In The Matter Of:

Pledger v.

Janssen

(Jury Trial-AM Session)

XII

February 10, 2015

John J. Kurz, RMR-CRR, Official Court Reporter

City of Philadelphia

First Judicial District Of Pennsylvania

100 South Broad Street, 2nd Floor

Philadelphia, PA 19110

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IN THE COURT OF COMMON PLEAS OF PHILADELPHIA COUNTY
FIRST JUDICIAL DISTRICT OF PENNSYLVANIA
CIVIL TRIAL DIVISION

IN RE: RISPERDAL® LITIGATION : March Term, 2010, No. 296

Phillip Pledger, et al., Plaintiffs, : APRIL TERM, 2012
v. : NO. 01997

Janssen Pharmaceuticals, Inc., Johnson & Johnson Company, and Janssen Pharmaceutical Research & Development, L.L.C. Defendants.

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TUESDAY, FEBRUARY 10, 2015

- - -

COURTROOM 425
CITY HALL
PHILADELPHIA, PENNSYLVANIA

- - -

B E F O R E: THE HONORABLE RAMY I. DJERASSI, J., and a Jury

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JURY TRIAL - VOLUME XII

- MORNING SESSION - (AMENDED)

REPORTED BY:
JOHN J. KURZ, RMR, CRR
REGISTERED MERIT REPORTER
CERTIFIED REALTIME REPORTER
OFFICIAL COURT REPORTER

APPEARANCES:

SHELLER, P.C.
BY: STEPHEN A. SHELLER, ESQUIRE
CHRISTOPHER A. GOMEZ, ESQUIRE
E-mail: Sasheller@sheller.com
E-mail: Cgomez@sheller.com
1528 Walnut Street, 4th Floor
Philadelphia, PA 19102
Phone: (215) 790-7300 Fax: (215) 546-0942
Counsel for Plaintiff(s)

KLINE & SPECTER, A Professional Corporation
BY: THOMAS R. KLINE, ESQUIRE
KRISTEN LOERCH SIPALA, ESQUIRE
E-mail: tom.kline@klinespecter.com
E-mail: kristen.loerch@klinespecter.com
1525 Locust Street, 19th Floor
Philadelphia, PA 19102
Phone: (215) 772-1000 Fax: (215) 772-1359
Counsel for Plaintiff(s)

ARNOLD & ITKIN, LLP
BY: JASON A. ITKIN, ESQUIRE
6009 Memorial Drive
Houston, Texas 77007
Phone: 713-222-3800 Fax: 713-222-3850
Counsel for Plaintiff(s)

Representing Defendants:

DRINKER BIDDLE & REATH, LLP
BY: KENNETH A. MURPHY, ESQUIRE
MELISSA A. GRAFF, ESQUIRE
One Logan Square, Suite 2000
Philadelphia, Pennsylvania 19103-6996
Phone: (215)988-2700 F:(215)988-2757
E-mail: kenneth.murphy@dbr.com
melissa.graff@dbr.com
Counsel for Defendant Janssen Pharma., J&J, and Janssen Research & Development

APPEARANCES: (Continued)

WEIL, GOTSHAL & MANGES, LLP
BY: DIANE P. SULLIVAN, ESQUIRE
ALLISON BROWN, ESQUIRE
(admitted pro hac vice)
301 Carnegie Center, Suite 303
Princeton, New Jersey 08540
T: 609-986-1100 F: 212-310-8007
E-mail: diane.sullivan@weil.com
E-mail: allison.brown@weil.com
Counsel for Defendant Janssen Pharma., J&J, and Janssen Research & Development

Also Present:

Priscilla M. Brandon, Esq., Sheller, P.C.
Marianne Mari, Tipstaff
Cory Smith, Video Technician
Ken Reed, Video Technician
Thomas F. Campion, Esquire
Benita Pledger

- I N D E X -

E X H I B I T S

(The following transpired in open court outside the presence of the jury:)

COURT CRIER: All rise.

(Call to order at 9:37 a.m.)

THE COURT: Good morning, everybody.

MR. KLINE: Good morning.

THE COURT: Virtually bright and early.

Okay. Yes, sir.

You can be seated, everybody.

MR. MURPHY: Your Honor, I just have a brief motion before we begin as to defendant Johnson & Johnson.

THE COURT: Yes.

MR. MURPHY: We move for a compulsory nonsuit as to Johnson & Johnson. The evidence presented by the plaintiff did not in any way implicate Johnson & Johnson as a manufacturer, distributor, or a marketer of the drug in question, Risperdal. It's beyond question that Johnson & Johnson is but a holding company. There's no evidence that's been presented by plaintiff that would allow them to pierce the corporate veil, as it were.

The only evidence regarding Johnson & Johnson that was provided to this Court was a LinkedIn page by the sales representative, Mr. Gilbreath, who in fact was employed by Janssen. There being no evidence as to Johnson & Johnson, we would move that --

THE COURT: Well, is Johnson & Johnson a different party from any of the other parties, or are they the same? I'm talking about Johnson & Johnson versus Janssen Pharmaceutica.

MR. MURPHY: A different company totally. It is a mere holding company.

THE COURT: Ah, I see.

Well, you know what, that's denied. We will cross that bridge when we get to it as far as the -- I mean, it's been pretty clear that the label involved in this case and the company that manufactured this was either Johnson & Johnson and/or Janssen Pharmaceutica. That was testified to by multiple witnesses in this case, ranging from Dr. Gilbreath to Dr. Mathisen to Dr. Kessler.

So the record will speak for itself.

We're not granting a nonsuit on that basis.

MR. MURPHY: Understood. I understand your ruling, Your Honor.

THE COURT: All right. Let's get the jury in here.

All right. I don't know whether you have the memorandum ready now or sometime later in the day.

There were two issues that were held under advisement on the directed verdict motion. I don't plan on reading it on the fly today, but if it's available sometime today, I would be happy to read it.

MR. KLINE: I don't believe I've seen it yet; is that correct?

MS. SULLIVAN: It's on its way, Your Honor.

THE COURT: Okay. No rush. Take the pressure off.

- - -

(Pause.)

- - -

COURT CRIER: All rise.

(Whereupon the jury entered the courtroom at 9:42 a.m.)

(The following transpired in open court in the presence of the jury:)

- - -

THE COURT: All right. Good morning. Please be seated.

JURY PANEL: Good morning.

THE COURT: Good morning, everybody.

All right. Now, members of the jury, as I told you yesterday, the plaintiff's side has rested and so now we are going to begin the testimony and evidence of the defense in this case, and for that purpose, I ask Ms. Sullivan to call your first witness when you're ready.

MS. SULLIVAN: Thank you, Your Honor.

Good morning.

THE COURT: Good morning.

MS. SULLIVAN: The defense calls as their first witness Dr. Ivo Caers.

Dr. Caers, if you could take the witness stand.

(Witness took the stand.)

COURT CRIER: Just remain standing. Please state your name for the record and spell it.

THE WITNESS: My name is Lodewijk Ivo Caers, but my call name is "Ivo."

COURT CRIER: Can you spell that, please.

THE WITNESS: L-O-D-E-W-I-J-K, I-V-O, C-A-E-R-S. I'm a Ph.D.

COURT CRIER: And raising your right hand.

- - -

... LODEWIJK IVO CAERS, Ph.D., after having been first duly sworn, was examined and testified as follows:

- - -

DEFENDANT'S EVIDENCE

- - -

DIRECT EXAMINATION

- - -

BY MS. SULLIVAN:

Q. Good morning, Dr. Caers.

A. Good morning.

Q. Good morning, everyone.

Dr. Caers, could you introduce yourself to our jurors; tell them who you are and where you work.

A. Well, as I told, I'm Ivo Caers. I'm a

scientist working with Janssen Research and Development. I'm actually living -- I was born in Belgium. I'm actually living in Belgium with my family in a small town, Beerse, somewhere in the north of Belgium, in Europe, middle Europe. And I'm still working there daily, on a daily basis.

Q. I think our jurors could tell it wasn't a Philadelphia accent.

A. I'm afraid not, no. But I'll improve on that during the day.

Q. And, Dr. Caers, for how long have you been at Janssen Pharmaceuticals?

A. More than 35 years. I've been working for Janssen R & D for more than 35 years now.

Q. And can you tell us a little bit about your educational background.

A. I studied -- I have a Master degree in biology, which I did at the University of Leuven in central Belgium. And the after that I did doctoral work, Ph.D., as we call it, in biochemistry, which I've terminated and completed in, I think, April 1979.

Q. And can you just walk us briefly through your career experience at Janssen. What did you do when you started back in 1979? And take our way through your career there, briefly.

A. Sure.

In May 1979, I actually started in a local operating company, Janssen the Netherlands. So the Netherlands are just north of Belgium. And I was there in a product development position and product management position for three years, up to 1982.

In 1982 -- always based in Beerse, Belgium. And in 1982, I switched to the clinical research group and did clinical studies in various domains: neurology, oncology, cardiovascular. I did that for five years about. Then later in 1987, about, I switched to what we called at that moment global studies in marketing, which is a commercial position, but more on strategic directions for drug development and line extension, so additional formulation development.

And during that time I also became available for the psychiatry products, including Risperdal. So me and my team, we did the global launch of Risperdal back in 1992, '93. And we are driving strategic directions for the compound up to -- and I've been doing that for up to 1999, when I switched again to the Janssen R & D organization.

Q. And R & D, Dr. Caers -- I'm sorry to interrupt -- is research and development?

A. Yes. Janssen R & D, yes, Research and Development.

So back in mid-1999, I was asked to become the team leader for Janssen R & D for Risperdal. And I have been doing that from 1999 up to 2009. After which, since then, I'm doing all the developments within Janssen R & D in other psychiatry products.

Q. And, Dr. Caers, we're going to talk about Risperdal and its development by Janssen. But first, can you give our jurors some background about your experience in drug development, in the discovery and development of medicines.

A. Well, you will understand in 35 years I've gone several times through the whole life cycle of the product. I've most -- I'm most familiar with Risperdal from the early days on up to 2009, as I said earlier. But I also been involved in developments in psychiatry, in the compounds for attention deficit hyperactivity disorders. I've been dealing with compounds in depression. I'm actually now still a compound development team leader for the depression compound. But as I said

earlier as well, I've started up new compounds that first we didn't make it because of efficacy or safety issues. So I'm pretty familiar with the first step, up to launch and beyond.

Q. And, Dr. Caers, Janssen Pharmaceuticals, when did that company become part of the Johnson & Johnson family of companies?

A. It was back in 1962, even before my time, that the company which was at that time also already based in Beerse, so it was north of Belgium where it still is, where that company was bought by Johnson & Johnson. And since then, Janssen Pharmaceutica is a member of the companies of Johnson & Johnson.

Q. And is Janssen named after somebody?

A. Yes, indeed. The company, the Janssen company was founded by Dr. Paul Janssen. Dr. Paul Janssen was a scientist in Belgium, grew up in Belgium, is from the region. And back in the early '50s, 1953, I guess, he started up his own lab looking and trying to invent new and better medicines; and he had been very successful, by the way. He has -- all of his career, he is the inventor of up to 80, eight-zero, new drugs for different areas of medicine. And that's why obviously, as I told earlier, back in 1962, that this company came under

the attention of Johnson & Johnson as a very productive laboratory and very successful laboratory and as an interesting company to join Johnson & Johnson.

Q. And, Dr. Caers, did you personally have the opportunity to work with Dr. Paul Janssen?

A. Oh, yes, very, very closely. I was actually sitting on the same floor when I was in clinical research; and my boss reported directly to Dr. Paul Janssen.

Q. And, Dr. Caers, we're going to talk a little bit about how to develop a medicine and then talk about Risperdal. And you've been involved in discovery and development of medicines including Risperdal?

A. Yes, indeed, yeah.

Q. And we have just as a demonstrative Defense Exhibit -- Ms. Brown, can tell me?

MS. BROWN: Yes; 54.

MS. SULLIVAN: And, Lamia, it's DG10.3.

MR. KLINE: I'll need to see it.

THE COURT: What is this now?

COURT CRIER: This would be D-54, Your Honor.

THE COURT: D-54.

(Whereupon Exhibit D-54 was marked for identification.)

MR. KLINE: I haven't seen this.

(Handing document to the witness.)

THE COURT: Counsel, I still -- I am going to ask that we follow the --

MS. SULLIVAN: Oh, you can take it down.

Yeah. I'm sorry. I didn't realize that they put it up, Judge.

THE COURT: D-54.

MR. KLINE: I've never seen it, Your Honor. And it was not produced.

THE COURT: Okay.

MS. SULLIVAN: It's a demonstrative. It's a timeline. I don't think it's controversial.

MR. KLINE: I have to see it first.

MS. SULLIVAN: I'll give them Dr. Caers' copy.

COURT CRIER: Let me run that off.

MS. SULLIVAN: That's okay.

COURT CRIER: The Judge needs one and counsel. Thank you.

MR. KLINE: Whether controversial or not, Your Honor, I object to the procedure.

THE COURT: All right. Mr. Kline, I'm going to ask you to speak into the microphone.

MR. KLINE: Yes. I object to the procedure. I'll look at the document, but we had an agreement to exchange all documents.

Now it's, quote, just a demonstrative.

THE COURT: Well, right now we're on court time here.

MR. KLINE: I understand.

THE COURT: We're going to proceed with this document one at a time.

MR. KLINE: I understand. I need to see it. I still haven't seen it.

THE COURT: Any objection?

MR. KLINE: Other than the one I raised, no, Your Honor.

THE COURT: No. It's all right. This is a demonstrative piece -- something to help explain something to the jury. It's okay.

Go ahead.

MS. SULLIVAN: Thank you, Your Honor.
COURT CRIER: D-54 to the witness.
MS. SULLIVAN: Ken, can we put it up?
(Document D-54 displayed.)
BY MS. SULLIVAN:
Q. And, Dr. Caers, can you walk our jurors through the process of discovery and developing a medicine in accordance with the FDA -- by the way, Dr. Caers, are you familiar with the FDA regulatory scheme as it relates to the development and labeling of medicines?
A. Yes, very much so, yeah.
Q. And is that something you deal with regularly in your job?
THE COURT: You know what, before we proceed, are we proceeding as an expert witness here or a fact witness? What is this?
MS. SULLIVAN: He's a fact witness, Your Honor, but he certainly has expertise in these areas.
THE COURT: Well, is he going to be offering an opinion of some sort?
MS. SULLIVAN: He's -- no. Factual testimony, Your Honor.

THE COURT: All right. Go ahead.
BY MS. SULLIVAN:
Q. And, Dr. Caers, can you walk us through -- just to back up.
Dr. Caers, how hard is it to get a medicine approved by the FDA?
A. Well, in all fairness, it's pretty hard, and I will explain to you why.
The whole process starts on the left-hand side. So the start is, you need to have an ID. So you have an ID that if you have a molecule that acts --
Q. Is that "idea"?
A. Say again.
Q. Did you say you need an "idea"?
A. You need an "ID," a hypothesis. And that tells you if I would have a molecule that has a certain activity, that may well be active in a certain disease area. So what you need on the left-hand side is a test and you need molecules. And we start making hundreds of molecules and we test them all in the lab to see whether this molecule may have had some activity that we want and that it is sufficiently powerful, this activity.
Out of a couple hundred, you may

select a couple, 10, 15, and you test them, and the next step is in animal models. You have a model where you can check whether indeed in living animals this molecule does what we hope to do; and, secondly, you check whether the safety, at least in animals, is good enough to go to the next step.
Q. And so, Dr. Caers, so that test tube, that relates to just trying to test and discover molecules in the laboratory?
A. That is correct.
Q. And is it true that most medicines never get approved by the FDA?
A. Well, as you can see, we start with a couple of hundreds. We selected a few tens, maximum, if not less, for testing in animals. Very few make it to the next step. And the next step is what we call Phase I studies. And that's the first time we give the molecule to a human subject.
Q. And do you need FDA approval before you can start testing a medicine in people?
A. If you want to do this in the US, you need to have an FDA approval. If you want to do it in other countries, you need to have other regulatory agencies' approval. Not an approval, an agreement. We talked -- well, don't mix it up with the final

approval at the end of the whole development.
Q. Yes. In other words, you need permission from the FDA before you can even test it?
MR. KLINE: No. Objection. That is not what he said. Objection; and she's leading.
THE COURT: All right. Sustained.
BY MS. SULLIVAN:
Q. Dr. Caers, do you need permission from the FDA before you can test in patients?
MR. KLINE: Objection; asked and answered.
THE COURT: All right. That has been answered.
So in the interest of time, you know, if you got your answer, let's get another new subject or new -- you know. We don't have to repeat everything.
BY MS. SULLIVAN:
Q. Dr. Caers, can you walk us through what the company looks for -- and, by the way, when companies test their medicines in patients, how is that done? Is that done by outside doctors?
A. Yes. So once we are beyond the human volunteers in Phase I and we still have a molecule

that shows safety and is pretty well-tolerated in non-ill subjects, you go to the next phase, which we call Phase II, where you do your first evaluation of efficacy. And here you use -- you need patients and you need investigators, clinical centers that have those patients, because we don't have patients. Patients don't come to us. They come to doctors. And we ask the doctors to do a certain study. And in this case we are in Phase II. The objective of that study is how is that efficacy as we hope that to be and is it pretty well-tolerated in the limited number of patients that we include in Phase II studies.

Q. And do these outside doctors and the company need informed consent from patients to participate in these studies?

A. Yes, absolutely. There is -- first of all, there's a protocol and the protocol describes from A to Z what the study is, what is the objective of the study, how it will be done, what type of patients you need, what type of patients you should not include, what should you assess for efficacy and safety. And there's always an informed consent.

And what is an informed consent? That is a short description in language that every

patient can understand that explains what the study is all about; what are the potential risks; what is known about the product. And only once the patient has signed and agreed that he has understood it and he agrees to enter the study, the physician and the investigator can enter that patient in the study.

Q. And what sort -- and so in these clinical trials -- and is that what they call clinical trials when you're testing it in patients?

A. That is correct.

Q. And in these clinical trials, what are the kinds of things the company and these outside doctors are looking for in terms of safety issues in patients?

A. Oh, always in clinical studies you have a range of safety assessments. You have blood level assessments. You have EKGs to test the safety on the heart. You also collect adverse events. Every adverse event reported or noticed with the patient is written down by the investigator. You may also have certain assessment skills that you follow a certain structured interview to assess certain particular elements for safety. And that is all written down per the individual patient in a patient record form.

Q. And, Dr. Caers, this testing in patients, do you look at the impact the medicine has on various systems in the body, blood, heart, lungs?

A. Yes, indeed, yes.

Q. And, in other words, are you examining, as you're doing these clinical trials, how the medicine affects the body?

A. To a certain extent, to a certain extent that it is possible to do so, yeah.

Q. And as you're going through these clinical trials, Dr. Caers, is the company collecting data, collecting information about side effects?

A. Collecting -- we are collecting information on all adverse events, side effects, safety assessment and efficacy assessments, yes.

Q. And is that side effect information that's being collected by the company from these outside doctors, does the company report that information to the FDA?

MR. KLINE: Your Honor, objection; leading. He's just saying "yes" or "no." And this isn't testimony.

THE COURT: Yes. I'll sustain that.

Also, you know, again, unless it's a very important aspect of this entire case,

these things can be summarized in a few minutes.

MS. SULLIVAN: Yeah.

BY MS. SULLIVAN:

Q. And, Dr. Caers, why don't you talk to our jurors about what information the FDA has given along the way in terms of the clinical trials.

A. Okay. Of every single study, once the study is complete, the last patient has completed the study, then all the data are collected and brought together in one single database. And at a certain moment when we have all the information available, then we close the database. That means all of the information as provided by the investigators is brought together. We analyze the study so that we know that whether the study shows efficacy and/or safety. This is written down in an extensive report.

Initially we go to a topline result report, but that's only 10, 20 pages for internal use. But the eventual result of every study is what we call a Clinical Study Report. And that's a 100- to 150-page document, plus an additional couple of thousand pages of tables and individual data. That is basically what we call the Clinical Study Report.

Q. And what kind of side effect information is the FDA provided by the companies as a result of these clinical trials?
A. Everything related to safety and efficacy is written down by the investigators and is included in the database and eventually described in the Clinical Study Report. And it's a full Clinical Study Report that is eventually shared with the FDA.
Q. And so, Dr. Caers, as it relates to Risperdal, for example, did the company conduct clinical trials as part of the FDA approval process for Risperdal?
A. Yes, of course.
Q. And as part of that process, did the company report side effect information to the FDA?
A. Yes, indeed.
Q. Including all the information about any patients that might have developed gynecomastia?
MR. KLINE: Objection; leading. It's all leading, including the information about the things. And he just has to say "yes" or "no." This is a direct witness, Your Honor. I object.
MS. SULLIVAN: I'll rephrase it, Your Honor.
MR. KLINE: I object to the

continuation of it.
THE COURT: That's sustained. Sustained. I mean --
BY MS. SULLIVAN:
Q. Dr. Caers, did the company provide side effect information to the FDA as it related to Risperdal as part of the clinical trials?
A. Yes.
Q. And what kind of side effect information was the FDA provided?
A. Well, all the side effects, all adverse events reported during the studies were summarized and described in the Clinical Study Report. But obviously, an NDA, a New Drug Application, there's more than one study. There might be 20 to 30 studies in such NDA. And every study has its own Clinical Study Report and with all the efficacy and safety information, including all adverse events, in your New Drug Application. That is the total package that you send to the FDA. You also have a summary on efficacy which summarizes the results of all the studies combined. And you do the same for safety information. All the adverse events reported and all the different study reports and studies done with the compound are summarized in an overview

report. And that's all part of what we call the New Drug Application.
Q. And, Dr. Caers, would that include any side effects the company saw about gynecomastia?
MR. KLINE: Objection; leading.
BY MS. SULLIVAN:
Q. Would that have been reported?
THE COURT: Sustained.
BY MS. SULLIVAN:
Q. Did the company report side effects including any prolactin-related side effects?
A. Yes, indeed.
Q. And what were some of those?
A. Well, there were cases of gynecomastia, galactorrhea and amenorrhea, so disturbance of the menstrual cycle in females, that was part of the adverse events that were in the data package submitted for the New Drug Application back in 1992.
Q. And was the FDA provided all of that information about those side effects?
A. Yes.
MR. KLINE: Objection, Your Honor.
THE COURT: Yes. Yes. Sustained.
MR. KLINE: The whole --
THE COURT: Was the FDA provided

with something, that's a leading question.
Maybe we can just do this: Kind of ask him what the story is or whatever.
MS. SULLIVAN: I was trying to move it along, Judge; but okay.
BY MS. SULLIVAN:
Q. The --
MR. KLINE: Your Honor, my other objection is that none of this that relates to the approval in 1992 has anything to do with children. And this drug was off-label from '02 to '06.
MS. SULLIVAN: Your Honor, this is not proper.
THE COURT: All right. Mr. Kline, I appreciate that.
MR. KLINE: That's my objection.
THE COURT: But, you know, this is a defense, and they're permitted to approach it any way they see fit, as long as it's admissible.
BY MS. SULLIVAN:
Q. And, Dr. Caers, can you talk about -- how long, Dr. Caers, for the first -- when was the first FDA approval for Risperdal?

A. The first approval for Risperdal was back in December 1993, and it was for the manifestations of psychotic disorders.
Q. And that was in adults, correct?
A. That was based on data collected in adults, including elderly.
Q. And, Dr. Caers, how long did Janssen study Risperdal and conduct animal testing, clinical trials, et cetera, before the FDA approved it?
A. Well, the molecule was synthesized first, invented basically in 1984, and we got our approval late 1993. So that's nine years of research.
Q. Nine years of study before FDA approved it?
A. Yes, indeed.
Q. And I'm going to mark Defense Exhibit...
MS. BROWN: 55.
MS. SULLIVAN: And this is DG6-1, a demonstrative.
MR. KLINE: Your Honor, again, we had an agreement to produce documents that are going to be used with the witness; and I object.
THE COURT: Let me see the document.
MR. KLINE: Before I even see it, we had a specific agreement.

THE COURT: Well, it may be. But right now I'm going to go one by one and then we'll look at it at another time.
MR. KLINE: At a break, may I have whatever is being used?
THE COURT: Pardon me?
MS. SULLIVAN: Your Honor --
MR. KLINE: All I ask is to be provided the documents ahead of time.
THE COURT: Well, nothing's going up on the screen or anywhere until you've seen it, until it's reviewed, until it's either objected to or not; and if it is, then I'll rule on it.
Do you have, actually, copies of these documents?
MS. SULLIVAN: We thought we did, Your Honor. I'm not sure what happened.
Your Honor, Mr. Kline provided us a whole bunch of documents the day his witnesses --
THE COURT: Well, I'm not really interested in a --
MR. KLINE: That's also not true.
THE COURT: -- back-and-forth between

counsel, I really am not. I don't think the jury is either.
Well, you know what, I'll permit you to use this after you've gone through these, you know, after all of these different points have been either stipulated to or testified to by your client. You may certainly use this as a summary of the points that you're making. But it is in the fashion of leading to put this particular document up there and then just have your witness kind of reply what's already in the document.
MS. SULLIVAN: Okay.
- - -
(Whereupon Exhibit D-55 was marked for identification.)
- - -
BY MS. SULLIVAN:
Q. Dr. Caers, has Risperdal been approved by the FDA for many different indications?
A. Yes, indeed.
After the first approval in 1993, there were additional approvals for Risperdal with different formulations, so with different ways of administration, such as a liquid, an oral liquid, or

a fast dissolving tablet which makes it easier for patients to take the pill; or in other indications such as bipolar mania, which is another psychiatric disease in which antipsychotics can be very effective.
It was also approved later, somewhere in 2006, I think, in irritability associated with autism, which is a primarily child psychiatric disorder. It was later then also approved for adolescents with schizophrenia and for children and adolescents with bipolar mania. Again, this is another age group as it was approved for in adults.
Q. And, Dr. Caers, when the company submits its New Drug Application for approval to the FDA after all of this years of testing, how long typically does it take the FDA to review all of the data and decide whether the medicine gets approved?
A. At that time it took about 12 to 15 months for the FDA to review all your data that you provided. And be aware, we not only give the paper document, they also get the database electronically. So they can check the analysis we do in the studies, whether they are appropriate and do justify, indeed, the conclusions.
After that review by the FDA, and the

whole file is distributed to different reviewers, different specialists within the FDA, they all make their assessment, bring it all together, and that eventually leads to a reply, first reply, which is usually an approvable letter that says, yes, okay, it looks good, but this and this and this we still want you to explore and justify.

And eventually then when you give your complete response and because you reply then, then they review that once more and then they can approve. And as part of the approval, they provide you the final label which is what they want to be said about this compound in the label to inform physicians how to use and prescribe this compound.

Q. And, Dr. Caers, when a medicine is approved by the FDA, do you get from the FDA an approval package?

A. Yes, indeed.

Q. And have you seen the FDA review memos that are part of that approval package?

A. Yeah. As I said earlier, so every -- the different parts of the file of the New Drug Application is reviewed by different specialists within the FDA. You have chemical; you have clinical; you have safety physicians; you have

pharmacokinetics; so they are experts on how the drug behaves in a body, et cetera, et cetera. So they all make their review, bring it all together in assessment reports, and those are, shortly after approval, available in the public domain on the FDA website. So we do have access to these assessment reports.

Q. And, Doctor, so you -- does the company see then the various review memos from the different doctors at the FDA on the medicine?

A. That is correct.

Q. And, Dr. Caers, I am going to mark as Defense Exhibit 56, DX207, the approval letter from the FDA for Risperdal in 1993.

MR. KLINE: Objection to FDA document.

THE COURT: Overruled.

MS. SULLIVAN: Do we have a copy for the Judge and for --

MS. BROWN: We do, yes.

THE COURT: Well, let me see you at sidebar.

Take that down, please.

(The following discussion transpired at sidebar out of the hearing of the jury:)

THE COURT: I don't mind the admission of this, but the contents of this are problematic, especially such that you highlighted that has the phrase, "safe and effective," which I did rule on in motion in limine. I don't want to get into the issue of safety and effectiveness as approved by the FDA.

MS. SULLIVAN: Well, Your Honor, I'll block it out here. I will not --

THE COURT: I don't know why you need all this. You have an approval. It's in the document, and that's it. The contents of this are problematic.

MS. SULLIVAN: Your Honor, Dr. Kessler said the drug's unsafe. That opens the door to this. It goes to negligence, Your Honor. This is the FDA standard. We've met it. It's evidentiary.

THE COURT: But it was unsafe perhaps for children. His point is well taken. This was an approval for adults. It's actually irrelevant. But beyond that, I'm telling you, we had a motion in limine ruling that specifically --

MS. SULLIVAN: I'll block out the safe and effective, then.

THE COURT: And I don't think the contents of this are admissible. They're not necessary.

MS. SULLIVAN: Well, this is the label, Judge.

THE COURT: Well, you have some testimony about the effectiveness and safety. You have testimony about it, or an opinion.

MS. SULLIVAN: I'll block it out.

THE COURT: But we're not doing it this way through the FDA.

MS. SULLIVAN: Okay.

THE COURT: We've ruled it out before.

MS. SULLIVAN: Okay. I'll block out the "safe and effective."

MR. KLINE: Well, no.

Your Honor, Your Honor, as I understood, the Court just told her not to display it; and her answer back on the way out was "I will block it out."

There's no good reason why this has to be displayed.

THE COURT: No. No. This document is not going up because the contents cannot be -- I can't -- I cannot --

MS. SULLIVAN: Your Honor, this is the label. And the FDA is saying this is the label you have to use.

THE COURT: I'm telling you, you have the approval. It's in the record, and it's admitted. But the fact of the matter is the contents of that document is not admissible. It's not subject to cross-examination. It's using a phrase that I had forbidden, and it's putting the FDA imprimatur of safe and effectiveness on this drug when in fact the issue has to do with children. And this particular label didn't have anything to do with children.

MS. SULLIVAN: And, Your Honor, just --

THE COURT: That's my ruling.

MS. SULLIVAN: I understand. But for the record, Judge, you initially ruled that the FDA defense is part of the case. This is the approval from the FDA.

THE COURT: Well, it has to be

according to --

MS. SULLIVAN: This is a business record and a public record.

THE COURT: It is not -- the contents of that document are not admissible in this case --

MS. SULLIVAN: This is the labeling.

THE COURT: -- for the purposes that you are presenting it. This is not a business record for whom the contents are admissible.

MR. KLINE: I have no objection to the label as a document being used.

THE COURT: That's already in evidence.

MR. KLINE: I have an objection to --

MS. SULLIVAN: But how about --

COURT REPORTER: One at a time.

MS. SULLIVAN: How about the statement from the FDA: This is the label you have to use?

THE COURT: I don't think you really need that.

MS. SULLIVAN: Well, Judge, that's our defense.

THE COURT: Your defense is that in 1993 the thing was approved. You have an official document to prove it.

MS. SULLIVAN: And the FDA says say this. The FDA says you have to say this verbatim.

THE COURT: You can use that.

MS. SULLIVAN: Thank you.

MR. KLINE: That would actually be misleading because --

MS. SULLIVAN: That's what it says.

MR. KLINE: Of course that's what it says, after a negotiation with them and having nothing to do with children.

MS. SULLIVAN: That's cross-exam.

MR. MURPHY: Your Honor, if I might.

THE COURT: The objection is sustained. I'm not going down that route.

MS. SULLIVAN: I can't show that the FDA says use this verbatim?

THE COURT: No, no. You can get that from your witness.

MR. MURPHY: Your Honor, just so --

THE COURT: Or get a stipulation. It's a can of worms that injects the FDA's

approval process as a -- without the FDA people being here or an expert witness testifying about these documents, just like Kessler did. You cannot use this document to speak for itself. You have to get an expert in here to testify about these documents. And that's my ruling.

MR. MURPHY: Your Honor --

THE COURT: That's it.

- - -

(Sidebar discussion concluded.)

- - -

(The following transpired in open court in the presence of the jury:)

- - -

THE COURT: All right. The objection is sustained, ladies and gentlemen. The objection is sustained.

This particular document here can be used for a particular purpose; namely, that an approval of the FDA took place in 1993, as we already know. That's it.

BY MS. SULLIVAN:

Q. And, Dr. Caers, as part of the FDA approval process, did the FDA also review the labels?

A. Well, part of the approval -- well, approval is the label. And the label is -- this is the document -- the FDA says this is the document that will be the label for this compound which is part -- an intrinsic part of the approval letter and document.

Q. And, Dr. Caers, can you talk about your experience with the FDA in terms of labeling for medicines including Risperdal.

A. Well, with every NDA, New Drug Application, you propose a certain label, but you write this label in line with the guidelines. There are FDA guidelines on how to structure a label and what should be in a label and what should not be in a label, and that's a proposal. Part of the review process by the FDA is reviewing that label and always they will make recommended changes and adaptations. They may delete certain things. They may add certain things. And at the end, with the approval, they say this is in our opinion what should be in your label and this is part of your formal approval, which means that basically this product is safe and effective for the use as described in that label and for the patients as described in that label. That's a very strict

process that is followed in that respect.

Q. And who, Dr. Caers, at the approval stage for a medicine, has the final say as to what goes in the label? The FDA or the company?

A. That's the FDA.

Q. And will the FDA permit you to market your medicine if you don't say what they tell you to say?

MR. KLINE: Objection.

THE COURT: All right. Sustained.

Is this an expert witness on pharmaceutical regulation, Counsel?

MS. SULLIVAN: Your Honor --

THE COURT: I'm going to ask you at this point to get into what this witness can testify as a fact witness about his involvement with the Risperdal approval process.

BY MS. SULLIVAN:

Q. And, Dr. Caers, do you have a significant amount of experience dealing with the FDA on labeling issues?

A. Yes, I do.

Q. And can you tell us whether a company can say something different from what the FDA dictates --

MR. KLINE: Objection.

BY MS. SULLIVAN:

Q. -- in the label?

THE COURT: Sustained. Sustained.

What we're looking for as admissible as a fact witness is about this individual's own experience with the Risperdal approval process.

BY MS. SULLIVAN:

Q. And, Dr. Caers --

MR. KLINE: I move to strike.

THE COURT: And we are going to strike anything that this witness has to say that has been objected to, any answers that's been -- please do not consider that.

He is not qualified here as an expert on pharmaceutical regulations.

If he were, I'd let you know.

BY MS. SULLIVAN:

Q. And, Dr. Caers, based on your experience with the FDA, do they have final say in what goes in your label?

MR. KLINE: Objection.

THE COURT: That's sustained. Sustained.

BY MS. SULLIVAN:

Q. When you get an approval letter from the FDA, what does it say about the label?

A. It has the label as it is approved by the FDA and as it will be used for the marketing of the product in this country.

Q. And what does that mean?

A. It means that the approved label as approved by the FDA describes, in the opinion of the FDA, all the relevant information that the physician needs to know in order to appropriately prescribe this medicine for his or her patients.

Q. And let's show our jurors the initial FDA approved label for Risperdal. Defense Exhibit 24, please.

COURT CRIER: D-57.

MR. KLINE: Your Honor, may we look at it first?

THE COURT: Of course.

MR. KLINE: Rather than to display, as per the Court's --

THE COURT: I thought I had made myself clear about that.

MS. SULLIVAN: Your Honor, this has already been admitted.

THE COURT: I don't care.

MS. SULLIVAN: Okay.
COURT CRIER: Previously marked as D-24, Your Honor.
THE COURT: Isn't that the same document as some other document we've had, plaintiff something?
MR. KLINE: No. It's the same as D-24. Now it's marked D-57.
MS. SULLIVAN: No. It's D-24.
THE COURT: D-24. Fine.
All right. That's been previously marked.
Go ahead.
BY MS. SULLIVAN:
Q. Dr. Caers, let's take a look at the initial FDA approved label back in 1993 for Risperdal.
And if we could go to the Precautions section, Ken.
(Technician complied.)
BY MS. SULLIVAN:
Q. And, Dr. Caers, can you talk about what was in the initial FDA approved label in terms of information about hyperprolactinemia or elevated prolactin and gynecomastia?
MR. KLINE: Objection; misleading. I

will not object if the word "adult" is used.
MS. SULLIVAN: Your Honor, I just asked him what was in the label. This is, you know --
THE COURT: Well --
MS. SULLIVAN: Everybody knows --
THE COURT: -- I'm not sure why we're going through this exercise.
I mean, the jury can read it for themselves or what. I mean, is there a question based on this label?
MS. SULLIVAN: Yeah.
THE COURT: All right. Then ask the question.
BY MS. SULLIVAN:
Q. And, Dr. Caers, in the FDA approved label, was there information for physicians about the fact that Risperdal could increase prolactin levels?
A. Yes, indeed. As you can see here, under the title "hyperprolactinemia," it says that as other products interfering with dopamine, and those are receptors, somewhere in the brain, also risperidone elevates prolactin in the blood, and that products that can increase prolactin in the blood; that certain adverse events such as galactorrhea,

amenorrhea, gynecomastia, have been reported with this type of drugs.
Q. And, Doctor, our jurors have heard the term "association" and "causation." Is there a difference between association --
MR. KLINE: Objection.
BY MS. SULLIVAN:
Q. -- and causation?
MR. KLINE: Objection.
THE COURT: Overruled.
THE WITNESS: Well, association means that these type of observations have been made while patients were treated with risperidone.
A causation means that the observations have been induced and caused by risperidone. And there is indeed a major differentiation, because it's not because it's associated that it is caused by it.
BY MS. SULLIVAN:
Q. And can you explain why something associated with something doesn't necessarily mean caused by it, based on your experience?
MR. KLINE: Same objection; expert testimony.

THE COURT: Sustained. Sustained. You're -- again, this is like expert testimony. If you want to qualify him as an expert, I mean, I don't understand what -- let me see -- what are we trying to -- he's a fact witness about what?
MS. SULLIVAN: He's a fact witness who's a Ph.D., and has significant expertise in drug development and drug labeling and is familiar with these concepts for over 30 years, Your Honor.
THE COURT: That's an expert.
MS. SULLIVAN: He's both.
THE COURT: Well, then, qualify him as an expert.
BY MS. SULLIVAN:
Q. Dr. Caers --
MR. KLINE: There's no report, Your Honor.
THE COURT: That's right. You can't qualify him as an expert, I guess, because we don't have an expert report.
MS. SULLIVAN: Your Honor --
THE COURT: So then the objection is sustained. This is not the right witness for

that.
MS. SULLIVAN: Your Honor, they've had extensive depositions of this witness.
THE COURT: Not the right witness. There's no expert report.
There are some Rules of Civil Procedure involved in Pennsylvania, and so, therefore, we're going to follow them.
I'm sure you have some other expert witnesses who are going to testify and they may do so properly. But this is a fact witness, I presume, about his own experience with this particular medication.
MS. SULLIVAN: And, yes, Your Honor, the concept of association and causation is in this label.
THE COURT: Well, ask him as relates to Risperdal.
MS. SULLIVAN: Okay. Fair enough.
BY MS. SULLIVAN:
Q. Dr. Caers, can you talk to our jurors about this label and Risperdal as it relates to these concepts "association and causation"?
A. Well, what this label reads is that the use of risperidone can be associated with the occurrence of

certain adverse events, such as galactorrhea, amenorrhea, gynecomastia.
Q. And, Dr. Caers, in your experience, if the FDA concluded Risperdal caused gynecomastia, have you seen labeling where they say the word "caused"?
MR. KLINE: Objection, Your Honor.
THE COURT: Sustained.
MR. KLINE: For many reasons.
THE COURT: Sustained.
BY MS. SULLIVAN:
Q. Has the FDA, Dr. Caers, in your experience with Risperdal, ever concluded that Risperdal causes gynecomastia?
MR. KLINE: Objection.
THE COURT: Sustained. Just not -- he's not qualified.
MS. SULLIVAN: That's not an expert. I said has the FDA ever concluded that.
THE COURT: I don't have a basis for his testimony on that from this witness.
MR. KLINE: That would be hearsay.
THE COURT: I mean, the labels speak for themselves. We don't need this witness to read the label to the jury. This jury has seen this label about three times already.

BY MS. SULLIVAN:
Q. Dr. Caers, because gynecomastia is listed in the label as a potential side effect, does that mean it causes it?
A. No.
Q. And can you explain that.
A. It is that it is observed in patients who are being treated with risperidone, but that does not necessarily mean that it is caused by it.
MR. KLINE: Your Honor, move to strike.
THE COURT: Well, it's --
MR. KLINE: I just couldn't be on my toes like on every question.
It's just every question.
THE COURT: That is stricken. That is as an expert -- that is the testimony of an expert.
He may be an expert, but you didn't follow the rules, so I can't help you on that. You have other experts, I'm sure, to get that particular testimony in if you have it.
Sustained.
Excuse me. Members of the jury, that

last question and that last answer is stricken. Just not the right person for that.
MS. SULLIVAN: And --
THE COURT: About the causation of -- this particular causation issue as to whether or not Risperdal causes this. He's not the right guy for that.
MS. SULLIVAN: And, Your Honor, the question related to labeling and what the FDA --
THE COURT: I'm sorry, Ms. Sullivan, sustained. You're going to have to play by the rules.
MS. SULLIVAN: Just trying to get a fair trial, Judge.
THE COURT: Well, you have to play by the rules to get a fair trial.
MS. SULLIVAN: The --
THE COURT: There are two sides to the coin. That's why we have Rules of Civil Procedure.
BY MS. SULLIVAN:
Q. And, Dr. Caers --
MS. SULLIVAN: Can we look, Jed, at

the safe and effective for children section?
BY MS. SULLIVAN:
Q. And, Dr. Caers, in the adult label from 1993, is there a section that tells doctors about safety for children?
A. The only reference to children in the label of '93 is a statement that the efficacy and safety of Risperdal in children has not been established.
Q. Okay. And that was in the adult label from the beginning?
A. That is correct. Well, it's in the Risperdal label, full stop.
Q. Yeah. Okay.
And, Dr. Caers, when the company got the FDA approval for Risperdal, was there review memos from the FDA as part of the approval package?
A. There are review memos, obviously, yes, we discussed earlier. Because the FDA experts summarize their findings in a review document, and those documents are available to the companies once your product is approved.
Q. And, Dr. Caers, is that information kept by the company as part of their regular and ordinary course of business?
A. Yes. Obviously we keep all the documents from

the FDA after we receive --
Q. And have you seen the review memos from the FDA for the 1993 approval?
A. Back in the early '90s, yes, yes.
Q. And I'm going to show you what's been marked for identification as Defense Exhibit 213.
MS. BROWN: It will be 57.
MS. SULLIVAN: 213A.
MR. KLINE: The same thing we went to sidebar on, Your Honor. I object.
THE COURT: I can't hear you.
MR. KLINE: This would be the same thing we went to sidebar on already. I would object. It's just another version of it, of an FDA document.
THE COURT: Is this an FDA document?
MR. KLINE: Yes.
MS. SULLIVAN: And also a business record.
THE COURT: We had a motion in limine about this entire subject. That is sustained, at least through this witness in this manner.
BY MS. SULLIVAN:
Q. Dr. Caers, are you -- are you -- do you know

whether the FDA noted that Risperdal could elevate prolactin in their review memos?
MR. KLINE: Objection, Your Honor.
THE COURT: Sustained as to what the FDA noted. This is -- you got a witness from Janssen. What did he know?
MS. SULLIVAN: Well, Your Honor, he just testified that this is part of what the company keeps as their business --
THE COURT: But you have other witnesses who are properly permitted to testify to these kind of things. This is not the right one. You didn't qualify him. He's not an expert on FDA pharmaceutical regulations or any of those kind of issues, Ms. Sullivan.
I really -- I feel that in the end, we have to enforce at some point the Rules of Civil Procedure.
MS. SULLIVAN: And, Your Honor, I'm just asking what FDA told Janssen.
THE COURT: What FDA told Janssen, why is that relevant to this man's testimony?
MS. SULLIVAN: Because he's Janssen.
THE COURT: I don't understand that.

MS. SULLIVAN: He's the doctor at Janssen that got this information.
THE COURT: If you establish some foundation for something, yeah.
MS. SULLIVAN: Yes.
THE COURT: But if you're just throwing documents out there for him to read them for the jury, that's not permitted.
MS. SULLIVAN: Well --
THE COURT: We went through that before the trial.
BY MS. SULLIVAN:
Q. Dr. Caers, you received the FDA review memos on Risperdal?
A. Yes, indeed.
Q. And --
THE COURT: When did he receive them?
THE WITNESS: Well, they were available from shortly after the --
THE COURT: Well, were you involved in this 1993 application?
THE WITNESS: I was involved in Risperdal -- in all Risperdal issues from 1991 on, yeah.
THE COURT: Well, if you establish

the foundation...
MS. SULLIVAN: May I show the document to the jury?
THE COURT: No. You have to establish a foundation as to how this witness can share something about this document that's meaningful for us.
MS. SULLIVAN: Okay.
BY MS. SULLIVAN:
Q. And, Dr. Caers, as part of the FDA review, did the FDA advise the company in the review memos that they knew that Risperdal could elevate prolactin?
MR. KLINE: Objection; leading.
THE COURT: Sustained. Sustained. Sustained.
MS. SULLIVAN: Sustained as to what the FDA told Janssen?
THE COURT: Absolutely. I don't understand in what respect this is relevant testimony here for this witness.
BY MS. SULLIVAN:
Q. Did the FDA also, Dr. Caers, have comparative data looking at Risperdal versus other medicines like Haldol?
MR. KLINE: Objection; repeated

violation.
THE COURT: Sustained. Sustained. Unless you lay a foundation as to this doctor's personal knowledge of the issues in play here and you set that up for us, we're not going to just be flinging documents out there. We've been here two and a half weeks. We cannot just fling documents.
MS. SULLIVAN: I wasn't flinging, Your Honor.
THE COURT: I think you are.
BY MS. SULLIVAN:
Q. Dr. Caers, did the company provide the FDA -- and you were involved in the approval process for Risperdal, right?
A. Yes.
Q. And did the company provide the FDA with information on comparative trials, Risperdal compared to other medicines?
A. Yes.
Q. And did the FDA -- and in those comparative trials that you gave to the FDA, did it show that Risperdal could elevate prolactin more than a first generation antipsychotic?
MR. KLINE: Objection. This is all

leading.
THE COURT: Yeah. Sustained.
MR. KLINE: She's just asking for a "yes" or "no."
THE COURT: Sustained.
I'd take a break right now except for the fact that I do have this meeting, and it's scheduled for 11 o'clock. I was trying to use our court time.
But these questions, as you're phrasing them, are impermissible.
MS. SULLIVAN: I understand the Court's position, Your Honor.
THE COURT: It is my position. And I hope you follow my position.
BY MS. SULLIVAN:
Q. Dr. Caers, did the FDA -- you already told our jurors you provide a comparative data as part of the initial approval process showing how Risperdal faired against other medicines on the issue of prolactin, right?
A. That is correct.
Q. And so, Dr. Caers, are you aware as to whether the FDA commented back in 1993 that they knew that Risperdal could elevate prolactin more than other

medicines?
MR. KLINE: Objection.
THE COURT: All right. That's another -- that's sustained.
That's, ladies and gentlemen, hearsay. That's a statement that's made outside of this courtroom not subject to cross-examination. It's forbidden by our rules of evidence except for certain exceptions. I'm finding that there are no exceptions at the moment. We cannot have testimony about from the FDA through this witness when that witness is not either here or some exception. That's what's going on here. And, you know, I just gave you an education on hearsay.
BY MS. SULLIVAN:
Q. Dr. Caers, did you provide the FDA with information that showed that Risperdal elevated prolactin more than Haldol?
MR. KLINE: Objection.
THE COURT: No. As to what he provided the FDA, absolutely permissible.
MR. KLINE: Why can't the question be: What did you show to the FDA, rather

than her giving him the answer?
THE COURT: I agree with that. But anything that he provided to the FDA or he knows the company provided to the FDA, that's fair game, absolutely.
THE WITNESS: Well, in our studies, we had Risperdal patients and we had patients on a reference compound, for example, haloperidol, also other first generation antipsychotics; and we had efficacy, safety, including prolactin levels, in all these different patients treated with different agents, including Risperdal and Haldol, yes.
BY MS. SULLIVAN:
Q. And did you review the FDA memos back when they were provided?
A. Well, we obviously had to look at them after the approval. But as I said earlier, we only had them available after the approval, so not during the approval.
Q. Yes. Did you review the FDA memos after the approval?
A. I did some of them, yes.
Q. For what purpose, Dr. Caers, would you look at the FDA approval?

A. Well, it's always interesting to see what the opinion of the FDA expert is after they have seen our full data set so that you understand their position and how they came to the label text.
Q. And what did you learn, Dr. Caers, about the FDA findings in the review memos on prolactin elevation and how Risperdal compared and what the FDA knew about that?
MR. KLINE: Objection, based on the Court's prior rulings.
THE COURT: Well, that's -- now we're getting closer to a permissible exception. You know, if you ask him what did he know that he then did on another test or something, fine.
THE WITNESS: Well, our data showed that the effective doses of Risperdal, there was prolactin increase in the Risperdal patients, but also in the haloperidol patients. So if you just compared one versus the other, it was not too much of a difference in the degree of prolactin increase compared to first generation antipsychotics such as haloperidol.
BY MS. SULLIVAN:

Q. And, Doctor -- and did you note that, based on your review of the FDA memos, that the FDA was aware of that?
A. Yeah, sure.
MR. KLINE: Object.
BY MS. SULLIVAN:
Q. And, Dr. Caers --
THE COURT: Overruled.
BY MS. SULLIVAN:
Q. And, Dr. Caers, did you -- did the company, after FDA approved Risperdal in 1993, continue to study the medicine?
A. Yes, very much so. We did additional studies on schizophrenia but also in other psychiatric disorders in order to further have approvals later on, as we already reviewed.
Q. And, Dr. Caers, once the FDA approved Risperdal, can you talk to our jury about the kinds of other studies the company did and the kinds of other indications the company saw, from the FDA?
A. From the early to mid-'90s we started exploring Risperdal also in children with conduct disorders or disruptive behavioral disorders. We studied Risperdal in patients with bipolar mania, again, another psychotic disorder where

antipsychotics can be very effective in. We started studying psychosis in the elderly with Risperdal. We started also studying Risperdal in adolescents with schizophrenia because schizophrenia can start up at the age of 12, 14, 16.
We also studied Risperdal in children and adolescents with bipolar mania. As I said earlier, we did additional studies in schizophrenia. And we also studied different types of administration in different psychotic disorders.
MS. SULLIVAN: And, Your Honor, I'm sorry, what time does the Court want to break?
THE COURT: In about five minutes.
BY MS. SULLIVAN:
Q. And, Dr. Cares, as Janssen continued to study the medicine -- and Risperdal is still on the market today, sir?
A. Yes, it is.
Q. Still being prescribed today?
A. Yes. Yes.
Q. And so it's been on the market for how many years, Dr. Caers?
A. It's about 20 -- 21, 22 years now, about.
Q. And can you give our jurors a sense of how

much safety data there is on Risperdal as of today?
A. Well, then you need to differentiate it in two databases. When I stopped working for Risperdal back in 2009, we had more than 16,000 patients documented in clinical studies with Risperdal. But apart from that, there's also another database that is based on spontaneous reporting. Physicians when they see an adverse event that is a particular concern of interest, they report it to the authorities. And that's another type of very huge database with thousands and thousands, even hundred thousands of patients of whom some are reported to have a certain adverse event on Risperdal, for example.

So that's a very -- thousands and thousands of patients safety database, apart from the clinical studies we had in our 16,000 patients.

Q. And, Dr. Caers, are you familiar, as part of your work in medicine development, with the FDA standards in terms of how many studies and how many patients you have to have to get FDA approval?
A. Yes. The minimum for an approval, but that's the absolute minimum, is you need to have 1,500 patients exposed to the product, different subjects exposed to the products. You need at least 3- to

600 patients exposed for six months. And you need at least 100 patients exposed for one year or more in order to have an approval package for one single indication.

Q. And, Dr. Caers, as it stands, how does what Janssen did in terms of safety testing on Risperdal compare with the FDA standards?

MR. KLINE: I have an objection, Your Honor.

THE COURT: That's sustained. That's sustained.

BY MS. SULLIVAN:

Q. Dr. Caers, did Janssen meet or exceed the FDA standards?

MR. KLINE: Objection. It's just a back door. Same question.

THE COURT: You're asking his opinion?

MS. SULLIVAN: Well, he's a fact witness, Your Honor. He knows.

THE COURT: All right. That's sustained.

MR. KLINE: That's an opinion question.

BY MS. SULLIVAN:

Q. Dr. Caers, do you know by how much Janssen exceeded the FDA standards?

MR. KLINE: Your Honor, objection.

THE COURT: Sustained. You are asking for some kind of evaluation, quantitative evaluation that only an expert can make. You know, you can ask him what he did, what he didn't do. But that's a fact witness. But to ask him for his opinion on whether he did enough, that's what the subject of this trial is about. Sustained.

We're going to take a recess right here till about 11:30, all right? I do have a meeting that I'm going to attend very briefly and then come back. So we're going to take a recess here till 10:30.

No. Then what's going to happen is we're going to return -- I mean 11:30. And then what we're going to do, we will return for another hour and then we'll take a recess for lunch is what we're going to do. I apologize at my end. But that way we didn't lose a whole morning for this meeting for us, all right? So we'll see you in about, I guess, at 11:30 I'll be here.

COURT CRIER: All rise.

THE COURT: You may go outside, of course, if you want to. You know, you don't have to stay here. Same rules apply.

- - -

(Whereupon the jury exited the courtroom at 10:42 a.m.)

- - -

THE COURT: Sir, you are excused till 11:30. But please do not discuss your testimony now with your lawyers.

THE WITNESS: I understand, Judge.

THE COURT: Yes, sir.

MR. KLINE: May I have whatever demonstratives are going to be used with this witness?

MS. SULLIVAN: Sure.

THE COURT: I guess that would be efficient for everybody.

MS. SULLIVAN: Yeah.

MS. BROWN: Yeah.

THE COURT: I do urge counsel to review the motions in limine. We spent a lot of time on them. And I hope that they're a guide to what this Court's rulings will be

here in court in front of the jury.
MS. SULLIVAN: And, Your Honor, other than safe and effective, Your Honor, I thought that Judge New ruled that the FDA issues could come into this case.
THE COURT: Well, the safe and effective, that particular language was forbidden. But I'm not, you know, going to jump over heels on it, because it was used just now by a witness and there was no objection.
But the reality of the matter is that the FDA documents were precluded for reasons that were stated on the record before. These are documents that fundamentally can be used if they are introduced through a proper foundation the proper way. But not in order to -- we went through the same thing with Mr. Kline when he had Dr. Kessler here, and we did not permit all of these documents to be admissible. Only certain ones came in.
If you want to run them by us ahead of time before the trial or before a witness, by all means. But it's at your peril if you're going to go against rulings that have

already been made on these subjects.
All right. We're at recess till 11:30.
- - -
(Whereupon a recess was taken.)
- - -
COURT CRIER: Come to order, please.
THE COURT: All right. Please be seated.
- - -
(Time noted: 11:36 a.m.)
- - -
(Witness resumed the stand.)
- - -
COURT CRIER: All rise as the jury enters the courtroom.
- - -
(Whereupon the jury entered the courtroom at 11:38 a.m.)
- - -
THE COURT: All right. Please be seated, everybody.
All right. Thank you for your indulgence, everybody. It was good. Thank you.

You may proceed when you're ready.
MS. SULLIVAN: Thank you, Your Honor. Welcome back, everyone.
- - -
EXAMINATION
- - -
BY MS. SULLIVAN:
Q. Welcome back, Dr. Caers. Let me just get moving here.
Dr. Caers, I wanted to talk some more about Janssen's study of Risperdal on children and adolescents; and you were involved with that, Dr. Caers?
A. Yes, I was.
Q. Can you tell our jury the nature of your involvement in Janssen's studying the medicine on children and adolescents?
A. Well, my team actually developed the study, the study protocols and actually run it by investigators, and also managed the analysis and the reporting of the study in the Clinical Study Reports, and eventually also managed and dealt with the composition of the New Drug Application -- in this case a Supplemental New Drug Application, which concluded -- which had all the information we have

collected in the different studies in a big file, which was eventually submitted to the FDA at different occasions.
Q. And, Dr. Caers, after the medicine was approved in 1993, did the company become aware that it was being prescribed off-label by physicians to children and adolescents?
A. Well, we had information, indeed, that in this country there were physicians that prescribed Risperdal for children or adolescents at that time.
Q. And so if the company was already selling the medicine for off-label prescriptions, can you tell us what the reason was the company continued to study the medicine in children and get towards getting additional approvals?
A. Well, for the company it's very important that there's appropriate information on appropriate use of this medicine in different populations, such as in this case pediatric population, such as children and adolescents. And although it was used in the marketplace, which we call off-label, it is important to document efficacy and safety, have that reviewed by the FDA, so that you have appropriate guidance in the label on how to use this medicine in this population and for which type of population

within this pediatric population.
Q. And, Dr. Caers, are there issues or challenges when companies try to study medicines in children?
A. Well, yeah. If you can understand, patients are requested and expected to give informed consent, as we discussed before the break, and particularly for children, this is not easy. I have three children as well. I have seven grandchildren. So you would think twice before you would conclude that you would allow your child or your grandchild to enter a study. Nevertheless, without the goodwill and the preparedness of these parents and children, we wouldn't be able to do these in clinical studies, and we would never be able to advise physicians on how to appropriately use this medicine in this population.
Q. And, Dr. Caers, while you were supervising some of these clinical trials on children and adolescents, can you tell us whether the FDA had any involvement in encouraging companies to study medicines?
MR. KLINE: Objection.
THE COURT: Overruled.
THE WITNESS: There are two ways that the FDA is involved. First of all, as we

said earlier, for every study you want to do in this country, you need to have at least permission by the FDA to run the study. But there is a particular legislation as well that came into effect by the late '90s, and that has to do with pediatric exclusivity. What does pediatric exclusivity mean?
Congress has voted legislation back in the late 1990s that said and that wanted to stimulate clinical research in children, because before actually we started in this area, there was no -- there was no research ongoing, not at all.
So Congress and the FDA wanted to stimulate the companies to study drugs more in children and adolescents. And that's how the legislation of pediatric exclusivity came into account.
And that legislation allowed and gave even the mandate to the FDA to tell companies this is the type of studies in this type of population that we want you to do. And if -- on the other hand, there's a benefit for companies as well in the same legislation by Congress. If you actually do them, these

studies, the way the FDA asked you to do it and you complete the studies, you make the Clinical Study Report and you submit this information to the FDA, and if this is, along with the written request, what the FDA asked you to do, then companies get an additional six months exclusivity, which basically means that you have six months more exclusivity on your product than without these pediatric studies. So that genetic companies can only come six months later on the market with a genetic compound. That's basically the benefit for companies first that they ask you to do.
BY MS. SULLIVAN:
Q. So the FDA and government provided incentives for companies to study the medicine in children?
A. Within the --
MR. KLINE: Objection. Objection.
THE COURT: All right. That's sustained. Sustained.
BY MS. SULLIVAN:
Q. And did you have meetings with the FDA, Dr. Caers, to get permission to study the medicine in children and adolescents?

A. We had meetings with the FDA on how to run these studies and how these studies would need to look like and what type of patients, et cetera, yes, we had several meetings of this kind.
Q. And, Dr. Caers, I'm going to put up an exhibit that has been up before. And this is DG6-3. And Ms. Brown can tell me what is the --
MS. BROWN: Yes. 58.
MS. SULLIVAN: Defense Exhibit 58.
(Exhibit D-58 marked for identification.)
COURT CRIER: Counsel have it?
MS. BROWN: Yeah, they have it.
MR. KLINE: This is the demonstrative. I have no objection.
BY MS. SULLIVAN:
Q. And, Dr. Caers, we're looking at Defense Exhibit 58. And can you tell the jury how many clinical trials Janssen did to support the approval of Risperdal in children and adolescents?
A. Well, in total, we did at least 18 studies in different populations of children and adolescents ranging from autism, disruptive behavior disorders, adolescent schizophrenia, children and adolescent bipolar mania. And they're, more or less, a little

bit listed here on this list.

And just for your information, on the left-hand side, Clinical Trial, the NED-9 is a study done in the Netherlands. The BEL is a study done in Belgium. International is an international study in different countries. USA is a USA study, and so on, Canada, Canada, and so on.

Q. Dr. Caers, what kind of safety information did Janssen collect in the course of these clinical trials in children and adolescents?

A. Well, similar to the adults, you collect basically all safety information. You do regular blood analysis. You also systematically measure prolactin in this population. We collected adverse events as reported by patients and by the investigator, which are written down by the investigators in the file. And all this information, apart from obviously the efficacy assessments, was all collected together in the database and eventually in the Clinical Study Report, just similar to what we discussed before the break on adult patients.

Q. And did Janssen provide all of the side effect information from these clinical trials to the FDA?

A. Yes, indeed.

Q. And, Dr. Caers, did Janssen also publish these studies for the world to see?

A. Yes. The different studies were, indeed, published in medical journals so that also the medical community and doctors could read about the experience and the findings in particular studies, both on efficacy and safety.

Q. And, Doctor, at this time was there any requirement for Janssen to publish their studies?

A. At that moment I don't think there was a requirement to publish the studies, but that was usually done.

Q. And, Dr. Caers, can you describe -- so there's been some discussion about the time lag between when a study is done and when it's published. Can you talk about the peer-review process?

A. Yeah. It's a -- there are different steps, obviously. Once you have your database closed and your analysis, the first thing you do is making sure you have the Clinical Study Report. And that's a hell of a job, as I said earlier. That's a 100- to 150-page document with thousands of pages of tables. And then the next step is you consider to publish the findings of the study in a peer-review journal. So you develop a manuscript, have it reviewed by

authors up and down and different versions. Then at the end you have a final manuscript which is submitted to a medical journal with requested publishes.

Peer review means that experts in the field review your paper, very often have comments, recommendations to -- can you say this differently, we don't think this is an appropriate phrase. Can you do that additional analysis? So the next step is you do, again, your additional things. You adapt your manuscript. You resubmit it and then very often it is either accepted for publication and it goes in the waiting list for the final publication, which may take another six to nine months. So overall, this period can take a few years even, usually.

Q. And, Dr. Caers, how did the company decide what kind of indications or reasons the company should study Risperdal for as far as children and adolescents?

A. Well, there are two sources to make that decisions. First of all, we had experts in the field and we did advisory panels because we knew --

Q. Is that advisory panels?

A. Yeah, advisory panels, yes. So that's a group

of experts in the field that you bring together and that you raise questions and you hear on their opinion. And they said -- because we knew there was widespread use in pediatrics of Risperdal -- and they said, well, where is this used most prominent? And consequently, that is where you have the most prominent, pronounced medical need.

On the other hand -- and also the FDA -- and remember the pediatric exclusivity law -- there, the FDA said we want you to do clinical studies in pediatrics in this indication, which was, in our case, schizophrenia and bipolar mania, because those are the two indications for which the product was approved in adults. And they said once this indication can also occur in pediatrics, we want you to study that field. So there are two different sources in making that selection.

Q. So outside experts, outside doctors would suggest ways that Risperdal may be helpful and then the FDA also gave you some information about what they wanted?

MR. KLINE: Objection; asked and answered; and simply repeating his testimony as she's inclined to do, so I object.

THE COURT: How about leading?

MR. KLINE: And leading, too.
THE COURT: Sustained. Sustained.
BY MS. SULLIVAN:
Q. And, Dr. Caers, I want to show you a document that was marked by the plaintiffs. It was Plaintiff's Exhibit 16, if I may.
MS. SULLIVAN: Okay. Is there any objection?
THE COURT: I don't know. What is this document?
MR. KLINE: I need to get the document in front of me.
MS. SULLIVAN: It's your Exhibit Plaintiff's 16.
MR. KLINE: I understand that. And there was a pile this high.
THE COURT: Okay. This is D-16?
MS. SULLIVAN: Plaintiff's 16.
MS. BROWN: P-16.
COURT CRIER: It was a plaintiff's exhibit.
THE COURT: P-16.
MR. KLINE: Your Honor, it's an FDA contact document, and it's a Janssen document. I just need to know what the

question is before the display.
THE COURT: Yeah, I agree.
MR. KLINE: Certainly every document doesn't need to be displayed.
THE COURT: All right. Why don't you ask your questions and see how you're going to use this document.
MS. SULLIVAN: Sure.
BY MS. SULLIVAN:
Q. Dr. Caers, were you involved with interactions with FDA and interactions with people in your group who interacted with FDA about what indications Janssen should seek approval for?
A. Yes, I was.
Q. And there are also meetings with the FDA on that issue?
A. Yes, there were.
Q. And, Dr. Caers, you're familiar with -- well, tell us about the conduct disorder issue.
A. Well, conduct disorder, that was back in the mid-'90s when the advisors, as I referred to earlier, advisors that this was one of the areas in pediatrics where there was a major medical need and where there was a substantial use already at that moment. And that's why in the mid-'90s we started

the whole development program to study Risperdal in, the umbrella term, "conduct disorder," or with other words also, disruptive behavioral disorders. And we did several double-blind studies.
First, there's placebo. That means you give one group the active compound and the other group you give a sugar pill, but that looks the same and you don't know which one of the two has the active and which one has the placebo, the sugar pill. And then you see whether you find a difference between the active and the placebo, which is the documentation of your efficacy, and obviously also document all safety. So this is the efficacy study.
On top of that, we did long-term safety studies where you have patients exposed to the compound over a long period and you document all safety aspects related to the product.
Q. And, Dr. Caers, you said it was already being used in conduct disorder. What do you mean, sir?
A. Well, as was mentioned earlier today, there was also in the '90s, there was a certain off-label use in the US of Risperdal in pediatrics. And based on the feedback we got from these experts, this was one of the areas where there was substantial

off-label use; but also that in their experience, there was a very substantial benefit. But obviously that had to be documented in well-designed studies.
Q. And, Dr. Caers, did the FDA have any concerns about Janssen seeking approval for the indication conduct disorder for children and adolescents?
A. Well, yeah. We consulted with the FDA to which extent the FDA thought that this would be a valid indication for Risperdal and they raised their concerns. They thought that this product, and particularly its use would be targeted towards aggression and agitation in conduct disorders' patients, and they didn't feel that aggression on itself was an appropriate indication for label --
MR. KLINE: Your Honor, please.
THE COURT: I'm going to permit him to finish his answer.
MR. KLINE: Yes.
THE WITNESS: They did not say it didn't exist, because there's a big book -- a thick book, the DSM-IV, which lists all the psychiatry disorders by the American Psychiatry Association. They said, yes, we recognize it's in that thick book, but, nevertheless, we don't think this is an

appropriate indication for label.
MR. KLINE: Move --
MS. SULLIVAN: And --
MR. KLINE: May I, please?
Move to strike. It's all hearsay based on what he says the FDA says.
THE COURT: Well, I am going to deny that motion at this time. I'm going to deny it.
But, again --
MS. SULLIVAN: May I use the document, Your Honor?
THE COURT: I don't know. You have to use that for a legitimate purpose. I mean, to refresh memory, some kind of reference, you know, something that has to be legitimate as far as being flashed up on evidence.
MS. SULLIVAN: Well, they've put it up. This is their document. They put it up.
THE COURT: It doesn't matter whether it's their document. They used it for a particular purpose.
BY MS. SULLIVAN:
Q. And, Dr. Caers, are you familiar -- the jury

has seen the term -- and Mr. Kline showed Dr. Kessler -- the term as it related to conduct disorder, the FDA's concern about, quote-unquote, a "chemical straitjacket." Are you familiar with that document?
A. Well, yes. Because that was in the minutes, I think, of that actual meeting.
Q. Yeah.
A. And that has exactly to do with the treatment of aggression. That's -- that's a delicate issue. Why do you treat aggression? Is it in order to help the patient or is it in order to help the environment?
Q. And, Doctor --
MR. KLINE: Your Honor, move to strike. He's not a physician. He's not even a physician.
THE COURT: Well, no. Overruled. Overruled.
It's still unclear to me, Counsel, exactly what role this witness had in all of this.
MS. SULLIVAN: Fair enough, Judge.
BY MS. SULLIVAN:
Q. Dr. Caers, can you describe -- can you tell

our jurors what role you had in the overall Risperdal approval process?
A. Well, not only in the approval process, my team, as I said earlier, which was managed by me, so headed by me, was dealing with all clinical studies done with Risperdal worldwide. We were dealing with all submissions. We were dealing with all the consultations with regulatory bodies, including the FDA, but not limited to the FDA. My team was dealing with all the studies with it, reporting them, putting the files together, submitting the files, negotiating and having meetings with the FDA before submission, if necessary after submission, and eventually dealing with the final label as approved by the FDA.
Q. And, Dr. Caers, as part of that process, would you review minutes of meetings with the FDA?
A. Yes.
THE COURT: And also, Counsel, would you ask him what the timetable of his involvement in this -- what he just described, what are we talking about? So I can understand for relevancy sake, once and for all --
MS. SULLIVAN: Sure.

THE COURT: -- what we're talking about.
THE WITNESS: If I may.
THE COURT: Yeah. Go ahead.
THE WITNESS: I played this role as a team development leader since 1999, mid-1999, but also before I was involved in the Risperdal strategy, but less so in dealing with the FDA meetings. But from 1999 up to 2009, I was involved with basically all these meetings.
MS. SULLIVAN: And so can I now display Plaintiff's Exhibit 16?
MR. KLINE: No. It's just full of FDA stuff, Your Honor.
I don't object to the "chemical straitjacket" part.
THE COURT: Pardon me?
Well, as far as I'm concerned, is this a document he's familiar with?
MS. SULLIVAN: Yes.
THE COURT: Why don't you just authenticate it in the usual way.
MS. SULLIVAN: Yeah.
THE COURT: And then we'll go for it.

BY MS. SULLIVAN:

Q. And, Dr. Caers, is this a document that you're familiar with; that you've seen?

A. Yeah, sure. Because Al Derivan is one of the gentlemen -- he was my clinical leader on my team as a child psychiatrist; Goedele DeSmedt. So, yes, all these people were a member of my team. And obviously I was involved from A to Z in preparing for this meeting. I was not actually at that meeting, but I was also involved in reviewing the minutes and the next steps.

MS. SULLIVAN: And, Your Honor, may I display the --

THE COURT: For what purpose?

MS. SULLIVAN: I wanted to talk about their -- in response to Mr. Kline's argument about chemical straitjacket, what was really going on here.

THE COURT: Well, why don't you have him review this document, look at the bullet point and ask him. You don't need to put the whole document up there because I don't believe this whole document was admitted before in its entirety, unless there's a reason for it.

MS. SULLIVAN: They had it up with Dr. Kessler, Your Honor.

THE COURT: Again, whatever -- I have to go through my notes as to what the reason was.

For the purpose that you're telling me now, you can have him comment on what was going on with that chemical straitjacket bullet point by refreshing his memory about that point without putting the whole document in there.

BY MS. SULLIVAN:

Q. So, Dr. Caers, can you talk about the FDA's concern on this chemical straitjacket statement that Mr. Kline referred to in his case and what the company's response was?

MR. KLINE: Object to the hearsay. No objection to the company --

THE COURT: No. As to his concern, FDA, or Janssen's response to that whole issue, absolutely.

You may proceed.

THE WITNESS: So as I said earlier, the FDA had concerns about treating aggression as a target, and they didn't say

no, because they don't -- they just raised a concern and referred to the term "straitjacket." But they also said, look, before we decide on this, you can go ahead, but we will bring it before a public advisory board. And a public advisory board is part of the review process with the FDA in which they ask, again, experts in the field, whether the experts support an approval, yes or no. So it's not you can't do it, but they said we are not convinced.

BY MS. SULLIVAN:

Q. And so what did Janssen do in response to that?

A. Well, we did two things, because, again, this is within the pediatric exclusivity legislation. Part of this meeting was as well. Our question to the FDA, this is the studies we have already done in pediatrics. Can this be used for submitting for the pediatric exclusivity?

And there, the FDA said, no, we don't think so because we -- we -- and this legislation was very new at that moment. The position by the FDA was we want you, first of all, to study, according to the pediatric exclusivity legislation,

we want you to study Risperdal in this case in schizophrenia and bipolar mania, because those are the two indications the product was also approved for in adults. And this indication, this disease can occur in children and adolescents, at least for schizophrenia in adolescents.

Q. And, Dr. Caers, did Janssen pursue those indications in children, schizophrenia and bipolar?

A. So as a consequence of this meeting, we definitely pursued and did studies in both adolescents with schizophrenia and in children and adolescents with bipolar mania, and we eventually got pediatric exclusivity approved.

Q. And was Risperdal approved for children with schizophrenia?

A. Not for children, but for only adolescents.

Q. Adolescents.

A. Schizophrenia doesn't occur before the age of adolescents. So it was adolescents with schizophrenia and children of 10 years and older and adolescents in bipolar mania.

Q. And can you talk to our jurors about how Janssen's decision to pursue FDA approval for kids with autism came about?

A. That's a whole different story.

It all started with a study and a consortium of US academic centers. And there they had to combine themself -- organize themselves under what they call the RUPP consortium. And RUPP stands for Research Unit for Pediatric Psychotherapy, or Psychopharmacology. And they concluded, with the sponsorship of the National Institute of Mental Health, which is a government organization that sponsors and that stimulates research in mental health, this consortium run what is called the RUPP study, or the USA-150, totally without really contacts and input from our side in the study design and the study conduct.

Q. And, Dr. Caers, you were familiar with the RUPP study?

A. Yes, I am.

Q. And can we -- and did Janssen -- well, can we mark -- I think it's already been used. Defense Exhibit...

MS. BROWN: It would be -- we're going to mark the flip chart as 59. So it would be 60, if we have not already used it.

(Exhibits D-59 and D-60 marked for identification.)

MS. SULLIVAN: Any objection?

MR. KLINE: Yes. Your Honor, the learned -- if it's learned treatise, it falls under Aldridge. And to the extent he testifies he knows it and the like, that's fine. To the extent it's going to be read, displayed, parroted, then I object, under Aldridge, specifically under the Aldridge case, which doesn't allow that.

MR. MURPHY: He's not an expert.

MR. KLINE: With an expert or a nonexpert.

THE COURT: Yes. Sustained.

BY MS. SULLIVAN:

Q. Dr. Caers, the study that you talked about, who funded that study, the RUPP study?

A. The RUPP study was funded by the National Institute of Mental Health.

Q. And that's the government?

A. That's a government-sponsored institute to stimulate research in mental health in the United States of America.

Q. And can you tell me -- and so Janssen -- did Janssen have anything to do with the RUPP study?

A. No. We were not involved in the design and the execution of the study.

Q. And what did this government-funded study find on the issue of Risperdal and whether it worked for kids with autism?

A. Well, the results which were published in 2002, I think, they showed that there was clear efficacy of Risperdal in the children compared to placebo. Remember, the sugar pill. It was a double-blind study. And there was very robust efficacy, particularly on what they call the irritability associated with autism, which are symptoms of agitation, aggression, restlessness and things like that. And they also obviously documented the safety in this study as described in the paper.

Q. And can you tell us whether the RUPP study got any press?

MR. KLINE: Objection, Your Honor. Whether it got press is irrelevant.

THE COURT: Whether it got press, sustained.

BY MS. SULLIVAN:

Q. How, Dr. Caers, if at all, did the findings of the RUPP study impact Janssen in terms of their research?

A. Well, the data were published in the New

England Journal of Medicine, by the way, which is one of the most famous medical journals here in this country and worldwide, by the way. But also we were contacted actually by the RUPP investigators, and they said look --

MR. KLINE: Objection to the hearsay.

THE COURT: Well, I'm really more interested --

MR. KLINE: "They said."

THE COURT: -- in what this witness did. So if you can -- you know, if it was in response to something --

MS. SULLIVAN: Yeah. It's offered for a non-hearsay purpose, Your Honor.

BY MS. SULLIVAN:

Q. So did the RUPP investigators communicate to you information that led Janssen to research this medicine in children with autism?

A. Well, as I was trying to say, the RUPP investigators contacted us and actually said, hey, you should really look at those data because we really think these are unique findings.

MR. KLINE: Objection to the hearsay, Your Honor. I can't cross-examine them.

THE COURT: You know what, so we're

really clear, what is easy to tell the jury about from a legal point of view is what you did in response to what you were told by the FDA. But you're really not allowed under the general rules to tell us what the FDA told you. So what you need to do is to say, I heard from the FDA and I did this.

THE WITNESS: I'm not referring to what the FDA told us.

MS. SULLIVAN: These are the --

THE WITNESS: I'm referring to what the RUPP investigators told us.

MS. SULLIVAN: These are the folks on the government study.

THE COURT: But that's still the same thing from a hearsay. That's still somebody else. That somebody else is not here to testify.

THE WITNESS: Bottom line is: Those RUPP investigators suggested to us to talk to the FDA regarding this data, and they suggested us to see what the FDA -- whether this data might be suitable for including this information in the label because they were convinced that this was very important

and relevant for the medical field.

BY MS. SULLIVAN:

Q. And the RUPP investigators, can you, Dr. Caers, based on your experience with them, describe for our jurors who they were and what RUPP was about.

A. Well, RUPP was, as I said, a consortium of academic child psychiatric centers all over the country, and so these investigators were prominent child psychiatrists linked to different universities in this country.

Q. And, Dr. Caers, can you tell us what the company did next as a result of this RUPP study and your communications with these outside investigators.

A. Well, then we had a consultancy meeting with the FDA on the database, on the data from the RUPP study, but also because, as I had told earlier, we had done substantial research already in disruptive behavior disturbance in children and adolescents. So we went to the FDA and said, look, this is valid data on the use of Risperdal in children with autism and beyond that. We have very substantial and large database on Risperdal in children and adolescents, more particularly in conduct disorder.

And the outcome of that meeting was that the FDA was prepared to accept such an SNDA, a Supplemental New Drug Application, for use of Risperdal in children and adolescents with irritability associated with autism. And that's important from the safety point of view with the much larger database we had collected in children and adolescents with conduct disorder.

Q. And, Dr. Caers, as part of the approval process for Risperdal for autistic kids, did the company do some of their own studies?

A. We had -- apart from the RUPP study, we had also a Canadian study which was company organized, which was also a double-blind study with active and the sugar pill, which the results of which were very much in line with the findings of the RUPP study. And that obviously was added to the weight of evidence in the SNDA. And, by the way, it was all information we had on the safety of Risperdal in children and adolescents.

Q. So, Dr. Caers, the safety data -- did the safety data that supported the autism approval with FDA include the safety data from this government-funded study, the RUPP study?

A. That is correct.

Q. And also some studies done by Janssen?

A. Yes.

Q. And, Dr. Caers, the plaintiffs in their case allege that the autism approval was pushed through --

MR. KLINE: Objection to the form.

THE COURT: The plaintiff's claim?

MR. KLINE: Yeah.

THE COURT: No; sustained.

BY MS. SULLIVAN:

Q. Dr. Caers, was the autism approval pushed through by Janssen or the FDA?

A. I'm afraid it's very difficult to push something through to the FDA. They are a fully autonomous body and they make up their own mind based on their own assessment by experts in the field within the FDA.

Q. How long, Dr. Caers, did it take between the time Janssen submitted the new drug approval package for autism to the FDA to the time the FDA ultimately approved the medicine for kids with autism?

MR. KLINE: Your Honor, objection.

THE COURT: Basis?

MR. KLINE: Basis is that the entire case here is '02 to '06. This is all about

getting approval in '06.

THE COURT: All right. I realize that.

MR. KLINE: We admit that, and everyone in the case agrees --

THE COURT: All right. I realize that. That's overruled.

I mean, in case we forgot, why don't you have him answer, just in case we forgot.

THE WITNESS: No. I think, to be honest with you, we submitted somewhere the SNDA for autism mid-2003 and eventually got an approval late 2006. So that is nearly two years and a half.

BY MS. SULLIVAN:

Q. So it took a couple years?

A. Yes.

Q. And the FDA -- and, Dr. Caers, was there interaction between the company and the FDA over those years?

A. Yes; several.

So first, that is, you submit your SNDA, and then the FDA reviews and they come back with the first feedback, after 10, 12, 15 months, which in this case was an approvable letter. That

means it looks okay, guys, but you need to provide more information. Do you have more safety information? Do you have more dose information? Because that was a critical issue in this submission.

We consequently brought additional data together and submitted them in what we call a complete response. Then the FDA once more reviews this additional information and then comes back with the next feedback and judgment, and that was an unapprovable letter. They said we still have decent questions about your dose recommendation, and that's -- that has technical reasons. I can elaborate upon, if you wish.

Then we had a meeting with the FDA, a face-to-face meeting on what we could do next in order to come up to their concerns, and particularly the dosing recommendations. And eventually they accepted that with some additional specific analysis of the data and the existing data. They accepted an approval with what we call a Phase IV commitment; that the FDA said, yes, we approve, but that means that you're going to need one additional study after we approve, which is a Phase IV commitment, on studying the lowest effective dose in children and

adolescents with autism.

Q. Did the --

MR. KLINE: Your Honor, we weren't told the year.

THE COURT: Well, again, there's an objection?

MR. KLINE: Yes. There's no objection if we're told the year of this.

THE COURT: I mean, if you want to, we can go back through all of that and give the relevant time periods, if you want.

THE WITNESS: Well, as I said, the first submission was in mid --

MR. KLINE: My objection was only to the year that it was approved.

THE WITNESS: The approval was in --

THE COURT: No. Counsel, that's overruled. Otherwise I would permit just putting the document up there that Ms. Sullivan wanted at the very beginning. We need to get through this.

THE WITNESS: Yeah. Once again, we did submit the SNDA in mid-2003, about, and then the different steps, which I don't know by heart the actual dates, but I do know I

think we had the final approval in October 2006.

BY MS. SULLIVAN:

Q. So, Dr. Caers, can you tell us whether the company satisfied the FDA's request for additional safety data, additional information, as part of the approval process?

A. Yes. Of course we did, because otherwise the FDA would not have approved the indication back in October 2006.

Q. And, Dr. Caers, I want to show you, and with permission from the Court, I want to show the jury the FDA October 23, 2006 approval letter for the autism indication.

MR. KLINE: Objection, based on the Court's rulings.

THE COURT: That's sustained. That's the same thing.

MR. KLINE: And she knows it.

THE COURT: We have a label in evidence. And we know that this document exists. The letter is -- you can mark it, put it into the record. But there's no reason to -- there is just no reason to put that up on the board. We know that.

MS. SULLIVAN: Well, Your Honor, at sidebar you said I could show the children and adolescent label.

THE COURT: I didn't say anything of the sort.

MS. SULLIVAN: I mean the approval letter.

THE COURT: I didn't say anything of the sort. We have the 2006 label. That's in evidence.

MS. SULLIVAN: I can't show that there was the approval letter from the FDA?

THE COURT: Was your application for autism in children approved by the FDA?

THE WITNESS: Yes.

THE COURT: All right. So much so.

BY MS. SULLIVAN:

Q. And, Dr. Caers, as part of the approval process, does the FDA send you an approval letter?

A. Yes, of course.

Q. And does the FDA communicate -- did the FDA communicate to Janssen what they could say on the FDA approved label?

MR. KLINE: Objection; violative of the Court's direction.

THE COURT: No. I mean, again, you're permitted to ask that, sure.

THE WITNESS: Well, as every approval letter, that gives you the label that the FDA wants us to use from the day one, which is obviously an updated label, because now it covers all the relevant information that is relevant for the appropriate use of Risperdal in children and adolescents with irritability and autism.

BY MS. SULLIVAN:

Q. And let's show -- and, Dr. Caers, were you involved in the 2006 autism approval process with the FDA?

A. Yes, I was.

Q. And can you tell the jury who made the final decision on what should be said in the label?

A. Well, that's obviously the FDA, as we alluded to earlier.

Q. And, Dr. Caers, I'm going to put up the FDA approved label for autism in 2006. It's attached to the approval letter, which I won't show per the Court's instruction.

Defense Exhibit...

MS. BROWN: 61.

MS. SULLIVAN: 61.

MS. BROWN: You're showing the label from the approval, right?

MS. SULLIVAN: Just the label. It's DX210. Now it's 61.

MS. BROWN: From the approval letter, the 2006 approval letter.

- - -

(Whereupon Exhibit D-61 was marked for identification.)

- - -

BY MS. SULLIVAN:

Q. And, Dr. Caers, in order to get FDA approval for children with autism, what did you have to establish with the FDA?

A. In order to get the approval, you need to submit your complete data set, obviously, as we did in different steps.

Q. And the FDA concluded it was appropriate for children?

A. Well, the FDA back in October 2006 concluded that Risperdal is safe and effective in the management of irritability associated with autism, which is basically the meaning of an approval.

Q. And if we look at the 2006 label, Dr. Caers,

you have it on your screen?

A. Yes, I do.

Q. Okay. And this --

MR. KLINE: Your Honor, this is -- oh. It's the label. Okay. No objection.

THE COURT: Okay.

BY MS. SULLIVAN:

Q. And, Dr. Caers, if we look at Page 11, it talks about the fact that it's now approved for irritability associated with autism, right?

A. That is correct.

Q. And it describes the symptoms. And if you could just read them for the jurors.

A. Yes.

As you can see here, these basically include symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods.

Q. And so the FDA specifically at this juncture approved Risperdal for this purpose --

A. That is correct.

Q. -- in children and adolescents?

A. That is correct.

Q. And is this the same -- so there's been discussion -- and you mentioned there was off-label

prescribing of Risperdal before it was approved in autism, right?
A. Yes.
Q. Is this the same compound, in other words, did the medicine change in terms of its compound or chemical make-up in 2006 as compared to what was being prescribed in '93, '94, 2002?
A. It's the same compound.
Q. So the same compound that was being prescribed off-label now had on-label?
MR. KLINE: Objection; asked and answered. She just repeated.
THE COURT: Yes. Sustained. That is sustained.
BY MS. SULLIVAN:
Q. And, Dr. Caers, if we look further in the label, there was a Precautions section in the label.
A. Yes.
Q. And you're familiar, Dr. Caers, with -- does the FDA have a format that Janssen has to follow in terms of how things are laid out in medicine labels?
A. Yes. The full format of the label is fully described in FDA guidelines and has its own fixed format and chapters.
Q. And does the FDA dictate the sections and the

type and things like that?
A. Yes.
MR. KLINE: Your Honor, this goes -- this goes to whether he's an FDA expert or not. And I just can't be on my toes all the time.
THE COURT: Again, that's true. Sustained.
You're going to have experts on this, aren't you?
MS. SULLIVAN: Well, Your Honor, this gentleman --
THE COURT: He doesn't know. He's not a member of the FDA, nor has been qualified as an expert. He knows from his own experience what he did and what kind of, you know, things that he had to do to get this thing approved for children.
BY MS. SULLIVAN:
Q. And, Dr. Caers, going further in the Precautions section, there's a section about elevated prolactin.
A. Yes, indeed.
Q. And can you talk to our jurors about what's in that section and why.

A. Well, as has been in the label since 1993, reference is made to the occurrence of hyperprolactinemia in drugs such as Risperdal who interact, as I said earlier, with the receptors in the brain, the dopamine 2 receptors, and that in patients treated with drugs, that can increase prolactin; that certain adverse events, such as galactorrhea, amenorrhea, gynecomastia, and impotence, have been reported.
Q. And, Dr. Caers, in the label there's also a pediatric section?
A. Yes, there is, yes.
Q. And there is separate information about the data in children and adolescents in the 2006 label, right?

Q. And can you talk to our jurors a little bit about what was in the October 2006 label on children and adolescents and elevated prolactin and gynecomastia.
A. First of all, it is repeated in this section that risperidone increases prolactin. And this was also the case in the studies we provided. And that in the clinical trials we provided up to 1,885 children and adolescents treated with Risperdal,

there were, indeed, adverse events reported, such as galactorrhea in .8 percent of patients, and gynecomastia in 2.3 percent of the patients in our database.
Q. And, Doctor, to get the 2.3 percent, did you look at all of the data in children and adolescents?
A. Yes. It takes --
Q. Go ahead.
A. It takes all the studies that were done with risperidone, Risperdal in children and adolescents together, and then you come to the overall incidence of, in this case, gynecomastia, in this total population of 1,885 patients.
Q. And, Doctor, there's been some criticism in this case about --
MR. KLINE: Objection. I don't object to straight questions.
THE COURT: Sustained. Sustained. I don't know what you're referring to. By whom?
BY MS. SULLIVAN:
Q. Dr. Caers, the jury has heard Dr. Kessler criticize --
MR. KLINE: Objection. It's not a proper way to start a question.

THE COURT: Why don't you rephrase it, Counsel.

BY MS. SULLIVAN:

Q. Dr. Caers, whose idea was it to pool, to include data on all of the children to get the 2.3 percent?

A. That comes from the FDA. That's common practice. That's the only way they systematically document incidences in labels, incidences of adverse events. They take all of the patients exposed for a couple of days, up to a couple of years, take all together and take one single database in which they calculate the incidences. And that's how it is reflected in the label.

Q. And, Dr. Caers, I want to show you what's been marked -- what will be marked as Defense Exhibit...

MS. BROWN: 62.

MS. SULLIVAN: 62.

BY MS. SULLIVAN:

Q. And it's a mark-up from the FDA of this 2006 label. And I'm going to ask you about it, if the Court permits.

It's D234.1.

MS. SULLIVAN: Do you have a copy, Dr. Cares?

THE WITNESS: I don't think so.

COURT CRIER: Not yet.

Mr. Kline.

THE COURT: It's been marked?

COURT CRIER: 62.

MS. BROWN: 62.

(Exhibit D-62 marked for identification.)

MR. KLINE: This is just the FDA track labeling?

MS. SULLIVAN: It's an e-mail from FDA to Janssen about the label.

MR. KLINE: I have no objection to the document.

THE COURT: It's now marked as P-62.

COURT CRIER: D-62.

THE COURT: D-62.

MR. KLINE: The document itself, not the e-mail. I have no objection to the mark-up of the label.

MS. SULLIVAN: I'm sorry, I didn't hear you.

MR. KLINE: I have no objection to the --

THE COURT: He has an objection to

the mark-up of the label?

MR. KLINE: I have no objection to what I believe is the mark-up of the label.

MS. SULLIVAN: And how about the e-mail from the FDA?

THE COURT: Who's this made out to, by the way?

MS. SULLIVAN: This is to -- this is from the FDA to Janssen.

MR. KLINE: Yes; that I do. It just -- it doesn't say anything. But I don't believe they come in under the rules.

But I don't object to the document you want to show.

THE COURT: The front page?

MR. KLINE: I do for the front page because it's the FDA document. But the going back and forth, which I think is what she wants to show, I don't object to.

MS. SULLIVAN: It's to Janssen, Your Honor. It's in their files. It's a business record, from their regulator.

THE COURT: Let me see counsel here at sidebar quickly.

- - -

(The following discussion transpired at sidebar out of the hearing of the jury:)

- - -

THE COURT: First of all, this is now going to be marked as what? D something?

MS. SULLIVAN: 62.

THE COURT: This discovery has been provided. There's no discovery issue here, correct?

MR. KLINE: No.

MS. SULLIVAN: No. We provided it.

THE COURT: Okay. So where is the section on gynecomastia?

MS. SULLIVAN: The section I want to show him is marked up by the FDA.

THE COURT: What page is that?

MS. SULLIVAN: It's Bates No. 752; and Page 24 of the document.

MR. KLINE: 752. Bear with me.

THE COURT: I don't have the mark-up. There's a mark-up there or something?

MS. SULLIVAN: It's 752, Your Honor.

THE COURT: So who's in the marking up here?

MS. SULLIVAN: This is from the FDA;

and he can talk about how they marked it up and what they told him to do. That's part of the discussions with the FDA.

MR. KLINE: My understanding from --

MS. SULLIVAN: And he can say he saw it; he knew it.

THE COURT: All right. Well, this is --

MR. KLINE: Well, he might have seen it, but he wasn't involved at all in this mark-up.

THE COURT: Yeah.

MS. SULLIVAN: Sure, he was.

MR. KLINE: He may have been the boss, but he wasn't involved in this mark-up, as I understand it.

THE COURT: The problem here is, is that unless this individual was the person who's involved in the FDA -- from Janssen in this correspondence, there's nothing to cross-examine this fella on.

MS. SULLIVAN: He was -- he was provided it at the time, Your Honor. He was the boss.

THE COURT: No. No. If he was the

one -- okay. If you lay the foundation that he was personally involved in it --

MS. SULLIVAN: Okay. Yeah. I'll do that.

THE COURT: And then he's subject to Mr. Kline's cross-examination, I'm fine with it.

MS. SULLIVAN: I'll do that, Judge.

- - -

(Sidebar discussion concluded.)

- - -

(The following transpired in open court in the presence of the jury:)

- - -

BY MS. SULLIVAN:

Q. Last point, Dr. Caers, before I think the Court wants to take a lunch break.

THE COURT: First of all, we're now on the record as to P-62.

COURT CRIER: "D."

MR. MURPHY: "D."

COURT CRIER: Defense Exhibit 62.

THE COURT: All right. This document is admitted for the purposes of its existence, and I think we are perhaps going

to be able to refer to two pages of this document, if the proper foundation has been laid.

BY MS. SULLIVAN:

Q. And, Dr. Caers, are you familiar with this document?

A. Yes.

Q. And were you involved at the time in the labeling decisions and discussions with the FDA?

A. Yes, I was.

Q. And I want to just show our jurors what's been marked as D-62.

And, Dr. Caers, this is an e-mail from the FDA, right?

A. Yes, indeed.

MR. KLINE: Your Honor, that's the exact document we didn't agree to at sidebar. But as long as I don't waive an inconsistency objection, she can show it.

THE COURT: Well, this appears -- no. I don't really have a problem. This is an e-mail to Janssen saying that we are negotiating and discussing this label; is that right?

MR. KLINE: It's a transmittal.

MS. SULLIVAN: This is a --

THE COURT: So we can now go to the actual points in question.

MS. SULLIVAN: Sure.

THE COURT: This witness was not on this e-mail, correct?

BY MS. SULLIVAN:

Q. But, Dr. Caers, you would have seen this document?

A. Yes.

THE COURT: So I'm interested in laying a foundation for the other questions involving the contents that are part of this document.

MS. SULLIVAN: Sure.

THE COURT: Of the attachment. And I don't need this particular document on the screen.

BY MS. SULLIVAN:

Q. Dr. Caers, did the FDA provide a mark-up to Janssen before approval -- this is a month before -- the September 28th date is a month before the FDA approves the medicine for autism?

A. Yes, indeed.

MR. KLINE: Objection; leading;

simply leading. It's asking to confirm.
THE COURT: All right. Well, she's attempting to lay a foundation, so that's permitted.
Overruled.
BY MS. SULLIVAN:
Q. And, Dr. Caers, did the FDA actually mark up the label and tell Janssen what it wanted?
A. Yes.
So what this is, is they identify track changes. So you can see what they delete. You can see what they add by underlining the letters. So you can see what changes the FDA proposes to the label in order to come to a final approved label for Risperdal in irritability associated with autism.
Q. And as part of the proposed label that the FDA marked up, did they make -- did the FDA comment on how Janssen should disclose the data about gynecomastia in the 2006 label, as it related to children?
A. Well, here it refers to, indeed, to the latest number of patients that we eventually had in the total file and consequently through the total incidence, in these 1,923, about patients that have

been documented with Risperdal.
Q. And did the FDA ask Janssen to pool all the data?
A. Oh, yes. That's common practice.
MS. SULLIVAN: Okay. It's a good time, Your Honor, if that makes sense for the Court.
THE COURT: Sure.
Pages 24 and 25; is that what we're talking about? Well, actually --
MS. SULLIVAN: That was Page 24, Your Honor, and also the first -- the document, the e-mail from the FDA.
THE COURT: All right. For the record, this is at JJRP00824751 and 4752.
You want to take a break now, Ms. Sullivan?
MS. SULLIVAN: Oh, I'm sorry, I thought we were.
THE COURT: No. We can take a break anytime.
MS. SULLIVAN: Okay. I thought it was a good spot, Your Honor.
Thank you.
THE COURT: You want to take a break

here?
MS. SULLIVAN: Yeah. That's good.
THE COURT: All right. Members of the jury, we are going to recess for lunch right here. Please come back around 1:30, and we will continue.
To our juror from McDonald's, all I can tell you is that I'm working on it, and I'm very surprised by the reaction of McDonald's, okay? We're working on it.
We will take a break here. Please do not discuss this matter with each other, and wear your yellow badges. And please do not refer to any outside source for any information about this case, all right?
Thank you.
See you at 1:30.
COURT CRIER: All rise as the jury exits.
- - -
(Whereupon the jury exited the courtroom at 12:36 p.m.)
- - -
THE COURT: All right. Then we're in recess till 1:30.

(Morning Session concluded.)
- - -
(Whereupon the Afternoon Session was reported and transcribed by Judith Ann Romano, CRR, Official Court Reporter.)
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C E R T I F I C A T I O N

I hereby certify that the proceedings and evidence are contained fully and accurately in the notes taken by me on the trial of the above cause, and that this copy is a correct transcript of the same.

I further certify that I am not a relative or employee of any attorney or counsel employed in this case.

_____

John J. Kurz, RMR, CRR
Registered Merit Reporter
Certified Realtime Reporter
Official Court Reporter

(The foregoing Certification of this transcript does not apply to any reproduction of the same by any means unless under the direct control and/or supervision of the certifying reporter.)

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