UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

GILDA HAGAN-BROWN, Plaintiff, v. ELI LILLY AND COMPANY, Defendant.	Case 1:14-cv-01614
JANINE ALI, Plaintiff, v. ELI LILLY AND COMPANY, Defendant.	Case 1:14-cv-01615 Day 4 (AM Session) Alexandria, Virginia August 27, 2015 9:00 a.m. Pages 761 - 930

TRANSCRIPT OF TRIAL

BEFORE THE HONORABLE ANTHONY J. TRENGA

UNITED STATES DISTRICT COURT JUDGE

AND A JURY

COMPUTERIZED TRANSCRIPTION OF STENOGRAPHIC NOTES

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I N D E X

Q Are you a board certified psychiatrist?
A Yes.
Q And are you a practicing psychiatrist?
A I am.
Q How long have you been practicing as a psychiatrist, Doctor?
A It's approaching 30 years now.
Q Well, before we get into the meat of your opinions, I'd like to talk a little bit about your educational background. Did you go to college?
A I did.
Q Where did you attend college?
A Brown University.
Q What did you study while at Brown University?
A I majored in psychology.
Q While you were at Brown University, did you know you wanted to get into mental health?
A Yes, that was one of the serious considerations.
Q Did you go to medical school?
A I did.
Q And did you graduate from Brown University with any honors?
A Yes.
Q Which honors was that?
A *Magna cum laude*.

Q Where did you attend medical school?
A Harvard Medical School.
Q What year was that?
A Let me think. In 1984 I graduated.
Q Can you just briefly explain to the jury what medical school entails?
A Sure. The first two years you're in the classroom. You have some exposure to patients, but most of it is sort of science courses, a wide range. And then the last two years you're doing a variety of rotations in hospitals. So you get exposure to surgery, pediatrics, psychiatry, OB-GYN so that you can decide what you want to ultimately do.
Q After you graduated from Harvard Medical School, what did you do next?
A I did my internship and residency at one of the Harvard teaching hospitals.
Q Which one was that, Doctor?
A It's called Cambridge City Hospital.
Q Could you just briefly explain to the jury what an internship and residency is.
A Sure. The internship is the first year. And again, it's general medicine. So I did emergency room, intensive care, medical wards, pediatrics. And then the residency is three years just of psychiatry,

specializing in psychiatry.

Q Why did you choose to pursue a career in psychiatry?

A It's always been an interest. It's of interest to me what makes people tick. I have really enjoyed working with patients who have symptoms and helping them overcome them, understanding why they have them.

Q And you mentioned previously that you're board certified?

A Yes.

Q Just briefly explain what board certification means.

A So when you finish all of that training, medical school, internship, residency, board certification is sort of one final overarching examination. It's just another credential.

Q Is your certification current?

A Yes, board certified in psychiatry.

Q Now, Doctor, following your residency and internship at Cambridge City Hospital, what did you do next?

A So since my -- since I finished my training, I have done a wide variety of things, which I've kind of been fortunate to do that. So I have had a big emphasis for a lot of my career on seeing patients. I

have published books. I teach. I have taught since I finished my own training, and maybe in about the last tennish years, I've been doing this kind of legal consulting.

Q All right. Let's briefly talk about each one of those, Doctor.

A Sure.

Q You said that you've been seeing patients. Do you operate a private practice?

A I do. I have a private practice in Harvard Square.

Q And have you operated that practice since you graduated from medical school?

A Actually, it was from when I finished my residency.

Q Fair enough, Doctor.

So how long have you been seeing patients privately as a psychiatrist?

A So since about 1988. So I guess it's coming up on about 30 years.

Q And in your private capacity as a psychiatrist, what sort of patients do you see?

A So partly because I trained at city hospital, I've also seen sort of the full spectrum of patients even in my private practice. So that means everything from

very low functioning psychotic, schizophrenic patients, kind of people on the margins of society, to super high functioning professionals.

Q Did you do any sort of other practicing as a psychiatrist following your completion of residency?

A Yeah. So the other piece of my clinical work was for 20 years I was part time on the staff of the Harvard University Health Services which serviced the Harvard community, the actual university community, students, faculty, and staff.

Q And what kind of work did you do as your work with the Harvard Health Services?

A So, again, there I liked seeing all comers, so to speak. I was in particular on the campus of the law school, and it was kind of community psychiatry. I got to know the deans, the faculty really well over 20 years. And if we had a student in trouble in the classroom, we could all collaborate around that.

Some of it was just developmental like my parents don't like my career choice. Well, it's your career choice. Some of it was people in the classroom and actually psychotic. How do you manage that in the dorm and in the classroom?

Q You said you no longer are working with Harvard Health Services; is that right?

A Right. I think it's about seven years ago that I retired from that position.
Q Was it your choice to retire, Doctor?
A Oh, yeah. In fact, I liked the job so much that I held on to it a year past when I reached Harvard's retirement age formula.
Q Well, Doctor, you said you also had done some teaching. Do you hold any academic appointments?
A Yes, I do.
Q What academic appointments do you hold?
A Since I finished my training, I've had a faculty appointment at Harvard Medical School. For most of that time, it's been called a clinical instructor in psychiatry. Just this year the university just changed the name for doing the same job to lecturer in psychiatry.
Q Now, Doctor, is that an appointed position?
A Yes. That's kind -- it's actually kind of an honorary position. It's a volunteer position. I volunteer my time to do that three or four hours a week.
Q And is it a selective position?
A Yeah. I think the year that I finished my training in my group, I think I was the only one who was offered that.

Q Why do you do this *pro bono* work? I'm sorry. Why do you this work for free, Doctor?

A So I actually felt like I got an enormous amount out of my residency, particularly in the city hospital. I was very close to a lot of the faculty, and it's been my way of kind of giving back.

Q And what kind of work have you done in this academic appointment?

A So for the bulk of it, I do what's called supervision, which means that psychiatry residents, sometimes psychology interns, sometimes social work interns will get assigned to me as a supervisor, and they actually come and meet with me one-on-one. The point of it is to get help and advice with their most difficult cases.

Q And are these students and residents who are in the Harvard Medical School system?

A Yeah. Most recently, maybe the last ten years, they've been focusing on giving me residents in their very last year of training. So they are quite senior. They're about to make the transition to practicing independently. I actually enjoy helping them with that transition.

Q You said you were also published; is that right?

A Right.

Q Are you published in the field of antidepressants specifically?

A Yes.

Q What have you published in the field of antidepressants?

A So I've written two books on antidepressants, these modern type of antidepressants that you've been hearing a lot about.

Q Can you please explain to the jury -- what are the titles of those two books?

A The first one is called *Prozac Backlash*. The second one is called *The Antidepressant Solution*.

Q *Prozac Backlash*, when was that published?

A 2000.

Q Briefly explain to the jury what *Prozac Backlash* was about and how it relates to antidepressants.

A So that was 15 years ago, and these modern antidepressants had become extremely popular. As I practiced as a psychiatrist, I was seeing side effects that I realized I didn't know enough about, and my colleagues felt the same. I was doing a lot of research and people referring me to patients who had some of these side effects. So half of the book is about side effects that in 2000 I didn't think doctors and patients knew enough about, especially primary care

doctors who were prescribing most of the drugs by that time. And the second half was sort of when the drugs are appropriate, how to make that decision either as a doctor or as a patient.

Q And what sort of work did you conduct researchwise in preparing that novel -- that book? Sorry.

A Well, first of all, I prescribe these drugs all of the time. So it was partly based on my own clinical experience, my education, my training, and then I did do a lot of research to master all of the literature that was out there. There's, I think, about 600 footnotes in *Prozac Backlash* to the medical literature, and there's probably about 350 *in The Antidepressant Solution*.

Q And, Doctor, did your career change in any way after your publication of that first book?

A Yes.

Q How so?

A So it's actually an interesting turn. I got a lot of requests from patients and from doctors for assistance with some of these side effects. The second book was an entire book on antidepressant withdrawal, which we're talking about here today. And then over time I started to get requests to assist people who are involved in lawsuits over some of these side effects.

THE COURT: Doctor, when were these books published again?

THE WITNESS: So the first one was in 2000. The second one was in 2005.

THE COURT: Thank you.

BY MR. WISNER:

Q Specifically, did the first book, *Prozac Backlash*, the one published in 2000, did that book or yourself receive any awards for it?

A Yes, actually.

Q Are you familiar with the American College for the Advancement of Medicine?

A Yes.

Q Did you receive an award from them?

A Yes.

Q What award did you receive?

A So they gave me their annual achievement award in medicine. I went and gave the keynote address at their annual convention, and that was for the first book, *Prozac Backlash*.

Q Let's talk about your second book, *The Antidepressant Solution*. Doctor, would you recognize the cover of the book if you saw it today?

A I think I would.

Q Doctor, on the screen, is that the book that you

published?
A Yes, sir.
Q And could you briefly just explain to the Court what *The Antidepressant Solution* is about.
A Right. So you can see from the subtitle it's a step-by-step guide to safely overcoming antidepressant withdrawal, dependence, and I put "addiction" in quotes because it's kind of what laypeople -- what patients will say if they're really having a hard time getting off the drug.

So the history of it is that one of the chapters in *Prozac Backlash* was about antidepressant withdrawal and had cases in it. They all did. But I got a lot of requests: Can you be more specific? Can you tell us kind of how to -- you know, like a cookbook of how to do that. So that's what this book is, just that one side effect.
Q Does this book go over your clinical opinions about how to properly discontinue an antidepressant?
A Yeah. I have tapered hundreds of people off of antidepressants, both when I was researching the book and particularly after it was published. A lot of colleagues would refer patients to me either for consultation -- help us, you know, do this -- and in some instances, to transfer the patient's care while

they were tapering off. And then some patients would just seek me out on their own.

Q And this book was published in 2005; is that right?

A Correct.

Q When was Cymbalta approved?

A Cymbalta was approved and came on the market just the year before in 2004. So there was very little information about Cymbalta at that time.

Q However, do you discuss Cymbalta in this book as well?

A Yes. It's included in various tables and absolutely what was known about it at the time.

Q And what sort of research went into researching this book, Doctor?

A Again, I tapered hundreds of patients off of the drugs and a lot of making sure that I was up to speed on all the medical literature. It was about 350 footnotes in that book.

Q Thank you, Doctor.

You mentioned that you've been doing legal consulting in forensic work; is that right?

A Right.

Q And you've been doing that for about how long, Doctor?

A It's roughly ten years now.
Q Does that work occupy a large part of your profession currently?
A Particularly in about the last five years, yes, since I retired from the health services. And my private practice is also smaller now; it's about a half a day to a day a week.
Q Now, Doctor, I don't want to get into any particulars about any one case that you've worked on, but can you generally explain what sort of work you've done in the field of forensic consulting?
A Yes. I've done, for example, medication side effects. I do some malpractice cases. I do cases, for example, involving off-label marketing of medications. It's actually a wide variety.
Q And have you testified -- I'm sorry -- worked with and against the government in different capacities?
A Yes. So I have done some cases for the government, and then if I think that the fact pattern actually more supports the other side of the case, I'll do that side.
Q How much time does it take to conduct an investigation into a particular pharmaceutical product?
A Some of these cases last five, six years, and can take hundreds and hundreds and hundreds of hours. It

can be very, very complicated to go through millions of pages of documents and try to cross T's and dot I's and put things together.

Q As part of these large scale investigations, Doctor, do you work for free?

A No, sir.

Q Do you charge an hourly rate?

A I do. I charge by the hour.

Q What is your hourly rate, Your Honor?

A It's $650 an hour.

Q All right. I want to talk to you about a few other issues. First, have you been present throughout the trial this week?

A Yes, I have been listening to the trial.

Q Why were you present, Doctor?

A You know, there's a huge volume of material in this case that -- well, the binders against the back wall are just a small fraction of it. These deposition excerpts are like maybe ten minutes to an hour of daylong depositions. So it's been helpful to sit here and hear exactly what the jury heard. It's also -- these cases are moving all of the time. So there's always new information. So this is -- you're hearing what's the most up-to-date, and to be here and hear that with you was helpful.

Q And to be clear, Doctor, have your opinions changed in any way because of what you've heard here today?

A Not at all. Again, as additional pieces of information come in, my opinions haven't changed but they help solidify them. They validate them actually.

Q During the time that you've been here all week, have you done any interviews or consultations with Ms. Janine Ali or Ms. Gilda Hagan-Brown?

A No, other than just saying hello in passing in the halls.

Q Okay. Doctor, have you ever been tendered as an expert in another court?

A Yes.

Q And you've been accepted before?

A Yes.

MR. SCHMIDT: Objection, Your Honor. He's also -- I don't want to do a speaking objection, but I don't think this is appropriate given the prior record on this witness.

THE COURT: I'll let him answer the question.

MR. SCHMIDT: Okay.

A Yes, I have been approved by courts.

Q And the method you used to render your opinions in this case, are those the same methods and approaches

that you used in those other cases?

A Yes, and actually in my clinical practice, same methodology.

Q And, Doctor, just a broad stroke overview, what is that methodology?

A It's called a differential diagnosis in medicine, and what it means is that you are sifting all the information through a kind of ultimate funnel of is it this, is it that, is it this, is it that kind of trying to parse out what happened in a particular case, whether it be a new patient who is sitting in front of you that you're going to treat or retrospectively looking at millions of pages of records and depositions and interviewing people.

Q And approximately how many hours have you worked on these cases specifically?

A So the science part of these cases, which, again, involves hundreds of thousands of pages of documents, I've spent about 310 hours on.

And then on the individual cases, in Ms. Ali's case, I've spent about 55 hours. And in Ms. Hagan-Brown's case, I've spent about 85 hours.

Q And the opinions that you are going to offer in this court, are they rendered to a reasonable degree of medical certainty?

A Yes.

MR. WISNER: Your Honor, at this time I'd like to proffer Dr. Joseph Glenmullen as an expert in psychiatry and antidepressants.

THE COURT: All right. Any objections?

MR. SCHMIDT: Just the objection we previously outlined, Your Honor, based on his qualifications and foundation.

THE COURT: All right. The Court is going to recognize Dr. Glenmullen as a witness qualified to express opinions concerning the issues of Cymbalta.

MR. WISNER: Thank you, Your Honor.

THE COURT: All right.

BY MR. WISNER:

Q Well, Doctor, what is Cymbalta?

A So I think you know by now Cymbalta is an antidepressant that is also used to treat anxiety, generalized anxiety disorder in particular, and several pain syndromes, including fibromyalgia.

MR. WISNER: Your Honor, permission to tender to the witness a binder that will be used throughout the testimony.

THE COURT: All right.

MR. WISNER: Defense counsel has received a copy of this.

THE COURT: All right.

BY MR. WISNER:

Q What kind of drug is Cymbalta?

A So it's an antidepressant. I think you've heard the terms SS -- no, SNRI, which means that the brain chemicals that it focuses on are serotonin, that's the S, and norepinephrine, the N. And it's worth noting that norepinephrine is the form of adrenaline that is found in the brain.

Q And what is a neurotransmitter, Doctor?

A So brain cells do not communicate. They don't send an electrical signal from one cell to the next. They actually send chemical signals, and these are two chemicals believed to be important in the modulation of mood, anxiety, pain.

Q Doctor, would use of a diagram of a neuron aid you in your testimony today?

A Yes, I think it would.

Q More importantly, did you use such diagrams in your book *The Antidepressant Solution*?

A Yes.

MR. WISNER: Your Honor, permission to publish to the jury what has been marked solely for identification purposes as Exhibits 151 and 152.

THE COURT: Any objection?

MR. SCHMIDT: No objection, Your Honor.

THE COURT: All right. Without objection, you may publish to the jury your exhibit.

Ladies and gentlemen, what you're going to see is purely for the purposes of helping you understand Dr. Glenmullen's testimony.

BY MR. WISNER:

Q Dr. Glenmullen, what is this a diagram of, which has been marked for identification purposes --

A So this is actually a diagram of two nerve cells. The body of the top nerve cell is here. The body of the second nerve cell is here, and you can see that they consist of a nerve cell body and then these very long branches through the brain or through the entire nervous system. And this juncture here is where they actually communicate, and I have another illustration of that specific interface or where they communicate.

MR. WISNER: Can we go to the next one.

BY MR. WISNER:

Q Okay. Doctor, so this is a blowup of that square in the previous diagram?

A Yes.

Q Okay. Would you please explain to the jury how Cymbalta interacts with this portion of the connection between brain cells.

A So this top, it kind of looks like a button. It kind of expands here at this top neuron. That's the neuron or nerve cell that's going to release a message. You can see that the messages are kind of contained in packets. The little dots are to represent the messages. Then this stem here is kind of the tail of that neuron that's going to receive the message.

Then what's important to see is that the packets actually merge with the cell membrane, and the chemicals are released. Then they go into a receptor, the little rectangles on the receiving cell. That's how the messages are sent, and then the messages go down. That's what the little jagged arrows are, the messages going down towards the cell body of the receiving neuron.

Q How does a drug like Cymbalta affect this area of the brain?

Do you want me to clear the annotations?

A Yeah, that would be helpful.

So you actually heard Dr. Ahmed talk a little bit about this. There's a mechanism by which the cell that released them kind of cleans them up, reuptakes them, and these drugs actually block that, which means -- I think she used the phrase that the chemicals hang around longer in the space. So you get more signals

for that chemical, but that's the way in which it happens.

Q Doctor, you've mentioned that Cymbalta is an antidepressant. How is it also used to treat pain?

A So it's believed that these drugs also modulate pain because these two chemicals are somehow modulators of pain in the central nervous system.

Q Doctor, are you familiar with a phenomenon known as withdrawal syndrome?

A Yes.

Q Does withdrawal syndrome relate to what is happening here in the neurons?

A Yes.

Q Could you please just explain to the jury how use of a drug and then discontinuation of it affects this portion of the neurons connecting.

A Sure. So what's interesting is that the receiving cells -- this cell down here -- is not passive in the face of any medication that crosses the blood brain barrier and reaches brain cells. So they react, and they always react to counteract whatever the drug was doing. We know that what they do in particular is they remove receptors. So they'll take some of these receptors out, and there's actually a technical term for it. It's called down-regulation.

So over time -- and this takes quite a long time, like months, because these receptors are proteins transcribed off of DNA. Over time they will make adaptations to living with higher levels of serotonin signals and the medication there 24/7.

And then when you stop the drug, they have to essentially reverse those changes. They're not going to see less serotonin signals. They need to put up more receptors. Again, that's going to take months.

Q This process of down-regulation where the receptors are removed, how are they brought back once the drug is removed from the system?

A So again, they're actually transcribed -- they're proteins transcribed off of the DNA through an intermediary -- they call it the MRMA -- that's related. But it's protein synthesis up in the cell bodies. Then they have to be moved down to the receptor sites and put up into the membranes, and it takes a while. It's a turnover.

Q And because this down-regulation is affecting the transmission of signals in the brain, can that lead to -- what does that lead to on the vis-a-vis symptoms?

A So what happens is if you don't allow the brain cells enough time to comfortably make that change, they essentially become very dysfunctional. They

malfunction. They are very stressed, and that literally produces the symptoms of antidepressant withdrawal. And that's true of all withdrawal from drugs that act on the central nervous system.

Q I want to talk a little bit about withdrawal specifically.

A Sure.

Q Have you treated antidepressant withdrawal syndrome before?

A Yes.

Q And could you please briefly explain to the jury what antidepressant withdrawal syndrome is.

A So different drugs that act on the central nervous system will have different withdrawal syndromes, meaning different clusters of side effects that are typical of that particular drug when you stop them or that class of drug. So the antidepressant withdrawal syndrome is these characteristic symptoms that you can see when one of these drugs is stopped.

Q Is there a difference between an antidepressant withdrawal symptom versus a syndrome?

A Yeah. So, for example, in the case of antidepressants, there are over 40 symptoms that have been identified as characteristic of antidepressant withdrawal. And then if you call it antidepressant

withdrawal syndrome, you mean that there's several of these.

Q Now, Doctor, drugs like Cymbalta you said are used to treat depression and conditions such as fibromyalgia; is that right?

A Right.

Q How do you know whether or not when someone discontinues Cymbalta those symptoms that you're seeing are withdrawal as opposed to a reemergence of the underlying condition?

A Well, you actually have -- it's really important to distinguish that. I think we'll get into some more detail about it. But number one are they the characteristic symptoms? You're not going to call something from out in left field that's not characteristic. Number two, are they new? Is this something that the patient didn't have before, or is it a preexisting symptom that's much worse? That's an important distinction. And thirdly, is it happening in the characteristic time frame? So again, if nothing happened until six months or a year later, you're not going to call that withdrawal. But if it happens in the initial days or weeks going off the drug, then you're going to be concerned that that's antidepressant withdrawal.

Q Are some of the symptoms of withdrawal also similar to the symptoms associated with the underlying condition?

A Yes. Again, there's a list of 40-some-odd symptoms, and they can include, for example, worsening depression, worsening anxiety, worsening insomnia, worsening pain. Then there are some that are highly unusual, like these electric shock sensations that you've been hearing about that occur in almost no other medical condition.

Q Now, Doctor, in your book *The Antidepressant Solution* you referenced something called the antidepressant catch-22.

A Yes.

Q Can you please explain to the jury what that means in relation to withdrawal.

A So this is a serious liability, so to speak, of antidepressant withdrawal. In addition to the acute symptoms that someone can get -- and they can be really debilitating. They can be life threatening if someone becomes suicidally depressed. There's another whole layer of concern, and that is that if a doctor doesn't really understand well enough what antidepressant withdrawal is, because it is overlap in the symptoms, it can be misdiagnosed as a serious psychiatric

condition or some other serious medical condition that the patient doesn't actually have. It can lead to very expensive testing. It can lead to patients being told that they have conditions much worse than they do. It can lead to patients being on medication long term that they don't really need because the withdrawal was misdiagnosed. That's what I call kind of a catch-22.

Q Now, Doctor, out of respect to your patients that you treat, but in a general sense, have you experienced that catch-22 in your clinical practice?

A Oh, sure. A lot of the consultations that I get are because that has happened. People have been to the emergency rooms. They have had CAT scans, MRIs, EEGs. They've been told they have seizure disorders.

MR. SCHMIDT: Your Honor, I don't think we're entitled to ask him about the details of his patients. So I don't think he should be testifying about it.

THE COURT: Overruled.

A So that's kind of on the medical side, the physical symptoms. Then on the psychiatric side, people can be told, Oh, you have very serious depression. Oh, you need to be on antidepressants for years. Oh, maybe you have bipolar disorder. You need to be on medications for that as well. Sometimes people get put on antipsychotics.

And then going back and trying to tease out when did these symptoms happen, what were the symptoms, were they new or worse, and if it appears that, in fact, it was antidepressant withdrawal, then you try removing the medications or -- for example, a neurologist might say an anticonvulsant is not needed. I don't think this patient had a seizure disorder.

Q How long in your clinical experience can antidepressant withdrawal last?

A For the drugs that are associated with particularly bad withdrawal, it can take four to eight months to get people off the drugs. And if they're still having significant symptoms despite the taper, it can last that long for sure.

Q And I want -- you said that it depends on how risky the drug is. Is there a way to understand the risks -- the different risks associated with a particular antidepressants?

A Yes.

Q And what is the way that you've identified?

A So there's two things. One is kind of a clue. It's what we call the half-life. I think you've heard this term a few times already this week. And then the definitive way to know is good quality studies, good quality studies.

Q By good quality, you're talking about prospective studies?

A Yes, prospectively designed studies specifically to measure the side effect and using the checklist as opposed to just these kind of open-ended questions to see what people spontaneously say.

Q We're going to get into the checklist in a minute. The jury has heard a lot about it. We'll get there soon. But I just want to stop and talk about antidepressant withdrawal specifically.

You said the half-life.

A Yes.

Q Can you briefly explain to the jury what a half-life is?

A Sure. So I think you've heard a couple of times it's the number of hours or days -- because it's a very wide range -- that it takes for half the drug to be out of your system, to flush out of your system if you stop it or lower the dose, the difference between the doses. Then once you get to half, it's the same amount of time for another half to be gone, which would get you to a quarter. Then the same amount of time for another half, which gets you to an eighth. The rule of thumb is that five half-lives roughly corresponds to when the drug is gone if you have stopped it.

Q Doctor, as part of your research for *The Antidepressant Solution*, did you evaluate the respective half-lives of modern antidepressants?
A Yes.
Q And did you compile that data in a chart?
A Yes.
Q Would going over that chart aid you in your testimony today?
A Yes. It's a table from one of the books. It's from *The Antidepressant Solution*.
Q Okay. Can you just turn to Tab 3 in your binder?
A Yes.
Q Is that a fair and accurate copy of that table?
A Yes.

MR. WISNER: Your Honor, at this time I'd seek permission to publish that table to the jury for demonstrative purposes only.

MR. SCHMIDT: No objection, Your Honor.

THE COURT: All right.

BY MR. WISNER:
Q Okay. Doctor, what is this a table of?
A So this is a table I made for doctors and patients, and it's looking at what we just talked about, the half-lives, and it's kind of listing all of these modern antidepressants from some of the ones with

the shortest half-lives.

Effexor you've heard about with five hours; Cymbalta with 12; down to the longest half-life, which is Prozac, which is 4 to 6 days, including -- you've heard it has an active metabolite that lingers a long time. And then this 90 percent elimination is that kind of five half-lives. So calculating that out and then the last column based on those figures is a typical onset of symptoms.

Q Now, Doctor, Effexor up there, it says five hours. Do you see that?

A Yes.

Q Is that a twice-a-day drug?

A There are now -- so Effexor XR is extended release, and that can actually be taken once a day.

Q But the original Effexor, that's twice a day?

A I think that's true. I don't recall. It's quite a while, but I think that's true.

Q Okay. And Cymbalta, that's 12 hours; is that right?

A Correct.

Q What drugs on this list are manufactured by Eli Lilly?

A So the two that are Lilly drugs are Cymbalta, and I think you've heard Prozac as well.

Q And so looking at Prozac, it says four to six days, right?

A Right.

Q How does that lengthy half-life affect the risk or likelihood of antidepressant withdrawal symptoms?

A So that very long half-life is kind of a slow built-in taper. As you lower the dose, it's almost a month of gradual change because the drug is lingering so long. So that means you don't have to make as many careful steps. You don't have to space them out over as long a time. And when you actually study Prozac in a high quality study with a checklist, it has the lowest rate at about 14 percent of patients.

Q Let's look at Cymbalta here. That has a 12-hour half-life; is that right?

A Correct. It's the second shortest.

Q And how does that, relative to Prozac's short half-life, affect the way you would have to taper a patient off of the drug?

A So again, this is now the opposite. It's going to flush out of the system very quickly. If you take -- even if you just make a step down, that difference in the dose, you're going to see a very quick change. We're looking at 2.5 days versus 25 days. That means that it's not going to be an uncommon side effect.

It's going to be common. You're going to have to be much more careful. You're going to want to space it out over a much longer time and much more gradual reductions.

Q Thank you, Doctor.

In your review of your materials today, did you have an occasion to review any documents showing the research that went into developing the relationship between half-life and antidepressant withdrawal?

A Yes.

MR. WISNER: Your Honor, at this time permission to publish to the jury Exhibit 78. It's already in evidence.

THE COURT: All right.

BY MR. WISNER:

Q Doctor, what is this document?

A So this is actually a journal. It's called a supplement to a journal. It looks like a little journal of its own. It's an entirely separate publication, and it's a summary of a meeting that Eli Lilly had in the mid-1990s, in 1996 where they brought together experts in antidepressant withdrawal from around this country and actually from around the world to talk about, when they were marketing Prozac, how best to study this phenomenon. And they published this

entire supplement. Again, Lilly sponsored that.

Q Let's turn to the second page on this document.

MR. WISNER: Let's call out that portion.

BY MR. WISNER:

Q Doctor, it says here a closed symposium December 17, 1996. Do you see that?

A I do.

Q What is a closed symposium?

A It's kind of a fancy term for they brought them all to a resort to talk about this. It means it was not open to the public. It was just this group of experts that Lilly brought together.

Q It says an unrestricted educational grant. What does that mean?

A So that means that Lilly paid for the meeting and paid for the publication.

MR. WISNER: Let's turn to the first article in the introduction to this publication -- actually, let's go to the table of contents.

BY MR. WISNER:

Q Doctor, this is the table of contents to the publication.

MR. WISNER: Let's look at the second article. It has all the names.

BY MR. WISNER:

Q Doctor, do you recognize some of the names of these individuals?

A Sure.

Q Who are they?

A So, for example, Alan Schatzberg is the chairman of the Department of Psychiatry and a professor at Stanford. Peter Haddad is from England. He was someone who had published a lot about antidepressant withdrawal before Lilly had this symposium. Jerrold Rosenbaum is the chairman of the Department of Psychiatry at the Massachusetts General Hospital and a professor at Harvard.

Q And do you know if these individuals that we just highlighted had any affiliation with Cymbalta specifically?

A Yes. A number of these people in this early meeting in the mid-1990s were advisors to Lilly on Prozac, and then they subsequently became advisors on Cymbalta. In particular, it's called the Global Cymbalta Medical Advisory Board.

Q And just briefly -- I believe the jury heard a little bit about this -- what is a Global Advisory Board?

A I think Dr. Detke testified that it was about 25 people, mostly academics, who would meet -- I think he

said a couple of times a year. They were consultants to the company.

MR. SCHMIDT: Your Honor, the jury has heard Dr. Detke's testimony.

THE COURT: I understand. Overruled.

Go ahead.

MR. WISNER: We're moving on, Your Honor.

THE COURT: Yes.

BY MR. WISNER:

Q Let's go to the first introduction to this publication. This is an article written by Alan Schatzberg; is that right?

A Correct, he wrote the introduction.

MR. WISNER: Let's go to the final paragraph of this. If we can call it up.

BY MR. WISNER:

Q All right. Doctor, it says here while discontinuation symptoms are generally mild and transient, the syndrome can be troublesome leading to missed work and reduced productivity. It can also be mistaken for a new physical illness or the return of the original depression. Misdiagnosing symptoms may lead to costly, unnecessary testing and treatment.

Doctor, how in any way does that relate to the antidepressant catch-22 you were discussing before?

A He's essentially saying the same thing that I just said, that this can be serious. You can end up with costly, unnecessary treatment. You can end up with misdiagnoses that you might live with for years if it wasn't -- if the distinction wasn't made. It's very serious.

Q It concludes with health care professionals should be educated about the management of symptoms that often accompany SRI discontinuation.

What is SRI discontinuation?

A SRI means serotonin reuptake inhibitor. It's just a shorter abbreviation than SSRI. Just to place this historically, this is the mid-1990s. Prozac would have come on the market in 1989, late '90s -- late '80s was the first. By the mid-'90s, there were additional drugs in the selective serotonin reuptake inhibitor class, particularly Paxil and Zoloft.

Q Well, Doctor, at this closed meeting in 1996, did the experts in any way develop a methodology for measuring antidepressant withdrawal syndrome?

A Yeah. So out of this meeting and additional work, the particular checklist that I'm talking about was developed by Lilly and its consultants at the time that they were marketing Prozac.

Q Doctor, let's just take a step back. What is a

symptom checklist?

A So the symptom checklist that you've heard so much about is these experts, working with Lilly, actually went through all of the previous medical literature and identified 43 symptoms that were considered the key symptoms of antidepressant withdrawal, and from that, they created a checklist to systematically be able to ask a patient: Have you had insomnia? Is it new or is it worse? Have you had nausea, vomiting, diarrhea? Is it new or is it worse? Have you had electric shock sensations? Are they new or worse? You go through the whole 43: Are they present or not? If they're present, are they new or worse or not?

Q Now, Doctor, what would be the alternative to a symptom checklist?

A So the alternative to that you've heard described as an open-ended question where you would just say, Is there anything new since I last saw you that you want to tell me about? It's also -- another technical term that you've heard is spontaneous reporting. And what that means is that the patient is just asked an open-ended question, and the burden is on the patient to spontaneously report something, which they may have no idea that they're feeling a lot more depressed has got anything to do with stopping the drug. It could be

a reaction to stopping the drug *per se* as opposed to a return of their original condition.

Q Doctor, in your professional opinion, what do you believe is the more appropriate method for measuring antidepressant withdrawal?

A The gold standard is to use the checklist.

Q Now, Doctor, you were here for the testimony of Dr. Detke, right?

A Yes.

Q And you heard him testify that he doesn't like checklists because there's a risk of false positives?

A Yes, he did say that.

Q Do you in your professional capacity agree with that sentiment?

A No.

Q Why wouldn't a checklist result in additional false positives?

A So the key here is actually the failure to use a checklist would give you many more false positives. If you just say to someone, Tell me whatever has happened in the last two weeks since I last saw you, when you look through some of these studies, people report, oh, I got pregnant. Oh, I had a bug bite. I had a tooth extracted. Well, obviously, those things have nothing to do with antidepressant withdrawal or taking a

placebo sugar pill. So that's the purpose of being focused.

And these checklists are widely used in medicine. They're used on the efficacy side when you're trying to test whether or not the drug works in all studies. There are other checklists for other types of side effects. They're the gold standard. So you would have far more false positives with an open-ended question.

Q Well, Doctor, we also heard testimony -- I forget from who -- that checklists are suggestive of withdrawal symptoms. Do you agree with that sentiment?

A So actually, this is an important point. A checklist is kind -- sorry. Suggestive is kind of a way of trying to disparage them, kind of cast a negative light on them. It's not a good term in my opinion.

MR. SCHMIDT: Objection, Your Honor. I don't think it's appropriate for him to say what other witnesses are doing in terms of disparaging.

THE COURT: Sustained.

MR. WISNER: Let me rephrase the question.

THE COURT: Go ahead.

BY MR. WISNER:

Q In your opinion, do you believe checklists are suggestive?

A I wouldn't use that term. Another term you've heard is elicited scale. So the whole point of them is to elicit specific symptoms, to focus on the particular antidepressant withdrawal symptoms or syndrome. So yes, you're eliciting. That's the whole point of it. You would do the same on the efficacy side. You ask about pain. You ask about depression. We always elicit. That's the gold standard.

Q Considering the potential similarities of the underlying condition with the symptoms of withdrawal, does the checklist in any way help rebut the potential of overlap?

A Sure. So, again, a patient could think, oh, I have insomnia. I've always had insomnia. It seems to be worse, but I don't understand why. They wouldn't necessarily even tell you if you didn't ask. Some of the things on the list are sensitive. You know, people don't always volunteer, I'm feeling depressed or I'm feeling anxious. Some people are very embarrassed to say that, especially if they become suicidal. They may well be too embarrassed to tell you that.

So again, we elicit these things. When you go to your doctor, the doctor asks, do you have this, do you have this, and do you have this. And you heard Dr. McCleary yesterday say checklists are the most

thorough. I agree with that.

Q Doctor, specifically, how does a checklist then distinguish between symptoms that were always there and symptoms that actually are related to withdrawal?

A So the actual Lilly checklist has columns for -- for any given symptom, there are four or five columns depending on the version of the checklist: So is it new, is it worse, is it old but not worse, is it old but improved, is it not here. This is -- you know, this person doesn't have insomnia. This person doesn't have nausea. So, again, very detailed, very thorough, all five pieces of information for all 43 symptoms.

Q And if a symptom is checked as old but improved, would that be considered a withdrawal syndrome?

A No. So the only two columns that are counted as antidepressant withdrawal would be new in the days or weeks after the person stopped the drug or old but worse. If it's old but improved or old and unchanged, it is not counted.

Q Now, Doctor, did Eli Lilly use the symptom checklist to study antidepressant withdrawal after the closed symposium in 1996?

A Yes.

Q All right. How did they do that?

A So some of these same people, for example,

Dr. Rosenbaum who we saw at the symposium, and people inside Eli Lilly designed and did a study to compare Prozac to its two competitors at the time, Zoloft and Paxil.

Q And just for quick reference, what are the half-lives of those respective medications?

A So both Paxil and Zoloft have fairly short half-lives. They're under 24 hours. I think one of them is 20 and one of them is 23, something like that. So kind of -- not as short as Effexor or Cymbalta but still much shorter than -- neither of which was on the market at the time yet. But it was much shorter than Prozac. Those three were the big ones on the market at this time.

Q So the drugs that were on the market were Prozac, Paxil, and Zoloft?

A Yeah. And then slowly Celexa and Lexapro came in. But both Effexor and Cymbalta were late entries. We're talking again -- time frame is important -- mid-'90s. The big ones are Prozac, Zoloft, Paxil.

Q Did Lilly publish the results of that clinical trial in a journal?

A Yes.

MR. WISNER: Please do not put this up.

BY MR. WISNER:

Q Doctor, could you please turn to Tab 5 on your binder. Is that a copy of that publication?
A Yes.
Q Is it a fair and accurate copy?
A Yes, sir.
Q And where is this article published?
A I'm pretty sure it's *Biological Psychiatry*. Hold on one second. Yes, it's a journal called *Biological Psychiatry*.
Q And is that a journal that involves peer review?
A Yes. This is a very scientific article published in a peer-reviewed medical journal.
Q And do doctors and scientists such as yourself rely upon journal articles such as this in evaluating clinical practice?
A Yes. It's a number of pages. It's a typical article size. It's very scientific. There's a lot of analysis in it. There's some discussion of -- there's the rates that were actually found, yes.
Q And then did you rely upon this article in coming to your opinions today?
A Yes.
Q And then looking briefly at the authors of this article, are there any actual employees of Eli Lilly who authored this article?

A So there are five authors, three of whom are actually in-house Eli Lilly employees.

MR. WISNER: Your Honor, at this time I'd like to move Exhibit 119 into evidence.

THE COURT: Any objection?

MR. SCHMIDT: Yes, Your Honor. It's not a Cymbalta article, and it doesn't have a nexus to Cymbalta.

THE COURT: All right. Over objection, the Court is going to allow Exhibit 119.

MR. WISNER: Publish it.

BY MR. WISNER:

Q Doctor, this is the article we were just talking about?

A Correct.

Q Okay. Let's focus in first on the authors. We have Jerrold Rosenbaum. Do you see that?

A I do.

Q We mentioned him previously as a Lilly consultant?

A He's the person who was at the symposium who is the chairman of the Department of Psychiatry at Massachusetts General Hospital.

Q And then Maurizio Fava. Do you see that?

A Yes.

Q Is he a doctor?

A Yes.
Q Who is Dr. Fava?
A So he's a colleague of Dr. Rosenbaum. He's also at the Mass General, also at the Harvard Medical School.
Q And does he have any relationship to Eli Lilly and specifically Cymbalta?
A Yes. He was an advisor of Prozac, and then he was on Lilly's Cymbalta Global Advisory Board.
Q And then Sharon Hoog. I believe we heard her testify yesterday.
A Yes. She was one of the videotaped company executives.
Q And then -- if you look here at the bottom, it has Eli Lilly and Company highlighted. Do you see that, Doctor?
A I do.
Q Then it has a bunch of letters?
A Yes.
Q What are those?
A So those are the initials, and you can see that -- Sharon Hoog, Richard Ascroft, and William B. Krebs, they are all at Eli Lilly.
Q Okay. Let's go to page 79 of the journal article.
MR. WISNER: It's the next slide.

BY MR. WISNER:

Q Doctor, you've been talking about the Lilly checklist. What is the title of the Lilly checklist?

A It's actually got a number of names. You've heard the original name, which is here, is discontinuation-emergent signs and symptoms, the DESS checklist. You've also heard DEAE, discontinuation-emergent adverse events. I think you've heard one or two acronyms for it. They're basically checklists.

Q Doctor, it says right here that the 43-item list was developed by investigators based on an evaluation of signs and symptoms reported in the available literature. Was that process done at the closed symposium in 1996?

A That's where it began. And that's what I was saying, that it was actually a review of the prior medical literature to find the key symptoms that you should focus on if you were going to study antidepressant withdrawal. They came up with -- Lilly and its consultants identified 43.

Q And then what was the general results of this study comparing Prozac to Paxil and Zoloft?

A So it was actually a very helpful study because it documented unequivocally that Prozac, with its longer

half-life, only caused withdrawal in about 14 percent of patients; whereas Paxil, with the shortest half-life of these three, caused withdrawal in 66 percent of patients; and Zoloft, which has a little bit longer half-life than Paxil, caused withdrawal in 60 percent of patients. So a wide range.

Q And, Doctor, are you aware of how Lilly -- did Lilly use the results of this study in any marketing capacity related to Prozac?

A Yes. Dr. Detke testified they used it as marketing -- when they were marketing Prozac versus Paxil and Zoloft.

MR. SCHMIDT: I object, Your Honor. There's no nexus to the facts of this case.

THE COURT: Sustained.

MR. WISNER: I'm sorry. Was that a relevance objection?

THE COURT: Yes.

MR. WISNER: Okay. I didn't know if it was a foundational issue.

BY MR. WISNER:

Q Okay. Doctor, let's move on. Specifically, if you were to see a copy -- have you seen the actual checklist that was used in this study?

A It's actually in a table at the back of this

publication.

MR. WISNER: Let's go to that table.

BY MR. WISNER:

Q Okay. Doctor, this is the actual symptoms that were used.

MR. WISNER: Let's call up the top part and just the first few symptoms.

BY MR. WISNER:

Q Okay. Doctor, nervousness and anxiety, just briefly explain what that is.

A So a few people become incredibly anxious, very, very much so during antidepressant withdrawal. Again, that can be new if they've never been anxious before, or it can be old and no different, in which case you wouldn't count it, or it can be old and much worse, in which case you would count it.

In this particular table, which was an appendix to this article, it does not have the five columns of the new, old but worse, old but not worse, old but better. So this is to give folks the list of 43. There are additional versions of it actually used in the study where you can see the columns.

Q Doctor, have you actually looked at the actual checklist that was used in this study?

A Yes.

Q Would you recognize a copy of that document if you saw it today?
A Yes.
Q Without publishing, could you please turn to Tab 6 in your binder.
A Yes.
Q What is this document?
A So this is the actual --
THE COURT: What exhibit number is it for identification?
MR. WISNER: Sorry, Your Honor. This is Exhibit 11.
THE COURT: All right.
BY MR. WISNER:
Q Doctor, what is this document?
A So this is the actual checklist that was used in that study by Lilly with Lilly's logo on it and all of the columns.
Q And did you use this document in rendering your opinions today?
A Yes.
Q Would discussing and showing this document to the jury aid you in your testimony?
A Yes.
Q To be clear, this was a document created by Eli

Lilly?
A Correct.
Q This was used specifically in the study that we've just been discussing?
A Yes.
MR. WISNER: Your Honor, at this time I actually move into evidence Exhibit 11.
THE COURT: Any objection?
MR. SCHMIDT: No objection, Your Honor.
THE COURT: All right. Without objection, Plaintiffs' Exhibit 11 is admitted and may be shown to the jury.
MR. WISNER: Put it up.
BY MR. WISNER:
Q All right. So, Doctor, this is the checklist that we were talking about?
A Yes.
MR. WISNER: Let's call up the top part.
BY MR. WISNER:
Q Okay. It reads Clinical Report Form. Do you see that, Doctor?
A Yes.
Q What is a Clinical Report Form?
A So that's the technical term in studies of medications. They're called Clinical Report Forms.

It's just a technical term for any kind of side effect report.

Q And it says below that Fluoxetine Versus Sertraline and Paroxetine in Major Depression: Comparison of Discontinuation-Emergent Symptoms.

What does that mean?

A So I think you've heard some about chemical names versus commercial or trade names. So fluoxetine is Prozac; versus meaning being compared to; sertraline is Zoloft; and paroxetine is Paxil. The patients in this study were being treated with one of these three drugs for depression, major depression, clinical depression. And it's specifically a study of discontinuation-emergent events, in other words, antidepressant withdrawal with these three drugs.

Q Just below that there's a bunch of letters listed, and it end with HCIT. Do you see that?

A Yes.

Q What does that mean?

A So when one looks in Lilly's database, every study has a code, and it's four capital letters. So this is the designation of that particular Lilly study.

Q Now, Doctor, in using this checklist, let's say a patient comes in and says, you know, since I stopped the drug, I broke my left foot. Would that data end up

being collected as a discontinuation symptom?
A No, because it's not one of the 43.
Q So doesn't this symptom checklist then limit the potential adverse events?
A No. Again, the point is to focus on the important ones and not have irrelevant data. So they would actually be asked specifically about each of these 43. Then if we look at the columns, they'll be asked, you know, is it new; is it old; if it's old, is it worse or better.
Q Doctor, when was this checklist created?
A So this study was done very close to the time of the meeting in Arizona in the mid-1990s, I think, if you look back to the publication. So the meeting was in '96. The publication of the meeting that we looked at was '97, and this study was published, meaning it had been done before that, in '98.
Q Have you seen any evidence in your review of the medical literature indicating that this list developed back then is still properly used more recently?
A Yes.
Q Would you recognize that article if you saw it today?
A Yes.
MR. SCHMIDT: Your Honor, this is the issue

we raised ahead of time. I think we're coming up on it.

THE COURT: All right. Let me see counsel at the bench.

(Conference at the bench, as follows:)

THE COURT: All right. I'm sorry. What are we --

MR. WISNER: This is the -- Your Honor, this is a journal article that was published in 2006 by Maurizio Fava, who was at that time on the Cymbalta Global Advisory Board. The document is *Prospective Studies of Adverse Events Related to Antidepressant Discontinuation*. This is actually Defense Exhibit 661. We did not object to it when they put it on the list. It goes into detail regarding the qualitative value of using checklists as opposed to -- I'm sorry. This is my version because, obviously, it's highlighted -- the qualitative value of using a checklist specifically versus spontaneous discontinuation. This journal was published after Cymbalta was on the market by an individual who was actually an expert of Eli Lilly on Cymbalta.

THE COURT: So what's the relevance of this?

MR. WISNER: This is going to go to support his opinion that, in fact, the symptom checklist -- it

states here that this is what is commonly used, it's a standard that's appropriate.

THE COURT: How does this not get into the area of -- it goes beyond what Lilly knew or had reason to know and gets into tests that they didn't conduct but you think they should have?

MR. WISNER: Respectfully, Your Honor, they presented testimony yesterday from several witnesses. They all said the checklist was not the standard used, that it's a bad checklist, that you shouldn't use it. This is a statement essentially by --

(Counsel confer.)

MR. WISNER: It specifically rebuts testimony from their own experts saying what those people you heard from yesterday that Lilly designated, not us.

THE COURT: What they said is they used it, and they explained why they used it.

MR. WISNER: They criticized it.

THE COURT: Now you want to put in that they should have used it?

MR. WISNER: No, Your Honor. I'm saying that they didn't use it. I'm not saying that they should have. I'm saying that they didn't.

This is important because in a minute we're going to get into clinical trials. And one of the big

distinctions in this case is that in 2011 they did a pool analysis of discontinuation symptoms, and that showed an 18 to 32 percent risk. Okay.

But none of the data used in that was used with a checklist, and in his opinion, the proper data is the time that they did use the checklist, not that they should have but that they actually did in 2005. That yielded 74 to 78 percent. So this validates the methodology and the reasoning why he has elected to testify that he thinks that the data that Lilly collected using the checklist is superior data to the data that was collected not using a checklist.

This is not presented to say that Lilly should have used a checklist and they did something bad. And if you want, I can admonish the witness to make sure he doesn't say that. He shouldn't. I've told him not to. But it does directly go to validity of his opinions about why he places significance and importance on the checklist data. And in cross-examination in California, that was almost the entirety of the attack against his opinions.

THE COURT: Mr. Schmidt?

MR. SCHMIDT: I think it's exactly what Your Honor said. This is failure to test. He's entitled to say -- we don't think he's entitled to say. He's been

allowed to say that he should have used a checklist. As Mr. Wisner said, he's shown the jury the checklist. He's shown the jury that it was out there.

THE COURT: Right.

MR. SCHMIDT: He's going to go through what the two checklist studies showed.

THE COURT: Is this information that Lilly knew?

MR. WISNER: Yes, absolutely. It's information Lilly knew in the sense that Lilly knows articles are published.

MR. SCHMIDT: What he's trying to do is attribute this to Lilly as something Lilly should have acted on, and that's the core failure to test problem.

MR. WISNER: Ultimately, Your Honor --

MR. SCHMIDT: Your Honor, may we finish arguing?

MR. STEKLOFF: We can add, Your Honor, there's no testimony --

THE COURT: Let me just hear from Mr. Schmidt.

MR. SCHMIDT: The argument he's making is we can fault you for not doing the checklist. If you respond by pointing out the limitations of the checklist, that opens -- or explain why you didn't do a

checklist, that opens the door for a full-fledged failure to test argument that includes suggesting that because someone had some affiliation with Lilly and they say they like checklists personally, that means Lilly knew they should have done a checklist and can be held accountable for not doing a checklist and all of our studies that didn't use a checklist are junk.

If he wants to take on our studies squarely, he's entitled to do that. He's entitled to get up and say, I reject all the science of the two studies. But to come in with an article and suggest this is Lilly's view or this is a Lilly affiliate, this proves they should have done more checklist studies, that's not appropriate.

MR. WISNER: I would be happy to have the jury instructed that they shouldn't consider this as Lilly's view and give it the weight it deserves.

Also, Your Honor, it goes to the adequacy of the label. One of Dr. Glenmullen's opinions is that the first part of the label says that the drug was systematically studied in placebo-controlled trials. It's the first sentence in the label. It says right here: Given that the systematic inquiry method is superior to the general inquiry approach, it is not surprising that almost all of the prospective studies

in the literature have used the same scale, the discontinuation-emergent signs and symptoms.

So why that's relevant is when you state systematic inquiry, it suggests a level of evaluation that they, in fact, did not do. And they're going to come back and say, Well, we think we did.

THE COURT: I'm still not clear on why this article is relevant to his opinions.

MR. WISNER: Because it validates his opinion. It's a piece of information that he relied upon. Respectfully, Your Honor, this is relevant to -- it shows directly that his opinions are, in fact, substantiated in the --

THE COURT: Well, his issue is whether there was an adequate warning based on what Lilly knew or should have known. How does this relate to that central issue?

MR. WISNER: Fair enough. It even relates to that because the first words in the label says "a systematic study."

THE COURT: Right.

MR. WISNER: This is saying the open-ended questions that they used is not systematic. So that shows right there --

THE COURT: Can't he say that? Why does this

article have to come in in order for him to give that opinion with respect to the label?

MR. WISNER: Well, how does it come in with regard --

THE COURT: If he's going to say it's systematic and he's looked at the clinical trials that Lilly had and they didn't systematically evaluate -- that's what you're going to say?

MR. WISNER: Yeah.

THE COURT: So how does this article --

MR. WISNER: Their witnesses are going to testify that this is not the appropriate way to study it, that it's not the standard in the industry, that it's a bad approach, and that it shouldn't be done. I think I should be able to support Dr. Glenmullen's opinion that that's just not true.

THE COURT: He can give that opinion, can't he, without this article?

MR. WISNER: He can give it, but it's just his opinion. They're going to go up there and say, None of these other people do it. That's not true. I mean, this guy is on the Cymbalta advisory board. He's not unrelated to Lilly. He's saying that all prospective studies have used this scale. I think that's a powerful statement not only of the adequacy of

the label, but it's a powerful statement of the fact that Dr. Glenmullen is taking this position about checklists is not some far-fetched or out there. It's something that Lilly's own guy is --

MR. SCHMIDT: Can I be heard on this?

MR. WISNER: I won't say it to Lilly's own guy, but it is a guy on the Lilly advisory board.

THE COURT: When did this come out?

MR. WISNER: In 2006.

MR. SCHMIDT: He wants to use it for the failure to test argument and just to bolster a view that Dr. Glenmullen is trying to put forward. It's interesting that if Your Honor looks at the statement that Mr. Wisner keeps saying about most or all of the studies that have done, it -- the only citation to that is the previous study. There's no other data supporting that citation.

When I asked Dr. Glenmullen three weeks ago, Can you tell me other companies other than Lilly who have used a checklist, three weeks ago he said no. That was the first California trial. Between then and the second, he came back and said, Well, now I found one or two.

They're trying to bolster something that we don't think is accurate with a hearsay statement that's

been used for the purpose of suggesting that Lilly should have been doing a study that it wasn't doing.

Your Honor has it exactly right. If they want to attack the label by saying, I think the systematically evaluated Lilly requires checklists, have at it. If they want to attack the label or the study data by saying the checklist data is the better data --

THE COURT: So the Perahia article did not use this checklist; is that right?

MR. SCHMIDT: It used interviews with patients, correct.

THE COURT: It used interviews with patients and those checklists?

MR. SCHMIDT: Yes. The article that they have been asking every witness about that they now want to disavow because it's not good data --

MR. WISNER: Now, Doctor -- I'm sorry. Your Honor, one last point -- and I think this sort of goes to the heart of this -- is that this is 2006.

THE COURT: Right.

MR. WISNER: One of the arguments that they are going to make attacking Dr. Glenmullen's approach is that that was the old way it was done. In fact, Dr. Detke testified to that yesterday. So here we have

evidence that people are saying in the medical literature that, in fact, it is being done that way.

I think on a technical level, Your Honor, on a purely legal point, they have waived any objections to relevance by putting this on their exhibit list and by me not objecting. The Court's original order in January said failure to object waives all objections. That's the first issue.

The second issue is hearsay. I can lay a foundation if this falls into hearsay. This is a medical journal that was published. So if the issue is relevance on a purely legal point, it's their exhibit.

MR. SCHMIDT: That's not accurate. We have always argued failure to test.

THE COURT: Was this on your exhibit list?

MR. SCHMIDT: We put it on our exhibit list because they raised the issue. It was purely a protective -- we objected to it throughout. In fact, Your Honor excluded it.

THE COURT: So what do you want to ask him about this? He's familiar with the article?

MR. WISNER: That's correct.

THE COURT: Then what?

MR. WISNER: Ask him who this guy is.

THE COURT: Right.

MR. SCHMIDT: Which is, if I may jump in, that he is Lilly's affiliate.

THE COURT: He's familiar with the article and then what?

MR. WISNER: Sorry. I'm going to show him this paragraph right here, the one that I showed you.

THE COURT: Right.

MR. WISNER: I'm going to ask him what does that mean, what is a prospective study versus a nonprospective study.

THE COURT: All right.

MR. WISNER: How this in any way supports the opinion that checklists are superior.

THE COURT: But you can do that without the article. You can ask him within the industry, within the standard methodologies that he's relied on, what role -- without the article.

MR. WISNER: If that's the case, Your Honor, if they come after him on the validity of using the checklist, that opens the door.

THE COURT: Well, I think you can get into all of this without specific articles. You can ask him about what extent were the checklists used, to what extent are checklists necessary in order to develop the data, and they can come in and say, Aren't you aware

that other people don't use checklists.

MR. WISNER: The last issue is --

THE COURT: I may have to revisit this based on what comes up.

MR. WISNER: Their expert relied on this. So I can take this out on cross-examination. Isn't that what 703 says?

THE COURT: We'll see.

MR. WISNER: Okay.

MR. SCHMIDT: Thank you, Your Honor.

(Proceedings continued in open court, as follows:)

BY MR. WISNER:

Q I apologize, Doctor. I hope you had a chance to get up and stretch.

A Yes.

Q Okay. Doctor, in your clinical practice, is the issue of antidepressant withdrawal symptoms something that you consider clinically an important issue in your evaluation of your patients?

A Yes.

Q I want to go over briefly: What sort of documents have you reviewed in rendering your opinions in this case?

A So it's been a very wide range of documents. I think I mentioned hundreds of thousands of pages of

documents. So, for example, I wanted to look at all of the Eli Lilly Cymbalta studies that could be found in the database. There were almost 30 of them where there was some assessment of withdrawal either with an open-ended question or with a checklist.

I wanted to review what's called the Clinical Study Reports, which are the internal company reports of those studies. I wanted to see any company memos or reports about the studies that weren't the individual studies; e-mails about withdrawal or the studies, the data, seeing what company executives were saying to one another about this issue; the published medical literature, which of the studies had been published, what was in the publications; the label; the official prescribing guidelines; the package insert. They're all the same thing, the package insert, the label, the official prescribing information, which has changed a little over time and to look at that and evaluate the label; all of the company executives who have been deposed either in their particular role or roles over the years or, as you say yesterday, one was designated as the spokesperson for Eli Lilly. So all of those depositions.

And then with regard to the two individual patients, all of their medical records and, again, the

depositions that had been taken in their cases, and then actually interviewing them by phone.

Q And, Doctor, in the context of reviewing that mountain of documents, did you have an occasion to see any surveys of physicians conducted by Lilly?

A Yes.

Q And Doctor --

MR. SCHMIDT: This, Your Honor, is the other issue we raised before.

THE COURT: All right. let me hear the next question.

MR. WISNER: If I could lay some foundation before we go to the sidebar, I will not cross the line.

BY MR. WISNER:

Q In those surveys, did you rely upon the information that you obtained in those surveys to form your opinion?

A I did.

Q Without getting into the content of those surveys or a survey, how did that inform your opinions in this case?

A Because the surveys indicated what was important to doctors.

Q And specifically, the surveys that you're talking about, were they related to Cymbalta?

A Specifically.
Q And were they related to the issues of withdrawal?
A Specifically.
Q And were these done prior to the approval of Cymbalta for sale in the United States?
A Yes, the surveys were done before.
Q And did these surveys -- without getting into the specifics of what they said, did these surveys evaluate the relative importance of issues for physicians of different products?
A Yes.

MR. WISNER: Your Honor, sidebar? I'd like to ask about the substance of those surveys.

THE COURT: All right.

(Conference at the bench, as follows:)

MR. WISNER: I assume that --

THE COURT: So what does this relate to? What opinion does this relate to?

MR. WISNER: Oh, I'm sorry. I thought he just explained. He said this relates to whether or not the issue of withdrawal was important in the medical field.

THE COURT: Why does that relate to any issues in this case? Why does that relate to whether Lilly gave an adequate warning with respect to the

withdrawal dangers that it knew or had reason to know?

MR. WISNER: Well, his opinion.

THE COURT: You're skirting around everything except the key issue here. The jury is not following. They have no clue why this witness at this point is on the stand. You need to ask -- what I'd like you to do is ask him what his opinions are.

MR. WISNER: It's literally after this document.

THE COURT: Well, let's do it now. Because I don't understand why this relates to the admissible opinion, which is that his view that the label did not adequately warn the physicians of the risks, the withdrawal risks that Lilly knew or had reason to know, right? That's the scope of the admissible thing I'm allowing in this case.

MR. WISNER: Fair enough. For his opinion, yes. We also have an obligation to prove fraudulent intent, and we are trying to lay the foundation for that.

THE COURT: Well, he's not going to be able to speak to any fraudulent intent.

MR. WISNER: We have no intention of doing that, but we'd like to use his testimony to lay the foundation to get the document in evidence. I can say,

Listen, in 2002, they knew that the only way they could be competitive -- and that's what this document says -- against other antidepressants was to minimize the risk of withdrawal.

THE COURT: But he doesn't add anything to that. You're just using him to get in a document that has no relationship to the scope of his expert opinion, and he's just going to repeat what the document says. The document may or may not come in, but it has to come in on its own terms.

MR. WISNER: I have no intention of offering the document into evidence. I just want to ask him what it says.

THE COURT: I'm not going to allow that. Let's get to his opinion.

MR. WISNER: Can I have at least -- just for the record lay the foundation that it's an accurate copy of the document, and then I can move on? Just because I'm going to have an authenticity issue on cross-examination.

MR. SCHMIDT: We deposed Dr. Glenmullen on this document. In the middle of my deposition in April, he went out to his car, got this document, and said, I'm ready to testify about this document.

THE COURT: Is there any issue of

authenticity?

MR. WISNER: Just --

MR. SCHMIDT: There's no issue as to authenticity, just admissibility.

THE COURT: All right.

MR. WISNER: If it's authentic, then I should be able to cross-examine any --

THE COURT: We'll see. Let's get to the opinion.

MR. WISNER: I'm there. I just wanted to get all of the foundational stuff out of the way.

(Proceedings continued in open court, as follows:)

MR. WISNER: We'll get into the next part, Your Honor.

THE COURT: All right.

BY MR. WISNER:

Q Okay. Doctor, I want to talk to you about specifically the opinions that you've come to in this case.

A Sure.

Q What opinions, if any, have you come to in this case in a general sense?

A So broadly speaking, I would say I've come to three opinions:

That the risk of withdrawal with Cymbalta when

studied in the gold standard way is 75 percent, about 75 percent, about three out of every four patients.

My second opinion is that Eli Lilly's label, the official prescribing information for doctors and patients, is misleading. It does not adequately or reasonably convey the risks.

And thirdly, that both Ms. Ali and Ms. Hagan-Brown's symptoms at the time that they stopped this drug are consistent with Cymbalta withdrawal.

Q Okay. Doctor, I'm going to try to note these down. Withdrawal risks is --

A 75 percent.

Q -- 75 percent.

Okay. Two, the label is misleading; is that right?

A Correct.

Q And three --

A Ms. Ali and Ms. Hagan-Brown, their symptoms were consistent with Cymbalta withdrawal.

Q I just apologize now for my handwriting. I'm of a generation where we type everything.

All right. Dr. Glenmullen, let's start off with your first opinion.

A Sure.

Q You say that the risk of withdrawal is 75 percent. How did you come to that opinion, Doctor?

A So one protocol for two studies, a pair of studies, with a -- I was able to locate it in Eli Lilly's databases, a Cymbalta study in which a checklist was used.

Q Now, Doctor, how many clinical trials did you review specifically before coming to this opinion?

A So there were close to 30 trials, which is a technical term for a study. There were close to 30 studies of Cymbalta in which there had been some assessment, either the open-ended question or the checklist of withdrawal. And of those, there was one pair, two studies, that used the checklist.

Q So 28 of the other studies, they were nonchecklist studies?

A Yeah. The remaining studies were all open-ended questions, all spontaneous reporting.

Q Now, let's talk about the two studies that did use a checklist.

A Yes.

Q Would you recognize a copy of the protocol for those if you saw it today?

A Yes.

MR. WISNER: Your Honor, permission to

publish Exhibit 69 to the jury. It is in evidence.

THE COURT: All right. You may.

BY MR. WISNER:

Q Okay. Doctor, what is this document?

A So this is what's called the protocol. You've heard a little bit of testimony about that. It's written prior to the study beginning. It's kind of the ground rules for the study so that it's clearly identified prospectively what you're going to study, what drugs or placebo are going to be used, and how you're going to do the study and what the measurements are, so to speak, what the bar is.

MR. WISNER: Can we call out some stuff here? There we go.

BY MR. WISNER:

Q All right. This is HMBU. Do you see that, Doctor?

A Yes.

Q What is HMBU?

A So I said earlier that all of the Eli Lilly studies in the database have a four-letter code, four capital letters. So this study is called HMBU.

Q And it says here duloxetine versus venlafaxine. We've heard duloxetine is Cymbalta. What is venlafaxine?

A So venlafaxine is the chemical name for Effexor. So this is a comparator study of Cymbalta and Effexor. I think I mentioned earlier that by the time Cymbalta came on the market, there was kind of a different set of drugs that were competing in the marketplace, and Effexor was already on the market.

Q Were those different drugs SSRIs and SNRIs?

A So by now, the newer drugs were SNRIs. Both of these drugs are selective serotonin and norepinephrine reuptake inhibitors. Again, a historical change from the mid-'90s that we were looking at earlier.

THE COURT: You said these are SNRIs?

THE WITNESS: SNRIs, both of them.

BY MR. WISNER:

Q Now, Doctor, it says here protocol approved by Lilly 3rd of December 2002. Do you see that?

A Yes.

Q At this time in 2002, how many SNRIs are you aware of were on the market?

A So Effexor at that time manufactured by Wyeth was the only SNRI. So Prozac is going to be coming out as a new -- I'm sorry -- Cymbalta is going to be coming out as a new SNRI to the market after Effexor is already established.

Q And this is approved in December 2002. Has

Cymbalta entered the market yet?

A No. It doesn't enter the market for two years.

Q Okay. Let's get into this document briefly. Let's turn to page 8 of the document of Exhibit 69.

MR. WISNER: Call out the bottom diagram.

BY MR. WISNER:

Q Okay. Doctor, what is this a picture of?

A So since this is a study prospectively looking at withdrawal side effects, there's going to be a focus on what's called the taper phase. And you can see that in this document up at the top, Study Period IV. So each period of the study, there's an earlier efficacy period. There's an earlier screening period. There's going to be the last period where people are going to stop their drugs with some taper in this case, one or two weeks. That's called the Phase IV taper period.

Q Now, it says up here duloxetine 90 and 120 milligrams daily. Do you see that at the top left?

A Yes.

Q What does that indicate when reading this diagram?

A So in the phases before, people are going to be on Cymbalta at 120 milligrams a day, 90 milligrams a day, and then the box below that you can see that some are also going to be on 60 milligrams a day. So we have people on different doses at the end of the trial, at

the end of the study.

Q So people who are taking, for example, 60 -- we'll stay up at the top -- 90 milligrams or 120, it looks like for the first step they're down to 60; is that right?

A Correct. So regardless of whether they were at 120, which is a 50 percent drop to 60, or at 90, which is a 30 percent drop to 60, those folks are going to go to 60 for the first week.

Q Okay. It says one -- is what that seven plus one day at the bottom means?

A You can see down at the bottom seven plus or minus one day. So each of these -- this is called a taper schedule. It's what steps you're going to take in reducing the dose and the time frame you're going to use to do that. So these are -- these folks are going to make a first step to 60 milligrams for about a week.

Q And then they go down to 30 milligrams for a week?

A Exactly, and then they will be one week off the drug while they're still being evaluated.

Q Now, to be clear, Doctor, below that you see there's a placebo and then it says no study drug? Do you see that?

A Yes.

Q What does that mean?

A So this was a comparator study. It's, as we said, the Cymbalta and Effexor. So placebo coming in here after the study is over and you're tapering, that's called placebo substitution. And what it means is that the people who are on 30, after one week, they're going to go to no medication but they're actually not going to know that. They're going to be given a pill that's identical to the medication pill, but it's actually what we would call a sugar pill. It's not really sugar, but it's just kind of a colloquial expression for it's inactive. So for the first week off of the Cymbalta, the people on 30 milligrams are still going to get a pill, but it's no longer Cymbalta. They have stopped. Then if you move into the last week, everybody is no longer taking a drug.

Q So the people in the last week know they're not taking anything?

A Yes. By the last -- in the last -- it's only in the last week that all of the patients know they're no longer on a medication.

Q And you see these study visits, 301, 302, 303, at the bottom?

A Right.

Q When was -- first of all, how was withdrawal studied in this protocol?

A So this is a checklist study.
Q Was it also studied without a checklist?
A Actually, that was a really interesting point about this study. They actually did it both ways so you could compare. So they asked the open-ended question: Is there anything you want to tell us about and then went on to use the checklist. So it has both types of data in this particular study.
Q And at which points were those checklists or open-ended questions used in assessing discontinuation here?
A So you see over on the left at the very bottom it says visit. Visit means an appointment. It means when the patient comes in to be evaluated. You can see the 301, 302, 303 are the codes. They're going to come in every week roughly three times during this Phase IV taper phase of the study.
Q And each time they come in, are they assessed with both of these methods?
A Correct. They're both going to be asked the open-ended question: Do you have anything you want to tell us about? And they're going to be asked in detail all 43 symptoms: New; old; if old, worse or not worse.
Q Okay. Let's move through that. Let's go to the results of the study. Let's put up Exhibit 111.

MR. WISNER: This is in evidence, Your Honor.

THE COURT: All right.

MR. WISNER: All right. Let's blow up the top part of this.

BY MR. WISNER:

Q Okay. Doctor, what is this chart reflecting?

A So this is actually the table with the data in it, and you can see here --

THE COURT: And this is from the same study?

THE WITNESS: This is that very study, yes, Your Honor.

THE COURT: All right.

A So this is Study Period IV, again, treatment-emergent adverse events collected by a checklist. That's the name of this checklist. All of the patients who entered the taper phase. You can see in the fourth line HMBU. That's the same code that we looked at at the protocol. This is the first of two studies, a pair of studies, using exactly the same protocol, same methodology.

Q And I see here that the total number of patients studied, that's 240.

A Right. So this is a large study. There are hundreds of patients in this study.

Q And does the number of patients involved in a

study affect the power of it?
A Yeah. So the larger the study, the more statistical power it has. There are sort of a couple of crucial variables. One is the quality of how the assessments are being made. In this case, it is using a checklist. The second is the size. So this is a large study.
Q And it says down here under dulox -- is that duloxetine in Cymbalta?
A Yes. Duloxetine is the chemical name for Cymbalta. Oh, and you're right. That's an abbreviation for it, dulox.
Q And it says 78.1. Do you see that?
A I do.
Q What does that indicate to you, Doctor?
A So what you're seeing on the top row here is any patient who had one or more of the checklist symptoms. So that's -- if you like the overall rate, then that is 78 percent in this particular study.
Q As a clinician, can you just explain what 78.1 percent means to you.
A That would mean that, based on this study -- and this was, again, a taper. It was after two-week taper, one to two weeks. If you taper patients off of Cymbalta one to two weeks, you'd still have three out

of every four patients having Cymbalta withdrawal, which is a very high rate.

Q Now, if you look to the right, there's something that says a p-Value. Do you see that?

A Right.

Q It says .082. Do you see that?

A Correct.

Q What is the significant of a p-Value?

A So a p-Value is a statistical term. It evaluates whether or not there's a significant difference between, in this case, the Cymbalta and Effexor. The cutoff is a p-Value less than 0.5. This is not less. It's larger. So what that means statistically or to someone who is a clinician is that there is no significant difference between Cymbalta and Effexor with regard to withdrawal. They both have very high rates.

Q Well, it says here venlafaxine is 67.5 percent, right?

A Right.

Q And duloxetine has 78.1 percent, right?

A Right.

Q Isn't that a difference?

A So it is a difference in terms of the percentage, but you run the statistical test. What the statistical

test is asking is is this difference likely to be due to chance, just chance variation in a study or is that highly unlikely. Again, the cutoff is a p-Value of 0.5 or less. And if it's less than that, then you say there is actually a significant difference. The difference between these two drugs is significant. And if it's not, which is the case here, you conclude that this was just kind of normal variation and there's no significant difference between the two.

Q All right. Doctor, I want to discuss a little bit about these symptoms that are listed below it.

A Yes.

Q Do you see dizziness right there?

A Yes.

Q Okay. It has an 18.4 percent next to it. Do you see that?

A I do.

Q What does that mean?

A So the ways these tables or the data is typically conveyed is the first row is the overall rate, and then below that you're looking at the rate for individual symptoms. That's an important distinction. I think that we should look at that again when we get to the label, the prescribing guidelines because there's two different types of rates, the overall rate and the

individual side effect rates.

Q And it says here 18.4 percent. So would it be fair to say that a person upon discontinuing duloxetine in this trial using checklist data, about 18 percent of people reported dizziness?

A Correct, with a taper, with a one- to two-week taper.

Q Thank you for the clarification, Doctor.

And then separately it says blurred vision has 14 percent?

A Right.

Q So there's also separately a 14 percent chance that you'll have blurred vision?

A Correct. For each of the individual side effects, it's a separate percentage. And if you were to add all of the side effect percentages up, they would be more than the 78 because lots of people were having more than one.

Q That's sort of what I wanted to get at, Doctor. It says patients with at least one DESS. Could a patient have a constellation of these symptoms?

A Yes. That's what we talked about earlier. Then you would call it not a symptom but a syndrome, an antidepressant withdrawal syndrome.

Q And then that person who is having a constellation

of symptoms, they would only be counted once in the first line; is that right?

A Yes. Yes. That's just the number of patients who had one or more.

Q Well, Doctor, you said there was a companion study to this; is that right?

A Correct.

MR. WISNER: Permission to publish to the jury Exhibit 112, which is already in evidence.

THE COURT: Doctor, before you go on, let me ask you a question just so I'm clear.

THE WITNESS: Yes, Your Honor.

THE COURT: The 78 percent -- 89 refers to the number of patients, the number of people?

THE WITNESS: Yes.

THE COURT: The 78 percent is the percentage that that number represents relative to the group of people being studied?

THE WITNESS: Right. It would be the 89 patients over the total number of patients that took Cymbalta, which is right below dulox. So the 114. The 89 over 114 gives you the 78.1.

THE COURT: All right. And is the 89 the sum of all the other numbers that's listed there?

THE WITNESS: No. In other words, if you

took -- and this is just a small portion of the list of side effects. If you took the 21 patients with dizziness, the 16 patients with blurred vision, etc., you'd get a larger number than 89.

THE COURT: I guess my real question is is there any way to tell whether the 14 patients with blurred vision are also among the group of 21 people experiencing dizziness or the 10 people experiencing increased dreams?

THE WITNESS: Good question. So you would have to have the raw data, the patient level data to identify that. But we know that because these numbers add up to more than 89, that at least some of the patients --

THE COURT: Do you know what the total number of patients are that have experienced symptoms?

THE WITNESS: That is the 89; 89 of the 114 had one or more.

THE COURT: All right.

MR. WISNER: Thank you for the clarification, Your Honor.

THE COURT: All right.

MR. WISNER: So let's go to the next result of the next study. I believe -- what was the -- let's pull up the next study. It's Exhibit 112. Okay.

Let's call out the top part again.

BY MR. WISNER:

Q Okay. Doctor, this is HMCQ, Study Period IV. Do you see that?

A Correct.

Q Is this the other study, the companion study to HMBU?

A Yes. Same protocol, same plan, so to speak, same prospectively designed to measure withdrawal side effects both by an open-ended question and a checklist. It would have been different patients, different study centers, but this pair of studies used the same methodology, the same design.

Q And, Doctor, what did the overall incidence rate for withdrawal indicate in this study?

A So you can see the 74.1. That is the overall incidence rate in this second study, very close to the 78 percent.

Q And because this study is using a checklist, are any of the symptoms that are going to be displayed here symptoms that would -- like bug bites or skin rashes or things that, you know, wouldn't normally be associated with withdrawal?

A But that's the purpose of using a checklist, to focus on the important side effects.

Q Thank you, Doctor.

And here, again, for example, dizziness, there's a 29.6 percent. Do you see that?

A Yes.

Q And so then this study showed, for example, a 30 percent chance that a person who discontinued Cymbalta would experience dizziness?

A Right. So one in three people still tapering one or two weeks is still going to experience -- and there's a fairly -- there's a particularly unusual form of dizziness that occurs in withdrawal. People feel like the room is spinning, and the particularly unique characteristic is that any movement greatly exacerbates it. So when people sit up out of a chair, they can feel like they're going to fall down. The same when they get out of bed. If they go up and down stairs, even -- if they have it severe, even if they just walk. And last but not at least, if it's really severe, people will report that even if they move their eyes, they feel very dizzy and like the room is spinning. That's one of the side effects that can make people bedridden. They literally can't get out of bed because of that dizziness.

It's compared in the literature to motion sickness. You know when you were a kid and you get

motion sickness on a boat or in a car. It's a particular characteristic form of dizziness.

Q Doctor, you said that these studies were also evaluated using a symptom checklist; is that right?

A These two, just these two.

Q I'm sorry they were also evaluated without a checklist using spontaneous questions?

A Yes, correct.

MR. WISNER: Your Honor, permission to publish to the jury Exhibit 110.

THE COURT: Is that in evidence?

MR. WISNER: Yes, Your Honor.

THE COURT: All right. You may.

BY MR. WISNER:

Q Okay. Doctor, this is a table. I'm going to take the bottom part of this page and then the table from the page following it -- because we're starting at the bottom here -- and put them together.

Okay. Doctor, this states HMBU and HMCQ, Study Period IV. Do you see that?

A Yes.

Q It says MedDRA preferred terms. Do you see that?

A Correct.

Q What does that indicate to you?

A So when patients report side effects, they're

coded in the database. There's a code for every side effect, dizziness, insomnia, nausea, and vomiting. They all have a different code in order to be able to go into the database. There's a particular dictionary of codes that's used. That's the MedDRA dictionary. That's what that's referring to. This is not a checklist, no. This is anything that the patients reported.

Q And you see over here on the right it has a total end of 523; is that right?

A Yes.

Q Is this the combined data of both the studies?

A Right. So it is -- and again, you can see that putting these two studies together, it's a lot of patients. It's roughly 500 patients. That's a large number of patients.

Q And in collecting adverse events without a checklist, what do the numbers reveal?

A So I thought that when I saw the results of those two studies it was particularly interesting that they had used both methods. So you can actually see in one study the difference that you get. So in this case, the two studies are not being reported separately. They combined the data. That's why it's 523 patients.

Without the checklist, they got 44 percent of the

patients reporting side effects, and again, this is kind of all over the place. This is not a focused list of side effects. So you get a lower number, and you get less valuable data because it's kind of anything they've said.

Q So, for example, on these symptoms, you could get like a bug bite for example?

A Sure. If you reported a bug bite or that you got pregnant or that you broke your leg or that you had a tooth extracted, it would go into this database even though it obviously doesn't have anything to do with withdrawing from a medication.

Q Now, Doctor, these two studies, HMBU and HMCQ, were they ever published in a medical journal?

A Yes, actually, they were.

Q And in that publication, did the results of the checklist data, the 74 to 78 percent, were those included in the publication?

A They were not.

Q What about the nonchecklist data, the 44.6 percent? Was that in the publication?

A They weren't either.

Q Let's talk about some published data, Doctor. Are you familiar with the Perahia article that we've been discussing at length throughout this trial?

A Yes.

MR. WISNER: Your Honor, permission to publish Exhibit 93 to the jury. It's in evidence.

THE COURT: Yes.

BY MR. WISNER:

Q Doctor, let's quickly go through some of these authors. Dr. David Perahia, do you know who he is?

A Yes.

Q Who is he?

A So he was in Eli Lilly's British offices. You heard him testify yesterday. He was very central to Lilly's studies of antidepressant withdrawal, Cymbalta withdrawal in particular.

Q And do you see Daniel -- I'm not going to pretend to pronounce that or the next one. But the next two authors, are they Eli Lilly employees as well?

A Yes, both of those authors. So in this case, three out of the four authors are actually in-house Eli Lilly employees.

Q And the last author, Peter Haddad, was he noted in the first publication we looked at from the symposium in 1996?

A Yes. When we saw the journal supplement from the Lilly meeting, I think I mentioned that he was someone who had published a lot on antidepressant withdrawal

even before that meeting back in the mid-'90s. He is also a British doctor.

Q And is he also on the Global Advisory Board for Eli Lilly?

A Yes.

Q Okay. Let's go into this document. Let's look at Table 2, which is a table that we've talked about before. Let's quickly just talk about the 44.3. What does that indicate to you, Doctor?

A So, again, the first line of this table is an overall incidence rate.

THE COURT: Which table is that?

MR. WISNER: Table 2, Your Honor, from the Perahia article.

THE COURT: All right.

A So you'll see it isn't -- the subsequent ones are not indented like the last table we looked at. But it's still the first line. It's the overall rate for the drug: 217 of 490 patients, which comes out to 44 percent, had withdrawal. This is actually six studies combined.

Q And with those six studies combined, the total number of patients, is that the 380 plus the 490?

A Correct.

Q Okay. And so the 44.3 percent, was that collected

with a checklist?

A No, this was not checklist data. This was all -- these six studies were done, again, before Cymbalta was approved, and these are six studies in which a checklist was not used.

Q Now, Doctor, I understand that the previous nonchecklist data we just looked at said 44.6 percent. Do you see that?

A Correct.

Q This says 44.3 percent?

A Right.

Q Is there any significance of that fact?

A Sure. They're obviously comparable, almost the same.

Q I'm going to mark on the board here for your opinions the data we've gone over so far.

A Sure.

Q So under checklist data, it's 74 to 78 percent; is that right?

A Correct.

Q Nonchecklist data?

A About 45 percent.

Q Well, the first one was 44.6, right?

A Sure.

Q Okay. And this one right here is 44.3?

A Right.
Q Okay. Now, Doctor, I want to make sure I get something straight here. There is a placebo rate of 22.9 percent, right?
A Right.
Q Wouldn't it be proper to just take 44.3 and subtract from it 22.9 to get the real risks?
A No. That's a common misperception. That's not why the placebo is in here. In real life, if you're treating patients, nobody is going to be on a placebo. They're all going to be on the drug. So what you want to know is in clinical practice, if I stop -- if I advise a patient to stop this medication, what percentage of them are going to report symptoms. And the number for Cymbalta in this study without a checklist is 44 percent.
Q How does the placebo number help validate the 44.3 percent?
A So the placebo number is being used statistically. The placebo number -- so we looked to a couple of studies where the comparator was an active drug, Effexor. Now, these are six studies combined where the comparator is a placebo pill. And what that does statistically is you compare the rate on the placebo with the rate on the drug. You use that p-Value to try

and determine if the side effect you're seeing is likely to be caused by the drug as opposed to not. So it's a kind of statistical test, and that's actually embedded in this table.

Q Now I want to look down at dizziness here. Under placebo, it has .08 percent [sic]; is that right?

A Correct.

Q That's for the placebo, right?

A Correct.

Q But then there's a 12.4 percent for duloxetine?

A Yes.

MR. SCHMIDT: And just for the record, Your Honor, I don't think he meant to misread it. Your Honor, it was 0.8.

MR. WISNER: Sorry. It's 0.8 percent. I apologize.

THE COURT: All right.

BY MR. WISNER:

Q And then it was 12.4 percent for duloxetine, right, Doctor?

A Right.

Q Now, as a clinician, how do you compare the relative risks of duloxetine to the sort of background rate?

A So what you see here is that only three patients

of 380 on placebo had dizziness. That's less than 1 percent, .8; whereas 61 patients on Cymbalta of 490 had dizziness. And that's 12 percent. That's obviously a very, very big difference.

But you still want to run the statistical tests to see, based on the number of patients that were in the study, is that actually what we call statistically significant. Is that a significant difference? Is it reasonable to attribute that to the drug? That's actually that little asterisk there.

Q And if you divide the numbers to each other, you get something around 26? Do you understand?

A Yeah. So that's another purpose of the placebo. You can actually do a ratio of the drug to the placebo. You can see that for overall rate, 44 percent versus 22 percent, being on the medication doubles your risks of having a side effect, one or more. And that has the asterisk. It is a significant difference. The asterisk goes down to the p-Value at the very bottom. That threshold that I told you about, the 0.5 or less.

Similarly with dizziness. Now we have a much, much bigger elevated risk. The difference between 12 and .8 is -- I think you said something like 20-fold increased risk.

Q That characterization, a 20-fold increased risk,

is that a significant way of describing a risk in your clinical practice?

A Oh, sure. Like, that's the kind of information you want to know. That's what the placebo is helpful for.

MR. SCHMIDT: Your Honor, just based on Your Honor's pretrial rulings, I'll ask him to keep his opinions to what he might want to know, not to speak to other physicians.

MR. WISNER: He did that, Your Honor. I don't know why we're talking about this.

MR. SCHMIDT: We're talking about it because he said that's what you would want to know. By definition, that's not him.

THE COURT: All right. Ladies and gentlemen, we're going to take our morning recess at this time. You're excused to the jury room. We'll take about a 15-minute recess. Please do not discuss this case among yourselves during the recess.

You may be excused.

(The jury exits at 11:32 a.m.)

THE COURT: All right. We'll stand in recess.

Doctor, do not discuss your testimony during the recess.

(Recess from 11:32 a.m. until 11:48 a.m.)

(The jury is not present.)

MR. SCHMIDT: Your Honor, we have an issue to raise. I don't want to interrupt the examination.

THE COURT: Yes.

MR. SCHMIDT: The first is the reason I objected when he was asked have you been qualified by other courts, has your methodology -- I don't think that's appropriate in the first instance, but he has been limited by other courts. In fact, just a couple of weeks ago he was threatened with contempt from the judge for not answering questions. The judge actually cleared the jury out and told him, If you keep doing this, if you keep not following my instructions -- I think the door has been opened to asking him about the fact that he's also been limited by courts. The sensitivity I have there is I don't think that gives him a license to say, Oh, that was another Cymbalta trial. So I just want to bring that to the Court's attention. That's the first issue.

The second issue is I would ask that the witness be directed by his counsel to be very careful. He is a very precise witness. He has corrected me a number of times on my grammar and terminology in depositions. I would ask that he be directed by

counsel not to testify about what other people might think, as he did.

Frankly, I'd ask that he just be a little more responsive to the questions, which is what he got in trouble with in California, just so we can move things along. The question was about dizziness. Three minutes later we are hearing about all different types of dizziness.

THE COURT: We'll get through it. I think he's done reasonably well in terms of responsiveness.

MR. WISNER: First of all, Your Honor, an out-of-context statement, he was admonished by a judge.

THE COURT: At this point, I'm not inclined to let you get into that on cross.

I think the parties are in agreement to stop. He is only going to speak to his own evaluation and not to what anybody else would view this as or what a reasonable physician would think of this. So just be sure you frame the questions in this fashion.

MR. WISNER: Sure.

MR. SCHMIDT: May I ask him if he's aware that his testimony has been limited by judges?

THE COURT: I'm sorry?

MR. SCHMIDT: May I ask him if he's aware his testimony has been limited by judges?

THE COURT: I'm not going to let you go into that. All right.

MR. WISNER: Yes, Your Honor. We're ready to proceed.

THE COURT: All right. Let's bring the jury out.

Dr. Glenmullen, come to the stand, please.

(The jury enters at 11:51 a.m.)

THE COURT: All right. Please have a seat.

We'll continue with the testimony.

Dr. Glenmullen, you remain under oath.

THE WITNESS: Yes, sir.

BY MR. WISNER:

Q Doctor, a quick cleanup question. I think on -- when I asked you that question, I asked you if the p-Value was .5. Is .5 the cutoff for p-Value?

A No. It's less than 0.05, less than 1 in 20 chance that it could just be due to random chance.

Q And that's reflected in the p-Value number on the bottom of this chart?

A Correct. That's the asterisk and every side effect that's asterisked. It was a significant difference between the medication and the placebo rates.

Q And, Doctor, we talked a little bit about the

differences between placebo and duloxetine and how we read those numbers. As a personal clinician, how would you advise your patient about the risks of withdrawal based upon the data in this table?

A I would tell them there was about a 45 percent chance that they would experience Cymbalta withdrawal based on this data. If they stopped the drug, that that -- and if they asked, I would explain that that's about double the risk. If they weren't taking the medication, that they would have some side effect -- some symptom.

And if we got into individual side effects, which I always do, and we happen to be looking at this table, for example, I would explain the nature of the dizziness that you can experience. And in this case, it's like a 20-fold elevated risk if you stop the medication.

Q I'm sorry. I think I might have misled you with the math. I think 12 divided by .08 is actually around 16.

A Great. Good clarification.

Q All right. Doctor, let's keep going through this article. Was this data, this 44.3 percent, was that collected using a checklist?

A No.

Q And did Dr. Perahia and the authors of this article acknowledge that fact in the publication?
A They do. They comment on that.
Q If we could just turn to the last paragraph, it says the main limitation of this review is that DEAEs were assessed by means of spontaneous reports rather than a symptom checklist.

Is that what you've been discussing here this morning about spontaneous and checklist?
A Yes. And the three Eli Lilly employees are acknowledging that that's a limitation. It is a significant limitation of the studies. And when you publish something like this in an academic journal, it would be important to make that kind of comment about the data. It's limited because a checklist wasn't used.
Q Well, that's where I was going, Doctor. This document was published in a peer-review journal, right?
A Right. That's a fairly thorough analysis. It went through the peer-review process. It is scientific data, but as part of that, in medical journals, you kind of -- it's important to say the strengths and limitations of any data. That's what this comment is, and I completely agree with it. That's my position as well.

Q It goes on and says the latter might be expected to produce high incidence rates. Just for clarification, what is the latter referring to?

A So that's referring to the checklist, and that's exactly what we saw in the other study where both methods were used. You had 44 percent, almost the same as this, without it and 75 percent, about 74 to 78 percent with the checklist.

Q Now, Doctor, I understand you have identified and you agree with this as being a limitation, but do you think that this data is valuable or is not valuable at all?

A Oh, no, no, no. I would not say that. When you evaluate scientific data, it's very important to keep in mind what we call kind of hierarchy of data. So the checklist data is higher quality. It is more valuable. But this is still useful. An analogy you might make is that the gold standard data is kind of like having gold coins, and this data would be more like having copper pennies or something. It's still valuable. You want to consider everything. But it's important to be aware of that hierarchy of the quality and value of the data as well.

Q Now, Doctor, I understand you reviewed -- you said previously about 30 or so clinical trials that measured

discontinuation data. Is that right?

A Yes.

Q And at any point did you review whether or not Lilly actually did a pooled analysis of their general database?

A Yes.

Q And did you review that pooled analysis as part of rendering your expert opinions?

A Yes.

Q Did you rely upon that data?

A Sure.

Q Did you consider it?

A Oh, I consider all of the data they find, absolutely.

MR. WISNER: Your Honor, at this time I'd like to move into evidence Exhibit 70. I don't believe there's any objection.

THE COURT: Any objection?

MR. SCHMIDT: There's no objection, Your Honor. It's our data.

THE COURT: Without objection, Exhibit 70 is admitted.

BY MR. WISNER:

Q All right. Doctor, this is the front page of Exhibit 70. Is that the pooled analysis you're

referring to?
A Yeah. I actually wouldn't use the term "analysis." This was the pooled study -- the pooled results that I was looking at. I wouldn't call it a study. I wouldn't call it analysis, just pooled data.
Q Doctor, did you refer to this as a pooled analysis in your reports in this case?
A Actually, I may have. Thanks for the correction.
Q All right. Doctor, I just want to make sure we're on the same page.
A All right.
Q It says here -- it says Supportive Optional Document to the Duloxetine Core Data Sheet Pre-Read Based on Clinical Trial Data in the Adult Population. What does that mean?
A So this is actually just a big compilation of data in tables. What I meant to say was it doesn't include any analysis of the data. It's just running all the data through standard formulas, so to speak. It's a huge report. I think it's a couple of thousand pages, and it's just updates of data, side effect data.
Q It says Confidential to Regulatory Agencies. Do you see that?
A Yes.
Q What does that mean?

A So this is kind of just an annual update just kind of given to regulatory bodies, like the FDA.

Q And it says, data from April 2010 through October 2011. Is it your understanding that this analysis or this data reflects the data Lilly possessed as of October 2011?

A Yes. This is the October 2011 update.

Q Okay. Great.

It says approval date, down there at the bottom, March 6, 2012. So it was actually -- is that when it was submitted to the FDA?

A It looks like it, in May 2012.

Q May or March, Doctor?

A Oh, I'm sorry. I should have put my glasses on. March.

Q Thank you, Doctor.

Let's get into this document. You said that it displayed a bunch of data. What does this document consist of?

A So it's really just tables, tables and tables and tables, lists and lists and lists of side effects. The emphasis is on side effects occurring while patients were on Cymbalta, but there are two tables for side effects occurring after stopping Cymbalta.

Q And is that data divided up in those tables in any

way?
A Yes.
Q How is it divided up?
A One of the tables is all the data from studies where the patients stopped Cymbalta abruptly, and the other table is all the studies combined where the drug was tapered over a week or two and sometimes three.
Q When you say they were tapered, is there a standardized tapering regimen used in all of these studies?
A No. This is an incredible -- it's every study. There's a lot of what we call apples and oranges just kind of put all together.
Q Let's first look at the abrupt table. Let's turn to the table. I believe this is page 2212 of the document. I'm sorry. Yeah, 2212.
All right. Doctor, this is your abrupt data; is that right?
A Correct.
Q You can see up at the top where it says Table 3.6, Abrupt Discontinuation-Emergent Adverse Events. There is about 2212 pages into this submission?
MR. SCHMIDT: Your Honor, can we not lead? I haven't been objecting.
MR. WISNER: It's foundation only.

MR. SCHMIDT: It's not resulting in short answers. We're getting the narratives still.

THE COURT: Go ahead with your next question.

MR. WISNER: Yes, Your Honor.

BY MR. WISNER:

Q What does this -- I have called out the top part of it. What does it reflect?

A Just that this is all the data from any studies, any different methodologies, many different conditions that it was being studied in. Some of the conditions never approved or marketed. So it's just a kind of putting all the data in long, long tables.

Q And there's some results here. It says 32.4 percent under the duloxetine heading. Do you see that?

A Correct.

Q And there's a 22.2 percent for placebo?

A Yes.

Q What does this, if anything, indicate to you in your analysis?

A So in this -- using this particular methodology with just all the data thrown together, at this point in time, that was the rate -- the two rates for the medication and the placebo when you don't use a checklist in any of the studies but you abruptly stop

the drug. As you can see, it's still significant. The p-Value is actually highly significant.

Q Doctor, how do you know there was no checklist used in this data?

A All of the studies were placebo-controlled studies, and Eli Lilly never used a checklist in a placebo-controlled drug study.

Q More specifically, Doctor, did Eli Lilly ever use a checklist again after that study we looked at earlier?

A No.

MR. SCHMIDT: Objection based on Your Honor's rulings.

THE COURT: Overruled.

BY MR. WISNER:

Q Well, looking at the data, there are 32.4. Is that statistically significant?

A Yes. At the very far right, you see Fisher's exact p-Value, and it's less than 0.001. It's highly significant.

Q And, Doctor, how would you characterize the risks relative to placebo here?

A So 32 versus 22, it's about a 50 percent increased risk.

Q These numbers, Doctor, in your professional

opinion, do you think that they're reliable?

A In my opinion, they're not reliable by comparison with the earlier studies we've looked at.

Q Why don't you think that this data is reliable, Doctor?

A There's actually a number of problems with this particular table in addition to not having used the checklist. For example, when we looked at the Perahia data, those were six studies where there was a lot of similarity in the methodology. All the patients had the same condition. That was published in a peer-review scientific journal. The limitations of the data were stated. And again, in this hierarchy of science, the checklist studies are the best. When you do that kind of rigorous analysis and you publish it and it's peer reviewed, that would be next. This is really just tables. It has no analysis with it. As I said, apples and oranges, all kinds of methodologies, all kinds of conditions. Many of the patients in these studies were being studied for conditions that Eli Lilly has never received approval for that condition. It was never marketed for it.

So when you have that kind of very broad brushstroke, just throw everything in, that's worth even less. That -- again, I would use a kind of gold

standard versus -- this is really what I would call the copper penny. Is it still worth something? Sure, everything is. You want to consider everything, but this would be much lower on the list.

Q I want to go through a couple of those points just very briefly, Doctor. The first one is you said there's no peer review of this data. What does that mean?

A So this was just thousands of pages of tables given to regulatory bodies. That's very, very different from an actual analysis of a group of studies that have been picked for a particular reason, pooled for a particular reason, consistency relatively speaking of methodology, patients, the conditions they were being treated for, peer reviewed so there's some scientific standard. I wouldn't really consider this scientific. It's just putting all the data in one place.

MR. SCHMIDT: I'll object to that, Your Honor. I think that's not appropriate.

THE COURT: Overruled.

A So, again, hierarchy of value.

Q Okay. Doctor, let's go into another point you mentioned. You said there's different methodologies being pooled together here. Is that right?

A Right.
Q Can you just briefly explain what you mean by that?
A Well, for example, some of the studies were depression. Some were fibromyalgia. Some were anxiety studies. Those three all ended up approved conditions, but there is the other studies for osteoarthritis, urinary incontinence. There's a wide range. Actually, hold on. I have another table that's got that. So you have a whole range of conditions.

I think when I looked at it, about a third of the patients of these -- I think it's around 3,000 were in studies for conditions that actually the drug didn't appear to work, and there was never approval for them. They also vary widely in the doses that people were given. They vary widely in the duration that people were treated. So, again, it's sort of -- it's too varied. It's too scattershot to be considered of the same scientific quality of the 45 or of the 75.
Q Were any of the data -- the studies that underpin this data, were they specifically created for a label?
A No, none of these studies were prospectively designed to have that as a focus in the way that we saw in the checklist study.
Q Okay. Doctor, I want to ask you another question.

It says up here -- it has -- well, let's go into the taper data first. Let's go to the next table. I believe it's Table 3.5. This is on page 2171 of this document.

All right. Doctor, we have called out this table again. This is the other part -- the other table you mentioned in this document.

A Right. These are the -- you see at the very top Tapered Discontinuation. So these were the studies where a relatively short-term taper, again, one, two weeks, at most three.

Q Did Lilly, to the best your knowledge, ever study a taper beyond two weeks?

A No, Lilly never studied it beyond two weeks.

Q Now, it says here 18.6. Do you see that?

A Yes.

Q What does that reflect? What does that number mean to you?

A So that means that this particular large group of varied data, the number that this table showed was 18 percent for people who did a taper.

Q Doctor, I have marked up here on the board 18 to 32 percent to reflect the tapering and the abrupt data from this pooled analysis.

A Correct.

Q Just so you know, I added the word "withdrawal." Even though I said it on the record, I didn't write it. So I just want you to know that.

A Fair enough.

Q Okay. Looking at this chart, Doctor, there's some questions I have. It is right here, 5,951 patients. Do you see that?

A Correct.

Q Does that volume of patients suggest that this data is more reliable than the 500 patients in the checklist data?

A No.

Q Why is that?

A Because again, it's not just the number. The number, you always look at that, but it's the quality as well, both. It's kind of like the difference between 500 gold coins and 5,000 copper pennies. The scientific value of the checklist studies is much, much higher.

Q Well, Doctor, this was a 2011 pooled study; is that right?

A Correct.

Q So that data was -- and this trial -- the checklist data, that was back in 2004?

A Correct.

Q Isn't this 2011 data more current and, therefore, better?

A Again, the answer is no, and again, it's the quality. You want to know the most recent largest study that's the highest quality, and that remains the checklist study with 500 patients, roughly the two together dating back to about 2004.

Q Okay. Doctor, now, just before I move on, this data in these tables, was it ever published or made available to physicians such as yourself?

A Oh, no. You would have to have analysis. You would have to pass peer review. You'd have to have all kinds of things. This is just a statistical table.

Q Is there any narrative at all in this document?

A There is no narrative. There is no discussion, no analysis. It is not scientific. It's simply tables.

Q Thank you, Doctor.

I want to transition on to your second opinion in this case, specifically, that the label is misleading. Do you see that?

A Yes.

Q We're referring to Cymbalta here, right?

A Correct.

Q Okay. One second.

MR. WISNER: Your Honor, permission to

publish Exhibit 22 to the jury.

THE COURT: Any objection?

MR. WISNER: It's in evidence. It's just a Cymbalta label.

MR. SCHMIDT: No objection, Your Honor.

THE COURT: You may publish.

BY MR. WISNER:

Q All right. Doctor, What is Exhibit 22?

A So I think you've seen this a number of times. This has been called the label, not meaning a label on a bottle but actually the kind of fine print information that you might see on one of those accordion sheets when you open the box. It is also published in large books for doctors, also called the product insert if it's in a box with a bottle. And what it really is is the official prescribing information from the manufacturer to doctors. In some cases, patients read it as well.

Q Doctor, in your clinical practice, how do you use the Cymbalta -- I'm sorry. How do you use the labeling of a drug?

A So the label for me is the most authoritative, the most important source of information. That's where I would go first if I wanted to find out about dosing, if I want to find out about side effects, if I want to

find out what it's actually approved for. This is coming directly from the manufacturer, and it's the most authoritative piece of information for me.

Q And in your review of the documents in this case, have you looked at the various versions of the Cymbalta label since it was approved?

A Yes, I looked at all of them. It has changed over time. For example, the original one was just for depression. Then generalized anxiety disorder was added. It was changed when fibromyalgia was added. It was changed, and I've looked at all of them.

Q And you have looked at the changes as well?

A Yes.

Q Is there a section in the label that was specifically meant to disclose the risks of withdrawal?

A Yes.

Q What section is that, Doctor?

A So I think this has been looked at a number of times. It is Section 5.7.

Q All right. Let's turn to that section. These are the three paragraphs we've read to the jury. I can't imagine how many times. Do you have an opinion that these three paragraphs are misleading? Is that correct?

A I do.

Q I understand -- what have you done -- I understand you have highlighted some portions that you want to talk about. Is that right?

A Yes.

MR. WISNER: All right. Let's highlight those.

BY MR. WISNER:

Q All right. Doctor, what do these highlights reflect?

A So they are portions of this part of the label which -- and I think it's important to say this is the particular part of the label that I, as a practicing doctor, would go to to find out information about the risks of Cymbalta withdrawal or discontinuation syndrome and how to manage that risk, how to manage patients when we are ready to stop the medication.

Q Now, Doctor, I -- you heard the testimony of Dr. Wohlreich yesterday?

A Yes.

Q And did you hear her testify about the label not being a compendium of how to practice medicine?

A I did.

Q What is your view about the role of the label in your practice of medicine?

A Well, the label is still supposed to be the most

important information. It's supposed to be what a reasonable doctor should know in order to reasonably inform a patient. I agree that it's not a book, but there's still a responsibility to have the key information. I think you've seen the admissions information. That's no bigger. It is actually smaller than that. I think we're going to look at that. In my opinion, you can get the most important information into something this size no questions asked.

Q All right. Doctor, of these various portions that are highlighted, what do you believe is the most misleading portion?

A To me the most misleading is the 1 percent or greater.

Q And why is that misleading to you, Doctor?

A Because that's the only percentage given in the label. It suggests to me that the overall rate is about 1 percent. You heard both treating doctors say the same. It suggests to me that withdrawal is going to be very uncommon. It suggests to me that this is not much of a concern with this particular drug.

Q Doctor --

A I'm sorry. Go ahead.

Q Well, Doctor, all of these different symptoms, dizziness, nausea, headache, paresthesia, doesn't that

information convey that these are risks associated with the drug?

A So the problem is that, as a practicing doctor, when you see 1 percent -- abruptly 1 percent, you just think this is not that big a deal. You hardly pay attention to the rest of the information.

Q And well, what about this part after it? It says at a significantly higher rate in duloxetine-treated patients. Doesn't that suggest that the rate is much higher than 1 percent?

A Actually, you're misreading that. What that's saying is that it's -- it's not saying it's significantly higher than 1 percent. It is saying that the 1 percent or roughly 1 percent to me for Cymbalta is significantly higher than placebo. And I would read that exactly the way Dr. Ahmed read it, that if the drug is about 1 percent and it's significantly more than placebo, it is going to be at a tenth of a percent.

MR. SCHMIDT: Objection, mischaracterizes her testimony.

THE COURT: Yes. That testimony is stricken.

Ladies and gentlemen, it's your recollection of what the other witnesses testify in this case, not the recollection or characterization of any other

witness.

Doctor, don't characterize the testimony of other witnesses.

THE WITNESS: Sure. Absolutely. Thank you.

BY MR. WISNER:

Q All right. Let's turn to -- your opinion here -- and we've discussed this previously -- is that a risk is about 74 to 78 percent or 75 percent, right?

A Roughly, 75 percent. If there was going to be 1 percentage in this, that's the one that I would want.

Q Now, Doctor, let's assume for a second that you're wrong.

A Okay.

Q Let's say the real risk, and this latter analysis is 18 to 32 percent. Okay?

A Okay.

Q Would your opinion be that this label was still misleading?

A Sure. Because to me as a practicing doctor, the 1 percent or greater doesn't suggest 18 percent, doesn't suggest 32 percent, doesn't suggest 45 percent, doesn't suggest 75 percent. It suggests a very low risk, something that's going to be really uncommon. I would want to know any of those numbers.

Q Now, Doctor, seeing that 1 percent or greater, how

would that influence your evaluation of discussing these potential risks with your patient?

A I would think it was not too important.

Q We're going to come back to this in a second, Doctor. I just want to ask you about something.

MR. WISNER: Could you go to the full page of the document. I think it's page 6. Go to the next one. All right. Let's focus in on the section immediately after 5.7, 5.8.

BY MR. WISNER:

Q Doctor, I do not want to get into a conversation about activation of mania or hypermania, but in this sentence, which is immediately following -- it's in the same general section of the label. It says activation of mania or hypermania was reported in 0.1 percent of duloxetine-treated patients and 0.1 percent -- no. It's the first sentence -- 0.1 percent of placebo-treated patients. Do you see that?

A I do.

Q Now, is that the same -- is that the threshold?

A No. That's telling you the actual number. It's actually even giving you more. It is giving you the data. It is telling you how many patients out of how large a group.

MR. WISNER: All right. Let's go back to the

discontinuation section.

BY MR. WISNER:

Q Okay. Great. All right. Doctor, I think we've covered the 1 percent or greater portion here. Let's move on to the first part, the systematically evaluated.

A All right.

Q Why in your opinion is the statement that it was systematically evaluated misleading?

A I think there are actually at least two problems with that.

Q Okay. What's the first problem, Doctor?

A The first one is that systematically to me indicates that a checklist was used. That's kind of the definition of a checklist, and this is not checklist data. So that is suggesting that the quality of the data is high, which is not true now that I know that it's not checklist data.

Q Now, Doctor, just on a side note here, when a drug company is evaluating the efficacy of a drug, whether or not it actually works, let's start with MDDs since that seems to be what you're familiar with, major depressive disorder. Do they use checklists to evaluate efficacy?

A Most of the studies, the purpose, their focus is

whether or not the drug works, efficacy, and they always have to use a checklist for efficacy. It's kind of -- some of the side effects are studied with checklists, and some are not. Eli Lilly in the Cymbalta studies only used a checklist twice.

Q Okay. You said there was a second reason why systematically evaluated was in your opinion misleading. What is that second?

A So the second one, we've talked about that a little bit. Over half the patients in that Perahia publication data, over half the patients still had withdrawal side effects after two weeks, and that was not studied. It was not studied beyond two or, in some cases, three weeks. To me, systematically would mean that you'd really look over a very long period of time. You would want to find out when do people stop having these side effects, how long can they go on, what kind of tapering schedule should you use. So systematically, again, implies to me that it's been very thorough, that everything possible had been done. And I find it misleading to discover that that's not the case.

Q Is there any statement in the label that indicates the duration or potential duration of withdrawal reactions?

A No.
Q Okay. Let's go to this last one here. It says patient should be monitored for these symptoms. Actually, before we get there, Doctor, are you aware of whether or not anyone within Eli Lilly specifically recommended to Lilly's executives whether they should study withdrawal for longer than two weeks?
A Yes.
Q And have you reviewed that document?
A Yes.

MR. WISNER: Your Honor, permission to publish Exhibit 93 to the jury.

THE COURT: All right.

MR. SCHMIDT: I'll object as to duplicative and him not having foundation to offer that testimony.

THE COURT: What is that?

MR. WISNER: This is the Perahia e-mail when it discusses the possible ways of studying the drug.

THE COURT: I'm going to sustain the objection. It's already in evidence.

MR. WISNER: Fair enough, Your Honor.

BY MR. WISNER:
Q Let's go down to your last highlight portion.
A Sure.
Q It says, Patients should be monitored for these

symptoms when discontinuing treatment with Cymbalta. A gradual reduction rather than an abrupt cessation is recommended whenever possible.

Why is that portion of the label misleading to you?

A Because it's very unhelpful. It provides very little information. Going along with the 1 percent, it suggests that this is no big deal. You would stop it over a couple of weeks in pretty big dosage reductions. It doesn't at all suggest that it could take four to eight months in very small dosage reduction in order to try to keep people comfortable and safe. It doesn't give a starting point. It doesn't say, you know, start by reducing the dose by 25 percent and make reductions once a month. There's no -- and then if that doesn't work, slow it down even more. It's just -- it's almost no information about how to do it. That's not helpful. When I go to this portion of the label wanting to know what the risks are and how to manage it, that doesn't give me enough -- just a basic reasonable enough information to how to go about this.

Q Well, Doctor, in your review of the clinical trial data, did Lilly ever prospectively study whether or not abrupt versus tapered discontinuation of Cymbalta affected how people suffer from withdrawal?

A Yes. Yes.
Q Please describe to the jury the nature of that study that you reviewed.
A So there was one study where that was prospectively the design. It was a two-week taper only, and there wasn't a significant difference between tapering for two weeks or just stopping abruptly.
Q Well, Doctor, I want to get a little bit more meat on the bones here. How do you study tapered versus abrupt in a clinical trial?
A So the proper way to do it is you're looking at patients in one trial, and you go through the efficacy portion of the trial seeing whether or not the drug works. And then at the end, there's kind of a fork in the road. It's called the arms of a trial or two different groups. So you split the patients into those who are going to abruptly stop versus those who are going to be tapered over two weeks, a short-term taper, and you compare those two. And that's the only study where Eli Lilly prospectively designed a study to do that.
Q Doctor, what were the results of that study to the best of your recollection?
A So the result was that there was not a significant difference between a two-week taper and just stopping

the drug.

Q Now, Doctor, I want to be clear. In that study, was there a placebo control?

A Let me just think. It was a generalized anxiety disorder, and the two arms that I'm talking about are patients who were on the drug and either abruptly stopped or were tapered over two weeks. Off the top of my head, I don't recall if there was another group that got placebo.

Q Okay. And in the two arms, the people who stopped abruptly and the people who stopped over a tapering period of two weeks, you said there was no significant difference. What does that mean?

A So that, again, is statistical tests. There's going to be some difference. And the question is if you do the statistical test, is that not meet the test and the difference was probably just due to chance or it does meet the test and you think that there is a significant -- it represents a significant difference between those two options, abrupt and taper. And in this case, there was no significant difference.

Q What, if at all, significance of that study does it have to your opinion of the label?

A So that study actually showed that two weeks is not enough. So if the label suggests that it's not a

big deal, just a small percentage of patients and you should just monitor them and gradually taper them and it's not a big deal and you can do it over two weeks or four weeks -- if there's actually data to show that that is not enough, I would want to know that, and I would like data to show how long you need to taper. Two months? Four months? Six months? Eight months? At what point does it make a difference?

Q And, Doctor, is it your opinion that patients should not taper?

A No. But based on this study, it needs to be a long enough taper to make a difference. I would want to know that. I would want to know at a minimum two weeks isn't enough. Then if I saw that, I would obviously want to know, well, what is enough?

Q Okay. Doctor, we have talked about how this label is misleading because of the statements in it. Okay.

I want to show you a document that -- how it contains language that Lilly has admitted is accurate and true as of today. I'll get a board for that because we need to keep the screen up.

Doctor, can you see the board?

A I do.

MR. WISNER: Hopefully everyone can see the board. Your Honor, I'm probably blocking your vision,

but I think you've seen the document before.
BY MR. WISNER:
Q All right. Doctor, have you reviewed this language in rendering your opinion today about the adequacy of the Cymbalta label?
A I have.
Q And did you rely upon this language is assessing the adequacy of the Cymbalta label?
A Yes, I did.
Q I'd like to go through this language and see how, if at all, it impacted your opinions regarding the adequacy of the Cymbalta label, okay?
A Sure.
Q So what language in here did you rely upon?
A So the -- starting with the first two words, "withdrawal symptoms."
Q Why does the statement withdrawal symptoms in any way affect your opinion of the Cymbalta labeling?
A For me that's much more helpful. That's much more kind of real world, plain English. This is what happens when you stop the drug and you go into withdrawal. Discontinuation is kind of confusing because that term can also be used for having to stop a drug because of side effects. So calling it discontinuation as opposed to withdrawal, in my

opinion, is much less helpful.

Q Okay. What other language in these admissions do you think is helpful to your understanding of the Cymbalta label?

A So the next one that would be very helpful is "are common."

Q Doctor, why is the fact that this admission says that they're common -- well, first of all, is the word "common" used in the Cymbalta label?

A No, neither is withdrawal symptoms.

Q Why is that relevant to your analysis of the Cymbalta label?

A Because this is really why I'm going to the labeling. I want to know is this side effect common or rare. So it's extremely helpful to point it out straight up: It's common. Then I can tell my patients it's common. I know that -- we're going to have to be concerned about it.

Q And the rest of the sentence reads particularly if discontinuation is abrupt, right?

A Yes.

Q Does that comport with your understanding of the risk of Cymbalta discontinuation?

A Sure.

Q All right. What's the next part of this language

here that informed your understanding?
A The 45 percent. So 45 percent of the patients.
Q Doctor, why is that relevant or helpful in your assessment of the Cymbalta label?
A It's an overall incidence rate. It's not a threshold. It doesn't say 1 percent of data. I need some indication of what the actual rate is. I can tell from that that it's common. So now I've been told twice that this is common.
Q Now, it says here 23 percent of patients taking placebo, right?
A Sure.
Q Is that helpful to you as well?
A Sure. Then I know that, as we talked about, it's a doubling of the risks compared to if you were on that sugar pill.
Q Okay. What other language -- what other language in this language influenced your opinion?
A So the next language that was particularly helpful is duration and dose of therapy.
Q Doctor, how is that relevant to your analysis of the Cymbalta labeling?
A So this, again, is giving me really helpful information that the longer a patient is on the drug and the higher the dose, the higher the risks. So

again, I'm getting really helpful information about this side effect, when to be most concerned about it.

I'm going to want to -- when I'm ready to stop a patient, if they want to stop and I agree with that, how long they've been taking it is going to matter in terms of how long we may have to take to get them off and what dose they're on. There's a big difference between 120 milligrams and 60 milligrams. That's telling me that that matters right there.

Q All right. Doctor, is there any statement in the Cymbalta labeling regarding dose and duration?

A No.

Q All right. What else about the language on this board influenced your understanding of the Cymbalta label?

A The next one I go to is occur within the first few days.

Q Okay. Doctor, how does that have any import to you as a physician?

A So again, helpful detailed information. You're going to watch particularly in the first few days for these symptoms to occur. That's when you evaluate them in terms of whether they're due to the drug or due to an underlying condition. That's when you really start to look closely. This can happen fairly quickly, very

helpful.

Q Now, it says in the U.S. labeling that patients should be monitored. Do you see that?

A Yes.

Q Doesn't that tell the doctor that you should be paying attention?

A But again, it's so vague with the 1 percent. You might think, oh, I'll tell them to come back in a month. This tells you you need to talk to them within the first few days or within the first week. It's very helpful information.

Q What other language on this board helped influence your understanding of the adequacy of the Cymbalta label?

A So the next particularly helpful phraseology is inadvertent -- patients who have inadvertently missed a dose.

THE COURT: Counselor, let me see counsel at the bench.

(Conference at the bench, as follows:)

THE COURT: There hasn't been any objection. I think the jury is going to get confused the way you're framing your questions. The issue is not whether this language should have been used, this language as opposed to some other language. The only

issue is whether the labeling adequately conveys or adequately warns of the dangers that are reflected in this description of Eli Lilly's knowledge. All right. You're framing it in terms of whether this language should have been used. That's not the issue.

MR. WISNER: Fair enough.

MR. SCHMIDT: Your Honor, I haven't been objecting because I thought we raised the objection earlier. It was overruled several times. I do agree obviously. I appreciate Your Honor raising that.

THE COURT: I admitted this only as to an admission to what Lilly knew, not that this is what should have been put on the label.

MR. WISNER: If I were to phrase the question this way, Your Honor, assuming this statement is true, why do you think that the Cymbalta label is misleading, I guess --

MR. SCHMIDT: I think at this point we should move on, Your Honor.

THE COURT: I think I'm going to let you ask one overall question, whether the language in the labeling adequately reflects the information in this description.

MR. WISNER: Yeah.

THE COURT: All right.

MR. WISNER: Okay. Let me -- I'll move on. I just want to ask one more question about the duration, two or three months, is that true? Is that something you'd want to know?

THE COURT: The question is whether the label adequately reflects the dangers associated with the information in this labeling.

MR. WISNER: Okay.

THE COURT: All right.

MR. WISNER: I'll ask that question.

THE COURT: Then let's move on.

MR. SCHMIDT: Your Honor, because we did object to this before -- because I think they did something similar with the doctors -- could we get some kind of instruction just that this is being considered as information that Lilly should have had, not as a specific warning?

MR. WISNER: Your Honor, that's argument. I think they can say that in closing. It would be inappropriate coming from the bench, I think.

THE COURT: All right.

MR. SCHMIDT: Then maybe an instruction is --

MR. STEKLOFF: I think, Your Honor, something along the lines to the jury, it's your job to decide whether Lilly adequately warned of the information it

had knowledge of so you can consider this information on the board in connection with whether they adequately warned with it. You shouldn't consider whether that language itself should have been put in the label.

MR. WISNER: I think it actually caused more problems on this board. If you want to do that, that's fine.

MR. SCHMIDT: Well, the judge is going to give an instruction.

THE COURT: All right.

(Proceedings continued in open court, as follows:)

THE COURT: Ladies and gentlemen, this exhibit that's been admitted was admitted for the purpose of evidencing what information Lilly knew about the risks and dangers of Cymbalta. It is not language that was admitted for the purpose of demonstrating what should have been on the label. So the only issue is whether the label adequately reflected the risks and the risks that are reflected in the information in this description.

So with that context, you may continue.

BY MR. WISNER:

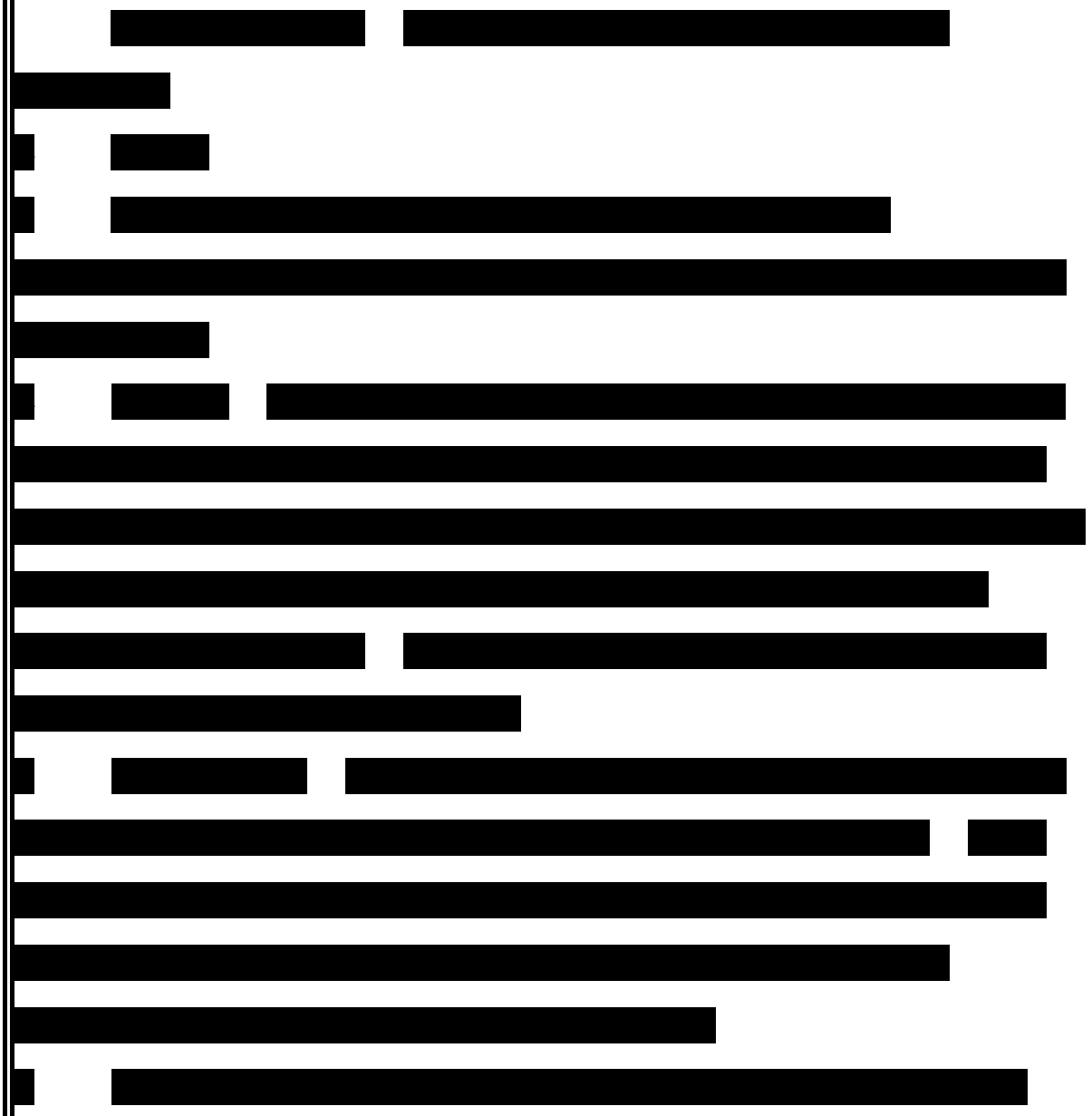
Q Doctor, this language states that that potential risk of Cymbalta withdrawal can be prolonged two to three months or more. Do you see that?

A Yes.

Q Looking specifically at the Cymbalta label, do you feel that that Cymbalta label adequately warns that Cymbalta withdrawal could last two to three months or more?

A No, I don't see that information in the label.

Q Thank you, Doctor.



(The jury exits at 1:01 p.m.)

THE COURT: Doctor, do not discuss your testimony during the luncheon recess.

We'll stand in recess until 2:00.

Time: 1:04 p.m.

I certify that the foregoing is a true and accurate transcription of my stenographic notes.

/s/
Rhonda F. Montgomery, CCR, RPR