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

WENDY B. DOLIN, Individually and as Independent Executor of the Estate of STEWART DOLIN, Deceased, Plaintiff, -vs- SMITHKLINE BEECHAM CORPORATION, d/b/a GLAXOSMITHKLINE, a Pennsylvania corporation, Defendant.	Case No. 12 CV 6403 Chicago, Illinois March 22, 2017 1:30 p.m.

VOLUME 6-B
TRANSCRIPT OF PROCEEDINGS - Trial
BEFORE THE HONORABLE WILLIAM T. HART, and a Jury

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(Proceedings heard in open court, jury not present:)

[redacted]

(Jury enters courtroom.)

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

You may proceed, sir.

MR. BAYMAN: Thank you, your Honor.

DAVID ROSS, PLAINTIFF'S WITNESS, PREVIOUSLY SWORN.

CROSS-EXAMINATION

BY MR. BAYMAN:

Q. Good afternoon, Dr. Ross.

A. Good afternoon.

Q. I just want to establish something at the outset. While you've worked for the FDA in the past, you're not speaking here today on behalf of the FDA, correct?

A. Correct.
Q. And you don't have authority to speak on behalf of the FDA, correct?
A. No.
Q. So, that's correct, you do not?
A. Correct.
Q. And while you work currently at the U.S. Department of Veterans Affairs, you're not speaking today on behalf of the V.A., are you?
A. Correct.
Q. Or on behalf of the U.S. government at all, are you?
A. Correct.
Q. Now, when you worked at the FDA, you worked in the group responsible for anti-infective drugs, is that right?
A. That was one of the groups that I worked in.
Q. And that -- there's a separate group at the FDA, though, isn't there, called the neuropharmacology division?
A. Yes.
Q. And you never worked in the neuropharmacology division, correct?
A. Correct.
Q. And that neuropharmacology division is the group responsible for the review and analysis of psychiatric medications like Paxil, correct?
A. The review and analysis of clinical trials on drugs such

as Paxil.
Q. And also for reviewing and approving NDAs, New Drug Applications, for drugs such as Paxil, correct?
A. Correct.
Q. And even though you never worked in that division, you also never received any assignments from the neuropharmacology division while you were at FDA, correct?
A. Not that I can recall.
Q. And while you were at FDA, you never reviewed any safety data for any SSRI or any psychiatric medication, correct?
A. Not that I can recall.
Q. You did not work at the FDA, in fact, on any issue concerning an SSRI or a psychiatric medication and suicidality, correct?
A. Correct.
THE COURT: Doctor, move that microphone closer to you.
THE WITNESS: Sorry, your Honor.
THE COURT: There's another one there on the stand.
THE WITNESS: Yes, sir.
BY MR. BAYMAN:
Q. For instance, while at the FDA, you never analyzed any data with respect to any SSRI or psychiatric medication to assess whether they increased the risk of suicidality, correct?

A. That specific issue, no.
Q. And during your time at the FDA, you never worked on the labeling for any SSRI or antidepressant, correct?
A. Correct.
Q. You were familiar with something that the FDA calls an advisory committee, correct?
A. Yes. If I may, I apologize. I need to clarify my answer to your previous question. For at least one of the products that I worked on during the time that I was in anti-infectives, there may have been work that involved simultaneous labeling considerations for an antidepressant.
Q. But that wasn't an SSRI, correct?
A. You know, I'd actually have to look at that label for that product to be sure, so I don't know.
Q. Do you have your deposition with you, Doctor?
A. I'm not sure if it's in this binder.
Q. What is that binder?
A. This is the exhibits for direct examination.
Q. Let me hand you your deposition.
A. Thank you, sir.
MR. BAYMAN: Your Honor, may I approach?
THE COURT: Yes.
MR. BAYMAN: That's his deposition.
BY MR. BAYMAN:
Q. Dr. Ross, turn, if you would, to your deposition, which

was taken April 5 -- April 2nd, 2015, to page 77, lines 1 to 4.

MR. WISNER: Objection, your Honor. If I could get a copy of whatever he's showing the witness.

MR. BAYMAN: It's his deposition. I'm happy to give you one.

MR. WISNER: Thank you.

THE COURT: Page?

MR. BAYMAN: 77, line 1 to 4.

BY THE WITNESS:

A. Yes, sir.

BY MR. BAYMAN:

Q. The question was, "While you were at FDA, you never worked on the labeling for any SSRI or any psychiatric medication, is that true?"

And your answer was, "That is true."

Did I read that correctly?

A. Yes.

MR. WISNER: Objection. Move to strike as improper impeachment. He testified that he may have worked on labeling in the anti-infective area that there was overlap. This is just reading testimony in from the transcript.

THE COURT: All right. Let's proceed.

BY MR. BAYMAN:

Q. You talked on direct a little bit with Mr. Wisner about an

FDA advisory committee. Do you recall that?
A. Yes.
Q. And FDA often consults advisory committees for independent expert advice on scientific matters, correct?
A. Correct.
Q. And advisory committees are composed of, at least in the FDA's view, authorities in the field?
A. Can you clarify -- when you say authorities in the field, I just want to make sure I understand what field you're talking about.
Q. Well, whatever field the particular advisory committees impanel. Let's say, for example, psychiatric medications. The FDA considers those people on the advisory committees to be experts in that field, correct?
A. Well, because there are by -- I don't know if it's regulation or law on FDA advisory committees, individuals such as consumer or patient representatives, I want to make sure I understand what you mean by expert. They may not be clinical expert, but they bring the different perspective to that.

So, I think it would be fair to say that the members of an advisory committee are consulted by FDA to provide input based on their perspective and experience.
Q. Fair enough. There are -- there may be consumer representatives, but there also may be medical doctors, too, correct, on the advisory committee?

A. And there's, I think, almost without exception a statistical consultant on the committee.
Q. You anticipated my next question. In any event, FDA invites experts outside of FDA to participate in advisory committees, correct?
A. Yes.
Q. And you've never served on an FDA advisory committee that assessed whether an SSRI or psychiatric medication was safe and effective, correct?
A. Correct. Excuse me.
Q. You have never served on an FDA advisory committee that assessed whether an SSRI or any psychiatric medication increased the risk or was associated with suicidality, correct?
A. Correct.
Q. And while you were at FDA, you certainly had no responsibility for reviewing any data concerning Paxil, correct?
A. Correct.
Q. And you never had any responsibility for reviewing Paxil's labeling, correct -- while you were at FDA, correct?
A. Correct.
Q. And you never had responsibility at FDA for reviewing any post-marketing data on Paxil, correct?
A. Let me qualify my answer, because again, I want to try to

make sure I'm giving you clear answers. You know, for example, you had previously said that I -- you know, during the deposition, I said I did -- I'm going to answer your question -- that I worked on the labeling. At the time of the deposition, my interpretation was you meant directly on the labeling, and that is correct.

It occurred to me, and this is probably because of the example I used earlier, that there was labeling that I worked on for anti-infectives that had implications for antidepressant labeling.

But to answer your question, while there may have been adverse event reports involving patients who were receiving Paxil along with other drugs, I was not responsible primarily for assessment of those reports with respect to Paxil.

Q. Thank you. Now, as I understand, you left the FDA in 2006 and began practicing at the Veterans Administration or V.A., is that right?

A. Well, actually, no. I had already been on staff practicing at the Washington, D.C., V.A. from 1998 onwards. In 2006 -- and I continued that activity while I was at the FDA up through the present day.

In 2006, I left the FDA to assume the -- direct the V.A.'s HIV, hepatitis C, and what's now called related conditions program.

Q. So, the V.A. became your employer in 2006?
A. Correct.
Q. And your role at the V.A. is that of a general practice doctor, is that right?
A. I'm sorry. I'm not trying to be difficult, but when you say general practice, tell me what you mean.
Q. You're an internist, correct?
A. Among other things, yes.
Q. Okay. And you have a specialty in infectious disease, correct?
A. Correct.
Q. But you treat patients at the V.A., correct?
A. Yes.
Q. And adult patients, correct?
A. Yes.
Q. And you testified yesterday that in your practice, you do not prescribe SSRIs, including Paxil, correct?
A. Let me clarify that in the sense that other providers, particularly in mental health, may initiate therapy with an SSRI, and I may order a new prescription or refill for a patient. And in doing so, even though it's another physician who initiated it, I take the legal and ethical responsibility for renewing it.

So, maybe that's -- I'm just trying to clarify that point, that I've not initiated treatment of patients with

Paxil.
Q. You've not written the first prescription for Paxil for a patient, correct?
A. Correct.
Q. And when you talked about medicines that you prescribed yesterday, you were talking about antidepressant medications that are in a different class than Paxil, correct?
A. Correct.
Q. Those would be benzodiazepines, is that right?
A. Well, benzodiazepines are generally not antidepressants.
Q. Okay. But you prescribe benzodiazepines, correct?
A. If they are clinically indicated, yes.
Q. Okay. Now, correct me if I'm wrong, but I think you testified yesterday that you don't prescribe Paxil or other SSRIs because you believe they cause people who take the medication to commit suicide in some cases, correct?
A. No, that is not what I said.
Q. Okay. I believe you said based on the information you learned in this case, you don't prescribe Paxil to patients, didn't you?
A. Correct.
Q. Okay. But when you see a patient who's taking Paxil prescribed by another doctor, you have a conversation with that patient about your opinion regarding the relationship between Paxil and suicide, correct?

A. To be honest with you, I cannot recall the last time I saw a patient of mine who was on Paxil.
Q. What about other SSRIs?
A. If there are other SSRIs that they're on, as a matter of course, I do what's called a medication reconciliation, which means that I go through their medications, and I say, "Are you taking this? Are you taking this?"

One of the challenges in my patient population is I frequently will have patients who are on literally 25 different medications. And one thing I'm always looking to do is say, "Is this medication really needed, or is it the right medication?"

So, I do go through them, and that's part of -- as part of that, I'm also assessing what is going on with the patient, including things such as depressive symptoms and the like.

Q. I think you said this morning that your healthcare organization manages patients and informs them about the risk of suicide, correct?

MR. WISNER: Objection. Vague.

THE COURT: Overruled. You can answer it if you can.

BY THE WITNESS:

A. When you say the risk of suicide, in what context?

BY MR. BAYMAN:

Q. Well, I think -- again, correct me if I'm wrong, but my

notes show you testified that suicide is an enormous problem with veterans, correct?
A. Yes.
Q. And that you work with a high-risk population, I think was the word you used this morning?
A. Yes.
Q. You know, though, don't you, that other doctors at the V.A. prescribe Paxil and other SSRIs to veterans, correct?
MR. WISNER: Objection, your Honor. You stopped me from going down this inquiry about his work with V.A. and SSRIs, and now he's doing it. So, he objected. I think it should cut both ways.
MR. BAYMAN: He talked this morning about how he counsels veterans who he sees about the risk of --
THE COURT: Well, very limited, and I'll allow very limited cross. It was very limited.
BY MR. BAYMAN:
Q. Okay. You know that other doctors at the V.A. prescribe Paxil and other SSRIs to veterans, correct?
A. I believe it's available to them. I actually would have no idea of how often it's used compared -- or how infrequently it's used compared to other drugs.
Q. You know that the V.A.'s formulary permits physicians to prescribe generic paroxetine, correct?
MR. WISNER: Your Honor, we're going into formularies

now? Objection. This is irrelevant.

THE COURT: Sustained. I think we ought to stay on track, sir.

BY MR. BAYMAN:

Q. You're familiar with the -- well, you were with the Veterans Administration in 2010, correct?

A. Yes.

Excuse me. If I could, I apologize, your Honor. It's actually Department of Veterans Affairs. Veterans Administration was the name about probably 20, 30 years ago. So, just in the interest of clarity.

Q. Okay. Why don't we just say V.A. Would that --

A. That would be even better.

Q. And then given your expertise in treating patients and in counseling them on the risk of suicide, you know that the deputy chief officer at the V.A. has testified that antidepressants lower the risk --

MR. WISNER: Objection. Move to strike. This is hearsay and irrelevant.

THE COURT: Well --

MR. WISNER: He's about to quote someone who's not even a witness in the case, and I had to interrupt him before he got the hearsay out, your Honor.

MR. BAYMAN: I'm just asking if he knows that the deputy chief officer at the V.A. testified that

antidepressants lower the risk of suicide among veterans when he testified in front of Congress.

BY MR. BAYMAN:

Q. Do you know that?

THE COURT: Objection?

MR. WISNER: Objection, your Honor. Hearsay. Move to strike.

THE COURT: It's sustained. The testimony is stricken -- question is stricken.

BY MR. BAYMAN:

Q. You're not a psychiatrist, correct?

A. No.

Q. You're not a member of any professional organization that focuses on psychiatry, such as the American Psychiatric Association, American College of Neuropsychopharmacology?

A. Correct.

Q. The focus of your career has not been on suicide or suicidality, correct?

A. That is correct.

Q. You don't consider yourself an expert in suicidality, correct?

A. I haven't claimed to be.

Q. I want to make sure that the record's clear. You've never had any conversations with any of your patients about the risk of suicidality and the use of SSRIs, correct?

A. You know, I'm -- and again, I'm not trying to be difficult. It doesn't stand out in my mind. Let me put it like that.
Q. You -- and you testified a minute ago that you treat patients at the V.A. who may be taking SSRIs prescribed by other doctors, right?
A. Yes.
Q. But you don't stop their prescriptions of SSRIs based on what you know from this case, correct?
A. That's -- I'm sorry. I've got to again give some context to this. You -- that's not the way things work in an organization where you've got teams of physicians. We're not in these little silos.

We have a record where I can see what's going on with the patients, what other prescribers are saying. I don't just say, "Well, I'm going to stop this," unless it's a clinical emergency.

So, before doing anything, where I said, "Boy, I really don't think this patient should be on this drug" -- and that has happened with psychiatric drugs, where they can interact with some of the HIV drugs -- I'm going to have a conversation with their prescriber.
Q. So, I guess the answer to my question is if a patient presents and they're taking an SSRI, you don't automatically stop that SSRI because of what you've learned in your work as

an expert in this case, correct?
A. I don't think there's any -- as a physician, there's no one-size-fits-all rule. If somebody came in and they were taking cyanide, yes, that, I would stop. But for a drug that they're on, you know, you assess the situation.
Q. You don't -- you don't address any issues concerning the safety or efficacy of SSRIs, antidepressants, or any psychiatric medications as part of your work at the V.A., correct?
A. I apologize. Can you -- I just want to make sure I'm answering this.
THE COURT: Read it back.
THE WITNESS: Thank you.
(Record read.)
BY THE WITNESS:
A. I, as part of my work, address approaches and treatments for depression, but I do not work on SSRIs directly.
BY MR. BAYMAN:
Q. You don't have a degree in epidemiology, correct?
A. I have training through the FDA in epidemiology, but not a Ph.D. in epidemiology.
Q. You don't have a degree in statistics, correct?
A. Again, training, not only through the FDA but also as part of my biomedical informatics training, but not a Ph.D. in statistics.

Q. You're not an expert in psychopharmacology, correct?
A. No.
Q. You're not an expert in neurology, correct?
A. No.
Q. You've never done any clinical research regarding Paxil or any other SSRI or any psychiatric medication, correct?
A. That is correct.
Q. And you've never done any clinical research on whether any medication increases the risk of suicidality, correct?
A. There are hepatitis C drugs that are known to induce suicide or suicidal behavior, and I believe I've looked at that issue.
Q. Do you have your deposition there in front of you?
A. Yes, sir.
Q. Could you look at page 62, line 22?
A. Um-hum.
Q. Have you got that?
A. Yes.
Q. The question was, "Have you ever done any clinical research on suicidality for any medication?"

And your answer was, "No."

Did I read that correctly?
A. Yes. At that time, that was a correct answer. That was two years ago.
Q. You've never designed any clinical trial intended to

determine whether a medication increases the risk of suicidality, correct?
A. Correct.
Q. And you've never been involved in any clinical trials where the trials were designed to determine whether any medication causes or increases the risk of suicidality?
A. Correct.
Q. You've never conducted any research on the subject of the effects of psychiatric medications, correct?
A. Not that I can recall.
Q. You've never lectured on the subject of the effects of antidepressants, anti-anxiety medications, or psychiatric medications, correct?
A. Correct.
Q. And you've never conducted any scientific research of any kind involving an SSRI, correct?
A. Not to the best of my recollection.
Q. You've never lectured on the subject of the effects of psychiatric medications, correct?
A. Not that I can recall.
Q. You've never published any articles in the professional literature about Paxil, correct?
A. No.
Q. Or any other SSRI or psychiatric medication for that matter, correct?

A. Correct.
Q. You've never published anything in the scientific literature about suicidality and Paxil or other SSRIs, correct?
A. Correct.
Q. You've not authored any publications concerning when or how to change a prescription drug labeling, correct?
A. No.
Q. You've not authored any publications concerning industry standards for prescription drug labeling, correct?
A. I'm sorry. Could you read the question back.
(Record read.)
BY THE WITNESS:
A. I believe that guidance documents that I've worked on -- worked on when I was at FDA may have addressed some aspects of drug labeling.
BY MR. BAYMAN:
Q. You've never published any article that specifically discusses the regulatory standards for when an adverse event should be included in labeling or how it should be included in labeling, correct?
A. Not that I can recall.
Q. And you've never published any articles that specifically discuss -- strike that.
You've never published any article in which you form

an opinion about the adequacy of a medication's labeling, correct?
A. I'm not sure I would agree with that statement.
Q. Which article do you have in mind?
A. So, I published an article in *New England Journal of Medicine* in -- boy, it's been a long time, I believe it was either 2007 or 2008, that at least indirectly addressed that by discussing the integrity of data in the trials and the safety and efficacy of a drug.
Q. It indirectly addressed it?
A. Well, that's the basis for labeling, so yes.
Q. You've never worked at a pharmaceutical company, correct?
A. No.
Q. You've never been retained as a consultant of any kind by either a generic or a brand name pharmaceutical manufacturer of any psychiatric medicine, correct?
A. I'm not sure.
Q. You don't recall?
A. I've been retained once by a pharmaceutical company, but I don't know if they're a manufacturer of pharmaceutical medications.
Q. Of psychiatric medications?
A. I'm sorry, I apologize, of psychiatric medications. They both begin with a P.
Q. Well, let's narrow it down. You've never been retained as

a consultant by any generic or brand name SSRI manufacturer, correct?
A. Again, I -- in the one instance, I don't know if that entity manufactures SSRIs, either as a generic or as a brand name.
Q. Can you turn in your deposition to page 62.
A. Yes.
Q. Starting at line 1.
A. 62, line 1. Yes.
Q. The question was, "Have you ever been retained as a consultant of any kind by a generic or brand name manufacturer of any psychiatric medication?"
Your answer was, "No."
Did I read that correctly?
A. The -- my retention occurred after this deposition.
Q. Okay. Now, you're here testifying as an FDA regulatory expert, correct?
A. Correct.
Q. And so you claim to understand the laws and regulations that control between the FDA and pharmaceutical manufacturers, correct?
A. I'm not sure I completely -- when you say control between the FDA and manufacturers, can you be a little more specific?
Q. The laws that impact the relationship between the FDA and pharmaceutical manufacturers.

A. With respect to the focus of my testimony, the laws and regulations concerning labeling of drugs and the standard for including information in the label.
Q. You testified about it a little more broadly yesterday. In fact, you testified that the FDA was privately funded by drug companies under what's called user fees, correct?
A. Yes.
Q. The user fees that you're talking about are derived from the Prescription Drug User Fee Act, correct?
A. Well, there's other user fee acts besides that, the Generic Drug User Fee Act, for example.
Q. Well, the one you were referring to yesterday was what we call PDUFA, P-D-U-F-A, correct?
A. Correct.
Q. And that's an act of Congress, right? It's passed by Congress?
A. That's correct.
Q. The user fees are not optional payments by the drug companies, are they, Doctor?
A. They can be waived by the FDA under certain circumstances.
Q. The user fees, Doctor, that the FDA collects from the drug manufacturers are mandated by law in that statute, correct?
A. Actually, no. They are -- part of what are called PDUFA agreements, there's what are called side letters. The actual legislation is fairly broad. So, on the one hand, the agency

sets the fees; and on the other hand, there's an agreement about how fast the FDA will review the drugs -- or the applications, I should say.

Q. Okay. But when a company wants to get a new drug approved, they have to file an application fee, correct?

A. Correct.

Q. And that application is -- application fee can be as high as $2 million, correct?

A. Actually, I think for FY '16, it may be more like 2.3 million.

Q. Okay.

MR. WISNER: Your Honor, they objected when I asked questions about this. You sustained the objection. I feel we're again in a goose-gander situation. I'd move to stop this line of inquiry because it's not fair.

MR. BAYMAN: He was asked a number of questions before my objection was sustained.

THE COURT: I do recall testimony about user fees, so I'll allow some liberality.

BY MR. BAYMAN:

Q. Okay. A user fee is just -- for example, it's like getting your driver's license; you pay an application fee, correct?

A. No, it is not just like a driver's license. There is a guaranteed standard of service that FDA agrees to provide in

exchange for that fee.
Q. But the people who pay the fees are the people who are getting the service; that's why it's called a user fee, correct?
A. Correct.
Q. Have you ever informed the FDA about the opinions that you're offering in this case?
A. I don't believe so.
Q. You've never informed the FDA that you believe there's an association between the use of paroxetine or Paxil by adults older than 24 and a risk of suicidality, correct?
A. Correct.
Q. You've never told the FDA that you think the FDA-approved labeling for Paxil is inadequate or false or misleading, correct?
A. Well, with the qualification that it's actually GSK's responsibility to do that, no.
Q. We'll get into that later. You've never submitted the opinions that you offered yesterday and today in response to Mr. Wisner's questions for review by your peers in the medical community, have you?
A. I'm not actually sure, given the fact that some documents are, I believe, under seal, that I would be able to do that.
Q. You've never published your opinions in any peer -- about Paxil and suicidality in any peer-reviewed publication,

correct?
A. I would give you the same caveat that I would have to back those up, and I'm not sure if I would be able to do that given the sealing of documents.
Q. No professional or scientific medical organization has ever sought out your opinion about Paxil's labeling, correct?
A. Not that I'm aware of.
Q. You generated your opinions about the adequacy of Paxil's labeling regarding suicidality solely for the purposes of this litigation, correct?
A. Hum. With the caveat that the principles that I based it on are in data analysis, which is the same science that was used at the FDA, is something that I did not discover for purposes of this litigation, I would say that I provided the opinions on the basis of the data that I was provided as well as data that I requested.
Q. Well, you provided them in the context of this litigation, this case, rather than in some other scientific context, correct?
A. If you mean that I didn't go looking for this, you're correct.
Q. Well, maybe I can make this easier.
Other than this lawsuit, has there been any time anyone else other than the plaintiff's lawyers have asked you to determine if there's reasonable evidence of association for

suicidality for any SSRI, antidepressant medication, or psychiatric medication?
A. I've not been in a position before where someone would ask me to do that.
Q. So, the answer is no?
A. Correct.
Q. And you're paid for your testimony in this case, correct, an hourly rate?
A. Yes.
Q. And how much do you charge?
A. I am being compensated -- I currently charge $550 an hour, but for this litigation, I'm charging $480 an hour.
Q. I want to turn now to the FDA approval process.
A. Okay.
Q. You know that when it -- or you agree that when it comes to prescription medications such as an SSRI, that the FDA has the sole and exclusive authority to approve that medication for use in the United States?
A. Could you reread back the last line.
THE COURT: Read it back.
(Record read.)
BY THE WITNESS:
A. With the caveat that other government entities, excuse me, and I think the example I mentioned in my deposition was the Drug Enforcement Administration, may have authority over some

aspects of that, I would say -- I would say the FDA has authority over that.

BY MR. BAYMAN:

Q. Could you look in your deposition at page 79, line 24. And it carries over to page 80, line 4.

Are you there?

A. Yes.

Q. Are you there?

A. Yes.

Q. Okay. The question was, "But you agree that when it comes to prescription medications such as an SSRI, that the FDA has the sole and exclusive authority to approve that medication for use in the United States?"

And your answer was, "Yes," correct?

A. Well, the qualification that I gave immediately before that was that this has gotten a little confused because of the advent of medical marijuana. So, that's where I indicated that that statement may not be completely accurate.

Q. And that would be the DEA with respect to medical marijuana would be the other organization; is that what you're saying?

A. Well, I'm saying it would be both.

Q. Both.

A. And also -- I mean, the issue here, as I understand it, is: Is it going across a state line? So, when you say the

United States, I think -- what you're saying, I guess, is interstate commerce I guess is the legal phrase. Is that fair?

Q. But you agree when it comes to an SSRI --

A. Yes.

Q. -- that the FDA has the sole and exclusive authority to approve an SSRI for use in the United States?

A. Yes.

Q. And to obtain FDA approval, manufacturers are required to prove that the drug is both safe and effective for its proposed indication, correct?

A. That's, in basis -- there's more qualifications to that, but yes.

Q. And it's the FDA that makes that determination whether a drug is safe and effective, correct?

A. Based on the information provided by the manufacturer, yes.

Q. And the FDA has to approve all prescription drug labeling, correct?

A. Eventually, yes.

Q. Do you agree that the Federal Regulations provide that the FDA has the final say on what should be included in prescription drug labeling?

A. So, I would say that leaving aside issues about the jurisdiction of the courts in this, I would say the sponsor

has the ultimate responsibility. The FDA is the ultimate authority in that context.

Q. You agree that the FDA makes the determination that the labeling and information evaluated with respect to a drug is sufficient so that in the FDA's judgment, it provides adequate directions for safe use to the prescriber, correct?

THE WITNESS: Your Honor, could I ask that the last question be read?

THE COURT: Yes, read it back.

(Record read.)

BY THE WITNESS:

A. Again, based on the information available to the FDA from the manufacturer at that point in time, yes.

BY MR. BAYMAN:

Q. And would you agree that the FDA's mandate is to ensure that the manufacturer's label contains relevant information regarding effectiveness -- accurate and relevant information regarding effectiveness and safety, correct?

A. Among many other things, yes.

Q. But it's the FDA that makes that determination, correct?

A. Again, based on the information provided to it, yes.

Q. You agree with me that the FDA has been charged by Congress with ensuring that drugs are safe and effective and that their labeling adequately informs users of the risks and benefits of the product and that it is truthful and not

misleading?
A. One non-trivial correction. The Congress, the last time I looked at the Prescription Drug User Fee Act, said that it wants the FDA to get safe and effective drugs to the market. And that was a revision back in, I think, the FDA Modernization Act.
But substantially, yes.
Q. And you would agree with me that Paxil could not remain on the market if the FDA was of the view that it was not safe and effective for use in accordance with the approved labeling, correct?
A. When you say, "could not remain on the market," could you clarify?
Q. That the manufacturer of either Paxil or generic paroxetine could not sell it in this country if the FDA were not of the continuing view that it was safe and effective for use in accordance with the approved label, correct?
A. That's one possible outcome.
Q. Now, we talked about GSK's New Drug Application. You talked about that with Mr. Wisner on direct, correct?
A. Yes.
Q. And that was submitted to the FDA in November of 1989, correct?
A. I believe so.
Q. And the applicant for an NDA -- I'm sorry, the company who

files an NDA is legally obligated to provide full reports of investigations which have been made to show whether the medication is safe and effective, correct?
A. It is -- I would say it is required to do so, yes.
Q. And those reports include safety data and other information about the medication from the clinical trials, correct?
A. Yes.
Q. And the Paxil NDA included data from the clinical trials conducted to that point, correct?
A. Yes.
Q. You talked yesterday about how much data is included in an NDA submission. You're not suggesting that a manufacturer should not provide all the data that the FDA requires or requests, are you?
A. I don't believe I was saying that.
Q. And along with the data, the New Drug Application, the NDA, must include proposed labeling for the medication, correct?
A. Yes.
Q. In addition, the manufacturer must furnish substantial evidence of adequate and well-controlled studies, correct?
A. I apologize. I would say it's substantial evidence from adequate and well-controlled studies.
Q. Thank you. And once the FDA -- or the NDA is filed, the

FDA's doctors and scientists review that submission to determine whether the drug is safe and effective for its intended uses, correct?

A. Based on the information provided by the company, yes.

Q. And you'd agree with me that the FDA's process for a New Drug Application is rigorous, correct?

A. When you say rigorous, I just want to make sure we're using -- on the same page. Please tell me what you mean.

Q. Rigorous. Thorough.

A. Well, okay. So, I think that with the understanding that there's different levels of rigor. There's rigor looking at the summary tables. There's rigor looking at -- going further and looking at individual what we call case report listings, looking at case report forms, and then finally, going back to the raw data.

The FDA's process is rigorous with the data it receives, but it does not get the raw data.

Q. But it can request that if it wants it, correct?

A. If it knows to request it, yes.

Q. You mean to tell the jury that the FDA doesn't know there's raw data behind the summary reports that are done?

A. Well, there's too much for the FDA to get all of it. You have to focus. And so if, for example, to take a hypothetical example, you don't know that emotional lability really means attempted suicide, then you won't know --

MR. BAYMAN: Your Honor, this is beyond the scope of my question. I move to strike it.

MR. WISNER: Your Honor, he was asking his question. He asked an open-ended, vague question. He can answer it.

THE COURT: You may finish your answer.

BY MR. BAYMAN:

Q. You would agree with me that the FDA is comprised of hundreds of scientific experts, correct?

A. I would actually go further and say it's composed of hundreds of scientific experts who have to review thousands of submissions a year.

Q. And that includes medical doctors, correct?

A. Yes.

Q. It includes chemists, correct?

A. Yes.

Q. It includes biostatisticians, correct?

A. Yes.

Q. Toxicologists, correct?

A. Yes.

Q. Pharmacologists, correct?

A. Clinical pharmacologists.

Q. Epidemiologists, correct?

A. Yes.

Q. And many of those people have advanced degrees, do they not?

A. Yes.
Q. And you agree with me that the reviewers at FDA, based on your experience at FDA, bring scientific and technical expertise and a strong commitment to public health to the issues which they address, correct?
A. The ones who I've worked with, yes.
Q. Are you aware of anybody who worked in the neuropharmacology division at FDA during the time that Paxil and the other SSRIs were approved as safe and effective who did not have the necessary expertise to evaluate the safety and efficacy or effectiveness of those medications?
A. Well, I guess the way I would answer that is looking at the reviews and other documents that I've seen, it's not only a question of expertise. It's a question of execution.

So, I would say do they have -- you know, expertise is one thing, but being able to actually put it into practice and use it effectively is another.
Q. Well, let's get back to my question. Do you know anybody during the time period that Paxil and SSRIs were approved as safe and effective that did not have the expertise to evaluate the safety and effectiveness of those medications?
A. Not directly.
Q. You would agree with me that the FDA reviews the safety data of a medication that is part of an NDA in order to satisfy itself that the drug is safe and effective, correct?

A. I don't think it's a matter of the FDA satisfying itself. I think it's a matter of complying with its responsibilities under the law.
Q. And you would agree with me that the experts at the FDA will do their own analysis on the information and data that is supplied by the drug manufacturer in an NDA, correct?
A. Well, it varies. I mean, there's some things where they do their own analyses, and there's some where they simply accept what the sponsor said.
Q. Well, let's talk about safety and adverse events. You would agree with me that's one of the areas that the FDA will specifically look at and review on its own, correct?
A. Well, when you say review on its own, I mean, to the extent that they are doing things beyond what the sponsor gives them, I would say yes.

If they are simply taking tables and graphs that a sponsor -- text that the sponsor's provided and cutting and pasting it into a document without adding substantive additional commentary, it's hard to say if that's independent or not.
Q. You know from your own experience that FDA does independent reviews of the data provided by a sponsor, correct?
A. In some instances, there -- and again, we're talking -- you're saying FDA. FDA is a huge organization. I know what

people in my office and my division do, and certainly, there's some things where you go -- divisions, because there were multiple offices that you worked in.

But, you know, if somebody's got an adverse event -- table of adverse events, there are some instances in which the FDA reviewer will seek to independently verify that; and there's others in which they'll say, "Well, I don't see any reason to do that. I'm just going to accept what the sponsor has said."

Q. And you don't know what the FDA did when they reviewed the NDA for Paxil in this case, do you?

A. Actually, I can make a pretty good guess.

Q. I don't want you to guess.

A. Okay. So, the --

Q. There's no question. I just said, "I don't want you to guess."

A. No, I understand.

MR. BAYMAN: Your Honor, I don't have a question.

THE COURT: Wait for a question.

THE WITNESS: I'm sorry, your Honor.

BY MR. BAYMAN:

Q. You would agree with me that the FDA is not limited solely to information submitted by the manufacturer, but can rely on other information that exists in the world of science when deciding whether to approve an NDA or drug labeling, correct?

A. It can.
Q. One of those things might be scientific literature, correct?
A. Yes.
Q. And, in fact, when you were at the FDA, you considered it part of your responsibility to keep up with the medical literature and scientific advancements in your field of infectious diseases, correct?
A. Well, I think this actually is a good illustration that answers a question you asked previously about independent review. So, in one of the Paxil applications, I believe --
Q. Can I get an answer to my question first?
A. Yes, I'm going to answer it, but I want to qualify it because you've been talking about the FDA and you've been talking about me. I want to clarify the distinction.

In that application, the sponsor told the FDA review division that there was no relevant literature. The reviewer simply said, "Okay. We're going to accept that." They did not -- even though they could have, they did not make an independent effort to verify that.

Now, I would not have done that. If I had verified it, I would have said, "The sponsor said this. I did a literature search on Pub Med," and that would be independent. But that did not happen in this instance.
Q. Doctor, you weren't at the division of neuropharmacology

when this NDA for Paxil was submitted, correct?
A. I'm actually talking about a supplemental NDA, and the sponsor did not -- just said, "The sponsor said there wasn't any new information in the literature," without any -- didn't say, "I reverified it." They said, "Therefore, there will be no review of the literature."
Q. You don't know what the reviewer did, do you?
A. No, I do actually. The reviewer wrote it down. It's available on the Internet for anyone to look at.
Q. You haven't talked to that reviewer, have you?
A. I don't have to. It's on the Web. There's one thing that FDA is very focused on through what are called good review practices is documenting what you do and providing -- we're scientists. You want to be able to tell another scientist what you did in such a way that they can replicate and verify or find issues with what you did. So, if it's not there, it wasn't done.
Q. We're going to get to what was done with respect to the NDA in a minute, but I want to make sure that I understand that -- I didn't really get an answer to my question, which is --
A. Yes, I would do my own independent analysis, correct.
Q. And when the FDA reviews a proposed label as part of a New Drug Application, it can edit and propose revisions to that labeling, correct?

A. The FDA review division can do that based on the information that it has available to it.
Q. And that happens frequently, doesn't it? A manufacturer submits labeling, and the FDA makes comments and revisions and sends it back, correct?
A. Based on the information provided by the manufacturer, yes.
Q. But the FDA makes its own comments; it doesn't just accept what the manufacturer submits, correct?
A. It may accept some things and not others.
Q. And sometimes the FDA, as we learned earlier, will call for an advisory committee to discuss the medication at issue, correct?
A. Sometimes.
Q. And you know there was an advisory committee impaneled in conjunction with the Paxil New Drug Application submission, correct?
A. For the original one. Is that what you're -- okay. Because they did not call one for other indications in supplemental NDAs.
Q. But the original one for major depressive disorder, right?
A. That's correct.
Q. And you agree with me that the FDA will not approve an NDA that fails to satisfy the standard of demonstrating the medication at issue is safe and effective when used in

accordance with the label, correct?
A. What I would say is the FDA, based on the information that's submitted to it by the manufacturer, can approve it, will approve it if the information that it sees from the manufacturer demonstrates safety and efficacy.
Q. But it's the FDA who makes that decision, correct?
A. Based on the information that it's provided, yes.
Q. And the FDA doesn't approve all NDAs that are submitted, does it?
A. No.
Q. And, in fact, if the FDA doesn't think it has enough information to make a decision on the drug's safety or effectiveness, it must reject the application, correct?
A. No, not necessarily. It really is: What does the labeling -- what does the labeling say, and what is the data?

So, for example, if an NDA, and this has happened, requests two indications, and the FDA says, "Well, we're going to grant this one, or we think there's enough information for this indication but not for another," it will approve the NDA but only for that indication.

Or to take it more broadly, if it has information saying that the use of a product is associated with an increased risk in a particular population, it will say, "We'll approve this if you change the label," if it knows about it.
Q. I think I understand. But you would agree with me that

approval of an NDA indicates that the FDA has concluded that the medication is safe and effective when used in accordance with the approved labeling, correct?
A. Based on the data it has at that time, yes.
Q. And for Paxil, the first approval for major depressive disorder was in December of 1992, correct?
A. That's correct.
Q. And at the time it approved that NDA, it -- the FDA also had to approve the Paxil prescription drug labeling that goes to the doctor, correct?
A. Well, yes. I'm sorry. I'm just trying to parse out the distinction between the drug and the label, but I agree.
Q. And the labeling approved by the FDA is an assessment by the FDA that it has determined that the label contains adequate information for the drug's use, including any relevant hazards?
A. Based on information given to it by the manufacturer, yes.
Q. And you talked some in your direct about misbranding. You would agree with me that a drug is misbranded when, among other things, its labeling is false or misleading in any particular way?
A. That's the verbatim language.
Q. And that the Food, Drug, and Cosmetic Act prohibits the misbranding of drugs, correct?
A. Correct.

Q. And if the labeling for a drug fails to include all necessary warnings, contraindications, adverse reactions, side effects, the drug is misbranded and in violation of the FDA statute, correct?
A. It can be found to be misbranded. I mean, it's not like throwing a switch.
Q. Can you turn in your deposition to page 93.
A. Yes.
Q. Line 18.
A. Yes.
Q. The question was, "And if the labeling of a drug fails to include all necessary warnings, contraindications, hazards or side effects, the drug is misbranded and in violation of the FDA statute" --
A. I see what you're saying. I guess what I would say is it's a little bit like if I take one step over the Canadian border, have I -- is there an invasion? Technically, but it doesn't mean we're necessarily going to war. I guess I should have clarified that back in 2000- -- whenever this was, two years ago.

I think -- what I'm saying is that the FDA has to reach the -- it's not like it's some physical law is, I guess, what I'm saying. The FDA has to go through a process where it says it's misbranded. It has to make that determination, and then it usually will offer to work with the company to get it

to correct the problem.
Q. Back to -- the question was, "If the labeling of a drug fails to include all necessary warnings, contraindications, hazards, or side effects, the drug is misbranded and in violation of the FDA statute," and your response was, "That is absolutely correct."
A. Yeah. I'll stick with that response. I'll just say there's a few intermediary steps. How's that?
Q. And if the labeling is also misbranded -- labeling is also misbranded if its labeling doesn't provide adequate directions for use, correct?
A. Correct.
Q. And violators can be subject to regulatory and enforcement actions, including injunction, seizure, and criminal prosecution, correct?
A. That is all possible.
Q. And if the FDA determines that the medication's labeling is false or misleading, the medication is subject to removal from the marketplace, correct?
A. It could be, sure.
Q. And you agree with me that the FDA may not knowingly approve any labeling that it knows to be false or misleading, correct?
A. Technically yes.
Q. After a drug is approved in a New Drug Application and

comes on the market, if a drug manufacturer wants to change the content of the labeling for an approved drug, it's required to work with the FDA regulatory process and file what's called a supplement to its approved NDA, correct?
A. That is correct.
Q. And if the manufacturer decides to change the labeling that's been previously approved, it has to submit those proposed changes to the FDA, correct?
A. Correct.
Q. And you also agree that there are situations where the FDA, in fact, drafts and proposes language itself and submits that language to manufacturers and says, "You need to implement these changes," correct?
A. Prior to about 2009, actually, FDA in general did not have that authority to order manufacturers to do that. It could request changes. From a practical point of view, if the manufacturer refused, the only option FDA had was to say, "Well, then we're going to declare you misbranded," which was not something that was practical to do on a large scale.
So, just to be clear, prior to that point, the FDA did not have the authority to order manufacturers to do it. It would have to go to court and attempt to do so. It's changed since then.
Q. All right. I'll come back to that.
You would agree with me that after a label has been

approved by the FDA, a drug's labeling must be revised when there's what's called newly acquired information, correct?
A. Are you talking about safety-related information?
Q. Yes.
A. Yes, that's correct.
Q. And newly required information is defined under the Federal Regulations, correct?
A. Yes.
Q. And it's defined as data, analyses, or other information not previously submitted to the agency, correct?
A. Correct.
Q. And the newly acquired information in the safety context must reveal a risk of a different type or a greater severity than previously submitted in submissions to the FDA, correct?
A. With the caveat that -- or the qualification, if you will, that it may be something that's closely related to something that's already in the label. The new information might be if the liver -- if the label says, for example, "elevated liver enzymes," and the new analysis shows liver inflammation, that would be an example of new information.
Q. But that's the language from the regulation, right, that I just asked you?
A. Yes. Yeah, I wanted to put that context in there. It's not like it has to be from a new organ system or something. But I agree with you.

Q. Fair enough. But a manufacturer is supposed to take those newly identified risks to the FDA and discuss whether and how the medication's labeling should be changed, correct?
A. Well, what the regulations provide for, as I said in the previous testimony, if a manufacturer wants to add or strengthen a regulation, it can do so without the FDA approving it.

It doesn't have to come in and discuss it. It can submit a -- what I mentioned is changes being effected supplement. But actually, generally, these things sort of landed on our doorstep. There was not any previous discussion.

Q. But ultimately, the FDA has to approve that change as being effective, correct, that change, correct?
A. It has to review it, and most of the time, those get approved.
Q. Well, turn in your deposition to page 107, line 10.
A. Okay.
Q. The question was, "And a manufacturer is supposed to take those newly identified risks to FDA and discuss whether and how the medication's labeling should be changed?"

And your answer was, "Yes," correct?

A. Yes. I don't think it's a -- what I'm trying to say here is the word "supposed to" I did not interpret as meaning a regulatory requirement. So, I'm just clarifying that ideally,

they would do that. They don't have to.
Q. But it's ultimately the FDA's decision to decide whether the newly acquired information submitted by the manufacturer will be included in the medication's labeling, when it will be included, where it will be included, and what will be said about the risk at issue, correct?
A. So, I think that, you know, basically, it's the sponsor's -- I'm sorry, manufacturer's responsibility to keep it updated. It's the FDA's -- has the authority to enforce that. So, the answer would be essentially yes to what you're saying.
Q. And part of the enforcement of that is, you would agree, determining where it will be included in the label, correct?
A. Yes. I'm sorry.
Q. What will be said about the risk, correct?
A. Yes, with -- again, with the caveat that it's not a yes-no thing. It's not like buying a lottery ticket.

The FDA may say, "You know, we're not sure why you're doing this. Can you come back and explain it?"

The manufacturer may say, "X, here's what we want to do."

The FDA says, "Oh, we understand now." Or they say, "Well, how about if we change this?"

There's, you know, that sort of discussion. It's not between two robots, far from it.

Q. There's a back-and-forth between the company and the FDA about what should be included, correct?
A. Correct.
Q. And where it should be included, correct?
A. If the sponsor proposes something, yes. And they can go to the FDA, you know, and say, "Well, we're not sure where it's supposed to go, but we think it needs to be in here. Can you tell us?"
Q. You would agree with me that the structure of the label is provided for by statute, the very sections in the label?
A. No, actually, it's provided by regulation.
Q. Excuse me. Regulation. But there is -- there are regulations that talk about the sections and what is to be included, correct?
A. That is correct.
Q. And it is -- I think you'll agree that in terms of the hierarchy of things, a warning is higher up on the hierarchy than, say, adverse reactions, correct?
A. All other things being equal, I would agree.
Q. Because the adverse reactions can include things that are serious and not serious, correct?
A. Well, again, I want to be careful because one of the -- and this is true -- much truer with a new format, more readable format. The Paxil label is in the old format.
But anyway, one of the things that people do try and

do and that labels are supposed to do in that laundry list adverse reactions section is capture things that aren't captured elsewhere.

Q. I think you said yesterday that the adverse reactions contains a listing of some side effects that are not as serious, as in the warnings, correct?

A. If it's not -- if it was serious enough to be in the warning, it should be in the warning section. And it can be in both places. I should clarify that.

Q. I don't mean to belabor this, but you would agree with me that the more serious risks, relatively speaking, are in the warnings section as compared to adverse reactions, correct?

A. Yes.

Q. So, in this debate between a manufacturer and the FDA, there might be some debate about where it should go in the label; and if the manufacturer says, "We think this should be in adverse reactions," and the FDA says, "No, this needs to be in warnings," it's the FDA's view that trumps that, correct?

MR. WISNER: Objection. Speculation.

THE COURT: Overruled.

BY THE WITNESS:

A. I think that really depends on the circumstances about -- I mean, there's no one-size-fits-all rule. But generally, when you're talking about fatal events, it's -- that are

occurring above some threshold -- and it may depend on the exact circumstances -- I've yet to hear a manufacturer argue, "Well, let's just bury it in the adverse event reaction and not mention it anywhere else."

BY MR. BAYMAN:

Q. Okay. Fair enough. But there -- you've seen in your experience times when the FDA and the manufacturer may disagree about where in the label an adverse event should go, correct?

A. Sure.

Q. And then if there's that disagreement, at the end of the day, it is the FDA's view that trumps or prevails, correct?

A. About where it should go?

Q. Yeah.

A. But both of them -- I just want to make sure I understand your question. This is on a circumstance where the manufacturer says, "Well, we think it should be in the label," and there's just a debate over where. Is that --

Q. Yes.

A. But the manufacturer wants it in the label somewhere?

Q. Right. In that hypothetical I gave you, the manufacturer says, "We think this adverse event should be in adverse reactions," and the FDA says, "No, this should be in warnings," it is the FDA's view that prevails, correct?

A. In that scenario, yes.

Q. And also, if there is a disagreement about what the language reporting on that adverse event should say, the manufacturer has one view of describing it, the FDA has another view of describing it, it's the FDA's view that trumps or prevails, correct?
A. Again, understanding that it is a negotiation and not -- a lot of times, FDA will take the manufacturer's arguments and say, "You know what, we agree with you." I agree with you on that.
Q. But it doesn't have to take the manufacturer's view, does it?
A. I think what I would say is it has to consider it. Perhaps that's the best way to put it.
Q. Okay. Consider it. But the FDA can consider it and say, "We disagree with you. We think it needs to go here," correct?
A. Yes.
Q. "And it needs to go here, and it needs to say this," correct?
A. Again -- and I'm just -- again, I -- it may be that the concept -- I mentioned before risk communication, and the issue may be less one of exact wording, although it can be. So, I just don't want to say -- when you say, "It has to say this," that's one event. It could be, "You have to express this concept, but we're flexible about the wording."

I'm just trying to indicate there's not always one thing. But in terms of the general concept that you're expressing, I would agree with you on that.

Q. And when that event needs to be reported in the label, again, if there's a disagreement between the manufacturer and the FDA, it again is the FDA's view that prevails or trumps, correct?

A. Yes.

Q. We talked about the standard when the manufacturer may revise its labeling. You remember that discussion with Mr. Wisner about when there is reasonable evidence of an association or of a serious hazard with a prescription medicine?

A. Yes.

Q. You agree with me that there's an important distinction between an association between a medication and a hazard and a causal relationship between the two, correct?

A. Yes.

Q. Reasonable evidence of an association does not equal causation, correct?

A. And the regulation recognizes that and says a causal relationship need not have been proven.

Q. An association, for you, represents reasonable suspicion that a drug may be related to a hazard from the drug, correct?

A. That's what I -- how I phrase it in my report, yes.

Q. You told the jury this morning in no uncertain terms that your opinion is that Paxil can induce suicide in adults of all ages, correct?
A. Yes.
Q. That opinion is not in your expert report, is it?
A. I believe that what I said is that the risk is not restricted to individuals under the age of 25, and what I said was there's -- it's not restricted to any one age group. So, that's in essence saying it can do it in all ages.
Q. Your opinion is that Paxil causes suicide in adults of all ages, correct?
A. Yes.
Q. Okay. Your opinion in your report says, "Paroxetine" -- which is the chemical name for Paxil, correct, and also the generic name, correct?
A. It's the -- what's called the United States -- well, never mind. Go ahead.
Q. Your report says, "Paroxetine is associated with an increased risk of suicidal behavior in adults relative to placebo, with the risk being higher than other antidepressants."

Did I read that correctly?

A. Yes.
Q. It doesn't say "cause," does it, Doctor?
A. I don't believe I -- I don't have the report right in

front of me, but --
Q. I'll be happy to get it for you.
A. Okay.
Q. Let me --
MR. BAYMAN: I have a notebook for you, your Honor, and for the doctor. May I approach?
THE COURT: Sure.
THE WITNESS: Thank you, sir.
MR. WISNER: Your Honor, while Dr. Ross is looking at that, can we have a short sidebar?
THE COURT: Do I need that?
MR. BAYMAN: This is going to be the exhibits that I was going to use with him, your Honor. We could take the other one away.
THE COURT: I've got the exhibit here.
MR. BAYMAN: I mean this is for the rest of the examination. So, I'll be happy to hold on to it until we get to another.
THE COURT: Hold on to it until I need it. I'm buried here.
MR. BAYMAN: Sure.
THE COURT: Give it to my law clerk.
MR. BAYMAN: Sure.
THE COURT: He doesn't have anything in front of him. All right. You have your report, Doctor?

THE WITNESS: I do.

THE COURT: Page, please, sir?

MR. WISNER: Your Honor --

MR. BAYMAN: Page 3.

MR. WISNER: I had requested a brief sidebar.

THE COURT: Oh, you want a sidebar. Okay. We'll go to sidebar while you're looking at that, Doctor. Give him the page number you want him to look at.

MR. BAYMAN: Page 3, summary of opinions, section B1, first one.

THE COURT: All right. We'll go to sidebar.

(Proceedings heard at sidebar:)

[redacted]

[redacted]

[redacted]

(Jury exits courtroom.)

[redacted]

(Recess from 2:53 p.m. to 3:15 p.m.)

(Change of reporters -- Volume 6-C)

(Proceedings heard in open court. Jury in.)

THE COURT: Thank you very much, ladies and gentlemen. Please be seated. We'll resume.

Doctor, you may take the witness stand.

THE WITNESS: Thank you, sir.

THE COURT: And we will proceed. Mr. Bayman?

MR. BAYMAN: Thank you, your Honor.

BY MR. BAYMAN:

Q. Before the break, Doctor, I asked you, isn't it true that your expert report said paroxetine is associated with an increased risk of suicidal behavior in adults relative to placebo with the risk being higher than other antidepressants. Did I read that correctly?

A. Yes.

Q. And when you were asked at your deposition if you had an opinion about causation, not association but causation, you said, "I don't address in my report the issue of a causal relationship." Isn't that correct?

A. That is correct.

Q. But today you told the juror -- the jury that Paxil causes suicide in adults, correct?

A. If I remember correctly, the word I used was "induce." I'm not -- if I used the word "cause," it was -- I misspoke. I intended to use the word "induce."

Q. And by "induce," that doesn't mean "cause"?
A. So "cause" has a very specific technical meaning, and so I'm not using that. I'm simply saying "induce."
Q. What's the technical definition of "induce"?
A. Technical -- no, I'm sorry. So there's a technical definition for "cause." I didn't say for "induce."
Q. So "induce" doesn't have a technical FDA regulatory definition, does it?
A. Not that I'm aware of.
Q. And you don't recall, right before the break when I asked you the question that you believe Paxil causes suicide in adult patients, you don't recall saying "yes"?
A. Oh, I do recall saying that, but you asked me if that was an opinion I expressed in my report. Those are two separate questions.
Q. Okay. I understand that. But I asked you here in this courtroom, you said Paxil causes suicide in adults. You said that right before the break, correct?
A. Yes.
Q. Okay. And that's not in your report, is it? Your report says "association," correct?
A. That's correct.
Q. And we established before the break that "association," you agree, is not equal to "causation," correct?
A. Well, I would say as a technical issue, if saying it's a

cause, it's also associated with. I mean, the two are -- it's not -- it can be association or cause if something causes something else that is associated with it.
Q. Association does not equal causation, correct?
A. It's consistent with it.
Q. But it doesn't equal it, correct?
A. I have never said it does.
Q. They're not the same thing, correct?
A. I've never claimed that they are.
Q. I just want to make sure it's clear. And when there's information that's added to a prescription drug label because of reasonable evidence of an association under the FDA regulations, that does not mean that the medication causes the adverse event or the outcome, correct?
A. You know, that's a really interesting question. If Paxil were -- under the rules that Paxil was approved under, there's reasonable evidence of an association. So under that standard, no, it does not mean that.
Q. It does not mean causation?
A. Correct. It doesn't exclude it either. I should be very clear.
Q. Let's turn, if you would, to your deposition, Page 150.
A. Uh-huh.
Q. Line 20. The question was, "And reasonable evidence of -- when there's information added to a prescription drug label

because of reasonable evidence of an association under the FDA regulations, that does not mean the medication caused the adverse event or the outcome, correct?"

And your answer was, "Correct."

Did I read that correctly?

A. Yes.

Q. And you used the word "signal" with Mr. Wisner. "Signal" does not equal reasonable evidence of association, does it?

A. Again, I'm -- I have not said that it does.

Q. And the FDA's regulations and requirements are designed to mandate warnings that reflect the known risk -- known risks based on reliable scientific evidence, correct?

A. Basically, yes.

Q. It's a well-worn concept at FDA that FDA requires valid scientific evidence to support statements in the label, correct?

A. Yes.

Q. So you said basically, when I asked you the FDA's regulations and requirements are designed to mandate warnings that reflect the known risk based upon reliable scientific evidence, the answer to that question is yes, isn't it?

A. Absolutely.

Q. Now, there was some discussion with Mr. Wisner about the ways that manufacturers have the ability to change their labelling. Do you recall that?

A. Yes.
Q. Okay. And there are different types of supplements depending on the type of labelling changes being proposed, correct?
A. Yes.
Q. One of those is a prior, what's called a prior approval supplement, correct?
A. Yes.
Q. And the other which you talked about with Mr. Wisner is what's called a changes being effected, or CBE supplement, correct?
A. Yes.
Q. And the FDA has the authority to determine whether a supplement should be treated as a prior approval supplement or a CBE supplement, correct?
A. In -- yes.
Q. And if a company decides to file a CBE, a change is being effected supplement, the FDA can decide to convert that filing to a prior approval supplement, correct?
A. In theory, yes.
Q. In theory, or it can be done?
A. In theory, yes.
Q. A prior approval supplement requires FDA approval before the labelling change can take effect, correct?
A. Yes.

Q. And among the labelling changes that must be filed as a prior approval supplement are changes to black box warnings, correct?

THE WITNESS: I'm sorry, your Honor. Could I have that question read back to me?

THE COURT: Read it back, please.

(Record read.)

BY THE WITNESS:

A. That is correct.

BY MR. BAYMAN:

Q. A manufacturer cannot use the changes being effected, or CBE supplement, to add or change the label -- the language of a black box warning, correct?

A. Yes.

Q. And other than a black box warning, the manufacturer can use a CBE to change the labelling before the FDA approves the label change, correct?

A. To add or strengthen a warning.

Q. But the FDA still must ultimately approve the CBE label change, correct?

A. Yes.

Q. And, in fact, the FDA has authority to retroactively block CBE supplements, correct?

A. In theory, yes.

Q. Turn, if you would, to Page 121 in your deposition, Line

11. Have you got that?
A. Yes.
Q. "Question: The FDA as the authority to retroactively block CBE supplements, correct?"
And your answer was, "Yes."
Did I read that correctly?
A. You did.
Q. Among the labelling changes that are eligible to be filed as a CBE supplement are those changes which add or strengthen a warning or precaution, correct?
A. I believe so.
Q. And a manufacturer can use the CBE supplement to make labelling changes to add or strengthen a warning, but it must give FDA a full explanation of a scientific basis for the change, correct?
A. As somebody who has reviewed hundreds of these, I would say yes.
Q. And if the FDA says before that CBE supplement is implemented it does not approve, the manufacturer can't move forward with implementing the CBE labelling change, true?
A. So I want to make sure I understand your question here. The CBE-30 -- there's a CBE-0, but let's leave that aside. A CBE-30 is, in essence, the manufacturer sending in changes to the FDA and saying, "We intend on implementing these in 30 days." And if the FDA were to reject that application or that

change within that 30-day period, it could be blocked.
Q. Thank you.
A. Is that -- no, no, I'm sorry. I wasn't answering your question. I want to make sure I understood your question.
Q. Well, my question --
A. I just want to make sure, is that your question, the FDA could block it in theory?
Q. My question was that -- yes. My question is that if a CBE supplement is implemented and the FDA -- or before it's implemented in the labeling and the FDA says it doesn't approve it, the manufacturer can't go forward with that labelling change, correct?
A. I don't think I can recall a single instance in which their CBE supplement has been reviewed by the FDA within 30 days of when it came in where there hasn't been some prior interaction and the FDA's rejected it, never has happened. If you can give me an example, I'll be happy to admit I'm wrong, but I would love to see an example of that.
Q. It's a simple question. I'm not asking you --
A. I understand. In theory, all the oxygen in this room could go to one corner. In theory, the FDA could review something like that in less than 30 days. I've never seen it happen.
Q. And if the FDA decides to convert a CBE labelling change to a prior approval supplement, the company cannot implement

that labelling change without the FDA's prior approval, correct?
A. At whatever point it would do so, and again, as somebody who has reviewed hundreds of these, sir, if that were to happen, the FDA were to say, well -- the change is already in effect. And I cannot recall an instance in my experience where that happened and the FDA said, "Now we're changing to a prior approval supplement, you've got to pull back all the labelling." That's all I'm saying.
Q. But it can do it?
A. In theory, that would be a theoretical possibility.
Q. Regardless of whether the submission is made by CBE or prior approval supplement, FDA does have a period of time to review the proposed labelling changes, correct?
A. Let me put it like this. Glaxo submitted a CBE in 2007. FDA did not complete its review until 2011. Okay. So it's four years. These are not activities that are supported by user fees, so there's no particular priority for them for the FDA usually.
Q. That wasn't my question.
A. I understand.
Q. Okay. My question was: The FDA has a period of time to review and comment and say it doesn't approve the label changes, correct?
A. In theory, yes.

Q. And it's FDA that has to approve all prescription drug labelling, correct?

THE COURT: I think we've been over this, haven't we?

MR. BAYMAN: Well, he said, "in theory," and I just want to make sure it's clear.

THE WITNESS: I want to make sure I'm giving you -- I swore to tell the truth, the whole truth, and nothing but the truth, so that's what I'm attempting to do here. The answer is, in theory, yes.

BY MR. BAYMAN:

Q. Turn, if you would, in your deposition, Page 96, Line 1.

A. Yes.

Q. "Question: And FDA has to approve all prescription drug labelling, correct?"

And your answer was, "Yes."

You didn't say "in theory," you said, "yes," correct?

THE COURT: All right. It's covered now.

MR. BAYMAN: Thank you, your Honor.

BY MR. BAYMAN:

Q. And you mentioned 2007 and the way things were before 2007. You recognize that before 2007, FDA had told manufacturers that they were declaring their products misbranded because FDA did not approve of labelling changes that either had been proposed or implemented by a company, correct?

A. I'm sorry. Could you point me to that line in there?
Q. Do you want to read the question back?
THE WITNESS: I'm sorry, your Honor. Could I have that question read back?
THE COURT: Yes.
(Record read.)
BY THE WITNESS:
A. I can't recall any instances of that happening. Misbranding has generally been where companies have promoted their drugs and not included risk information that was in the label. That's the basis for declaring it misbranded.
BY MR. BAYMAN:
Q. Take a look at your deposition, if you would, Page 92, Line 5. The question was: "You fully recognize before F-D-A-A-A, FDAAA, 2007, that FDA had told manufacturers that they were declaring their products misbranded because FDA did not approve of labelling changes that either had been proposed or implemented by a company, correct?"
And your answer was, "Yes."
MR. WISNER: Your Honor, I object. For completeness, if he could read the question before and the answer before.
MR. BAYMAN: I'm happy to have him do it on redirect or I'll do it now, your Honor.
THE COURT: You can do that on redirect, sir.
THE WITNESS: I'm sorry. Was there a question still

pending?

THE COURT: No, nothing pending, sir.

Go ahead. Ask another question.

BY MR. BAYMAN:

Q. Thank you. You would agree with me that the FDA regulations say that to permit or require statements of conflicting opinion in a label would destroy the usefulness of prescription drug labelling?

A. So I want to make sure I'm understanding you correctly here. Could you point to that in my deposition because that's a really, really good question you're asking, a really good question.

Q. It is Page 143, Line -- I'm sorry. It's at Page 142, Line 19.

A. Ah, okay. So --

THE COURT: Just read it to yourself, sir.

THE WITNESS: I'm sorry.

(Pause.)

THE WITNESS: Okay. And --

THE COURT: Well, wait a minute.

THE WITNESS: I'm sorry, sir.

THE COURT: Hold up.

THE WITNESS: Sorry, sir.

THE COURT: There's an objection.

MR. BAYMAN: There's no objection by Mr. Wisner, your

Honor.

THE COURT: Yes, there is, on Line 24.

MR. WISNER: That's what I see at Line 24 as well. I see, "Wisner, objection."

THE COURT: Wait.

MR. BAYMAN: I'm just asking if he agreed with the statement. I'm not -- I haven't tried to impeach him. He asked me if he could see his deposition. I'll get the regulations out, your Honor. I was just trying to move things along.

THE COURT: I don't think you ever got -- did you get an answer to that question?

MR. BAYMAN: Yes, I did, your Honor. Line 15 on Page 143.

THE COURT: Okay. Let me see.

Read the answer as well.

MR. BAYMAN: He just -- I'm not impeaching him. He just asked to see his deposition on the subject.

THE COURT: Okay. You want to go on to something else?

MR. BAYMAN: No. I just want to ask him if he agreed with the statement. I haven't impeached him. He just said, "Can I see my deposition?"

THE COURT: Okay.

MR. BAYMAN: And I said, "Sure."

THE COURT: Okay. All right.
BY MR. BAYMAN:
Q. So I'm just going to say that -- I would just say that the regulations say to permit or require statements of conflicting opinion in all of these matters would destroy the present usefulness of prescription drug labelling. Do you agree with that?
A. Well, allow me, if I could, to go to Page 145 of my deposition.
Q. No, sir. I'm just asking you --
A. No. Excuse me, sir. I am not going to simply answer that without going to an answer that bears on this later on in the deposition. And if there's some reason that you don't want it heard in court --
THE COURT: All right.
THE WITNESS: I'm sorry, sir.
THE COURT: Just go ahead and answer.
THE WITNESS: Okay. I point out that this is a document from over 40 years ago. Which you did not -- did not realize at the time was, this was a proposed rule in which manufacturers were trying to keep warnings out by creating false controversies. And the proposed rule -- this actually gets to a point that you've asked me about repeatedly, is the FDA's authority to say, there is no controversy here. There needs to be a warning. And that actually became the rule.

So this is about, the false controversies here are about those really created by manufacturers who were going around trying to create those controversies, sir.

MR. BAYMAN: Your Honor, I move to strike that as completely unresponsive to my question.

MR. WISNER: I oppose, your Honor.

THE COURT: All right. Let's go on to something else. It may stand.

BY MR. BAYMAN:

Q. You would agree with me that you are -- you agree with me that the FDA does its own analysis of the data provided by manufacturers and then makes a judgment call about what information in labelling there will be when you have a medical controversy about a particular issue?

A. In some instances, it does, and that's what I'm familiar with. I can't speak to every instance in the FDA where that happens.

Q. Look at your deposition, Page 147 at Line 14.

A. Ah.

Q. The question was: "Well, FDA does its own analysis of the data that's provided by manufacturers and then has to make a judgment call about what information in labelling there will be when you have a medical controversy about a particular issue?"

And your answer was, "Yes," correct?

A. Yes.
Q. Okay. Thank you. You're -- moving on to something else, you're familiar with the phrase "confounding by indication," correct?
A. I am.
Q. That means when you have an underlying disorder or disease that may cause an adverse event when it's difficult to determine also whether the medication or the exposure could have also caused that adverse event after the medication was started, correct?
A. Yes.
Q. For example, suicidality is associated with depression and anxiety for people who don't take any medication at all, correct?
A. It can be.
Q. And that's an example where you have the underlying disorder, the depression, being a confounder for trying to assess whether or not a medication such as an SSRI increases the risk of suicidality in patients who take the medication, correct?
A. Yes.
Q. And when that happens, it makes it more difficult and complex to determine whether it's the underlying disorder like the depression that's causing the suicidality or whether it's the medication, correct?

A. Difficult but not impossible.
Q. Now, in preparing your expert opinions in this case, you claim that you utilized the same methods as FDA reviewers, correct?
A. Yes.
Q. And you claim you work in -- you've worked in that manner in this case so you could show how your methodology tracks what the FDA did and how the FDA did it, correct?
A. I would say as -- frame it differently, that I'm doing that as a way of meeting the requirements regarding the reliability of methodology with respect to the opinions and the regulatory conclusions that I'm drawing.
Q. So you believe that the FDA's methodology is the correct methodology, correct?
A. Methodology for what, sir?
Q. For analyzing whether there's an increased risk with SSRIs and other antidepressants from 2004 forward.
A. Can you be a little more specific about which methodology just so we make sure we're both talking about the same thing?
Q. Okay. Sure. You agree that when the FDA assessed the issue of whether there was an increased risk with any SSRI or other antidepressant from 2004 forward that it turned to and analyzed randomized double-blind placebo-controlled trials?
A. I do agree with that.
Q. And let's turn, if you would, in your notebook, the big

one.
A. Yes, sir.
Q. I believe it's Tab 7. It's Joint Exhibit 13, your Honor, which is in evidence. It's the FDA's 2006 clinical review.
Do you have that?
A. I do, sir.
MR. BAYMAN: May I publish that, your Honor?
THE COURT: Yes.
MR. BAYMAN: Thank you.
THE COURT: Hang on.
MR. BAYMAN: Sure.
BY MR. BAYMAN:
Q. This is a copy, the jury has already seen it, of a -- the FDA clinical review relationship between antidepressant drugs and suicidality in adults. Do you agree?
A. This is the Stone/Jones report.
Q. What's called the Stone -- the review done by Dr. Marc Stone and Dr. Lisa Jones, correct?
A. Yes.
Q. They were FDA scientists, correct?
A. Yes.
Q. And you're familiar with this document, correct?
A. Yes.
Q. Okay. Turn, if you would, Page 8, Section 2.2, "Drugs studied." It reads: "In total, eight sponsors of 12

antidepressant products submitted data sets to the DNDP culled from all the randomized controlled trials of their respective drug products conducted in the adult population."

Do you see that?

A. Yes.

Q. And then if you would, sir, turn to Page 11, the second full paragraph at the bottom.

Can you pull that up, Roger?

"The FDA request letter" -- go ahead and highlight that, please -- "instructed sponsors that the search should be strictly limited to adverse events occurring during the double-blind phase of treatment or within one day of stopping, i.e., events occurring prior to randomization or more than one day after discontinuing from randomized treatment should be excluded."

Do you see that?

A. I do.

Q. What FDA did in 2006 was look solely at the randomized double-blind placebo-controlled portions of the trials to assess whether there's an increased risk with completed suicide in antidepressants, correct?

A. Yes.

Q. And you agree with me that the FDA included -- I mean, excluded events from the post-double-blind period, correct?

A. For purposes of this specific analysis, yes.

Q. Yes. And the reason they did that is because of uncontrollable confounding results from an array of various different treatment scenarios that may happen after a trial ends, correct?
A. For, again, the very specific question they were asking here, not whether these were -- there's reasonable evidence of association or whether the labelling should be modified, adjust for calculating odds ratios and the confidence intervals around those, yes, that's what they did.
Q. Well, you agree with me, sir, and with FDA -- or you agree with FDA, sir, that this is the appropriate methodology to use when looking at the issue of antidepressants in suicidality, true?
A. If -- and I know you're going to point me to my deposition but if you're looking, as I said, at that issue, that does not address the larger issue of whether there is reasonable evidence of an association. It's one piece of it.
Q. You recall testifying that you agreed with the FDA's methodology, correct?
A. With respect to calculating odds ratios and the confidence intervals around them, I agree, using data from uncontrolled trials portion might confound things but in terms of -- it's a question of what the question is that you're asking here.
Q. Excuse me, Doctor. I just need to get the report.
A. Sure.

Q. You agree with me that for the analysis that the FDA was doing, the FDA used the appropriate methodology by excluding events that did not occur during the control phase of randomized placebo-controlled trials, correct?
A. I'm sorry. Did you mean the uncontrolled phase?
Q. Sorry, the uncontrolled phase.
A. No, no -- okay. Yes, for this question, I would agree, that's the right way to do it.
Q. Okay. Take a look, if you would, at Page 50 of this document. There's a section called "Data submission."
MR. WISNER: Your Honor, during my direct of Dr. Ross, I was instructed to not cover things that were covered with Dr. Healy. This is almost verbatim the questions that were asked of him on cross. It seems like, you know, there was a concern that this was taking a long time, and I feel like this is exacerbating the problem, so I object, cumulative.
MR. BAYMAN: Your Honor, he used this document --
THE COURT: The objection is overruled.
MR. BAYMAN: Thank you.
THE COURT: You may proceed.
MR. BAYMAN: Thank you.
BY MR. BAYMAN:
Q. The FDA says there under "Data submission, In order to perform additional analyses investigating the relationship

between exposure to the drug of interest and PSRAEs." Now, PSRAEs are possible suicide-related adverse events, correct?
A. Yes.
Q. And the FDA goes on to say:
"When looking to assess those, among the subjects of interest, we would appreciate your submitting the following variables as outlined in the next table. As noted, we are requesting information from placebo controlled trials only. Please do not submit data from active controlled studies -- active control-only studies, uncontrolled extensions of placebo controlled studies, or combination drug studies."
Did I read that correctly?
A. You did.
Q. So when FDA did its analysis of Paxil and the other antidepressants which you've talked about on direct to assess the possible risk of suicidality, it looked exclusively at randomized double-blind placebo-controlled trials, correct?
A. That is what they asked for from the manufacturers.
Q. In fact, there's no statement anywhere in this document, is there, that says the FDA will evaluate data from non-placebo-controlled trials or uncontrolled extension phase or combination drug studies or active control studies to assess the risk of suicidality with the medication, correct?
A. I have never claimed that there is.

Q. And you're not aware of any time when analyzing the risk of suicidality with any SSRI or any antidepressant after 2004 where the FDA looked at something other than and relied on something other than randomized double-blind placebo-controlled trials?
A. That's correct.
Q. And when FDA made its labelling decisions with respect to adult suicidality and the use of antidepressants, the data it relied on was from the double-blind randomized placebo-controlled trials, correct?
A. It relied on the data that the manufacturers including GlaxoSmithKline had submitted to it and represented to be the universe of randomized double-blind placebo-controlled trials. The FDA did not independently verify that, in fact, that was what they got.
Q. Well, you don't -- the FDA requested that data, correct? They requested the data --
A. It did. It did.
Q. -- okay, from those trials, randomized double-blind placebo-controlled trials, correct?
A. That is what they requested. They did not validate that that is what they actually got.
Q. You don't know one way or the other --
A. Actually, we do, sir. If you look at the 2011 paper by Carpenter that was discussed during direct examination, a

number of randomized double-blind placebo-controlled studies were omitted from that.

Q. We're going to get to that, Doctor. You would agree that in March of 2004, six years before Mr. Dolin's suicide, that FDA required a labelling change for Paxil and other antidepressants to strengthen the warning section of the label to encourage close observation for worsening depression or the emergence of suicidal thinking and behavior in patients being treated with antidepressants, correct?

A. It requested one from the manufacturers.

Q. And so we're clear, it was requesting of all manufacturers in the class a new warning that had not been in the label previously, correct?

A. A general class warning, correct.

Q. And that class warning had not been in the label previously, correct?

A. Correct.

MR. BAYMAN: I want you, if you would, to turn in your book to Tab 8 which is, your Honor, Joint Exhibit 7 already in evidence. It's the May 2004 Dear Healthcare Provider letter.

THE COURT: Hang on.

THE WITNESS: Yes.

BY MR. BAYMAN:

Q. Are you with me?

A. I am.
Q. You've seen this letter before, correct?
A. Yes.
Q. And you're familiar with it, correct?
A. Yes.
Q. A Dear Healthcare Provider letter is a letter that goes out to doctors and other healthcare providers to notify them of changes to the product labelling, correct?
A. Correct.
Q. Let's take a look at the first paragraph. It says:

"On March 22, 2004, the FDA issued a public health advisory cautioning physicians, their patients and families about the need to closely monitor all patients being treated with antidepressants. This advisory arose from FDA's ongoing review of potential safety issues involving antidepressants in pediatric patients. Additional information concerning this review is expected later this year."

Do you see that?
A. I do.
Q. And then the letter goes on to say:

"These labelling changes, which have been finalized, describe that patients with major depressive disorder, both adult and pediatric, may experiencing -- may experience worsening of depression and the emergence of suicidal

ideation and behavior," and then there's a parenthetical, "suicidality" --
A. I'm sorry. I'm listening, sir.
Q. Okay.
A. Please go on.
Q. "-- whether or not they are taking antidepressant medication. The changes include a new warning recommending close observation of adult and pediatric patients treated with antidepressant drugs for worsening of depression or the emergence of suicidality, particularly at the beginning of treatment or at the time of dose increases or decreases."
Do you see that?
A. I do.
Q. And along with the letter, GSK provided the revised Paxil labelling to doctors at this time, correct?
A. It did.
Q. Okay. Turn, if you would, sir, to Page -- it's Page 23 and 24 of the exhibit, but it's Page 10 and 11 of the labelling.
A. I'm sorry, Mr. Bayman. If you could remind me which exhibit we're looking at here -- Exhibit 8. I apologize.
Q. We're looking at the letter which is Tab 8 --
A. Yes.
Q. -- in your book.

A. Tab 8.
Q. And I mentioned the attached label that was provided with the letter. And I was turning you to Pages 10 and 11 of the label which is actually Page 23 and 24 of the entire exhibit, but if you find the label.
A. Yes.
Q. I want to put up, I want to show on the screen the section entitled "Clinical worsening and suicide risk." This reflects the addition of the Paxil labelling of the FDA's new proposed warnings, correct?
A. Yes.
Q. And it says at Page 11:

"Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and non-psychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, and other symptoms described above as well as the emergence of suicidality and to report such symptoms immediately to healthcare providers."

Did I read that correctly?
A. Yes.
Q. Sir, that language was drafted by the FDA and required for all SSRIs, correct?
A. It was pro -- so not to play semantic games here, but it

was proposed by the FDA. And again, as I've said repeatedly, short of going to court and getting -- applying for a misbranding, or I'm not sure what the legal term would be, the FDA could not require people to do it. It's not a dictator. It operates within a legal framework.

Now, could it have done that? If it was willing to spend in the real world the resources to go after people, but I want to just be clear that this was proposed and not ordered. The FDA did not have that authority for several more years.

Q. Doctor, my question was simpler than that. This was the language -- the original draft of this warning was drafted by the FDA, correct?

A. Yes.

Q. It was not drafted by GSK, correct?

A. I actually don't think we know what input GSK or any other sponsor had into this.

Q. The original draft, Doctor, was language sent from the FDA to the various SSRI and antidepressant --

A. I --

Q. -- manufacturers?

A. I understand we do not know what conversations were had.

Q. I'm not asking you about the conversations. I'm just saying, the original draft, the draft language that was proposed was from the FDA, correct?

A. Once it was in this form, yes. I'm sorry, I'm not going to except implicit assumptions in these questions that I don't agree with.
Q. Well, you don't know. You just said a minute ago.
A. It could be or it may not be, but I just want that -- it's always best to make assumptions explicit.
Q. Well, you've seen no evidence that this language in this warning was prepared by GSK or any other company?
A. I'm not saying it was.
Q. Okay. I just want to be sure.
A. I'm not saying it wasn't.
Q. Let's go to the third paragraph starting, "The following symptoms." It says:

"The following symptoms -- anxiety, agitation, panic attacks, insomnia, irritability, hostility, aggressiveness," within parenthesis, "impulsivity, akathisia," and then parenthesis, "psychomotor restlessness, hypomania, and mania have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as for other indications both psychiatric and non-psychiatric. Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing

the therapeutic regimen including possibly discontinuing the medication in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms."

Did I read that correctly?

A. You did.

Q. And that draft, that language was also the FDA's language as originally proposed, correct?

A. This is the language that they sent out.

Q. And the warnings reflected in this labelling were not limited to a certain population or age of a patient, correct?

A. Well, they were not, but allow me to -- I'm sorry. I just again want to make a clarification here. The fact that the FDA requested this -- and by the way, I think it not stop GSK from proposing -- I want to give two examples here. They did not have to take it as it was.

I want to be very clear. The fact that the FDA drafted it, two things that could have been added here. One, they could have added the term "emotional lability" and explained what that meant and, two, they could have proposed the FDA adding the Paxil-specific information they already had here. In fact, they had the responsibility to do that. We've talked about the difference between authority and responsibility.

So the fact that -- again, it is not something where

the FDA is the king. The FDA, certainly when I was there, took its legal authority but also the limits of its legal authority very seriously.
Q. I'm sure the jury will remember your testimony earlier about the relative authority of the FDA and of the drug manufacturer, but with respect, all I'm asking is: This is language that is class language that the FDA proposed for all drugs of the class, correct?
A. Correct.
Q. And the manufacturer can't stick its own language into class labelling if the FDA says, "We want class labelling," correct?
A. They may not -- actually, I'm unaware at this point in time of GSK proposing to put anything anywhere. Certainly, in terms of later events, Glaxo never proposed putting it outside of class labelling.
Q. That wasn't my question. My question was: This -- these warnings that we've seen, that's class labelling that the FDA says has to go in all the drugs, SSRIs and antidepressants, correct?
A. They're proposing that it be put in. And again, again, I want to just speak to the implicit assumption that the -- of course, the FDA would like it if people didn't say, "Let's do something different," but they did not have the authority then to say, "You may not propose anything else." I certainly, in

the request that they sent out, did not see anything where they said that.
Q. But once adopted, once they're -- the FDA says, "This is the language we want," GSK couldn't have put anything different in there, correct?
A. No, that is not correct, sir. That is not correct. They could have proposed something else. They can do a prior approval supplement and propose anything they want. The FDA can turn that down, of course, but the -- GSK certainly could have. That is what I'm trying to say. It's not like they would have gone to jail for proposing something, putting in that risk information that they already had. I'm sorry for raising my voice.
Q. But if FDA says, "No, you can't do that," GSK can't put anything else in this language, this class labelling, correct?
A. If they actually ask. And I'm again not talking about in the middle of the class labelling, talking about putting it somewhere in the label. We went over this at length during my direct examination.
Q. Agreed. It's not the middle of the label. They can't put it anywhere in the class labelling, correct?
A. We're not -- I'm sorry. I'm not talking about the middle of the class labelling. I'm saying could they put it below that class labelling, above the class labelling. If they don't ask, it certainly won't go in there. If they ask and

FDA says no, that's a different issue. You know what, there's no law, there's no communication from FDA saying, "do not do that."

Q. We're going to get to that. I think you agreed with me that this is not restricted to any particular age group, correct?

A. It's disease management, I would say. I mean, this would be good disease management, you know, 20 years ago. So I would agree with you, it doesn't mention a specific age limit.

Q. And you -- you talked about the original label and Mr. Wisner showed it to you having some language about disease management. This is different language than was in that original label, correct?

A. The words are different. Again, let me get to the meaning. It doesn't speak to the risk specifically of Paxil. It doesn't say anything to say it's any different from any other antidepressant or that there's information available about Paxil that is not available that the sponsor has.

Q. It's class labelling, correct?

A. Sir, I think we've established that.

Q. So if we --

THE COURT: I think you covered it. Now let's go on.

BY MR. BAYMAN:

Q. Do you agree that the warnings that went out in May of 2004 alerted -- as reflected in the Dear Healthcare Provider

letter and in the attached labelling, alerted physicians that if the medication is started, to be on the lookout for emerging suicidality and clinical worsening of the conditioning -- of the condition or worsening depression?
A. Do I agree that they did it? Again, this is -- I almost feel like I'm being asked if I am beating my wife. The question is, does this adequately warn in terms of the information that's available.
Q. That wasn't my question. My question was: The warnings that went out in May of 2004 by GSK by the Dear Healthcare Provider letter and the attached label alerted physicians that if the medication is started, to be on the lookout for emerging suicidality and clinical worsening of the condition or worsening depression, correct?
A. That would be true no matter what -- the question is not what it says. It's what it doesn't say. Let me just put it like that. The message is not to put in statements that individually are true. If the label, not the label statement, is false or misleading, but the label is false or misleading either by commission or omission, then the drug is misbranded. And that's what I'm trying to get across here.
Q. So this labelling, this class labelling was false and misleading?
A. With respect to Paxil, I would say yes.
Q. You would agree with me, though, this is 2004, six years

before Mr. Dolin's suicide, there was a label change, correct?
A. Yes.
Q. And that label change included warnings about the need to closely monitor patients for clinical worsening and suicidal thinking and behavior, correct?
A. For any antidepressant.
Q. And that would include Paxil, correct?
A. As a prescriber, it wouldn't tell me which one I should pick or whether there were special considerations for Paxil.
Q. Paxil --
A. That is part of adequate directions for use.
Q. Paxil is an antidepressant, correct?
A. If it's a more risky antidepressant, that is important for prescribers to know, or if there's information that's available, let's leave -- suppose there's no other information about Paxil -- I'm sorry, for other drugs but Paxil had it, then that's important information to know.
Q. Sir, you'll get time to give your views when Mr. Wisner asks his questions. I just asked a simple question. Paxil is an antidepressant, correct?
MR. WISNER: Your Honor, if counsel -- I'd request that the Court not -- I would request that Mr. -- Dr. Ross not be admonished by counsel but by the Court. He's trying to answer his questions that are complicated.
THE COURT: He's doing fine. Let's proceed.

MR. BAYMAN: You would agree with me --
THE COURT: We've covered that already. We know it's an antidepressant. Let's not cover that.
BY MR. BAYMAN:
Q. You would agree with me, six years before Mr. Dolin's suicide, the Paxil label was changed to tell doctors about the possible emergence of akathisia following Paxil use, true?
A. I'm sorry. Could you remind me what akathisia is?
Q. Well, you talked about it on direct so --
A. I did, but it's after lunch. But akathisia, I'm just a little hazy on --
Q. Just highlight that.
A. Oh, yes. That's the condition that's associated with suicide and -- okay. So the answer -- I just want to make sure I'm talking about the right thing. Yes, that's correct, it mentions it but not suicide.
Q. You don't think that's a warning to be on the lookout about akathisia and the emergence of suicidal impulses?
A. It does -- I don't see any wording there that tells a provider what -- why akathisia is important. I mean, that is an unusual word.
Q. Well, does it not say that akathisia and the other symptoms have been reported in adult and pediatric patients being treated with antidepressants for major depressive disorder as well as other indications, both psychiatric and

non-psychiatric?
A. Let me put it like this. Let's replace that with atrophy of the corpus callosum and say, do we know that that -- what that means.
Q. I just --
A. And this is prescribed by a lot of primary care providers. In fact, that's -- from what I've seen, that's what a lot of the marketing is. The average physician certainly may not know what akathisia is and why it's important.
MR. BAYMAN: Your Honor, I move to strike that as totally unresponsive to what I asked him. It's not even close.
MR. WISNER: Oppose.
THE COURT: It may stand. Proceed.
BY MR. BAYMAN:
Q. You would -- you would agree with me that the best way to know what a primary care physician understands about what akathisia is would be to ask that doctor, correct?
A. That would be one way of doing it. I mean, I think you could also say, what is the curriculum in prime -- you know, go to the American College of Physicians and see how often they have sessions on akathisia.
Q. My question, a particular primary care physician, if you wanted to know his or her understanding of what akathisia means, the best way to find that out is to ask that doctor,

correct?
A. I would say that is a way.
Q. And so I guess I want to understand, it's your testimony then that this label, this warning doesn't alert doctors to be on the lookout for akathisia because it's -- it has been reported in adult and pediatric patients taking antidepressants?
A. Again, context is everything. If you don't know the significance of that, it's not a real warning.
Q. And you don't believe although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, and it goes on about other things you might do?
A. Let me put it this way. If I'm parking over near Cook County -- or actually, I should say Washington Hospital Center where is where I'm from, and there's a parking space near an oxygen tank, I'm going to react differently to "consider not parking here" versus, "don't even think of parking here." That is very muted language.
Q. So you think that warning is not clear?
A. All I'm saying is, you're talking about a fatal event. It's -- you would expect with a fatal event to see the equivalent of danger. And, in fact, there are labels where it

says, let me take clindamycin, antibiotic, you should never give that quickly pushing it into a vein. You will cause the patient to go into cardiac arrest. And the language on that is very, very clear: This may kill people.

This sounds like, well, maybe it's a problem, maybe it's not. I'm saying this not so much as a primary care physician that as someone who has done a lot of labelling. And the principles are the same. It's a risk of communication. It doesn't matter what the therapeutic area is so much. Yes, the details are certainly important, but if I want to say, "stop, this is really something to think about," not just for when the patient is on the drug but do I start this patient at all on a drug, do I choose something besides drug therapy, if you really don't think it's that big a deal or that's -- maybe this is appropriate, but again, we've seen from the data analysis, and I'm talking about GSK's own data analyses, that the company has known for a long time that there's an increased odds ratio of Paxil versus placebo.

Q. We're going to get to that. My question was a lot simpler. You don't think that warning is clear to alert a prescriber to be on the lookout for akathisia and about a possible link to suicidality?

A. It's not specific for Paxil. It's not -- again, getting into these yes/no things, this is a question of, is this adequate directions for use.

MR. BAYMAN: Well, let's -- we've been talking about akathisia. Let's move to the next exhibit, which is Tab 9. That, your Honor, is Joint Exhibit 6. It's already in evidence. That's the February 2005 Dear Healthcare Provider letter.

Have you got that, Doctor?

THE COURT: Pull it up on the screen.

MR. BAYMAN: It is.

THE WITNESS: Yes.

BY MR. BAYMAN:

Q. Let's -- you're familiar with that letter, correct?

THE COURT: Just put your question, sir. We'll see it --

MR. BAYMAN: Okay.

THE COURT: -- without trying to --

BY MR. BAYMAN:

Q. Sure. This is a letter that told doctors that the Paxil label was being revised to add additional warnings, correct?

A. Yes.

Q. Okay. And the second -- on the second page, first full paragraph, blow that up and highlight it, the letter says:

"The new warning also emphasizes the need for close monitoring of patients, especially at the beginning of therapy or with changes in dose. The monitoring recommendations include a suggested schedule for

face-to-face visits with patients or their family members or caregivers."

Did I read that correctly?

A. That is the text on that page, that's correct.

Q. And that, that warning was also class labelling for all SSRIs, correct?

A. That is correct.

Q. And look at Pages 4 and 5 of the document.

THE COURT: What's your question, sir?

BY MR. BAYMAN:

Q. This is the new warning that was added to the labelling in January of 2005, correct?

Can you highlight that, please, Roger?

A. I believe so, yes.

MR. BAYMAN: No, highlight the warning.

THE WITNESS: I'm sorry.

BY MR. BAYMAN:

Q. And this label includes additional recommendations for close monitoring of patients including adult patients, correct?

A. Yes.

Q. And look at the top of Page 5, the first full sentence.

A. Yes.

Q. "It is also unknown whether the suicidality risk extends to adults." Did I read that correctly?

A. You did.

Q. And as of January 2005, FDA didn't make GSK remove that statement from the Paxil labelling, did it?
A. Given that GSK had not provided the accurate odds ratios showing that the risk did extend to adults, no, FDA did not. You are correct in that, sir. So that statement, what I'm trying to say is, is false.
Q. Okay. We're going to get into the odds ratios. Look at the third full paragraph on Page 5.
A. I'm sorry. Did you say third?
Q. Yeah.
A. Okay. Go ahead.
Q. It's on the screen.
THE COURT: It's on the screen, Doctor.
MR. BAYMAN: Yes.
THE WITNESS: Oh, I'm sorry, your Honor.
BY MR. BAYMAN:
Q. It says at the end of that section, again, "Although a causal link between the emergence of such symptoms and either the worsening of depression or the emergence of suicidal impulses has not been established," and then it refers to the symptoms up above, correct?
A. It does.
Q. And that -- those symptoms again include akathisia, correct?
A. This is the same language that we were discussing with the previous exhibit --

Q. And --
A. -- with the same flaws.
Q. And this is class labelling again, this part of the warning is class labelling, also, correct?
A. Correct.
Q. Let's turn to Page 6 of the exhibit and the section called "Precautions," and let's go to akathisia. You -- you know that beginning in January 2005, the Paxil labelling said, had a section in the precautions that went in that said:

"The use of paroxetine or other SSRIs has been associated with the development of akathisia which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment."

Did I read that correctly?

A. That is the text on that page.
Q. And this is something that GSK added to the Paxil label, this is not class labelling, correct?
A. I'm actually not sure because it refers to the use of paroxetine or other SSRIs.
Q. The label also had in the precaution section a section on clinical worsening and suicide risk.
A. Yes.

Q. Do you see that?
A. I do.
Q. And again, that's class labelling, correct?
A. That is correct.
Q. And there's akathisia again, correct?
A. Again, it does not indicate that that may be associated with suicide or suicidal behavior, I should say. Sorry.
Q. It says that patients, their families, and caregivers should be encouraged to be alert to the emergence of certain symptoms such as akathisia, worsening of depression, suicidal ideation. So you don't think that's a warning to be alert for the emergence of suicidality?
A. Well, if we can highlight the many, many words in between that -- hypomania, mania, other unusual changes in behavior -- I think the issue is these are not all of equal significance. Akathisia, to my mind as a clinician, would be -- many people have trouble sleeping. Insomnia is pretty common. But akathisia, but it doesn't indicate that that's of particular importance. This is a laundry list. It doesn't say "particularly akathisia."
Q. But --
A. So again, this is a question of omission. The statement before that the risk doesn't extend to -- it's not known if it extends to adults, that is a sin of commission, if you will.
Q. And that's -- again, that phrase is FDA class labelling,

correct?
A. That is correct.
Q. And the title of the section is called, "Clinical worsening and suicide risk." Is it your testimony that this does not alert a healthcare provider that some of these symptoms could be associated with a suicide risk?
A. It doesn't do a very effective job, again, for two reasons. One, some of these are common issues. Insomnia, if I thought every patient of mine who was an insomniac was automatically suicidal, then I would become a psychiatrist. On the other hand, akathisia or agitation are things that are rather unusual. So again, it's grouping all these events or all these terms without any indication that some may be more important than others.

The second thing I'd say is, akathisia, as I've said before, is not only an unusual event, it's an unusual word.
Q. My only question was, you're not saying -- you're saying you don't believe that this section links those symptoms with the possible emergence of suicidality given the title of the section?
A. The question is -- and again, I'm going to have to speak as a regulator here. The regs don't say, does this label give directions for -- needs to give directions for use. It needs to give adequate directions for use.
Q. So you believe then that the label, the FDA-approved label

as of January 2005 was false and misleading?
A. For Paxil, and that is, again, based on the information that FDA had from GSK. The FDA is not telepathic. People sometimes think we are, but no.
Q. I want to make sure I'm clear that what information it is that you thought the FDA did --
THE COURT: I think we're going to recess now until 9:30 tomorrow morning. Ladies and gentlemen, thank you very much for your careful attention. You are excused. And we'll have your coffee on time tomorrow. I've spoken to people about that, that it's important and it should be done.
(Proceedings heard in open court. Jury out.)

[redacted]

[redacted]

(Proceedings adjourned from 4:28 p.m. to 9:30 a.m.)

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C E R T I F I C A T E

We, Charles R. Zandi and Judith A. Walsh, do hereby certify that the foregoing is a complete, true, and accurate transcript of the proceedings had in the above-entitled case before the Honorable WILLIAM T. HART, one of the judges of said Court, at Chicago, Illinois, on March 22, 2017.

/s/ Charles R. Zandi, CSR, RPR, FCRR March 22, 2017

/s/ Judith A. Walsh, CSR, RDR, F/CRR March 22, 2017

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