didn't say we don't want it anywhere in the label. So starting out with a black box --

10:16:43

10:17:06

BY MR. WISNER:

Q. I'm going to stop you right there, Doctor, before we move off the topic.

A. Yes.

Q. I want to be very clear, did GSK ever attempt to put the statement that Paxil induces the risk of adult suicidal behavior over the age 24 anywhere in the label?

10:17:13

A. No.

Q. Okay. Sorry, you were explaining about the black box. I wanted to make sure it didn't get lost.

A. No. No. They didn't.

10:17:27

So let me just walk through this. There's no reason, except the FDA said, well, we don't want it in the middle. Okay, it could've gone at the end of this (indicating).

MR. BAYMAN: Objection, Your Honor. Again, this is a new opinion. May I have a continuing objection?

10:17:46

THE COURT: Yes, you may.

MR. BAYMAN: Thank you.

BY MR. WISER:

Q. So you said right here at the end (indicating)?

10:17:53 A. Yes.

Q. Can I draw an arrow?

A. Sure.

Q. All right. So what I'm going to do with my terrible handwriting is try to keep a counting of all this. So I'm

10:18:04 going to put number 1 here, all right?

A. Okay.

Q. So they could've put it right here at the end of the class portion of the black box warning, is that right?

A. Yes.

10:18:13 Q. All right. Could they put it somewhere else?

A. Yes, they could've put it immediately below the black box warning.

Q. And if you want to point to it on the screen, Doctor. I think it's actually touch-sensitive.

10:18:29 A. This is what happens when you get too highly specialized.

I'm sorry, I'm touching it but --

Q. Just underline it.

A. Okay.

Q. Perfect.

10:18:40 So right here (indicating) then?

A. Yes.
Q. Okay. Great. All right. So now we've -- and I'll clear it each time so we can keep ourselves on track here.
All right. So we have it now just above the
10:18:54 description. And do you think it would've been smart, from a regulatory perspective, to put this risk right smack on the first page just before you get into all the nitty-gritty of the label?
A. Yes.
10:19:05 Q. Why is that?
A. This is -- except for -- we used to say the FDA, except for the nerds who are looking at that chemical structure immediately below, most physicians are going to look at two things, the warnings and how much do I give.
10:19:28 Q. All right. So we go into the description section. Is this the area that you would've suggested that they put a suicide warning for adults over 24?
A. In clinical pharmacology information?
Q. Yes.
10:19:45 A. No.
Q. So we're going to go to the next section after clinical pharmaceutical, and now we're here in this section entitled Clinical Trials; do you see that, Doctor?
A. Yes.
10:19:55 Q. All right. Do you have an opinion about this?

A. Yes.
Q. What's your opinion?
A. So the clinical trial section gives the actual -- or summary of the actual information that the FDA has relied on in approving the drug.

10:20:07

And in this instant -- incidence there was clinical trial -- I'm sorry, clinical trial data across all indications, as well as trials for Paxil and depression showing an increased risk of suicidal behavior.

10:20:27

So you certainly could logically say, since it's across all indications, and the clinical trials go over the various indications that were studied, you could put it right here (indicating).
Q. Okay.

10:20:46

A. So it's the first thing to say -- because that was the result where you combined trials for all indications.
Q. Okay. Great. Where else could you put it?
A. Well, certainly look at major depressive disorder, specifically you could put it here (indicating) or you

10:21:05

certainly could put it -- just to be clear, number 3, that would be -- this is a general warning or general indication about the risk, that 2.76 here (indicating). If you were looking specifically at major depressive disorder, you could put it at the beginning or at the end.

10:21:28

Q. So what I'll do is I'll put it in here and put "4" and then

draw an arrow up, is that fair?
A. Yes.
Q. Let's keep moving on. We got Obsessive Compulsive Disorder, Panic Disorder, do you see that, Doctor?
10:21:46 A. Yes.
Q. Okay. All right. Social Anxiety Disorder. Do you know -- have you seen any studies, clinical studies that focused on any of these specific indications other than MDD?
A. I have seen clinical studies but not analyses that
10:22:04 specifically address the suicide risk on the way they have for MDD.
Q. Okay. All right. We got Post-Traumatic Stress Disorder. Now, we're in "indications and usage," do you see that, Doctor?
A. Yes.
10:22:20 Q. We're on page 8 of Joint Exhibit 1.
What, if anything, could go in here?
A. So this -- so just to be clear, "Indications and Usage" goes to what conditions the drug has been studied in and for which there is evidence, what I'll call substantial evidence of
10:22:48 efficacy, but it's not just the diseases, it's also the populations. So, for example, kids are considered a different population than adults.
Q. So this is more for efficacy, is that right?
A. Yeah.
10:23:00 Q. So you wouldn't put a suicidal warning for adults over 24?

A. No. No.
Q. All right. Post-Traumatic Stress. So let's go through the whole section.
All right. Now we're in the warnings, do you see
10:23:15 that, Doctor?
A. Yes.
Q. All right. What is the warnings section and do you believe that there could've been a warning about adult suicidal behavior over the age of 24 in the warnings?
10:23:24 A. Yes. So the warnings section warns about side effects that are particularly severe, even fatal.
Q. All right. So where would you put it?
A. So, again, there are multiple areas where this could go. And again, the goal is not to -- so much to just to obey the
10:23:46 regulations, although that is obviously critical, we want to tell people about what's going on. And I rely on these labels when I'm prescribing. So you could put it before everything else.
Q. So right here before the class labeling, right?
10:24:04 A. Yes.
Q. Now, actually I just ask to clarify. There's a section that says "Clinical Worsening and Suicide Risk," do you see that?
A. Yes.
10:24:10 Q. And it extends to this page, has a chart up here, and then

it goes down to this page, and then it ends on this page (indicating)?
A. Yes.
Q. Okay. So all that class-wide warning, is that specific to Paxil?
10:24:27
A. None of it is.
Q. What is it specific to?
A. It addresses the general issue of suicidal behavior in patients on antidepressants.
Q. And this was the class warning that was focused on under 25 years old?
10:24:36
A. Yes.
Q. So it could've gone right here (indicating). Where else could it gone, Doctor?
A. So actually before I get to that, one other very important point: I mentioned that there are circumstances in which a manufacturer can go ahead and add or strengthen a warning without getting prior clearance from the FDA; this is a section where you can do that.
10:24:48
Q. So you're telling me, without getting prior approval from the FDA, GSK said right here, under the warning section, this drug induces suicidal behavior in adults over 24?
10:25:05
A. That's correct.
Q. Have you seen any evidence or any submissions by GSK that they ever tried to do that?
10:25:24

A. Not in a way that I would regard -- well, let me put it like this, you asked if they had added that information earlier if they would have made it not false or misleading and I said no. They had added information --

10:25:39 Q. Doctor --

A. I'm sorry.

Q. -- I don't want to get into that conversation.

A. Okay.

Q. I want you to focus on my question.

10:25:48 My question was, have you seen any evidence --

A. No.

Q. Hold on. Let me ask the question.

A. I'm sorry.

Q. Have you seen any evidence that GSK tried to put a

10:25:57 statement that Paxil induces the risks of adult suicidal behavior over 24 in this part of the label?

A. I apologize for assuming. No, they have not.

Q. Again to clarify, have they ever made that proposal anywhere in the label?

10:26:14 A. No.

Q. All right. So we got the warning section here. And do you think it would've been appropriate from a regulatory perspective, and as a clinical practitioner, as a physician, to put that suicide risk as it relates to Paxil smack at the

10:26:34 beginning of the warning section?

A. Yes.
Q. Why?
A. That is the most prominent place. I mean, you're talking about a long, intense label. In the first, it makes it more likely that people are going to see it.
Q. All right. So then we get into the class-wide warning. Do you see this whole section, Doctor?
A. Yes.
Q. And you mentioned earlier that GSK would not have been allowed to put it in the middle of any of these paragraphs, is that right?
A. Correct.
Q. Could they have put it at the beginning of it?
A. Yes.
Q. Do you have an opinion about whether or not GSK could've or, quite frankly, should have put in a warning about adult suicidal risk for Paxil over 24 in the clinical worsening suicide risk section?
A. I think they absolutely could have, should have, and could have done it without getting prior approval.
Q. Okay. And so could you mark on the screen where you think it could have gone? At the beginning, I assume?
A. Yes.
Q. All right. So I guess right after the colon, so right here (indicating). And I'll call it number 6, okay?

A. Yes.
Q. And then separately, I'm going to go to the end of the class warning.
A. Before you do that, could I just add one comment here?
10:27:46 Q. Sure.
A. If you go to down to the second paragraph, and I'll just -- I don't want to mark up the screen, but on the 2, 3, 4, 5, on the 6th line of that paragraph "there was considerable variation in risk of suicidality among drugs."
10:28:01 Q. Yes.
A. So what that doesn't say is -- when they say variability, they mean that you've got a drug like Paxil with a very high risk with a confidence interval that shows that -- we know that that is real, but it doesn't mention that. It just is sort of
10:28:29 like language, but that is the underlying thing and does not -- by not having that information there, that 2.76, that is misleading.
Q. In your opinion, Doctor, this statement that there was considerable variation of risk among drugs, without having any
10:28:51 Paxil-specific information, does that cause problems?
A. Yes.
Q. Okay. Would you like me to underline that, because you pointed it out.
A. Please.
10:29:00 Q. In red?

A. Please.
Q. All right. So there was considerable variation in risk among drugs with --
Is that it, Doctor?
10:29:11 A. Yes.
Q. Okay. Great. Okay. And, quite frankly, we're actually going to go into this in a minute and go trough the class warning, I just want to get to the places where they could've warned. We're talking about what they haven't done and then
10:29:25 we're going to talk about what they did do, okay?
A. Okay.
Q. All right. So this is the class warning, right. And you would agree they couldn't put it in the middle of any of this, right?
10:29:32 In the middle of any of this?
A. Yes.
Q. All right. All this stuff keeps going. And we're going to talk about that that says in just a minute, Doctor. And then we get to the end of the class warning right here, before
10:29:40 screening patients?
A. Yes.
Q. Do you have an opinion about whether or not GSK could've added Paxil-specific language here?
A. Yes.
10:29:56 Q. What's your opinion?

A. It could have.
Q. Okay. Where? Could you point on the screen.
A. So it could've gone right here (indicating) after the class labeling.
10:30:06 Q. So right there, Doctor (indicating)?
A. Yes.
Q. Sorry.
A. My drawing is not too good these days. I mean, it really could come -- it's --
10:30:18 Q. Let me clear it.
A. Yeah. So as long as it did not go in the middle of the class labeling section. It could go before, it could go after.
Q. All right. So why don't we put the arrow. Right here (indicating).
10:30:34 What number are we at, do you know? 7?
(Brief pause).
BY MR. WISNER:
Q. All right. And then moving through this warning section, it keeps going, it has all these different warnings, could GSK
10:30:44 have put a warning section in after the class-wide warning in a separate section for Paxil?
A. Yes.
Q. All right. So then for the 7, how should I represent that on this? You tell me.
10:30:56 A. I think you could just draw an arrow down through this

entire warning section and say it could have gone -- you know, a separate section could have gone anywhere under the regulations.

Q. All the way down here (indicating).

10:31:10 Is that right?

A. No, I would not put it in the pregnancy section, obviously, but, you know, it would be -- I think as a separate section it could go, you know, in someplace where it's not a subhead under another.

10:31:31 Q. So, for example, slide it in right there (indicating)?

A. Right.

Q. Okay. So I'm going to keep going through this. We're on the next page. It keeps going.

All right. Now, we get to precautions. Just to be

10:31:51 clear, we just went through all those different sections and the warning, and we're going to go into more detail in class portion in just a second --

A. Uh-huh.

Q. -- but do you recall whether or not GSK requested or even

10:32:07 attempted without prior approval to put a warning about Paxil-induced suicidal behavior in adults over 24 in the entire section for warnings?

MR. BAYMAN: Your Honor, this has been asked about 3 or 4 times now.

10:32:21 THE COURT: I think it's covered.

MR. WISNER: Okay.
THE COURT: Proceed.
MR. WISNER: Fair enough, Your Honor.
BY MR. WISNER:
10:32:43 Q. I want to make sure I get the record clear. So you said it wouldn't go in the pregnancy three, do you recall that?
A. Yes.
Q. All right. I'm going to mark it again so there's actually a record of it because the screen gets cleared and you don't
10:32:48 see it.
So it was right here is the arrow that we pointed to, is that right?
A. Yes.
Q. Okay.
10:33:14 (Whereupon, there was a conference had between counsel off the record).
BY MR. WISNER:
Q. Okay, Doctor, I want to clarify. When you have this arrow, it keeps going, an arrow down like that (indicating). Just to
10:33:24 clarify, you mean it can go in the pregnancy or does that have to go before or after?
A. It would have to go before or after.
Q. Okay. And so for all of these folded sections, is that what you're referring?
10:33:33 A. Correct. It would not go --

Q. Right here, for example, on page 13 (indicating)?
A. Correct. And, for example, there's things about animal effects, you know, it would have to go outside one of these sections with -- it would be a section that would have one of
10:33:48 these kind of headings like potential for interaction with monoaminoxidase inhibitors.
Q. Okay. So I'll do another section like there here, serotonin syndrome, do you see that?
A. Yes.
10:34:02 Q. Now is that a different font or color?
No, it's the same. Okay. Just bad lighting from here.
So to be clear, it could be any of these sections? I just want to make sure the record is clear.
10:34:17 A. Yes.
Q. All right. Okay. Now to the precautions section.
A. Yes.
Q. What's the difference between a warning and a precaution?
A. So a precaution is just what it sounds like, a section
10:34:36 where you say certain things might happen during treatment and here's the rate at which they happen.
So, for example, under seizures, one out of 1,000 pages got seizures. Paxil should be used cautiously in patients with a history of seizures. But here you're getting
10:35:03 kind of more detailed information about things to be careful

about specifically with this drug.
Q. All right. And, again, do you have an opinion about whether or not GSK could've requested to put an adult specific warning over 25 in the precaution section?
10:35:25 A. Yes.
Q. What's your opinion?
A. My opinion is that it certainly -- it could've and would've made complete sense to do that.
Q. Okay. So where would you put it?
10:35:37 A. I would put it at the beginning.
Q. So right under "precautions"?
A. Yes.
Q. Okay. All right. And anywhere else you could've put it?
A. In precautions? I mean, it really can go anywhere in this
10:35:58 section. I think the most logical place would be at the beginning, but you could simply create -- I mean, you could put it under -- you could put it anywhere. I think the most logical place would be at the beginning to increase its chances that the prescribers and patients are going to see it.
10:36:17 Q. All right. Let's move to the precaution sections. And let's talk for a second, because I know this is going to come up at some point, see this sentence where it says "akathisia"?
A. Yes.
Q. All right. Anywhere in this akathisia warning, does it
10:36:35 relate akathisia to suicidal behavior?

A. No.
Q. Do you think that's a problem?
A. Yes.
Q. Why?
10:36:43 MR. BAYMAN: Your Honor, again objection. He's not expressed an opinion on this in his report, in his deposition testimony, and it's not been supplemented. So we object to this entire line.
MR. WISNER: In his report he does discuss akathisia.
10:36:57 MR. BAYMAN: It's not an opinion about what should in the label about it.
THE COURT: You may proceed.
MR. WISNER: Thank you, Your Honor.
MR. BAYMAN: Continuing objection to this line, Your
10:37:07 Honor.
THE COURT: Yes.
MR. BAYMAN: Thank you.
BY MR. WISER:
Q. So what's the problem of this akathisia discussion not
10:37:12 including a discussion about suicide?
A. Well, it doesn't say that akathisia is not just some funny word. It is something that is associated with suicidal behavior.
If I can just go to the section right below it and
10:37:36 just to contrast this?

Q. Sure.
A. So it's talking about the possibility that SSRIs can lead to hyponitremia, which is just low sodium in the blood, and it says cases with serotonin sodium lower than 110 millimeters
10:37:53 have been reported. Normal sodium is like 145.
Q. This line right here (indicating)?
A. Yes, I'm sorry. At 110, any physician, general internist, primary care physician, certainly a psychiatrist would say, whoa, that is a life threatening level. The significance of
10:38:17 that is pretty clear, it's a basic thing in medicine. Akathisia would not be and, therefore, this is where you got to spell it out.
Q. Well, I see under -- how do you say that hypo--
A. Hyponatremia.
10:38:35 Q. Okay, hyponatremia. It says here at the bottom, do you se it says "death"?
A. Yes.
Q. Is there any statement in akathisia about that leading to death?
10:38:41 A. No.
Q. Is that a problem?
A. Yes.
Q. All right. Do you have an opinion about whether or not in this portion of the label with regards to akathisia, GSK
10:38:53 could've put information?

A. Not just could've but should've.
Q. And where would that have gone or could've gone?
A. I think you could put that at the end and say -- for example, and say "akathisia is associated with suicidal
10:39:16 behavior and this is data that the company has published." Most suicides happen early on, that are induced by Paxil, happen early on in treatment.
Q. Okay. So here's another place they could've added something.
10:39:32 All right. Let's keep going through the label here. You mentioned that -- all right. So here we go. There is a section here, Doctor, that says "clinical worsening in suicide risk," do you see that?
A. Yes.
10:39:55 Q. All right. Is this actually the same warning that's in every antidepressant?
A. Yes.
Q. Okay. Can you just tell me what, if anything -- do you have an opinion about whether or not GSK should've added
10:40:04 anything to this section?
A. Well, again, this is disease management. And it's fine as far as it goes. I mean, there's nothing wrong with it, but it has to do with taking care of patients with depression in general, not with the risks of the drug. It doesn't say
10:40:20 there's something unique about Paxil in terms of the data we

have available, that's just not in there. So --
Q. So --
A. Go ahead.
Q. So, Doctor, it says here:
"Patients their families and their caregivers should be encouraged to be alert ..."
and it lists all these different things:
"... worsening in depression and suicidal ideation especially during antidepressant treatment and when the dose is adjusted up or down."
Does that say anything that the drug itself is causing suicidal behavior?
A. No.
Q. Is that a statement or -- is that an instruction of how to practice medicine?
A. It's -- it's really about, I would say, disease management in the sense of what kind of discussion do you have with patients.
Remember, when I describe something, it's not just an order, here take this. I sit down and I say, here's the pros, here's the cons, here's what could happen. And if there's a member in the family in the room I'm going to talk to them too. If there's something where -- you know, like I think something might happen that I want to call out to them, then this gives

me guidance on what to do, but this has nothing specific about Paxil.

Q. So to be clear, Doctor, if you have a patient that's depressed, and let's say you're not giving them an SSRI at all, what conversation do you have with them about paying attention to clinical worsening and depression and suicide?

10:41:50

A. Well, that things can get worse quickly. That they -- you know, this is not -- don't be afraid of calling me, don't be afraid of calling the emergency room. But people's threshold for -- I mean, they're not, you know, going to know necessarily is this worse or not if they know something specifically like this really might increase the risk of this happening.

10:42:14

Q. We're talking about a person that you're not prescribing --

A. That I'm not prescribing I'm sorry.

Q. Do you talk about watching out for suicidality because they're depressed?

10:42:33

A. Yes. Yes. And, I mean, that's one thing, if somebody -- one thing as a matter of course that's done, not just for me, I'm not trying to say, you know, I'm perfect, but this is actually done in my health core organization, the system prompts' providers to ask on a regular basis about depression specifically. And if what we call the score of depression symptoms is high, you would ask more questions. And if that's positive, do something, don't just stand there. So that's just the sort of general procedure, and I work with a population

10:42:45

10:43:12

that is at a high risk for depression.
Q. How does the conversation change when you're talking to someone who has depression and there's obviously a risk of suicide associated with depression, how does that change when
10:43:31 you say in addition to depression, we have this other risk, SSRIs? How does that change?
A. Well, I want to let them know not only that such might happen, but what it's due to and what to do about it. And it's -- it's -- it's a conversation. It's not simply my lecturing
10:43:55 them, the patient. So I might say, you know, I'm thinking about -- and I do this all the time in terms of other classes of drugs, I'll say, well, here's what I'm thinking about this drug. And the patient will say, well, how many times a day do I have to take it; once; great. Or this might give you trouble
10:44:16 sleeping, it might give you weird dreams; well, I'm not sure I really like that.

So if I'm saying this is not just a discussion about what to do when you're prescribing it, it's also starting it. So if I say, well, this drug has an increased risk of inducing
10:44:35 suicidal behavior, a patient might very well say, well why are you giving it to me. And I might say, you know, that's a good question. Or I might say, you know, it's a risk, we know it's a risk, but I don't have any other alternatives.

But that's a discussion, but certainly the patient
10:44:54 needs to know, because really we're talking about informed

consent for treatment.
Q. If you don't know that the drug can cause already depressed people to become more suicidal, can you have that discussion?
A. No.
10:45:10 Q. Okay. So back to this portion of the label that talks about being alert to anxiety and suicidality. You said this is disease management, is that right?
A. Yes.
Q. Now, would this warning or this discussion about disease
10:45:24 management shift if before it starts talking about patients it said "Paxil induces the risk of suicidal behavior in adults over 24," how does that change the caricature of this warning?
A. It gives me more information that I can provide to the patient -- well, first off, that I can take into consideration
10:45:45 myself. I mean, we're talking about the patient section, and more information I can give the patient.
Q. Now, to be clear, do you have an opinion about where in this clinical worsening in suicide risk section GSK should have discussed Paxil specifically inducing suicidal behavior?
10:46:07 A. I really think at the beginning.
Q. So right here (indicating)?
A. Yes.
Q. What number are we at, Doctor, do you recall? Number 10?
A. 10, yes.
10:46:21 Q. And while we're here, I just want to be clear. This

section about clinical worsening and suicide risk, this disease management language, has that been in the label since the beginning?

A. There has been all along, going back to earlier classes of antidepressants, this kind of I don't want to say boilerplate because it does mean something, but disease management.

I mean, if you go back, for example, there's a section that said, under warnings, Paxil, you should prescribe the fewest number -- the lowest number of tablets of Paxil that you can in this, and that's something that was written down in the labels for the older antidepressants like tricyclics. So this is nothing new.

Q. And if a person has been using labels for antidepressants, SSRIs, from the beginning, from the '90s onward, does this give you any new information about whether or not Paxil itself induces suicidal behavior over 24?

A. No.

Q. All right. So we have a bunch of other stuff here. We have stuff about, you know, alcohol and pregnancy and nursing, do you see that, Doctor?

A. Yes.

Q. Do you think a suicidal warning goes into any of these type of things?

A. It could be a separate section in here. Again, I would put it up at a -- at the beginning.

Q. Would it be fair to say that when it comes to the precaution section, the three places we've marked, which is here at the beginning (indicating), here in akathisia (indicating), and here in the clinical worsening and suicide
10:48:12 section, those are the places in the precautions that it made the more sense to a Paxil-specific warning?
A. Yes.
Q. Okay. Let's keep going through this. Let's get to the end of the precaution section because there's a bunch of -- oh,
10:48:23 sorry, I skipped a section.

(Brief pause).

BY MR. WISNER:
Q. All right. So all these are referring to using it with another drug, is that right?
10:48:40 A. Yes.
Q. Okay. So I'll skip through all this.

All right, now we're in the next section. There we go.

What is this section, Doctor.
10:48:54 A. So this section lists side effects, both those that were observed in terms of the original trials and then later on adverse events that have been observed either in postmarketing trials conducted after approved or just from side effect reports that get submitted to the FDA.
10:49:17 Q. And adverse reaction, is suicide attempt an adverse

reaction?
A. Yes.
Q. A suicide is an adverse reaction?
A. Yes.
10:49:30 Q. Would you characterize it -- how would you characterize it in the spectrum of adverse reactions?
A. Those are serious adverse events.
Q. All right. So right here at the beginning of adverse reaction, you see "associated with discontinuation of
10:49:40 treatment"?
A. Yes.
Q. That word "associated," does that have any special meaning in the context of regulatory speak?
A. So basically "associated" means it happens more often in
10:49:57 people who get the drug than people who don't.
Q. All right. And do you have to have a statistically significant increase to say you have an association?
A. No.
Q. What do you need?
10:50:09 A. You need reasonable evidence of an association.
Q. And when you look for that reasonable evidence, do you exclude adverse reactions that happen in clinical trials that weren't placebo controlled?
A. No.
10:50:23 Q. Why not?

A. You -- actually let me go back for a second. I want to clarify something. When I say it happens more often in people who take the drug than those who don't, that's one factor. If it's something where you don't have enough numbers to show that
10:50:52 that happens but the circumstances are so overwhelming you know that the drug had something to do with it, like you gave the person the drug and they dropped dead a minute later, that's sort of the thing. You know, it's out of one, as we say it's one person, but that's extremely compelling evidence. And
10:51:19 sometimes that has been used on the basis of case reports that are compelling submitted to the FDA and I personally would approve those kind of supplements.

Q. What about other types of analysis like challenge, de-challenge, re-challenge?

10:51:37 A. Yes, exactly. If something happens when you take the drug and then when you take the drug it goes away, that's called a de-challenge. A challenge is when you give it and something happens and you take it away is called a de-challenge, and if the side effect goes away, that's pretty good evidence it has
10:51:57 something to do with it.

Q. And then what about re-challenge?

A. Re-challenge, if it happens again -- I'm sorry, I've got to use this line: There's -- there's a James Bond novel where Fleming wrote the first time it happens, it's coincidence, the
10:52:13 second time is happenstance, the third time it's enemy action.

So that's really --

MR. BAYMAN: Your Honor, I object to that. Move to strike that.

THE COURT: Yeah, that may go out.

10:52:24 BY MR. WISNER:

Q. All right. So adverse reactions, do you have an opinion about whether or not GSK could have or should have put the adverse reaction of suicide attempt or suicides in this section?

10:52:41 A. Yes.

Q. Where could they put it?

A. There's a number of places. So what the adverse reaction section is, and it's not just something that's mutually exclusive with warnings, this gives actual frequencies.

10:52:56 Q. So where could they have gone?

A. So if we could go to the next page.

Q. Sure.

Doctor, before we go on to the next page, I just want to ask you a quick question before we go there.

10:53:06 A. Yes.

Q. There's a section here that says associated with discontinuation of treatment, do you see that?

A. Yes.

Q. Could you have created a section right here (indicating)?

10:53:16 A. Oh, yeah. I'm sorry. Yes, you absolutely could do that.

There's no question about it.
Q. Okay.
A. Again, if you want to make it more prominent calling it out at the beginning and having a separate section is something you
10:53:31 can absolutely do.
Q. All right. Well, let's go through here. And you said there's like a table here for discontinuation and there's a bunch of percentages and stuff, do you see that?
A. Yes.
10:53:37 Q. Showing, you know, what shows like, you know, dizziness, do you see that?
A. Yes.
Q. Let's go to tremor, do you see that?
A. Yes.
10:53:47 Q. And it has 1.1 percent right here (indicating)?
A. Yes.
Q. And then .03 percent, do you see that?
A. Yes.
Q. So what does that tell us based on -- and it's also under
10:54:01 major depressive disorder, do you see that?
A. Yes.
Q. So what does that tell us about agitation for people taking Paxil?
A. It's more than two times greater in patients with MDD than
10:54:12 a placebo.

Q. And you're making that calculation because they're comparing .03 percent to 1.1, is that right?
A. No, I'm sorry, 0.5 percent with 1.1 percent.
Q. Oh, you're talking about agitation?
10:54:27 A. Yes.
Q. Okay. So there's a doubling of the incidents of agitation for people who are depressed who take Paxil versus people who take a sugar pill?
A. Yes.
10:54:37 Q. Okay. Tremor, what was the increase there?
A. Almost 4 times.
Q. Okay. Great. And then you see all these numbers for all these different indications, do you see that?
A. Yes.
10:54:43 Q. Including, for example, like PTSD?
A. Yes.
Q. And I know you have some experience with PTSD because you treat veterans. Do you see this number here 1.2?
A. Yes.
10:54:57 Q. What does that tell you about tremor?
A. Well, if you have a PTSD patient and this was -- I'm sorry, I gotta mention this just in terms of interpreting this data, this was not a real world PTSD patient population --
MR. BAYMAN: Your Honor, I object to this. We're now
10:55:13 getting into PTSD patient populations and discontinuation, I

don't see what this has to do with this case. It's entirely irrelevant and prejudicial.

THE COURT: All right.

MR. WISNER: Your Honor, we're just trying to understand how the label is read.

10:55:27

THE COURT: To the extent that you raised the point that it is not part of the case, I'll sustain the objection. To the extent that you're trying to explain how this fits in the chart, he may answer that question; in other words, why is PTSD over here rather than somewhere else.

10:55:43

BY MR. WISNER:

Q. So, Doctor, I don't want to hear about the population.

A. Understood. I apologize.

So these are the indications in which Paxil has been studied, and PTSD is one of them, so the incidents of tremor in patients with PTSD who got Paxil is 5 times than in patients who just got a placebo.

10:55:56

Q. All right. If you go down to some more of these adverse reactions you see "commonly observed adverse events, major depressive disorder," do you see that?

10:56:19

A. Yes.

Q. So this is where you could list common events that you would expect to see with people who are depressed?

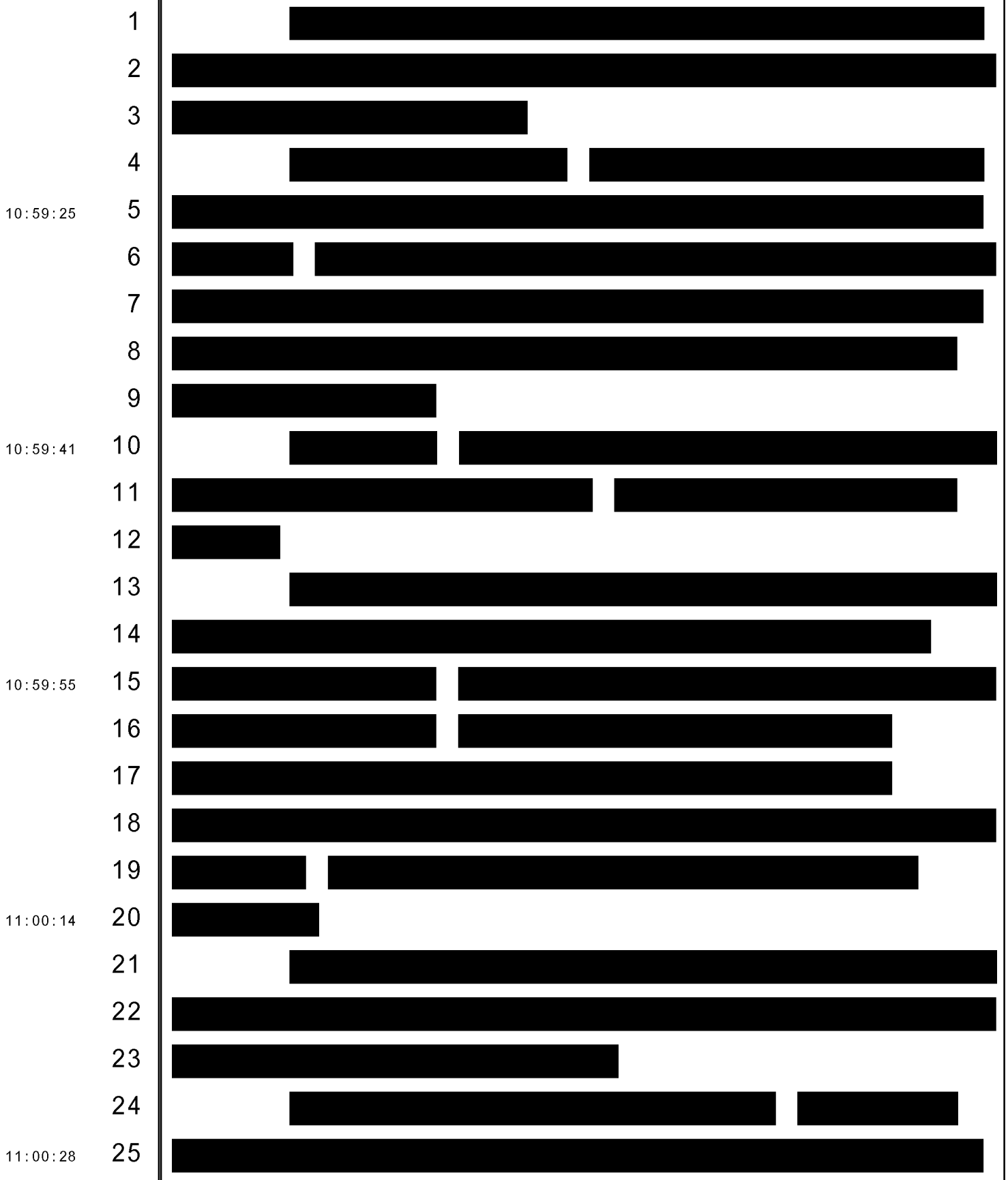
A. Yes.

Q. Okay. And it has different things in here. It has

10:56:27

asthenia, that's not akathisia, right?
A. Correct.
Q. And you have a bunch of different here, sweating, nausea decreased appetite, et cetera, do you see that?
10:56:46 A. Yes.
Q. And those are all just adverse reactions?
A. Yes.
Q. Okay. So this is for the area of associated with discontinuation, is that right?
10:56:52 A. Yes.
Q. Okay. Let's move on.
I just want to take a second to discuss this. So just for discontinuation there's a chart, there's a section, do you see that?
10:57:04 A. Yes.
Q. All right. And it keeps going, do you see all that?
A. Yes.
Q. And then we get to a new one here which is incidents of controlled clinical trials, do you see that?
10:57:16 A. Yes.
Q. So there's already almost a page and a half, two pages, just devoted to discontinuation symptoms?
A. Can you -- I just want to make sure I'm understanding it correctly. Can we go back.
10:57:31 Q. That's the first part (indicating).

A. Right.
Q. By the way, you have a copy of it in your binder.
A. I'm sorry, which?
Q. Joint Exhibit 1.
10:57:38 A. Joint Exhibit 1.
Q. That actually might be helpful in case you want to look at something I'm not showing you.
We're on page 25, Doctor.
THE COURT: We'll take a recess at this time, ladies
10:58:06 and gentlemen.
Mike, open the door for them.
(The following proceedings were had out of the presence of the jury in open court:)
[redacted]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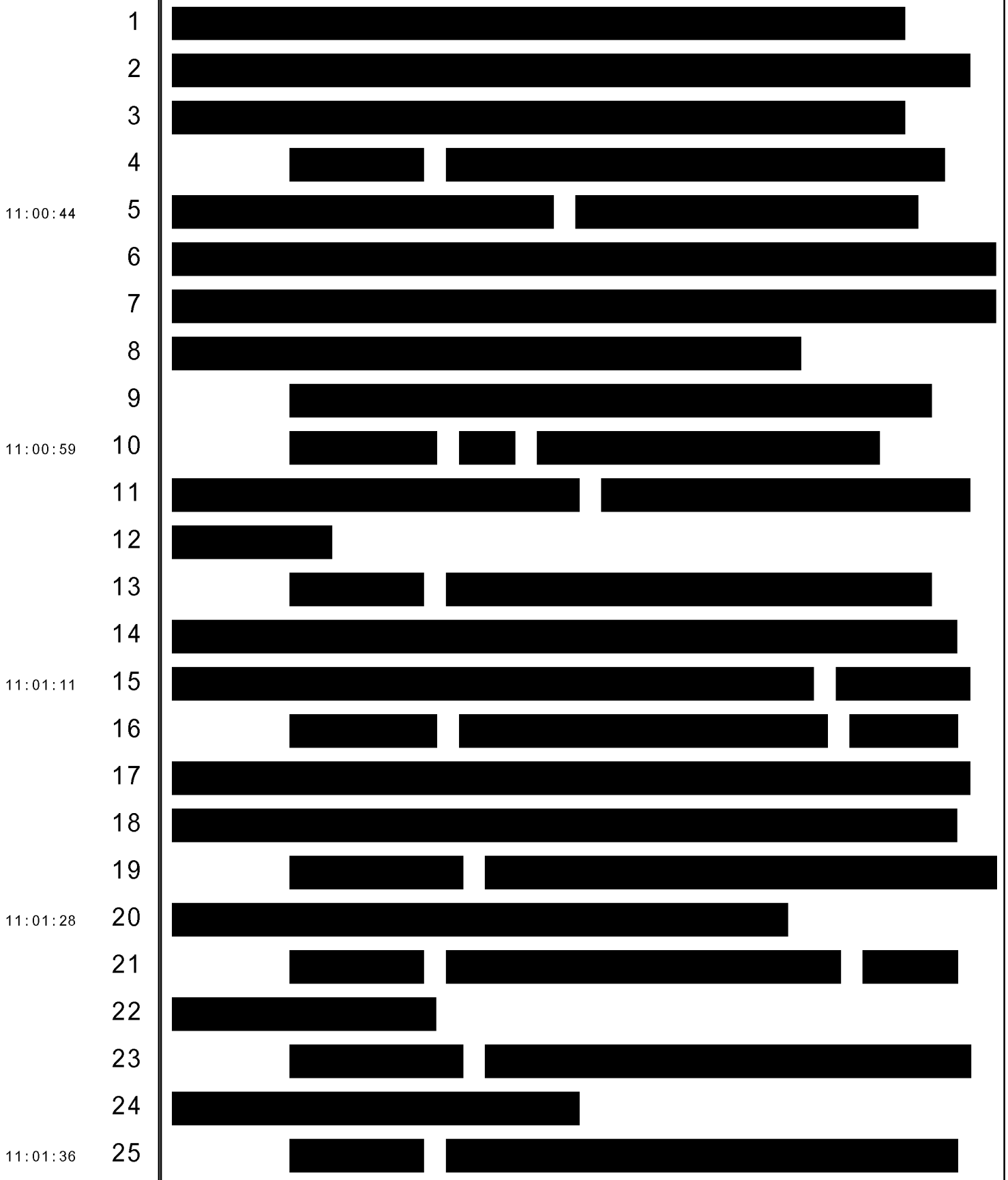
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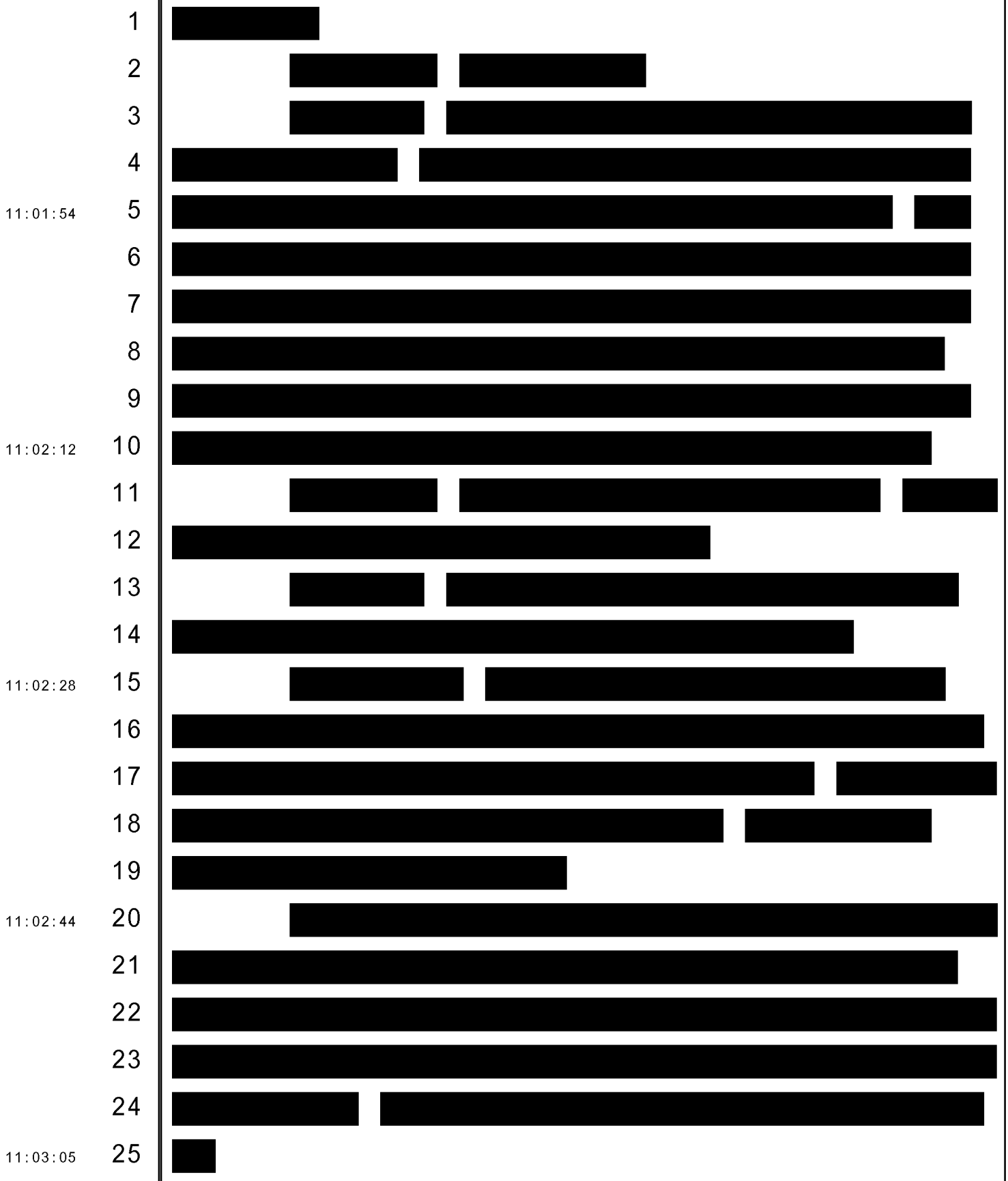
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[redacted]

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

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

We will proceed.

Doctor, if you will.

THE WITNESS: Thank you.

(Brief pause).
BY MR. WISNER:
Q. Okay, Doctor, you have the water there.
A. Thank you.
11:22:06 Q. All right. So before the break we were talking about adverse reactions and relating to this section right here, do you see that?
A. Yes.
Q. Okay. And just for the record, we're on page 25 of Joint
11:22:26 Exhibit 1.
A. Yes.
Q. This states:
"... adverse reactions associated with discontinuation of treatment."
11:22:33 Do you see that?
A. Yes.
Q. Is this section referring to the reasons why in clinical trials patients stopped participating in the trials?
A. Yes.
11:22:46 Q. Okay. So that's a little different than, for example, the symptoms that somebody has when they stopped taking the drug, in general?
A. Well, these -- these refer to -- is this working (indicating to the microphone).
11:23:03 These refer to symptoms that are sufficiently severe

that they lead to either the patient or the investigator at the site saying let's take you out of the trial.
Q. So, for example, it says right here "discontinue treatment due to a adverse event," that's what you're referring to?
11:23:23 A. Yes.
Q. So these were so severe that in the clinical trial itself patients were actually removed from the trial?
A. Yes.
Q. Okay. And then we go to this chart, it talks about, for
11:23:36 example, major depressive disorder, do you see that?
A. Yes.
Q. And that's referring to clinical trials related to major depress disorder, right?
A. Yes.
11:23:46 Q. And while on that point, I just want to make sure we have an understanding, is there a difference between what we see in people who have commonly known depression and major depressive disorder?
A. Well, the definition of major depressive disorder --
11:24:02 everyone feels down once in a while. A major depressive disorder is a specific diagnosis in which --
Is this working (indicating microphone)?
Q. Yes, it is.
A. A patient has 5 out of 9 specific symptoms for majority for
11:24:26 at least 2 weeks.

Q. And for -- and our understanding of depression, as we understand it today in common parlance, is that different than the type of depression that we were talking about in the 1950's, line melancholia?

11:24:45 A. Yes.

Q. And has the general definition for depression expanded in people that we considered depressed over the years?

MR. BAYMAN: Objection, Your Honor. No foundation for this testimony from this witness. He's not a psychiatrist. He

11:24:56 is an internist with a specialty in infectious disease.

THE COURT: Overruled.

BY THE WITNESS:

A. Thank you.

So in terms of the -- first let me clarify. The

11:25:11 mechanism -- I'm sorry. Depression as a primary care disorder, I am revising an edition of a book on primary for veterans with HIV, one of the major chapters is depression with the implication that this is something that the primary care providers should be responsible for.

11:25:35 Having said that, the criteria for diagnosing it have been refined and improved considerably over the last several decades. So that it's no longer when you're feeling down once in a while, that's too broad, too vague. On the other hand, there's an appreciation that certain symptoms that previously

11:25:59 had not been thought of as depression--for example, insomnia or

hypersomnolence--may actually represent signs of depression.
Q. Sorry, Doctor, hypersomnolence?
A. Sleeping a lot.
Q. Okay. All right. So we're looking here at a table and we
11:26:22 have major depressive disorder, and these are all side effects
that cause people to leave the study, is that right?
A. Correct.
Q. Okay. So with that in mind, 1 percent of all patients in
depression trials who took Paxil quit the trial because the
11:26:46 tremors were so bad?
A. Yes.
Q. 1 percent of patients who took Paxil had such bad agitation
that they left the trial?
MR. BAYMAN: Leading, Your Honor.
11:26:59 BY THE WITNESS:
A. Correct.
BY MR. WISNER:
Q. What does that 1.1 percent mean with agitation, Doctor?
THE COURT: Excuse me. Did you say something?
11:27:09 MR. BAYMAN: Objection. Leading, Your Honor.
THE COURT: Oh, leading, yes. Don't lead. Just ask
the questions.
MR. WISNER: I'll rephrase. I'm sorry. That is open
ended question.
11:27:16 BY MR. WISNER:

Q. What does that 1.1 percent agitation mean?
A. So of the -- hang on here.
If I can just go up to the introductory paragraph.
Q. So own page 25 here.
11:27:28 A. Yes.
(Brief pause).
BY THE WITNESS:
A. So if you look at the first sentence, 20 percent, one out of every 5 patients who received trials -- I'm sorry, Paxil in
11:27:48 clinical trials in major depressive disorder, and that's about 1200 patients, stopped the drug because of a side effect. That's where it says at the end, "discontinued treatment due to a suicidal event."
Q. Okay.
11:28:09 A. And sometimes patients can stop for more than one.
Q. All right. And then we have a bunch of other types of things in here, do you see that?
A. Yes.
Q. So, for example, like nausea. So what does that 3.2
11:28:19 percent mean?
A. Those patients, or 0 those 1200 patients who stopped, 3.2 percent discontinued because of nausea as opposed to only 1 percent in placebo patients who stopped treatment.
Q. And so for -- when we go back up here like tremor, the 1.1
11:28:39 percent, how many percent greater is that than placebo?

A. That's almost 4 times greater.
Q. So in all MDD clinical trials, what does that tell you about the people quitting the trial because of tremor?
A. Well, it's I don't want to say statistically significantly
11:29:04 greater, I haven't done that analysis on this, but it's a lot more.
Q. All right.
A. May I -- if I may just offer one observation which I believe is important in terms of understanding this table.
11:29:18 So if --
MR. BAYMAN: Objection, Your Honor. I don't see what this has to do with any of the issues in this case.
THE COURT: We'll see.
BY THE WITNESS:
11:29:28 A. I mentioned earlier that depression requires a diagnosis according to current criteria 5 out of 9 symptoms over a period of 2 weeks. If you break up those 5 symptoms in just -- if somebody has 5 of those symptoms that you count them independently and you don't consider them together, then you
11:29:51 will conclude that the reason for discontinuation is that particular symptom rather than depression.
So, for example, the first line is somnolence, sleeping a lot. The question here is, if you say, well, it turns out that patient also had anxiety and insomnia, and what
11:30:24 can be mixed with somnolence and so on and they really had

depression, you are going to shift what -- the reason for adverse events should be depression -- discontinuation, rather, should be depression, but here it gets to capture somnolence. So it's a question of how it's covered.

11:30:46 Q. All right. That said, in a clinical trial if a patient on Paxil or placebo attempts suicide, are they typically removed from the clinical trial?

A. Typically, yes.

Q. So suicide attempt would be a reason for discontinuing from

11:31:04 a clinical trial?

A. Yes.

Q. Do you see anywhere here any statement about suicide attempts or the likelihood of it occurring in these various indications?

11:31:13 A. No.

Q. We know, Doctor, from the 1989 data, what was the risk ratio between suicide attempts in Paxil and suicide attempts in placebo?

A. I believe it was roughly a non-fold difference, if I'm

11:31:31 remembering correctly.

Q. So that if it were to be written in here, it would say suicide attempt and then 9 percent, is that right?

A. Well, no, not 9 percent, but the --

Q. Well, the incidents --

11:31:46 A. The incident events would be greater. The odd -- it might

not be 9 percent, but it certainly would be listed in this table with the incidents. This table does not give odds ratio, but you can calculate them like we just did with tremor where the odds ratio there is almost 4.

11:32:09 Q. Now, we also looked at a re-analysis done by GSK in 2002 just looking at placebo-controlled date, do you recall that?

A. Yes.

Q. And we just put the placebo number aside for just one second and we looked at just suicide attempt and the incident

11:32:25 rate, do you remember that?

A. Yes.

Q. And do you recall it was about 1.2 percent?

A. Yes.

Q. So 1.2 just the placebo controlled data of people who

11:32:37 attempted or committed suicide in the MDD trials, is that right?

A. Yes.

Q. And 1 percent of those incident rates for suicide attempts, in your opinion, should that information have been put right

11:32:49 here in this table as a reason for discontinuing the study?

A. Yes.

Q. All right. Doctor, let's move on. We're in the process of exploring places where they could've put warnings. Are we in one of those areas now?

11:33:09 A. Yes.

Q. Where would you have put it?
A. So now keeping in mind that this section generally provides numbers --
Q. Hold on. Before we get to that.
11:33:34 A. I'm sorry.
Q. On this table right here, could they put something?
A. Oh, yeah. In fact, if you look at -- there's a couple of different ways. They could put -- you know, on suicide attempt would not necessarily go under CNS, but it could, but certainly
11:33:57 it should be in there.
Q. So you said it could've have been CNS, what about under other, could it have gone there too?
A. Yes. Although, again, I think that's sufficiently important that you'd want to put it someplace prominent.
11:34:12 Q. All right. So should I put an arrow under CNS and other there?
A. Yes.
Q. All right.
THE COURT: Again, what does CNS mean?
11:34:33 THE WITNESS: Central nervous system, Your Honor.
THE COURT: Ah, central nervous system.
BY MR. WISNER:
Q. What number are we at here, doctor, do you know?
THE COURT: But you're saying that it could have been
11:34:36 -- more data could have included, is that what you're saying?

Or should've been?

THE WITNESS: Yes, the latter, Your Honor.

THE COURT: But we don't know what the drop-out rate was -- well, we know what the base was, the base was the 20 percent shown at the top, right?

11:34:56

THE WITNESS: Yes, sir.

THE COURT: Okay.

BY THE WITNESS:

A. If I may just add one comment?

11:35:03

There are a number of areas on this table where there's dashes. And so if there's not sufficient numbers or you can't calculate an exact rate but you know that it is something where it's greater in Paxil than placebo, it could also be put in in that form.

11:35:23

BY MR. WISNER:

Q. Sure. But we know as of 1989, before the drug ever came on the market, there was 1.2 percent increase?

A. Correct. But certainly if those patients are discontinued, that enumerator would be 47, assuming all 47 of them were discontinued because of the suicide attempt.

11:35:46

Q. So I'll number this as 11, Doctor.

THE COURT: I'm sorry, what enumerator are you referring to? On page 25?

THE WITNESS: No, Your Honor. This was an analysis that --

11:35:59

THE COURT: But the enumerator is not on page 25, is it, that you're referring to?

THE WITNESS: No, sir.

THE COURT: Okay.

11:36:08 BY MR. WISNER:

Q. Just to be clear, Doctor, the enumerator would be suicide attempts, right?

A. Correct.

Q. And there's no statement of the number of suicide attempts

11:36:15 here at all?

A. That's exactly.

Q. All right. Let's keep going.

So, Doctor, let's look at that next section and it actually starts at the bottom of that page that we were just

11:36:36 on. It says "Commonly Observed Suicidal Events, Major Depressive Disorder," do you see that?

A. Yes.

Q. So in this section of commonly observed adverse events, what's supposed to go in there?

11:36:47 A. So these are events that occur in 5 percent of more patients receiving Paxil and where the incidents is at least twice that as what is observed in a placebo.

Q. All right. Now, we know, Doctor, from the FDA study that there's a doubling of the risk with Paxil, is that right, over

11:37:07 placebo?

A. Yes.
Q. But that 2.76, that's not high enough incident rate to meet that 5 percent threshold, is that right?
A. Correct.
11:37:17 Q. All right. So this next section goes -- breaks it down by different conditions, do you see that, Doctor?
A. Yes.
Q. Okay. Let's move on to the next section, Incidents of Controlled Clinical Trials, what does that refer to?
11:37:37 A. So this refers to how frequently -- or less, actually, suicidal events that were observed in uncontrolled clinical trials not -- it excludes trials where that were uncontrolled, basically.
Q. All right. And you have one here for major depressive
11:38:08 disorder, do you see that?
A. Yes.
Q. And it says, table 2 enumerates adverse events that occurred of an incident of 1 percent or more?
A. Yes.
11:38:19 Q. So let's look at the table, all right. Can I turn the page?
A. Yes.
Q. All right. So now we're looking at "treatment emergent adverse experience," do you see that?
11:38:26 A. Yes.

Q. What does that mean in basic English?
A. Side effects that happen while you're getting the drug or after you've started the drug.
Q. So, for example, there was an incident that happened, you know, in the washout period before you started, would that qualified as a treatment emergent adverse experience?
11:38:41
A. No.
Q. Okay. All right. And so we have here a bunch of different adverse effects, do you see that, Doctor?
A. Yes.
11:38:57
Q. And we have the percentage of people who are experiencing it on Paxil versus placebo, do you see that?
A. Yes.
Q. And these percentages here reflect the results from MDD trials, is that right?
11:39:10
A. Correct. Placebo-controlled MDD trials.
Q. Thank you, Doctor.
And so we have here "nervous system" and we have all these different things that would be classified under nervous system, do you see that?
11:39:23
A. Yes.
Q. Now if there was -- and it all starts at 1 percent and moves up to 23 percent, right?
A. Correct.
Q. And so let's take a quick look at tremor, 8 percent.
11:39:30

A. Yes.
Q. What does that mean relative to the 2 percent on placebo?
A. So tremor happened 4 times more often in patients exposed to Paxil than in those who received placebo.
11:39:46 Q. I mean this might sound obvious to some, but what is "tremor"?
A. It's where you're shaking.
Q. Okay. We also see nervousness here, do you see that?
A. Yes.
11:40:02 Q. And again, is that an elevated incident rate with Paxil?
A. Yes. And, again, just to clarify, these are treatment emergent. They weren't there from the get go.
Q. This is after they started taking the drug?
A. Correct.
11:40:17 Q. Okay. "Drugged feeling," what's that?
A. You feel out of it.
Q. And again, we also have zero percent on confusion and 1 percent for Paxil, do you see that?
A. Yes.
11:40:29 Q. Okay. And again, this is an elevated incident rate of Paxil versus placebo, is that right?
A. Yes.
Q. Now, I see this goes down to descending order.
Is suicide attempt in there?
11:40:47 A. No.

Q. And do we know that it should be?
A. So it should be. The incidents in MDD studies altogether was greater than in placebo.
Q. And you know that from the data from 1989?
11:41:07 A. Yes.
Q. Okay. So where would we put it in here? I guess it's 1 percent, so is it above or below "confusion"?
A. It would be above.
Q. Okay. All right. So another area they could've put
11:41:25 something, right?
A. Yes.
Q. Okay. And then it goes on. And I don't want to spend too much time because we'll be here all day. This is a fairly lengthy label. But you have the same charts for obsessive
11:41:38 compulsive disorder, panic disorder, social anxiety disorder, do you see that?
A. Yes.
Q. And then it has another chart there with all the different frequencies, and that's on page 30. Then there's a whole
11:41:49 section that specifically relates to generalized anxiety disorder, do you see that?
A. Yes.
Q. And again, if we turn -- that's page 31, if we turn the page to page 32 we have the chart here, is that right?
11:42:07 A. Yes.

Q. And the way we read the chart for depression, you could read the chart here the same way?
A. Yes.
Q. All right. So we're not going to go through all those again.
11:42:17
Down here it says "dose dependency of adverse events," what does that refer to, Doctor?
A. So if a drug causes an adverse event, the more the drug you give, the more frequent the side effect, more often it should happen.
11:42:40
So if you compare what happens on different doses, it's useful in saying is this a side effect that is associated with use of the drug.
MR. BAYMAN: Your Honor, once again, Dr. Ross has given no opinions on dosage and I would like a continuing objection to this line of questioning, to the extent I haven' already.
11:43:00
THE COURT: Yes, so noted.
MR. BAYMAN: Thank you.
BY MR. WISNER:
11:43:10
Q. All right. So let's turn to the table that comes with dose dependence.
Do you see that, Doctor?
A. Yes.
Q. And that's table 5 in the adverse event section, is that
11:43:19

right?
A. Yes.
Q. All right. This is page 33.
So we have here, on the top, we have the placebo, right?
A. Yes.
Q. And can you have different doses of placebo? Is that possible?
A. Ah, no.
Q. Okay.
A. It's a fair question, but no.
Q. Okay. And then you have 10 milligram, 20 milligram, 30 milligram, 40 milligram, do you see that?
A. Yes.
Q. Okay. And this shows the various symptoms that occur based on increase the dose, is that right?
A. Yes.
Q. So again look at this nervous system. I just want to point out a few just so that we can get a sense of it.
Let's look at "nervousness," right here (indicating). Do you see "nervousness"?
A. Yes.
Q. At dose is the incidents of nervousness the highest for Paxil?
A. According to this table, 10 milligrams.

Q. So, in fact, the lowest designated dose actually causes the most amount of nervousness, do you see that?
A. Yes.
Q. Okay. And we see this -- we see different percentages, but we also see a significant amount for other things like anxiety, do you see that? 2 percent experienced anxiety?
11:44:42
A. Yes.
Q. And we don't see any -- we see paresthesia, what is that, do you know, Doctor?
A. It's when your foot feels like it's falling asleep. You get tingling or numbness usually in the feet.
11:44:57
Q. Okay. Are you aware of whether or not it also applies to the psychological phenomena in your head? I'm just curious if you know anything about that.
A. It certainly can be exacerbated by that.
11:45:13
Q. Okay. All right, this is a section -- I mean, Doctor, have you seen any data about the dose relationship in suicidal attempts or is that something you haven't seen?
A. No, but I just want to call attention to the line -- sorry, this is "marked somnolence," and this is a really good illustration of what we refer to as a dose-response effect.
11:45:36
So the placebo rate of somnolence, and again this sleeping a lot, or feeling like you want to get in bed and pull the covers over your head, placebo at 7.8 percent, at 10 milligrams 12.7 percent, it increases to 18.3 percent if you go
11:46:03

to 20 milligrams, 30 milligrams it goes up to 20.8 percent, and then at the highest dose tested at 21.6 percent.

I mean, you don't necessarily expect as you double the dose, the incidents of something is going to go up in the same proportion, but this is a clear dose-response trend.

Q. Okay. Thank you for explaining that, Doctor.

All right. Let's clear this out.

(Brief pause).

BY MR. WISNER:

Q. It goes on to explain other types of stuff like adaption of adverse events, to certain adverse events. What does adaptation of adverse events mean?

A. You get used to it.

Q. Have you heard the word habituation?

A. Yes.

Q. What does that mean? Is that the same thing?

A. It's close in meaning.

Q. Well, what does it mean --

MR. BAYMAN: Objection, Your Honor. I think we're now getting into causation opinions here, going into habituation. So I would object to this line of questioning also. It's not in his report or in his depression.

MR. WISNER: I'm asking what it means.

THE COURT: Habituation?

MR. WISNER: Habituation, yes.

THE COURT: Do we need it?

MR. WISNER: Well, we heard Dr. Healy talk about it. I just wanted to see if it's the same thing.

MR. BAYMAN: He talked about causation, Your Honor, 11:47:31 that's what Dr. Healy talked about. I object to this line of questioning.

MR. WISNER: Well, I asked about causation. He's the one that objected to it.

THE COURT: All right. Go on to something else.

11:47:42 MR. WISNER: Okay.

BY MR. WISNER:

Q. All right. It says here over 4 to 6 week period there was evidence of adaptation to some adverse events with continued therapy, do you see that?

11:47:51 A. Yes.

Q. And lists an example, nausea and dizziness, do yo usee that?

A. Yes.

Q. Okay. Is there any reference here to akathisia?

11:48:00 A. No.

Q. It says "asthenia," do you see that?

A. Yes.

Q. Is that akathisia?

A. No.

11:48:07 Q. Okay. What is asthenia, just so we're not falling asleep

on this.
A. Kind of like feeling weak, feeling tired out. It's actually a specific term in the coding dictionary.
Q. Okay. Then it goes into differences with males and
11:48:25 females, Doctor, do you see that?
A. Yes.
Q. All right. Let's go down here, it has discussions, it has hallucinations, do you see that?
A. Yes.
11:48:35 Q. All right. So now let's get to the next section. What is that section, Doctor?
A. So anything that wasn't captured above, basically, that did not -- was -- was -- was not -- didn't meet the definition of common, or discontinuation, or frequent. Basically, this is
11:49:06 almost like a miscellaneous listing of things.
Q. Is this where you look to if you missed anything earlier?
A. If -- yes.
Q. All right. And yesterday we went through the 1992 label for Paxil, do you recall that?
11:49:25 A. Yes.
Q. Is this the same section where we saw the "emotion lability" term?
A. Yes.
Q. And that was back in 1992, right?
11:49:34 A. Correct.

Q. So this is 2010. How many years later is this?
A. 18.
Q. Okay. All right. And we have the same text, essentially, that we saw in the '92 label, is that right, Doctor?
11:49:47 A. Yes, with the exception that, you know, there may have been some things added and this would be through CBE, change being affected in supplements.
Q. Okay. And, for example, the number of patients has obviously increased?
11:50:02 A. Yes.
Q. Okay. Now, the bottom here it says:

"The events are further categorized by body system and listed in order of decreasing frequency according to the definitions."

11:50:14 Do you see that?
A. Yes.
Q. And is that the same definition of "frequent" that you discussed with the jury yesterday?
A. Yes.
11:50:19 Q. And so it's still in the label today?
A. Correct.
Q. All right. Let's turn the page.

Remember yesterday we discussed the nervous system?

A. Yes.
11:50:32 Q. And the listing of frequents adverse events?

A. Yes.
Q. Do you see a frequent adverse event in there of suicide attempt?
A. No.
11:50:44 Q. What do you see?
A. Emotional lability.
Q. That's the term we looked at yesterday where the FDA was talking about coding maneuvers, is that right?
A. Correct.
11:50:58 Q. Doctor, in your opinion, is that use of emotional lability misleading?
A. Yes.
Q. Why?
A. It should have been coded. These events were actually
11:51:16 suicide attempts, that's number one. From a regulatory point of view -- so if you saw "suicide attempt" there, that means it's something very different than emotional lability.

Number two, and this is a regulatory issue, it says "a standard COSTART based dictionary terminology." Suicide
11:51:33 attempt -- so the specific terms, not -- these are technical terms, even though they may have a common meaning, COSTART--and that dictionary is no longer in use--but suicide attempt is the appropriate COSTART term.
Q. So emotional lability, it wasn't that they had to use it,
11:51:55 they could've used "suicide attempt"?

A. I'm not even sure --

MR. BAYMAN: Objection; leading, Your Honor.

THE COURT: He may answer.

BY THE WITNESS:

11:52:02 A. I'm not even sure that emotional lability is a term in COSTART. I mean, it might be, but it's -- it's -- it's something that -- it's not the right word. It's just not.

Q. Since we're on this point, Doctor, I've pulled up the red pen. Is this a good time to use it?

11:52:22 A. Certainly.

Q. All right. What should I circle or underline?

A. I would circle "emotional lability."

Q. And what do you have to say about that, Doctor?

A. Well, it's not only the wrong term, but it's buried. I

11:52:44 mean, the average prescriber is not going -- I don't go through these list unless I've got some patient with an extraordinary unexpected event, and I say has this ever been reported anywhere.

So it's -- it's -- you can say, well we said there's

11:53:05 emotional lability, you'd have to know what that meant and then you'd have to go through this whole label. It's not an effective warning.

Q. So it would be fair to say suicide, suicide hidden?

A. Suicide not even mentioned.

11:53:19 Q. So no suicide?

A. Correct. Or suicide attempt. Again, those are two different concepts, or suicidal behavior.
Q. My handwriting is terrible, but did I write "no suicide, or suicide attempt, or suicidal behavior"?
11:53:49 A. Correct.
Q. Okay. And just to be clear, Doctor, I mean, this is the current label, is this the same thing that's happened since 1992?
A. Yes, this is -- well, again, just to be clear, this is the
11:54:04 2010 label.
Q. I'm sorry, Doctor. This is a 2010 label. Is this the same thing that's happened since 1992?
A. Yes.
Q. And in your opinion, as a regulatory expert, did GSK have
11:54:17 an obligation to fix this term right here (indicating) with "suicide attempt"?
A. Yes.
Q. And after the FDA investigated this issue with regards to the pediatrics, did that add a heightened obligation on GSK to
11:54:36 change the label?
MR. BAYMAN: Objection, Your Honor.
THE COURT: Overruled.
BY THE WITNESS:
A. Yes.
11:54:39 BY MR. WISNER:

Q. Did they ever try?
A. I'm not aware of any attempt.
I want to clarify one thing, though, because we did agree this was the June 2010 label, but I actually looked last
11:54:56 night and the most recent --
MR. BAYMAN: Your Honor, you restricted the evidence.
THE COURT: There's no question pending, Doctor. I'm afraid you're going to have to wait for a question.
THE WITNESS: I apologize, Your Honor.
11:55:09 MR. WISNER: Well, I guess I have to ask the question and see if --
THE COURT: No, you won't.
MR. WISNER: Okay.
THE COURT: You ask your question.
11:55:18 MR. WISNER: Okay. I'll move on.
THE COURT: You ask the questions, he gives the answers.
MR. WISNER: Yes, Your Honor.
THE COURT: That's the way it works.
11:55:23 MR. WISNER: I just don't want to ask a question that gets me in trouble.
THE COURT: Well, and that's why we don't allow the witness to volunteer.
BY MR. WISNER:
11:55:31 Q. Okay. Dont' answer this question until he's objected.

A. I understand.
Q. Does the current label for Paxil still have this emotional lability language in it?
A. The most recent label was approved in -- the labeling supplement was approved in January of 2017. And so that is like all other versions of the label, available on the web. It still contains the same language.
Q. 2017?
A. That would be about 2 months ago.
Q. So we're 25 years later, from 1992, and to this very day the label has never told people that emotional lability is referring to suicide attempts, is that right?
A. That's correct.
Q. All right. Let's continue. Let's go to page 37, Doctor.
And we went -- sorry, let's go back to 36. This is a nervous system and then there's all these other sections of the body, right?
A. Organ systems, yes.
Q. Okay. And then we get to the next page, page 37, and after the various organ systems there's one that says "Postmarketing Reports," do you see that?
A. Yes.
Q. And I don't want to spend much time on this, Doctor, because I don't want to take up everyone's entire day, but what is a postmarketing report, generally?

A. So once the product is approved, a product drug is approved, it gets out into general use and can be and is used not only for the indications that were studied, but also other indications that may or may not have been studied. It's used in groups of patients who it's never been tested on, and so on.

11:57:25

So the FDA has a system in place where adverse events that happened in practice, in the real world, are collected. It's all voluntary. So it's estimated that only, at best, 10 percent of side effects in the real world ever get reported, at most. They can be sent to the manufacturer who turns them into the FDA. They can be sent directly to the FDA. And there's a standard form for doing this.

11:57:51

Q. And actually this is a question about the FDA that I want to clarify. Does the FDA only collect data from placebo-controlled trials?

11:58:09

A. No; of course not.

Q. What other types of data do they collect about suicide risks or adverse events?

A. Anything. First off, randomized controlled trials are very useful, but they are not the only source of evidence, by any means.

11:58:25

Secondly, randomized controlled trials only study a narrow carefully defined population. So it's important to know how a product is going to be used and what happens in the real world. So these adverse event reports say what happens when

11:58:43

you get out of the lab and go into the real world.
Q. Scientifically, do you think it's appropriate, both from a scientific perspective as well as ethical perspective, to exclude looking at data of an adverse event just because it
11:59:08 didn't happen in a placebo-controlled trial?
MR. BAYMAN: Objection, Your Honor, to "ethical."
MR. WISNER: I think this is a part of science, Your Honor.
THE COURT: Well, I'm going to sustain. We're not
11:59:20 going to get into the ethics.
MR. WISNER: Fair enough.
THE COURT: I know there's an ethical problem, but, I mean, in every activity, but we haven't opened that door yet. So stay with the relevant part of your question.
11:59:34 BY MR. WISNER:
Q. Let me ask the question again, Doctor.
Is there -- is it scientifically legitimate to just look at suicides or suicide attempts that occur in placebo-controlled clinical trials?
11:59:57 A. No.
Q. All right. So we have postmarketing reports, and then we get into this next big section here, Doctor, "drug abuse and dependence," do you see that?
A. Yes.
12:00:07 Q. And then we get to overdosage, do you see that?

A. Yes.
Q. What is the purpose of the overdosage section?
A. Overdosage provides information for patients and physicians about whether there's any information on what happens if
12:00:28 somebody takes too much of a drug, and also what kind of things that results in terms of symptoms, and then what to do about it.
Q. Now, it says here:

> "... since the introduction of Paxil in the
12:00:43 United States, 342 spontaneous cases of deliberate or accidental overdosage during Paroxetine treatment have been reported worldwide circa 1991."

Circa 1991, what does that suggest about what this
12:01:02 data is referring to?
A. No information --

MR. BAYMAN: Objection, Your Honor. I just want to make another -- I think I have a standing objection to the entire exhibit, but I just want to make it clear we're now
12:01:12 going into another area --

THE COURT: I don't think dosage is an issue in this case and I'll sustain your objection. I don't think we should go into dosage.

MR. WISNER: Your Honor --

12:01:20 MR. BAYMAN: I ask the jury to disregard his comments

about that.

MR. WISNER: Your Honor, it says "deliberate or accidental overdosage," deliberate overdosage is a suicide attempt.

12:01:33 THE COURT: There's never been an issues, as I understand the case, with all the issues and problems we have, when the idea of dosage has been contested.

MR. WISNER: Absolutely, Your Honor. We're talking about -- fair enough. I'll move on.

12:01:47 BY MR. WISNER:

Q. Okay. Great. All right, in the next section here, Doctor, is "dosage and administration," do you see that?

A. Yes.

Q. And this is one of the last sections of the label. What

12:02:08 does that refer to?

A. So this is how much of a dose to start with, whether you should take it with food, how many times a day. It may depend on what exact condition you're treating, who you're treating, how frequently you should make changes to the dose.

12:02:31 Q. Now, it says "administration," do you see that?

A. Yes.

Q. Is that about how you give a drug to somebody?

A. Yes.

Q. And do you believe that there are Paxil-specific

12:02:40 information that a prescriber would need about how to properly

administer Paxil, particularly in the early part of the treatment?
A. Well, let me -- yes, in -- in the sense -- yes.
Q. What is that?
12:02:57 A. So again --
MR. BAYMAN: Your Honor, again getting into dosage.
THE COURT: I'm going to sustain the objection. We've got a lot of issues in the case, we don't need to get into dosage.
12:03:11 MR. WISNER: Yes, Your Honor.
BY MR. WISNER:
Q. All right. Okay. So let's go to the last part of the label, Doctor.
This is a section that's included, it's called the
12:03:23 "medication guide," do you see that, Doctor?
It's on page 42.
A. Yes.
Q. What is a medication guide?
MR. BAYMAN: Your Honor, objection. Again, Dr. Ross
12:03:33 had no opinions about this, and I just would like a continuing objection to this line of inquiry.
MR. WISNER: I think he's made that continuing objection for the last hour. I don't know why he keeps making it.
12:03:44 MR. BAYMAN: Well, it's a different document, Your

Honor, which is why.

THE COURT: Is the medication guide been an issue in the case?

MR. BAYMAN: No, sir.

12:03:51 MR. WISNER: It they stipulate to not discussing or mentioning the medication guide in any way, we will not discuss it now.

THE COURT: They don't have to stipulate. You'll object and I'll sustain your objection.

12:04:00 MR. WISNER: Sounds good, Your Honor.

THE COURT: All right.

BY MR. WISNER:

Q. All right. So, Doctor, we just went through the label and pointed out, I think we got up to 11 or 12 times places that

12:04:14 GSK could have added an adult suicide warning over the age of 24, is that right?

A. Correct.

Q. Okay. And on the first page here we highlight, we underline in red and we did it in a couple of other sections as

12:04:26 well, portions that you thought were really a problem, is that right?

A. Correct.

Q. Now I want to clarify something. The statement here as it relates to all antidepressants, is that itself untrue?

12:04:40 A. No.

Q. The statement, if you'll apply it to Paxil, is it untrue?
A. Yes.
Q. What, if anything, does that -- how does that relate to your opinion?
12:04:52 A. If you don't give that information, it is misleading.
Q. All right. In a minute I'm going to pass you along to opposing counsel and there's going to be a discussion of this section, before that happens I want to just quickly run through it very quickly with you, Doctor, okay.
12:05:20 This first section right here where it says warnings, clinical worsening and suicide risk, do you see that?
A. Yes.
Q. And it has a discussion in here, do you see that?
A. Yes.
12:05:32 Q. All right. And it discusses:

> "... patients with major depressive disorder, both adult and pediatric, may experience worsening of their depression and/or emergence of suicidal ideation and behavior, suicidality, 12:05:44 or unusual changes in behavior whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs."

Now, this is the language that we talked about 12:05:55 yesterday for quite some length, isn't it?

A. Yes.
Q. Do you believe this language right here is stating to physicians that Paxil can induce adult suicidal behavior?
A. It's not specific. It doesn't say anything specific about
12:06:08 Paxil.
Q. Does it say anything specific about drugs actually doing anything?
A. No.
Q. In fact, Doctor, the sentence we just read it says:
12:06:20 "... whether or not they are taking antidepressant medications."
Do you see that?
A. Yes.
Q. Does that in any way suggest -- what does that suggest to
12:06:29 you?
MR. BAYMAN: Your Honor, I think we covered this 3 or 4 times.
THE COURT: Yeah, I think you covered this, sir.
BY MR. WISER:
12:06:36 Q. All right. Let's talk about this page here, this page we did not cover.
Is there anything in this part of the class warning that is misleading? We're on page 12, Doctor.
A. Yes.
12:06:48 Q. That is misleading or inappropriate without a

Paxil-specific warning?
A. Yes.
Q. Can you please point it out to us.
A. So this table is for all antidepressants as a group. And
12:07:03 it says people who get an antidepressant -- people under 24 who get an antidepressant, you may see more suicide.
Q. You are referring to this portion right here, Doctor (indicating)?
A. Correct.
12:07:17 Q. Okay.
A. For all antidepressants as a group more than placebo, but if you once you get over 25, it's less.
Q. So it says here "one fewer case," does that mean for patients 25 to 64 the use of antidepressants decreases suicidal
12:07:38 behavior?
A. That is what this table says, but it's for antidepressants as a group.
Q. So, Doctor, is it all right if I circled that one fewer case right there in red (indicating)?
12:07:51 A. Yes.
Q. Does this sentence or this statement hold true when it comes to Paxil?
A. No.
Q. What do we know about Paxil?
12:07:59 A. It increases the risk.

Q. Specifically, what do we know about Paxil for this age group?
A. We know that that increases the risk.
Q. All right. Is there anything else in this that you think needs to be pointed out to the jury?
A. I would just say just one other thing, and I just want to make this very, very clear, as I said yesterday, the label is -- in terms of how the FDA considers this, there's -- these concerns regarding the label extend to things are, from a regulatory point of view, part of the label, such as advertising, print ads. And if -- I'm trying to clarify this, and if I'm -- I don't want to go beyond the line here, but the medication guide is part of the labeling --
MR. BAYMAN: Your Honor, we just objected to the medication guide and you sustained the objection. That was the last document which he wanted me to stipulate to and you sustained my objection.
THE COURT: Yes. It's not clear what the point is here, sir. Ask another question.
MR. WISNER: Sure.
BY MR. WISNER:
Q. Doctor, my question was, is there any specific sentences in this section of the label that I should highlight to the jury?
A. Is there any --
THE COURT: I think we've been over this, sir.

MR. WISNER: No, this actually we have not covered.
BY MR. WISER:
Q. Let me just draw your attention.
Doctor, the sentence right here, "there were
12:09:37 suicides," do you see that?
A. Yes.
Q. Do you have a problem with that sentence?
A. Yes, I do.
Q. What's your problem with that sentence?
12:09:41 A. There were suicides in the adult trials but the number was
sufficient to reach any conclusion about drug effect on
suicide, that is not true for Paxil.
Q. What do we know about Paxil?
A. Paxil increases the risk of suicide in adults at all ages,
12:09:57 including adults older than 24.
Q. And can I bracket that or is that not --
A. Please.
Q. All right. Okay, Doctor, and the rest of this we covered
yesterday, so I don't want to get into it in any detail. Do
12:10:11 you believe that this constitutes a warning about
antidepressants or does it constitute disease management?
A. Disease management.
Q. Okay. All right.
MR. WISNER: Your Honor, at this time I'm going to
12:10:37 mark this as Plaintiff's Exhibit 70. And this is the markup

version I was discussing with Dr. Ross.

And one second.

(Whereupon, there was a conference had between counsel off the record.)

12:10:55 MR. WISNER: At this time, Your Honor, we move Plaintiff's Exhibit 70 into evidence.

MR. BAYMAN: I object to that, Your Honor. That's the marked up version which is demonstrative.

THE COURT: You may use it at some other point in the
12:11:06 trial, sir, but I'm going to receive it in evidence, as such.

We already have the unmarked-up-exhibit in evidence, we have the record, we have the doctor's testimony. So we will not receive it in evidence. You may have some use of it for demonstrative purposes.

12:11:24 MR. WISNER: Sure. Sounds good.

(Brief pause).

THE COURT: Do you want to start your cross-examination, sir?

MR. WISNER: I have a few more points and then I'm
12:11:35 done.

THE COURT: I thought you had tendered the witness.

MR. WISNER: No, not yet at this time, Your Honor.

THE COURT: We're trying to help you, sir.

MR. WISNER: I know. I'm just moving over to my other
12:11:43 device because I'm no longer using the camera.

THE COURT: All right. Proceed.
BY MR. WISER:
Q. Okay, Doctor, we just went through that label. Have you seen any statements publicly made by GSK employees that they have not warned about drug-induced suicidality in the label?
12:11:59
A. Yes.
MR. BAYMAN: Objection, Your Honor. That's not disclosed. It goes into motive and intent and it's also hearsay.
12:12:12
MR. WISNER: It is in his report and I can show you the page site, if you'd like.
THE COURT: Just a minute.
(Brief pause).
THE COURT: All right. You may proceed.
12:12:24
BY MR. WISER:
Q. Are you aware of any statement made by GSK, Doctor?
A. Yes.
Q. And where was that statement made?
A. That was made in a publication by GSK employees that was -- I believe it was the Journal of Clinical Psychopharmacology. It was submitted to that journal in 2008, I believe published in either 2010 or 2011. The first author on that, I believe, was Mr. Krause.
12:12:43
Q. All right, Doctor, could you please turn in your binder to Plaintiff's Exhibit 285.
12:13:09

(Brief pause)
BY MR. WISNER:
Q. Are you there?
A. I am.
12:13:31 Q. Is this that article you were referring to?
A. It is. I apologize, the first author was Mr. Carpenter.
Q. Okay. Is this document that you cited in your report?
A. Yes.
Q. Is this a document that you relied upon in forming your
12:13:48 opinions?
A. Yes.
Q. Would discussing the contents of this document aid you in your testimony today?
A. Yes.
12:13:53 MR. WISNER: Permission to publish, Your Honor.
THE COURT: All right.
(Exhibit published to the jury.)
BY MR. WISER:
Q. So we're looking at the journal article here, Doctor. I'm
12:14:03 just going to call out the title and the authorship here.
What is the title on this document, doctor?
A. (Reading:)
'... meta analysis of efficacy and treatment emergent, suicidality in adults by psychiatric
12:14:15 indication and age subgroup following initiation

of Paroxetine therapy: A complete set of randomized placebo-controlled date trials."

Q. What does that mean in layman's terms?

A. They combined all the trials and they looked to see if people who received Paxil were more likely to kill themselves or try to kill themselves compared to placebo and they looked at it by age as well.

Q. Okay. Great. And you mentioned the authors here. I want to point out one. Do you see this person, John Kraus?

A. Yes.

Q. Who is he?

A. Dr. Kraus is a GSK employee.

Q. And was he heavily involved in the 2006 analysis that yielded that 6.7 risk ratio we discussed yesterday?

A. Yes.

Q. Okay. Let's look at this first paragraph here -- and just to be clear, Doctor, you said this was published when?

A. I'm sorry, it was accepted in 2010 and then published in 2011.

Q. Okay. So this was -- was this after or before the class warnings that were instituted by the FDA?

A. After.

Q. Okay. So this is hard to read, but let's see if I can do it. It says:

"... while these agents are efficacious and

generally well tolerated, standard precautionary statements regarding suicidality have existed in SSRI and other antidepressant prescribing medication for more than a decade."

Do you see that, Doctor?

12:16:07

A. Yes.

Q. Is it your understanding that there had been standard precautionary kind of suicidal warnings in SSRIs for over a decade?

A. If they're talking about the -- only with regard to the disease itself, not with regard to the potential for a drug to -- one of these drugs to induce suicide.

12:16:20

Q. Well, let's go to the next sentence:

"... these precautions, however, did not explicitly alert prescribers to the potential that the medication itself could induce suicidality."

12:16:46

Do you see that, Doctor?

A. Yes.

Q. How does that in any way relate to the opinions you gave this jury about whether the Paxil label addresses whether Paxil itself induces adult suicidal behavior?

12:16:54

MR. BAYMAN: Objection, Your Honor. This is talking about the early label. Not the 2010 label, it's very clear.

THE COURT: I beg your pardon. I didn't quite hear

12:17:11

what you said.

MR. BAYMAN: I'm sorry. Objection, Your Honor, he is mischaracterizing this. This talks about the early label, not the label that he was questioned about. It is misleading.

12:17:25 THE COURT: Okay. Well, you can cover that on cross examination.

You may answer.

THE WITNESS: I'm sorry, could you read the question back to me.

12:17:40 (Question read.)

BY THE WITNESS:

A. Well, I think it's an acknowledgement, admission, whatever, that the statements in the label for Paxil have never, not just in '92 but going forward as I said yesterday, never explicitly

12:18:04 alerted or even hinted at the potential that Paxil could induce suicidality.

BY MR. WISNER:

Q. All right. We talked a bit about whether or not there was any analysis that looked at whether Paxil increased suicidality

12:18:19 or suicidal behavior in adults specifically over 24, remember?

A. Correct.

Q. Let's take a look at this article.

All right, Doctor, I'm on page E7 of this article. And I called up a table here, table 6, what is it titled,

12:18:55 Doctor? I have it blown up on the screen if you want to look.

Your copy might be clearer because it's a little blurry here.

(Brief pause).

BY THE WITNESS:

12:19:06 A. Yes.

BY MR. WISNER:

Q. So what's the title of that table?

A. (Reading:)

"... "definitive suicidal behavior or ideation

12:19:13 by indication, treatment, and age as a risk factor."

Q. All right. And if you look here, we have ages 25 through 64, do you see that, Doctor?

A. Yes.

12:19:30 Q. Okay. So now we're looking specifically at that age bracket that we were talking about a minute ago.

A. Yes.

Q. Okay. And then we have MDD, do you see that?

A. Yes.

12:19:41 Q. All right. And then it lists all the data for it. And if we look over here -- sorry. I had the wrong part.

If we look at over here, under the section "definitive suicidal behavior," do you see the number presented for MDD?

A. Yes.

12:20:07 MR. BAYMAN: Objection. I object to this line, Your

Honor, also. This is not in his expert report, or in any of his disclosed opinions, nor in his deposition testimony. So I object to this entire line.

MR. WISNER: For the record, it is in his report. He cites this article. And they never questioned him at his deposition.

THE COURT: Proceed.

BY MR. WISER:

Q. All right, Doctor, do you see this line here that it refers to MDD and definitive suicidal behavior alone?

A. Yes.

Q. All right. I'm just going to blow that up even closer so that we can all see it.

So on the left side we have the incident rates for Paxil, is that right?

A. Yes.

Q. And then in the middle we have placebo, is that right?

A. Yes.

Q. 8 on Paxil, zero on placebo, is that right?

A. That's correct.

Q. And then a risk ratio represented in the far right, do you see that?

A. Yes.

Q. It says "infinity," is that right?

A. That's correct.

Q. What does that mean from a statistical perspective?
MR. BAYMAN: Same objection, Your Honor.
THE COURT: Overruled.
BY THE WITNESS:
12:21:11 A. So just want to be clear about what we're looking at the risk up here --
BY MR. WISNER:
Q. Doctor, please answer my question.
A. Okay. Okay.
12:21:19 Q. What does "infinity" mean here?
A. "Infinity" means that it's an extraordinarily high risk. And if you look at the confidence interval, that lower number of 1.3 means that we can be sure about that, that this is not just a chance finding.
12:21:36 Q. So to be clear, Doctor, GSK's own employee, Dr. Kraus, published an article that acknowledged that the definitive suicidal behavior for people over the age 24 but under 65, there was a nonrandom increased risk in suicidal behavior, is that right?
12:21:58 MR. BAYMAN: Objection; leading, Your Honor.
THE COURT: Overruled.
BY THE WITNESS:
A. Yes.
BY MR. WISER:
12:22:04 Q. Since this article was published or proposed for

publication in 2008, did GSK ever add a warning about definitive suicidal behavior in adults over the age of 24?
A. So just to make sure I understand. By "definitive suicidal behavior," you mean not just -- the way it's defined, it's just
12:22:27 behavior but combined by suicide attempts and completed suicides?
Q. That's right. I'm talking about in the chart, it says "definitive suicidal behavior," did GSK--
A. No. No. Absolutely not.
12:22:38 Q. All right. Let me ask just ask the question so we get the record clear.
A. Sure.
Q. Since this article was prepared in 2008, did GSK ever put in the --
12:22:48 MR. BAYMAN: Your Honor, objection. This is 2011, the article clearly states that. It's not 2008, it's 2011 after the events leading to --
MR. WISNER: Your Honor, it was submitted it 2008. He's testified to that several times.
12:23:00 MR. BAYMAN: It was published in 2011, Your Honor. It's clear on the document.
THE COURT: Submitted when?
MR. BAYMAN: It's published in 2011, Your Honor. On the first page of the document, which is, I think, beyond the
12:23:14 event. It was accepted May 26, 2010 and it was published in

2011. It says clearly on the article --

MR. WISNER: Respectfully, Your Honor, it says submitted December 8, 2008. So this was prepared over 2 years before his death.

12:23:32 THE COURT: Yes.

MR. BAYMAN: And published after his death, Your Honor.

THE COURT: I understand.

BY MR. WISER:

12:23:38 Q. All right, Doctor, let me ask you my question. Let's go back to this table.

Doctor, after this was submitted for publication in 2008, did GSK ever attempt to put a warning for adults over the age of 24 for definitive suicidal behavior in the Paxil

12:24:04 labeling?

A. No.

Q. Has GSK in the entire 30 years that this drug has been on the market ever put in the label that this drug can cause adults to kill themselves?

12:24:16 A. With the clarification that it's actually a quarter century rather than 30 years, no.

MR. WISNER: Thank you, Your Honor.

One minute, Your Honor. Let me check with counsel.

(Brief pause).

12:24:29 MR. WISNER: We pass the witness.

THE COURT: All right. We'll break now until 1:30.

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

[redacted]

12:25:03

(Luncheon recess taken from 12:25 o'clock p.m. to 1:30 o'clock p.m.)

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

S/Blanca I. Lara March 22, 2017