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, by BENITA PLEDGER, as Guardian of his Person and Conservator of his Estate, Plaintiffs, v. JANSSEN PHARMACEUTICALS, INC., JOHNSON & JOHNSON COMPANY, and Janssen Pharmaceutical Research and Development, L.L.C. Defendants	:	APRIL TERM 2012 NO. 01997

WEDNESDAY, FEBRUARY 11, 2015

VOLUME XIII
AFTERNOON SESSION

COURTROOM 425
CITY HALL
PHILADELPHIA, PENNSYLVANIA

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

REPORTED BY:
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(Hearing is reconvened at 2 o'clock p.m. with all parties present.)

(IVO CAERS, Ph.D., having been previously sworn, resumes the witness stand.)

THE COURT: On the jury front, counsel, I am probably in a position needing to excuse one of the jurors, the McDonald's one by Friday afternoon. And other issues are coming up involving funerals, involving leaving early on Friday, for some kind of event at a school. There are a lot of issues here. So the quicker we can try this case, the better. Or settle.

MR. KLINE: I am here at the Court's pleasure.

MR. MURPHY: Since you are talking about the scheduling issues, after today, Your Honor, tomorrow we have video clips of the treating doctors. We could provide the Court the parties', with respect to objections and counters, we can provide it this evening or we can provide it tomorrow morning.

THE COURT: Do you have any live witnesses at all? I don't need to meddle with

your order unnecessarily, but for me personally, and the case, it's a lot more important to get the live people in and out.

MR. MURPHY: Understood, Your Honor, and that's been part of our challenge. Our next live witness is available on Friday. So the next we have is the video evidence to provide to Your Honor.

THE COURT: As long as a live witness is in on Friday, I don't have a problem with it, whatever you want to do.

(The jury enters the courtroom at 1:02 p.m.

THE COURT: Good afternoon, everybody. Mr. Kline, when you are ready you may proceed with your cross examination.

MR. KLINE: Your Honor, good afternoon. Good afternoon, everyone, thank you for your patience and thank you for your patience with me.

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CROSS-EXAMINATION (Continuing)

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BY MR. KLINE:

Q Good afternoon, Dr. Caers.

A Good afternoon.

Q I would like to discuss with you the 18 studies. I believe there was a document which we have seen marked as DG63. I am not asking for it to be displayed yet, but it's a document that has on it the clinical trial, the trial length, the number of patients on Risperdal, the reports of gynecomastia, and the gynecomastia rate.

Do you recall that document?

A Yes.

Q By the way, sir, the document that we went over of the placebo-control studies, I believe I heard you say yesterday that you had helped in the preparation of that document. Do you recall, sir?

A No, I have not. No.

Q You did not help in the preparation of that document?

A No.

Q Okay, then we will just have to check the record for my recollection. Did you help in the preparation of any of these demonstrative exhibits?

A No.

Q No? Okay, thank you. What I would like to review with you, sir, is on these various clinical trials, and I believe there were 18 of them -- I am going to refer to Exhibit No. P-28 in connection with what I would like to discuss, and perhaps we could display DG6-3, to look at some of the points.

Again, sir, very respectfully, I would like to ask some direct questions and hopefully get to the bottom of certain information which I am seeking to elicit.

The first thing is, sir, of the 18 studies, and I am referring to the exhibit that counsel put up for the company and an exhibit that I have here, of the 18 studies, sir, ten of them were short-term. Can we agree?

A Yes, except for the USA-150. This is the only first eight weeks of the 150. There was a follow-up in the USA-150 of four months open-label followed by another two months double-blind, placebo-controlled.

Q So if I can now focus on my issue here at hand, P-28, can you see it across the room? You don't have to see me now, we are far away.

A No, that's fine. I can see that, yes.

Q We have seen in the label this number 1885,

which is the total number in the studies, okay?
A Yes.
Q And if we take the short-term studies --
THE COURT: Counsel, what do you mean by short-term?
Q I believe we defined short-term, but short-term was less than six months?
A Well, that's up to you. If you want to call all the studies up to ten weeks short-term and everybody agrees, then I am fine with that.
Q Well, that would be ten, and I believe they are the same ten studies that I have on this board, by now seems to be a century ago.
Let's agree. Let's agree. So 1075 of the 1885 that you put up there, for the jury, on that display chart are short-term studies, meaning that they are ten weeks or less, by our agreement, correct?
A Yes.
Q So in terms of the number of patients that were studied long-term, and when I say patients we are talking about children and adolescents with mental disabilities, correct, sir?
A Yes.

Q And of the children and adolescents with mental disabilities that were not short-term, that is to say not less than ten weeks, we are really only left with 810 children. And I have the math here, by the way, to help us along easily, sir. I will give you a calculator if you would like, but we have done this?
A No, no, yeah, 1885 minus 1075, that's fair.
Q And so we know that in RIS-41, the RIS-41 study up there, International-41, 504 of the patients are in that study alone, correct?
A Yes.
Q So 810 minus 504, in these 18 studies, 18 studies which you have described, only 306, there are only 306 long-term children who are not in RIS-41. Correct?
A I guess that's correct. I can't see the figures here but, yes. It must be something like that.
Q I am sorry, sir?
A It must be something like that. I can't see the figures but --
Q I am going to move away, I didn't expect all of these things to be flying at me. I have the

figures here for you.
1885, which is this large number of studied, of which when you come right down to it, other than RIS-41, you have 306, divided by 1885, 16 percent of the overall kids are in long-term studies that are not the International-41 study, correct?
A Yeah, except again, there were more patients in USA-150 involved which are not listed here. But that's fair enough.
Q This is your chart, sir.
A No, that's fair enough.
Q Who prepared that chart?
THE COURT: He said fair enough, counsel.
MR. KLINE: Okay.
Q So if you take 16 percent of the kids, children, 16 percent of long-term, not in RIS-41, and in fact, of the -- okay.
So, now, the next thing that I would like to discuss with you, and tell me if you have done this ahead of coming into Court with us today. The next thing I would like to discuss is the ages of the kids in all the studies. Have you done that?

A I don't know them exactly by heart, but obviously --
Q You are generally familiar?
A Yeah, yeah, yeah.
Q Okay, good. Well, if we go down the list, and these are the short-term and the long-term studies. We have NED-9, and the kids were it 12 to 18. Does that sound roughly familiar?
A I have to tell you, that may be correct but I cannot check that here. I don't have that all right -- readily available.
Q Okay. Belgium-22. And I am going to ask you if you have anything to contradict this, maybe would be a better way to do it.
Belgium-22, the kids are three to 14. That's BEL-22.
BEL-24, the kids are six to 14.
USA-93, the kids are five to 12.
USA-150, the kids are five to 17.
Canada-19, the kids are five to 12.
Canada-20, the kids are five to 12.
USA-97, the kids are five to 12.
Canada-23, the kids are five to 12.
HUN-4, the kids are six to 16.

International-70, the kids are six to 15.

International-79, the kids are five to 17.

International 84, the kids are five to 17.

USA-231, the kids are 13 to 17.

S-C-H, what is S-C-H?

A Schizophrenia.

Q Thirteen to 17.

BIM -- what's BIM?

A Bipolar mania.

Q Ten to 17.

USA-234, 13 to 17.

Now, all of these studies were considered, and in fact, they were part of the 1885 in the label, correct? The 2006 label?

A No, the schizophrenia studies and the bipolar studies are not among the 1800.

Q Which are they, down here? Just give me the numbers and we will take them out quick.

A The BIM-3001, the schizophrenia 3002, the USA-234, and the USA-231 were not in the autism submission.

Q Okay, and of course, according to the published report, INT-41, why that's published at six to 15, as SHAP(A), correct?

A That may well be, yes.

Q Now, of all of these studies, they are all combined by the discussions and eventual resolution that you had with the FDA, those were all combined to make up that 1885 number. Correct?

A That is correct. Those are unique numbers. So if you have a patient that was first in the 1019 and then goes further on in the INT-41, for example, that is counted as one patient, obviously, although the numbers come back in two studies.

Q I don't think I will get in trouble for saying this, great point, and in fact, if some of these kids were carried, this jury has seen, from 41 to 70, you would count it as one unique person, correct?

A One unique patient.

Q Got it. But in so far as counting all the numbers up, when the label ended up saying 2.3 percent gynecomastia rate, which is what you and I both know it says, correct?

A Yes.

Q All of these studies were taken into account, correct?

A Yes.

Q Not a one of these studies has a cutoff -- let me stop. Other than RIS-41, SHAP(B), not one of these studies has a cutoff at age ten, correct?

A No, and -- yes, that's correct.

Q And in fact, by age 12, you have the onset of puberty, generally speaking, correct? Generally speaking?

A Well, in boys, yes. According to experts, they started counting puberty in boys from the years of ten and older.

Q Ten and older is considered pubertal, generally speaking. I know every individual, every human being is different, but ten and older is pubertal, correct?

A In boys.

Q Every one of these studies, every study that makes up the 1885, does not eliminate kids under ten. Correct?

A That's correct.

Q Every one of the studies, you had a consultation with outside experts, correct?

A For every of the study I am not sure.

Q You don't know?

A No, I am absolutely sure that not for each individual study we had a separate consultation. We had consultations on autism, we had consultations on conduct disorders, we may have consultations on the schizophrenia and bipolar, but not necessarily on each individual study.

Q Let me ask it a little different way, sir. There was, generally speaking, consultation with experts including in the expertise of psychiatry as well as the expertise of endocrinology, which would have in one way or the other covered every one of the studies; can we agree?

A In reviewing the data, definitely, also, the endocrinologist. In setting up the studies, we primarily worked with child psychiatrists, though.

Q Well, you didn't work with child psychiatrists only with the pooled analysis, correct?

A Definitely not regarding child psychiatrists, no, that's correct.

Q Well, you worked with endocrinologists on the pooled analysis before you even went to work on drafting those papers, correct?

A Drafting the papers, when we were doing and in preparation of the explorative analysis, as I referred to yesterday, yes, we started consulting with child endocrinologists, yes.

Q Sir, we have seen in this courtroom four drafts, a final paper, E-mails. Do you know somewhere -- and this is a very specific question to get to a very specific point -- do you know somewhere where the word, relating to the pooled analysis, the word "exploratory analysis" appears, yes or no?

A That I don't know.

Q Have you seen it, sir, as you sit here today, do you recall seeing that word anywhere in writing as it relates to the pooled analysis, yes or no?

A Not to my -- I don't remember that. No.

Q Let me give this -- Mr. Gomez, quickly, an exhibit number.

THE COURT CRIER: P-99.

MR. GOMEZ: P-99.

(P-99 is marked for identification.)

Q I am marking it as Age of Children in Studies.

And, sir, in doing any one of those 18 studies, 17 excluding RIS-41, some of those studies

study the prolactin levels, don't they?

A About all.

Q All. Yeah.

A I am not sure -- there might be a few where prolactin levels were not available. But the vast majority, yes.

Q The vast majority of them do. The vast majority studied prolactin levels in boys, correct?

A Both boys and girls.

Q Well, my question was about boys and then I would get to girls. In the vast majority of the studies it measures the prolactin levels in boys, correct?

A Yes.

Q And in the vast majority of the studies it measures the prolactin levels in girls, correct?

A Yes.

Q And in every one of those studies, and then we will get to 41, in every one of those studies they include somewhere between the age of 12 and 15, correct -- 12 and 18, I am sorry, all the way up to 18. Correct?

A I thought there were a few studies that had an upper age limit of 12, but that was on your previous

sheet.

Q Yes, which I am trying to find.

No one ever went back in any of those other studies, correct me if I am wrong, no one ever went in back in any of those other studies, other than the five pooled ones which you did after you got the results of SHAP(A), no one ever went back in any of the other studies and did a SHAP(B) analysis, correct?

A Not to my knowledge.

Q To this day, as we sit here, correct?

A Not to my knowledge, yes.

Q And in fact, NED-9, you couldn't do it because it was all children over puberty, correct?

A It may be that we don't have -- those two are maybe the two studies in which we didn't have prolactin levels.

Q Now what happened in the five pooled cases -- let's see if I can get my chart up for this -- this was a group of cases, a group of studies which you all called Disruptive Behavior Disorder studies, correct?

A Correct.

Q And by the way, in some of the studies you had

all autistic kids and in some of the studies you had behaviorally disruptive kids, in some of the cases you had bipolar kids, but the measurements of some of the parameters were the same, for example, doing prolactin levels, even whether it was autistic kids or bipolar kids, correct?

A Yes.

Q Now on the DBD studies -- let me get my numbers out again. These studies as designed, CAN-19 -- I am marking on P-31, so the record is clear -- were five to 12s, CAN-20 was five to 12s, USA-93 were five to 12s, USA-97 was five to 12s, and INT-41 was six to 15s. Correct?

A Yes.

Q Now the spread, of course, of ranges -- when I say six to 15, is it inclusive of 15, sir?

A I would need to look at the paper, but --

Q What is it generally?

A I would think it does, yes.

Q So it would be six, seven, eight, nine, ten, 11, 12, 13, 14, 15. It would cover ten years, correct?

A Yes.

Q Of which five are in the 11, 12, 13, 14, 15

range. The over-ten range, correct?
A Yes.
Q And of course, here, in all these other studies which didn't have as much gynecomastia reported, you only lose two years, correct?
A What do you mean by you lose?
Q Well, you are cutting off two years rather than cutting off five years. Correct?
A In determining -- you mean the adolescent boys?
Q I didn't say anything about adolescents --
A We didn't cut off anything, obviously.
Q Well, when you did SHAP(B) -- maybe we should do it this way. For the over and under ten, for over and under ten, here we have five to ten is five years, five, six, seven, eight, nine. And then it's ten, 11, 12. You correct me if I am wrong, so we have eight years to deal with, so we have five, six, seven, eight, nine, and then ten, 11 and 12.

So in these studies, if you make your cut point at ten, then you keep five of the eight in CAN-19. Correct so far?
A Yeah.
Q You keep five of the eight for CAN-20,

correct?
A Yes.
Q You keep five of the eight for CAN-93?
A Yes.
Q You keep five of the eight for USA-97?
A Yes.
Q And you keep ten of the 15, that is to say two-thirds of them, for INT-41. Correct?
A I am not sure I follow you when you say "keep."
Q Keep?
A Yeah. What do you mean with "keep"?
Q I mean you keep them in?
A In what?
Q In other words, if you divided --
A Keep them in what?
Q Sir, may I? You have SHAP(A) and SHAP(B). Do you see that?
A Oh, that's what you mean. Okay, but that is a fundamental flaw in your thinking.
Q Okay, I was using a colloquial expression, I am sorry. So what you end up here with INT-41, you lose five of the years for SHAP(B) and you lose three of the years for all the other ones. Is that

correct?
A No, you don't lose those. No.
Q Well, as to counting them in SHAP(B). That's my point.
A If --
Q That's my point. You lose them?
A No, you don't lose them.
Q Tell me how you don't lose them?
A Because what you do, you keep them in the denominator, but you say because of this and this reason, this type of events that fall under SHAP(A) do not fall under SHAP(B). So consequently, you have a reevaluation of your nominator, but your denominator remains the same. You don't exclude the roughly ten years from your population, you just say for this and this reason, I exclude a number of the SHAP(A)s in SHAP(B). That's what you do.

Do I make myself clear?
Q My question had nothing to do with the denominator. Here is my question. When you were picking off SHAP(A) and SHAP(B), here is my simple question: When you split International-41 study, you got the six to 15s of the SHAP(A), the six, sevens, eights and nines get into SHAP(A).

Is that correct? Six, seven, eight and nine. It's actually four, I can tell you that.
A No. All the SHAPs identified in the six to 15 age group are in SHAP(A). Yeah?
Q Yeah.
A And in SHAP(B) you have all the same SHAPs excluding, for example here gynecomastias in boys ten years and older, because they do not fall in the definition of SHAP(B).
Q Yes, and I think we are on the same page. So SHAP(B) would only be -- I know what I did wrong here. Let's go back.

THE COURT: Do you want to do another page?

MR. KLINE: Yeah. My bad. I am going to try to correct this. My bad.
Q SHAP(A) is all inclusive, correct sir?
A Yes.
Q Let's try this again and we are going to go to a different page.

CAN-19 were kids that were five to 12, correct? Correct so far?
A Yeah.
Q I represent to you and the Court that that was

the ages of the kids. Can you stick with me so far?
A That was the age of what?
Q Five to 12?
A Yeah, yeah.
Q Okay. I didn't want to get hung up on that but I see we are.
CAN-19, five to 12. SHAP(A) would be all the years five to 12, correct?
A All the SHAPs in the five to 12s are in SHAP(A), yes.
Q SHAP(B) would be just the five to nines, correct?
A As far as gynecomastia in boys is concerned, yes.
Q Correct, thank you. As to -- you pronounce is Jinocomastia (sic)?
A Yeah, I guess I need to follow you in the right pronunciation because it's not my strength.
Q Do you know the derivation of gynecomastia?
A I guess it comes from Greek, but I am not so sure. I never studied Greek. I did Latin but not the Greek.
Q That's the mastia part.
CAN-20 were five to twelves, so SHAP(A)

were five to 12, but SHAP(B) were simply the five to nines, correct?
A Simply? Correct, they were the five to nine.
Q And USA-93 was five to 12s, and then SHAP(A) would be five to 12 but your so-called SHAP(B) would be five to nine, correct?
A Yes.
Q By the way, when the articles were being drafted, who is Olga Mitelman, sir?
A Say again?
Q Who is Olga Mitelman?
A It doesn't ring a bell to me.
Q Okay. USA-97. USA-97 was five to 12s, and of course, the SHAP(A)s, that's allcomers would be five to 12, and SHAP(B) would be five to nine.
And then finally, RIS-41, which was kids six to 15, SHAP(A) would be six to 15, that would be six, seven, eight, nine, ten, 11, 12, 13, 14, 15, ten years of them. And my point here was SHAP(A) in all the others are five, six, seven, eight, nine, ten, 11, 12, which is eight years of them, and over here on the right side for SHAP(B), you only get six to nine, three years of them. Six, seven, eight, nine -- four years of them. Correct?

A Yes.
Q And of course, in terms of the numbers in the study -- by the way, which studies of these were short-terms? Two of them were just short-term studies, what are they?
A CAN-19, and USA-93.
Q These are just short-term, and here, we have in RIS-41, we know we have -- let's look up at the board -- we have 504 kids, correct?
A Yes.
Q I will put "Number of Kids," 504. How many do we have in USA-97?
A 107.
Q And how about in CAN-20, is the only other one I need?
A Seventy-seven.
Q Seventy-seven, yeah. So you can see, sir, here, that the -- and the majority of the cases of the gynecomastia, the large, large number of them in these five, came from RIS-41, correct?
A Yes.
Q And in terms of the numbers in the study, of the three long-term studies, and you would agree with me that it's more likely to find gynecomastia

in a long-term than a short-term study, we can agree on that basic proposition, correct?
A No, we can agree that the longer you observe, the more chance you have to observe something.
Q Let me understand what you said and we will just leave it at that to see how far we can agree.
The longer you take the drug, the more chance you have to observe something. Is that what you said?
A No, that's not what I said. The longer you observe somebody, the higher the chance that you are going to see something.
Q Thank you.
MR. KLINE: I think I will mark this as the next Exhibit.
(P-100, is marked for identification.
MR. KLINE: P-100, a milestone, P-100 is the chart showing the --
Q And sir, you would agree -- withdraw that question.
Now that's the DBD studies. So those studies are combined together, and when they are combined together -- again, let's aim towards everything to see what we can agree to -- when they

are combined together, there is an exploratory -- what's the word you now use?

A Exploratory analysis.

Q Exploratory analysis, okay. Exploratory analysis. By the way, sir, in addition to not being in any paper, you have testified in depositions for hours and hours in these Risperdal cases. You know that?

A Yes.

Q I have one depositions of yours that's 12 hours?

A Yes.

Q You never used that term before, before you came in front of this jury?

A No, but it's a very common terminology.

Q I didn't ask you if it's common terminology. My question is a simple one. You testified for hours and hours and hours in the Risperdal litigation. Prior to coming in front of this jury you never used that word before, correct?

A I cannot -- that may be, I don't know. I can't reread all my depositions.

Q Do you recall using the word before, sir, yes or no?

A That, I don't recall.

Q Now --

A But nobody asked me.

Q Sir, you are the one who used the word in the courtroom, correct?

A Yes, and it's --

Q You weren't asked a question. Let's not debate. Let's find what we can agree on.

A Okay.

Q Let's find the agreed points.

Now when the pooled analysis began, when it began, and before there were any statistics run a first time and a second time, before it began, there was the concept of the Janssen scientists, you included, to do a pooled analysis, correct?

A Yes.

Q And that pooled analysis, sir, did not have a plan to divide anything by SHAP(A) and SHAP(B); is that also correct?

A No, that is not really correct. The first consultation with it back in 2001 with Daneman, already brought up, which is the Toronto child endocrinologist, in that first discussion, Daneman said, yeah, but, guys, you need to be careful with

bringing these all together under the one umbrella SHAP, because there are certain of these observations that are most likely not prolactin-related.

At that time it wasn't called SHAP(A) and SHAP(B), but he said you cannot just clump them all together because, for example, gynecomastia in pubertal boys is so common and can occur up to 50, 60 percent of the boys, so that you cannot define them just as probably prolactin increase related.

So from the first discussion on with Daneman, that concept of differentiating this from the total umbrella came up.

Q Sir, if that were true, first of all, you never testified to that before, correct? That's brand new as well?

A That is not really new to me, but yeah.

Q Well, it's brand new testimony. And the fact of the matter, sir, is what you just said is not what is stated in the documents. Because there was a meeting in January of 2002, correct?

A That may be.

Q Yeah. A meeting in January 2002, and it talks about the endocrinologists that were there, Moshang

and Daneman, correct?

A That was the first face-to-face meeting because --

Q Were you there?

A I don't think so. Moshang came in later.

Q So now you are telling us something somebody said at a meeting you weren't at? Correct? Yes or no?

A I was not at that meeting.

Q Did you ever talk directly to Dr. Daneman, yes or no?

A No.

Q So anything you are telling us about what you say Dr. Daneman says, which is not in the meeting minutes, is something that you want us to believe that someone told you that he said. Because you didn't talk to him. Correct?

A I did not talk to him, that's correct.

Q Right. In fact, there was no plan from the beginning, no plan, to do SHAP(A) and SHAP(B). Would you admit it, sir?

A No, no, there was -- that's totally wrong. There was, as we discussed yesterday, by the way, what you thought and what you presented as an

analytical plan is not an analytical plan. I explained yesterday. These are the data we need before we can even start what I called yesterday and I keep calling an exploratory analysis of the whole cluster of data we have in this field in the studies that at that moment had been finished and on which we had both prolactin levels and potentially prolactin-related adverse events, which was called later on, on the advice of the endocrinologists, SHAP.

Q Sir, you said right here in your answer that SHAP(A) and SHAP(B) came later. Do you recognize that?

A The term, yes, that came later, yes.

Q Yeah, that's what I am talking about, SHAP(A) and SHAP(B). May I go on? Let's find areas we can agree. Okay? I will make a proposition to you, sir, okay? Would it be true that you and I will not agree on everything until we leave here today?

A That sounds reasonable.

Q Yes, okay. So let's find everything we can agree on. That's what I would like to do.

There was a meeting, sir, that you mentioned, and you weren't there but there are notes

of the meeting, and guess who was copied on the E-mail?

A I might have been copied on that E-mail, yes.

Q Yes, you might have been. You are.

A Okay.

Q And the fact of the matter is there is no mention of breaking the kids up in SHAP(A) and SHAP(B) at the beginning of this letter?

A That terminology came in later but the concept.

Q The concept is not in the E-mail either, I am going to show you?

A Show me the E-mail.

Q Let's look at the E-mail dated January 23, 2002, it's marked as P-31, the jury has already seen.

MR. KLINE: I believe it's been displayed without objection, Your Honor, and this witness is on the bottom half E-mail, and I will show the operator where, on JJRE02250121.

Q Do you see the E-mail, sir?

A Yeah, I am reading it.

Q In fact, sir --

THE COURT: Let him read it.

Q Okay, you tell me when you are done and when you are ready. I would like to ask you a few questions and then move to our next topic, sir, that's my goal.

A Okay.

Q Okay? I would like to go to paragraph one. One says, "A quick update on the prolactin expert meeting". So you had experts. And this is in January. Let's put it in context because it's been a long time for us.

In January is when the study gets started, correct?

A It's not a study, it's an analysis. The study had already been done, yeah.

Q Yeah. In January, sir -- we will go again -- in January an analysis was planned and there was a meeting in Toronto to discuss this analysis. Correct?

A That is correct.

Q And the fact of the matter, sir, is that after the meeting there was an E-mail about it, "Dear All," correct?

A Yes.

Q And you weren't there so this is a report to you. Correct?

A Yes.

Q Did you get conferenced in live, did you get conferenced in by phone, did you get conferenced it by telecommunications?

A No. Let there be no misunderstanding, I was not at that experts meeting.

Q You weren't?

A No.

Q I thought this was a very important meeting?

A Well, this is one meeting on one of the nine development plans I was running at that moment worldwide. This is one meeting. There were meetings going every day all over the world on Risperdal. How can I do that? I can't clone myself, you know?

Q Yeah, that's right.

A No, I cannot.

Q Neither can I.

A We agree on that.

Q We do. Now keeping in mind that you can't clone yourself and you got a meeting report, that means you know what's in the report, correct?

A I know what was discussed at that meeting.
Q From the report?
A From this debriefing. I don't know whether --
Q Your report says nothing about the endocrinologists told us that we are going to divide into SHAP(A) and SHAP(B), let's start there, correct?
A Again, the SHAP terminology came in later.
Q Right, by Olga Mitelman, she invented it, correct?
A That may be.
Q You don't even know who invented the term SHAP, correct?
A No.
Q At this point in time they were being called prolactin-related adverse events, correct?
A We said potentially prolactin-related.
Q No, they actually did not use potentially prolactin. I will show you the studies. They were called prolactin-related adverse events. We saw them here for days. Would you like me to show you a document?
A No. If you say that, we may even agree on that. You can show that.

Q There were no potentials or hypotheticallys at that point?
A Potentially, we brought in later.
Q Later, right.
A Because of this point.
Q I heard you yesterday. You said --

MS. SULLIVAN: Objection. I would just like counsel to let the witness answer the question.

THE COURT: You may have him explain that. He said later.

BY MR. KLINE:
Q Here is the point I wanted to get to. You said yesterday that the SHAP term, and I don't want to debate it with you, the SHAP term was a more prudent term. I heard your word yesterday, a more prudent term?
A Yes.
Q Let's just find out what the group said. It said here, and I would like to read the thing and I would like to move on because I have a lot of things I would like to talk to you about still.

"The group discussed that there are several factors which affect prolactin levels."

Now the group here, you see the report? The group includes T. Moshang, that's the endocrinologist from Children's Hospital, who is now, unfortunately, deceased. And D. Daneman, who is another outside expert. Correct?
A That's the Toronto guy, yes.
Q Those were the endocrinologists?
A Yes.
Q And the next paragraph: "The group discussed that there are several factors which affect prolactin levels. For example: Estrogen during adolescence increases prolactin, in the natural population, 25 to 40 percent of boys greater than eight years of age will develop gynecomastia which disappears."

By the way, let's highlight that.

According to your expert endocrinologists, sir, there, who were advising Janssen -- and you only hired the best, correct?
A We try to.
Q Pubertal gynecomastia, right there, according to the report you got, occurs 25 to 40 percent in kids above age will develop gynecomastia which -- do you see the word "disappears"?

A Yes.
Q That means you wouldn't expect, sir, based on what you recorded this day, in this thing, you wouldn't expect, sir, to see, based on pubertal gynecomastia, an adult male with large pendulous breasts from puberty when it disappears, would you? It says it right here it disappears, would you agree?
A In principle it gradually, during puberty it tends to disappear, yeah.
Q Right. Have you ever in all of this heard of the phenomenon, sir, of a boy getting pubertal gynecomastia and having size 46 double D women's breasts?

MS. SULLIVAN: Objection.

THE COURT: Overruled.

Q Have you ever heard of that?
A No, I have not.
Q Did you read the whole thing, sir, the whole document?
A Yes.
Q To maybe save some time, is there anything in that document where the endocrinologists suggested, anything where the endocrinologists suggested that

you only study children under the age of ten? Yes or no, sir?

A No, no. That's the wrong question. I am sorry.

Q No, that's my question.

MS. SULLIVAN: Objection, Your Honor, can he permit the witness to answer?

MR. KLINE: No, he said that's the wrong question, and I would like my question answered.

MS. SULLIVAN: And he tried to answer and you interrupted him.

MR. KLINE: May I restate the question?

THE COURT: The objection is overruled, and if you have a question then the witness is obliged to try to answer it.

Q Is there anything in that document where the endocrinologists suggested, sir, that you should study children under ten or break out the children under ten?

A The concept --

Q No, sir, I am asking you, is there anything in the document, that's my question?

MS. SULLIVAN: Objection.

THE COURT: I am going to permit him to answer that question as long as he is not characterizing whether your question is good or bad. I don't really care.

A The concept of the SHAP(B) is exactly in this E-mail, because what the endocrinologist says, Hey guys, be careful, up to 40 percent of the boys in puberty can develop gynecomastia spontaneously without having to do with prolactin.

That's the first -- let me finish.

The second one is in the third paragraph, They also stated dysmenorrhea must not be seen as a potential prolactin-related adverse event because it's not, and also, in girls that one month of gynecomastia or -- less than one month of gynecomastia in girls, neither should be related to prolactin, as well as one week duration of amenorrhea.

So those are exactly the four SHAP(B)s that they already describe back in 2002, that we should not regard those as prolactin-related. And consequently, the SHAP(A) and SHAP(B) concept is exactly in this E-mail right here, although the terminology came later.

Q Sir, let's read the rest of the E-mail and then you and I won't debate it. Let's read the rest of the E-mail for the jury.

Sir, you would agree with me that none of what you said there, none of what you said there is contained in that E-mail?

A No. It's all in there.

Q Let's look at the E-mail.

A Shall I explain once more?

Q No. I am going to ask you an unrelated question, though. Are you the guy they send to the FDA to make the arguments?

MS. SULLIVAN: Objection, Your Honor.

THE COURT: That's sustained.

Q Let's look at the E-mail, my word, third paragraph of the E-mail.

THE COURT: Who wants to read it? I will read it, as long as we keep moving.

Q "The expert endos agreed that the pediatric data shows no relationship to prolactin levels and prolactin levels decrease to within normal ranges by week 48 to 54. They clearly stated that prolactin levels over 200 indicate a tumor, prolactin levels 100 to 200 should incite clinicians to look for a

tumor. They also stated that dysmenorrhea is not a side effect of elevated prolactin, that one month of gynecomastia is not related to prolactin, nor is one week's duration of amenorrhea.

Next paragraph.

The expert panel requested more analyses looking at the ITT database without matching prolactin values to determine if there are potential prolactin-related side effects. They have asked us to list all prolactins over 30 and list all sexual side effects. Based on the stats reports they saw, the incidence of prolactin-related side effects is less than 5 percent and not cause for concern.

Next.

Can we agree that Piet doesn't relate to our discussion, sir?

A I agree.

Q Next. Can we agree, let's look down here: "Action Items: The additional analysis plan has been written."

Sir, what did they call it? A what kind of plan?

A An analysis plan.

Q Analysis plan?
A Yes.
Q There was an analysis plan, wasn't there?
A I haven't seen it.
Q But there was one, wasn't there?
A Well, that may be.
Q You told the jury no. You told the jury there was not an analysis plan, and you see it right there in black and white?
A I see analysis plan, but is that the one you showed me yesterday? That I would not call an analysis plan.
Q What does this say, sir?
A This says an additional analysis plan.
Q That's because if you are going to do an analysis you need a plan, correct?
A That's what you usually do, yeah.
Q Yes.
A And that's what we did, actually.
Q That's right, you ran the data, which included no SHAP(B) to start?
A No, no, no, no. The SHAP(B) is already in here.
Q Oh, my word. Let's go on here. You see where

it says, "analysis plan has been written up." Not only was it written up, it was sent to all participants to review. My word, if there was an analysis plan it would have to go to you, correct?
A No, no, no.
Q You are one of the participants.
A Look, I may -- I am not aware that I ever reviewed that analysis plan. And what I call an analysis plan, is that the one you had yesterday? I would not call that an analysis plan.
Q Why are you asking me, sir?
A Well, because you asked me yesterday.
Q Who works for Janssen, sir?
A Say again.
Q Who works for Janssen, you or me?
A I, I think, yeah.
Q Just to finish this up, then it's going to go to BrainWorks, they are one of those outside companies, to write the manuscript; correct?
A Yes.
Q So what we know here, and we are going to pick this right up after our break, what we know so far is that there was an analysis plan, and somebody was hired to write a draft based on the analysis plan,

correct?
A Not based on the analysis plan. Obviously, you cannot write a manuscript based on an analysis plan, you can only write a manuscript based on an analysis.
Q You do an analysis and you have a plan to do it, and then you write it up?
A You have a plan, you do the analysis, and then you have it.
Q Plan, analysis, write it up?
A That's correct.
Q So the first writeup would then be based on the plan, correct?
A No, no, no.
Q You wouldn't do a plan and then have a writeup that's consistent with the plan; is that what you are telling us?
A No, the manuscript doesn't give the plan. The manuscript describes the results of the analysis.
Q No, sir. Have you seen these drafts? Have you seen the drafts of the so-called Findling article, yes or no?
A I have seen at least one. I have seen one draft, and I definitely have also seen the final

manuscript before it was submitted.
Q Well, the second draft which we know came to you because he have an E-mail, has no breakout of SHAP(B). Correct?
A That may be, yes.
Q Maybe yes or yes?
A Yeah, well.
Q You know that for a fact?
A Yeah.
Q Yeah. Correct?
A Well --
Q You know for a fact that the draft that you saw, which wasn't the first draft, it was the second draft, that, sir, has no SHAP(B) analysis at all contained in it, correct?
A Okay. If you tell me.
Q You have read it.
A Well --
THE COURT: Is that a yes or no, sir?
THE WITNESS: I did see that manuscript, yes.
THE COURT: Anything else for this moment? We need to take a break.
MR. KLINE: Okay, Your Honor, thank you

for being indulgent with me to finish that.

THE COURT: So we are going to take a recess here for ten minutes, same rules, and we will be back in ten minutes.

(A brief recess is taken.)

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

THE COURT: You should know, tomorrow we have a request from the juror who is a member of the charter school community to adjourn at 3 o'clock to allow her to attend some kind of all-day teacher conference. So since tomorrow might be a video day, I told them that's a possibility since we won't have a live witness. So I think tomorrow we can expect to adjourn at 3 p.m.

MR. KLINE: Your Honor, is it okay as long as one counsel is here, with the videos, as long as one counsel is here? Is that okay with you?

THE COURT: For tomorrow?

MR. KLINE: Yeah.

THE COURT: I am hoping that we have four or five hours worth of video we can show

it.

MR. KLINE: But I mean we don't need to come in full team is my point.

THE COURT: No.

MR. KLINE: As long as there is a lawyer here representing the client.

THE COURT: Yes. If there are any issues before tomorrow we will address those. So I am looking to adjourn with this witness, hopefully, at around 4:30, quarter to five at the latest. I am available after quarter to five, but it would be nice to address the deposition issues before tomorrow morning.

(The jury enters the courtroom at 3:29 p.m.)

THE COURT: All right, Mr. Kline, when you are ready you may proceed.

MR. KLINE: Your Honor, thank you.

BY MR. KLINE:

Q Sir, when we left off, and I have asked the technician to pull this up, we were on Exhibit 31, and we were talking about this E-mail, and I have asked for the CC on it, which shows it's to you from Carin Binder, who we have discussed earlier.

By the way, sir, Carin Binder, one of the authors of this study, correct?

A Yes.

Q In fact, one of the Janssen authors of this study, correct?

A Yes.

Q Presumably, one of the people who would know the most about the study, writing this E-mail, correct?

A I wouldn't claim that. She basically organized and made it happen, but she is definitely not an expert in the field, as we can see. For Janssen we had Al Derivan, who is a child psychiatrist, and Goedel DeSmedt, who was a project scientist in the Janssen organization, who were at the meeting.

Q Her name is on the article, correct?

A Yes.

Q And she is the author of this E-mail?

A Yes.

Q And by your definition now, she is one of the organizers of this whole thing, correct?

A Yes, she organized this.

Q And by definition, and you weren't even there,

you were over a Belgium, correct?

A Yes.

Q So she would presumably know what she is talking about, correct?

A I would hope so.

Q And you see she is copied, and now at the very end, and this is where we were -- we are going to take a snapshot of this and we are going to mark it as P-101. We promise, Marianne, to print it out instantaneously and it will be a be piece of paper in your hand and marked.

(P-101 is marked for identification.)

Q Now, sir, this was in January. By August, the writeup of this reaches you. We know that because there is an E-mail transmitting it to you, and you have seen it in preparation for your testimony?

A Yes.

Q Will you move this along and say yes?

A Yes.

Q And there is an E-mail from Binder, same lady, to Caers. And here is Binder's E-mail, and I promised His Honor to do this as quickly as I can, and let's go to the next exhibit number, which is already marked P-38, so I know I can display it,

JJRE011568. I want to start at the bottom of the E-mail but then we are going to move our way up.

Once again, the E-mail is talking about what the message should be, correct?

A I haven't seen the E-mail yet.

Q I will get it in front of you, to make it easy. There you go, sir. We are old friends now.

A Absolutely.

Q And it says here, Binder to Goedel DeSmedt and Ivo Caers, and other people. The bottom E-mail we are looking at, August 15, 2002, 11:06 a.m. Do you see that, sir?

A Yes.

Q And it says, "Dear Pediatric Publication Team." There was a team involved in getting this data published, which eventually there was success in doing, correct?

A Be careful. This was a pediatric publication team that not only deals and was not only formed to do this publication, they dealt with all the publications in our pediatric studies.

Q Thank you for the clarification. But this E-mail is about the pooled subject. If my trusted Corey can follow along, the Subject: "Pooled

Prolactin Manuscript"?

A Yes.

Q And it says here in the second paragraph: "Key message." This is the message that is to be conveyed. "Prolactin rise is transient and not related to side effects hypothetically attributed to prolactin." Do you see that, sir?

A Yes.

Q That statement is inconsistent with what is behind this document. Correct?

A No, I disagree.

Q Okay, then we won't agree on that one and we will move on.

Up above there is an E-mail from Pandina, we talked about him, the psychologist, to you. And he says, "Dear Team." Do you see it?

A Yes.

Q And it says here, about the third sentence down, right in the middle -- I am hoping Corey can find this -- "If we can demonstrate". "If we can demonstrate." Do you see that?

A Yes.

Q Just the lead into that, sir, this is advocacy. If we can demonstrate something then we

will be okay, rather than letting the scientific chips fall where they may, correct? Or do you disagree with that? If you disagree, tell me and we will move on.

A No, no, I disagree because --

Q Okay.

MS. SULLIVAN: I am sorry, Your Honor, can he answer the question?

THE COURT: I thought he said he disagreed.

MS. SULLIVAN: He was about to answer it further, and Mr. Kline --

THE COURT: Why don't you ask another question.

Q It says here, "If we can demonstrate that the transient rise in prolactin does not result in abnormal maturation or SHAP, this would be most reassuring to clinicians." Do you see that.

A Yes.

Q Well, of course, it would be reassuring to clinicians if that were the case, wouldn't it be?

A Yes, because it would be important information indeed. That was what the article was all about.

Q Well, that's what the ultimate article was all

about?

A No, no, no.

Q Well, let's look at the article you got. Because I want to go back to the plan and whether there was a plan. Remember, like, when you do a study. By the way, sir --

A No, no, no, I need to repeat myself that this is not the same type of analysis, analytical plan, if at all, as you do for people who -- regulatory single study. That should be very clear. I call it for the sake of simplicity an explorative analysis and that's exactly what it is.

Q Sir, were you a biology or chemistry major?

A Biology, but within biology the specialty was biochemistry.

Q Do you remember the old experiments way back in college and high school? Remember doing an experiment in the lab, yes or no?

A Myself you mean?

Q Yes.

A Oh, yes. I have worked in a lab for seven years for my Ph.D.

Q Let's move off that point. I want to go right to this thing about whether there is a plan.

Now, you got this paper, P-39, previously marked during Dr. Kessler's testimony. Sir, you are familiar with it?

A With what?

Q Are you familiar with the document?

THE COURT: One second.

A With the manuscript you mean?

THE COURT: We need to get P-39 to him.

MR. KLINE: Sorry, I am rushing. I shouldn't be. I am sorry.

THE COURT: If we can't do it today --

MR. KLINE: No, I want to finish today.

Q You see, sir?

A Yes.

Q This is a manuscript?

A That's a draft manuscript, yes.

Q And we know it as Draft Two. Do you know if you saw a prior draft of this? It would help us. Yes or no?

A No.

Q In realtime, when this was all happening?

A I don't know whether I have seen a first draft. Unlikely.

Q Okay. But this document you did see at the

time, in August of 2002, correct?

A Yes.

Q We know, sir, that there was a statistical analysis that was run in May. You are aware of that fact, aren't you?

A Yes.

Q You are aware of Table 21, correct?

A Yes.

Q I want to ask you a very, very, very specific question: Table 21 -- you know what I am talking about, sir?

A Yes.

Q The very specific question that is capable of yes or no: Was Table 21, that actual table, submitted to the FDA? Yes or no?

A That table?

Q Yes. I don't want to know about anything else. I want to know if that table was submitted to the FDA, yes or no?

A I am pretty sure no.

Q Okay, thank you, sir.

Now, abstract, let's see what this abstract shows.

THE COURT: Abstract of what, sir?

MR. KLINE: I am sorry, of the manuscript.

THE COURT: P-39?

MR. KLINE: Yes. And to put it in perspective, and this is all my fault because I am rushing, but I am going to try to get back.

Q This document, sir, is a manuscript that was drafted by the outside people, BrainWorks, and then reviewed by the Janssen scientists. Is that correct?

A Yes, and to the experts.

Q And the experts. So it would have been circulated, just so we understand it, it would have been drafted first by the outside company, correct? I am not criticizing that, sir, by the way.

A No. I didn't say even anything.

Q And then it got through how many Janssen hands, would you say? Six? Eight?

A Simultaneously, yeah. That would be something like that, yes.

Q I am sorry, the number? I just didn't hear you.

A That may be something like that. I am not

surprised.

Q Yeah, six or eight. And including outside, including this Findling guy and Daneman and Moshang, the -- I will say it this way, I hope no one will object, the fancy pants endocrinologists. Correct?

A The endocrinologists, yes.

Q You use that term?

A No.

Q And the thing shows up on your desk. You don't disagree with me that this was not the first draft, it's the second draft. Can we just basically agree on that?

A Yes.

Q Okay, and now we are looking to see, to put it in context, whether there was a plan. And let's look at what the document says.

If I can, we are on P-39, and we are on the abstract, which is, of course, the abstract is the -- starts with the Background, correct?

A Yes.

Q And it says, "This -- do you see the word "analysis"?

A Yes.

Q Do you see the word "designed"?

(Caers - Cross)

A Yes.
Q "To investigate prolactin levels in children with long-term risperidone treatment and explore" -- do you see the next word?
A Yes.
Q -- "any relationship, with side effects hypothetically attributable to prolactin."
Do you see that?
A Yes.
Q That's what the study was designed to do, it says it in black and white.
A Explore.
Q How about explore the next two words, sir, "any relationship." It doesn't say some relationships, does it? Does it?
A No, it doesn't.
Q It doesn't say "relationships between children under ten," does it?
A No.
Q It says "any relationships".
And then it goes on to say, "Data from five clinical trials were pooled for this post-hoc analysis." We haven't seen that word. Could you maybe give us a sentence so we can move on. What's

(Caers - Cross)

a post-hoc analysis?
A A post-hoc analysis is an analysis you do with data off the primary preplanned analysis for the individual studies that have been done.
Q And we learn that, and it's right here, after consultation with the two endocrinologists, after the consultation with the six or eight Janssen people, it says here in black and white that the study is going to study kids five to 15?
A Yes.
Q Did I say six to 15?
THE COURT: Counsel, where is -- oh, I see. This is on 01115172.
MR. KLINE: Yes, Your Honor.
Q Now, if you will indulge me, sir, before we go further with this, if we put up Table 21, which is previously marked as Exhibit 34(A), you know, sir, and you discussed it with counsel for the Janssen --
THE COURT: Counsel, can you remind us where Table 21 came from?
MR. KLINE: Yes, it came from statistical runs of May 15, 2002, which is being reported on, I am sure this witness will agree, in this Abstract.

(Caers - Cross)

THE COURT: Okay.
Q And of course, Weeks 8 to 12, we are all familiar with that, sir, 20 to seven, 7.8 to 2.9, statistical significant finding at less than .02. Correct, sir?
A Not correct for multiple comparisons, as I tried to explain yesterday.
Q Sir, it's right in the study that we have a p-value of greater than two. But let's see what we can degree on, not disagree. Okay?
Now, the fact of the matter, sir -- we can take Table 21 down, and we are going to go to the draft study, the jury has seen it before, JJRE ending in 192, and if I can go to the top paragraph before the psychologist's comments, just the top, not the whole thing. I really just need up to the Comments. I need the text down to p-value of -- I still got to get p-value in there, please.
Okay, now, it says here in the writeup, based on the plan, based on the, to use the words of the study, "analysis," it says here, "The percentage of children with SHAP was assessed for patients with prolactin levels above the upper limits of normal versus patients with prolactin levels within the

(Caers - Cross)

normal range at the various analyses time periods. The proportions were all comparable except Weeks 8 to 12 time period, in which 7.4 percent of patients who had prolactin above the upper limits of normal had SHAP at some point during the trial, while 2.9 percent of the patients with prolactin levels within the normal range at Weeks 8 to 12 experienced SHAP at sometime during the study. P equals .02." Do you see that?
A Yes.
Q Are those the words which were written there?
A Yes.
Q Now I only have one question for you, sir, again, my goal to agree on what we can: This writeup, as we see here, does not appear in the Findling paper, can we agree?
A In the final paper, that's correct.
Q And we can also agree that this writeup is based on Table 21, correct?
A That is correct.
Q And did you see any of the E-mails in between, the E-mails talking about nauseating amount of gynecomastia, hiding data, or any of those E-mails?
MS. SULLIVAN: Objection, Your Honor,

(Caers - Cross)

it's cumulative. It's been asked and answered this morning.

MR. KLINE: I need to know whether to go into it.

THE COURT: It's compound.

Q Do you see any of the other E-mails or further drafts? I will ask it that way.

A Not the E-mails you refer to.

Q Did you see any of the further drafts? Because if you did I would like to examine you, and if you didn't then I want to know why.

A I am not sure. I definitely saw the final manuscript, but I am not sure whether I saw any in-between drafts.

Q When you say you saw the final manuscript, so we know, and again, I think I have a few questions on which we can agree. And we have heard a lot about it from you yesterday on direct examination.

When you saw the final manuscript, sir, did you see the final manuscript before it was submitted to the journal?

A Yes.

Q And did you make -- do you personally, Ivo Caers, make any changes or suggestions?

(Caers - Cross)

A That's what I don't remember, to be honest.

Q Did you at any point say we should put back in this information here about Table 21?

A I don't think so.

Q Okay, and we have heard why at length, I believe.

Now, the next thing I would like to do is, there was this SHAP(B) that was created, and I would like to talk about SHAP(B) and those tables. We are going to be going to the Findling article, I am sure, so we can have it cued up. But let's talk about the Findling data and SHAP(B).

It's the "real" SHAP, that's what you called it?

A The real SHAP?

Q I think you used the word "real" SHAP yesterday. Do you remember?

A It might be, yes.

Q Let's try to organize quickly, see if we can put a couple of things together.

Let's go to Findling and let's go to those tables, and let's go to that SHAP(A) table to get focused. And we know that the rate of gynecomastia is 5.1, correct, sir? In SHAP(A),

(Caers - Cross)

allcomers?

A Yeah, okay.

Q By the way, you know that the Abstract says that SHAP was reported in 2.2 percent of the 592 patients. You do know that?

A Yes.

Q But you know that the analysis plan said that it was to find all side effects, do you remember that, from what you just said?

A All SHAPs, side effect.

Q Maybe we can just agree with this, sir, the Abstract tells people that it's 2.2 based only on SHAP(B), correct?

A That's correct. It doesn't stay that it's based on SHAP(B), but it is.

Q That's right. Someone who read this journal -- by the way, the *Journal of Clinical Psychiatry*. All of these articles that you are publishing in the "published" literature, let's look at that. *Journal of Clinical Psychiatry*, sir, and *Journal of Adolescent Psychiatry*, those are small circulation journals which go to a subspeciality of practitioners, correct?

A I don't know the distribution and the size of

(Caers - Cross)

the distribution.

Q Well, sir, compared to the *New England Journal of Medicine*?

A Obviously, because this is only psychiatry and *New England Journal of Medicine* is all medicine.

Q That's my point. I think we can agree?

A Yes.

Q These articles when you are publishing them are published in, compared to the *New England Journal of Medicine*, a small circulation journal?

A Yeah, but to the right people.

Q In this case, sir, do you know who Austin Pledger's doctor was? Was he a psychiatrist, who was prescribing the drug for five years, do you even know?

A I don't know that doctor, no.

Q Yeah, he was a neurologist.

A Oh, okay.

Q Yeah, not a psychiatrist. And the fact of the matter is that SHAP(B) -- let's look at the SHAP(B). Oh, for SHAP(A), let's see if we can agree on some things, sir. Let's try to do it in hopefully an expedited fashion.

The way I see it, it was a pooled

analysis of 592, and the breakdown, you can find it in the paper, are 489 versus 103 girls. Does that sound about right?
A Yes.
Q And by the way, this is a paper that you have read in preparation for coming to Court? I would be shocked if you didn't.
A How do you know?
Q How many times?
A Yes.
Q Five? Three?
A The answer is yes.
Q Okay. And the fact of the matter is that boys under ten are about 255, the full girls, because girls under ten weren't excluded from SHAP(B), are 103, right?
A They were not excluded from SHAP(B). The events as described in the article that occurred in this population were excluded from the denominator.
THE COURT: I apologize, but again, we are focused on the record here, what is it that --
MR. KLINE: P-53. I have P-53 in front of the witness and in front of the jury, Your

Honor, thank you.
Q And the fact, sir, is that -- we are going to talk about the denominator, trust me -- total number of eligible subjects in the study who were included in the SHAP(B) group would be 358; is that correct?
A It was 592.
Q Sir, there are only 255 boys under ten?
A Yeah, so what?
Q Let's try to agree rather than disagree. Let's see what we are going to agree on. Let's get the SHAP(B) table up, Table 3, of the Findling article, which is P-49. Let's aim for all those things we agree on.
And what we can agree on is that when getting percentages of the rate of gynecomastia, having heard your explanation at length yesterday, what you did was you used a denominator using all of the children rather than just the children who would be eligible in SHAP(B). Do I have that correct?
A No, that's incorrect.
Q Okay.
A Because --
Q No, if it's incorrect, it's incorrect. And of SHAP(A), sir, the rate is 30 out of 592. Let's go

back up to SHAP(A), Table B. 30 into 592 is 5.1, correct?
A Yes.
Q So for all subjects in the study, the rate of gynecomastia in this long-term study which paid special attention to prolactin elevation and the outcome of gynecomastia, was 5.1 percent. Correct?
A No.
Q No?
A No. It's SHAP. SHAP is more than gynecomastia. So 5.1 percent of SHAP.
Q Thank you, 5.1 percent SHAP. That includes little girls who were lactating and girls who were not getting their period, that includes all of them, too?
A Yes.
Q And if you were to just look at gynecomastia, sir, that would be 22, but you have 3.7 percent because -- don't want to argue about it -- because you use the denominator of 592 rather than the denominator of only the boys, 489. Correct?
A Yes, of course.
Q Oh, of course. Did you approve this, by the way?

A Yes.
Q Did this get your final approval?
A Yes.
Q So what's here, we have the man who actually approved these numbers; is that correct?
A Well --
Q Yes?
A Yes.
Q And of course, you would agree with me, sir, that if I, Mr. Kline from Philadelphia, or let's assume it was Dr. Kline, the pediatric psychiatrist from Philadelphia --
A Don't do it now.
Q Too old to go back to school. If that were, sir, if a Dr. Kline were in Philadelphia, Pennsylvania, looking at this, and wanted to know how many boys, what percentage of boys got gynecomastia, would that be 3.7 percent, or would that be 4.4 percent? Which one of the two? Answer the question?
A If the question is on boys.
Q Yeah.
A Then it is 592, 4.4. But don't forget that within the 25 there was one girl.

Q I am sorry?
A There were --
Q I am not talking about girls, my question is, sir, if a pediatric psychiatrist in Philadelphia, Pennsylvania, or in, better than that, nearby Thorsby, Alabama, wanted to know the percentage of boys, all boys in the study who got gynecomastia, would that percentage be 3.7 or 4.4.
A That would be 4.4.
Q Thank you. Is that reported on that table, yes or no?
A No, because --
Q And --
A No, no, because 592 includes boys and girls, and few of these cases were in girls. So if you dismiss that, then obviously, you will never understand these figures.
Q Let's go forward. The pediatric neurologist in Philadelphia wants to know what percentage of girls get a prolactin-related adverse event, okay?
A Yes.
Q That would be eight out of 103 girls got an adverse event, correct?
A Yes.

Q 7.7 percent, correct?
A Yes.
Q Just so I can compare it, if my eyes were skimming down this, it would tell me that reproductive disorders female are 1.4 percent. Correct?
A Yes.
Q Is that correct? That's because you use 592 as the denominator, correctly so, right?
A I think so, yes.
Q Makes sense to you, correct?
A Yes.
Q And if we are just going to look at SHAP(B), and I want to get into these kids for my last part, hopefully, if you look at the SHAP(B) children, now, SHAP(B), you say that the denominator should not be 358, that we should go back and revert to the original denominator. Just yes or no?
A Yes.
Q But if one were to look at the number of children who had a SHAP-related event who were in the SHAP(B) group, that would be, 358 children are eligible in the SHAP(B) group, if someone were to ask that question, the answer would be 13 out of

358, if I wanted the universe of children in SHAP(B) and the number of SHAP(B)-related events, correct?
A No, because you cannot reduce the number of patients in which the total incidence is based on from 592 to 358. You can't do that.
And let me say in all transparency, and the fact that you are even able to do that without a Ph.D. in statistics shows that it is fully transparent in the paper.
Q If a doctor sits there and studies it. How long do you think it took me to figure all of this out?
A I don't know.
Q A few days, sir.
A Just like me, you don't have a Ph.D. in statistics, do you?
Q No. But unlike you, you would agree, that I wasn't sitting in Belgium giving final approval to this paper, correct?
A I wouldn't think so, no.
Q Yeah. And I wasn't the one who said divide SHAP(B) by 592. We can agree with that, too, can't we?
A You were not -- I wouldn't think so, no.

Q And if I wanted to know the rate of males under ten -- by the way, prepubertal, prepubertal. Now we have outlawed and we are back down -- let me start again.
Now when we have prepuberty, we are at the, to coin a phrase, I think you will agree, at the real SHAP, correct?
A That's what I called the real SHAP, yeah.
Q And that would be because you now know that this isn't puberty causing these five, correct?
A That is not assumed to be, indeed.
Q It's the first time I had real trouble understanding you, would you repeat the words?
A The prepubertal gynecomastias cannot be assumed to be due to puberty.
Q The prepubertal gynecomastia children, the so-called SHAP(B) children, the one thing we know for sure is that they are not due to puberty, correct?
A They cannot be assumed to be due to puberty, yes, that's fair.
Q Right. So now we have a rate, if you want to go -- if I can have SHAP(B) up there -- if you want to use the 592 denominator you have .8. If you use

the old Philadelphia math, you would have 2.0.

But have you looked at these five kids? They are right in one of the tables that we talked about?

A Which five?

Q Do you remember in your direct examination there was a discussion about Table 21 and there being other tables?

A Yes.

Q Have you looked at the table of five children which are in SHAP(B) that you discussed?

A The individual cases?

Q Yeah.

A No, I did not.

Q It's Janssen data, correct?

A Yeah, yeah.

Q And these are all children who would be not in puberty, correct?

A Yes.

Q So these are all kids who had gynecomastia not as a result of puberty, correct?

A That's the assumption.

Q And let's make a quick analysis of the five. I am going to give you, from the -- this, Your

Honor, is from the September 27, 2002 data run, when SHAP(B) was run. The data was run in May and then again in September, can we agree, to move it along?

A Yes.

Q There were statistics done, we have Table 21, to put it in perspective, is from May of 2002, and Table 20, which is the SHAP(B) counterpart, was September of 2002. You know that, correct?

A That may be, yes.

Q Yeah. And by the way, did you know, coming in here today, did you know that in May and September of 2002, when you were sitting in Belgium, that there was a little boy named Austin Pledger who was on this drug during that time?

A I have been told, yes.

Q You didn't know it at the time, did you?

A 2002? No.

Q You did know at the time there were thousands of Austin Pledgers because you knew the drug was widely used off-label?

A We knew that, yes.

Q And you knew you didn't have a full safety profile proven on this drug yet, correct?

A Not by the FDA approved.

Q You didn't have it by your own standards yet. You still hadn't sorted out whether there was or there wasn't a prolactin-related side effect, at that time?

A That's why we did the exercise.

Q In fact, sir, even that article today, even that article today that you all cite, the Anderson study, you know, the government study, do you remember talking about it?

A Yes.

THE COURT: For the record D-26.

MR. KLINE: D-26.

THE COURT: But, Mr. Kline, I don't think we have --

MR. KLINE: I am going to get through.

THE COURT: We haven't gone into the contents of D-26 before.

MR. KLINE: Okay, then I am going to not go there now. I will do it with another witness.

Q What we have, sir, is let's look at the five SHAP(A) -- that's called a lawyer almost getting off track, Your Honor -- and what we have here is --

MR. KLINE: Can we mark it and hand it

to the witness, please? Table 24, Chris, of the September 27, 2002 run, which are the five SHAP(B) children.

(P-102 is marked for identification.)

Q Can we put up, so the jury has context and for the Court's knowledge as well, displayed to the jury is Table 24 from the September 27, 2002 run of the data. That would be when Table 20 was run, to put it in context, the SHAP(B) table.

And it says here, sir, on it, "Demographic variables and prolactin levels in patients with prolactin-related side effects."

Do you see that?

A Yes.

Q And by the way, paren (SHAP), but the nomenclature, the nomenclature that's used if we can highlight it quickly, is right on the -- right here "prolactin-related side effects." That's the language was used when all of these tables were run, correct?

A Be aware, this is the title that is given by the statistician, the Ph.D. in statistics, on how you want to call this table. But obviously, the statistical person isn't aware of whether SHAP is

prolactin-related side effect or what it stands for. The statistical person just said you are going to look at this and this and this and this and analyze and give you the figures.

Q Let's go down them, sir.

A Okay.

Q You now have, of these children, you now have, remember, 14 -- is that right, Chris? 13? Or 14?

A It's 14.

Q Fourteen SHAPs. But each one of those 14 is a little child, correct?

A Absolutely.

Q And what you have here is -- let's pick out the boys first and then we will take a sampling of the girls.

You have Patient Number 3704, and that's a boy, 9.4 years old. Do you see it?

A Yes.

Q A little boy with a 77 IQ, and no puberty caused that, correct?

A That's assumed to be the case, yes.

Q Gynecomastia. And by the way, this table tells us what their pre-dose and what their prolactin levels became. And you see this little

boy? His pre-dose was at nine, jumped to 29, stayed about that at 21, and then tailed off. Correct?

A Yes.

Q That's what you would expect to see, correct?

A That is in line with the overall findings, yes.

Q And it's also in line with what you know, sir, that if you go do a prolactin test on one of these kids, two, three, five years later, it's not going to be elevated, correct? You know that?

A I can only see what the levels are up to Week 48.

Q But you know, you have been living in this world for a long time, you know that the prolactin levels eventually go back to normal, correct?

A Well, normally, people have normal levels of prolactin, yeah.

Q Yes. Now let's go to the next gynecomastia boy. By the way, with the increased prolactin at Four to Seven and Eight to Twelve.

Now let's go to boy Number 3004. He was 9.1 years old. His pre-dose went from 11.2 to 29. Do you see that?

A Yes.

Q He is another boy who had elevated prolactin and gynecomastia, correct?

A Yes.

Q It's a nine-year old. And now next, 3190. That's a 7.9 year old. He's a little mentally retarded child, if that's a correct term today, borderline retardation, with a 73 IQ, gynecomastia, and look what happened to his prolactins on this drug. Went from 7.8 to 34.3.

If you can save all of these as call-outs, but I want to do this quickly so I don't want to take up the time now.

3329, a five-year old. A five-year old, with female breasts. Do you see that?

A Whoa, whoa, whoa. Be careful. Gynecomastia does not necessarily mean female breasts.

Q Gyne, female, mastia --

A Gynecomastia --

Q Sir, respectfully, let's just go through the chart.

THE COURT: Is there an objection?

MS. SULLIVAN: I just want him to let him answer the question.

THE COURT: Again, unless you are

qualified to testify as an expert about this particular problem, about what gynecomastia is, we are going to move on.

MR. KLINE: I am sorry, Your Honor, I was rushing to it.

Q 3329, a five-year old, and look what happened to this 5.0 year old. Look what happened to his prolactin. It went from five to 38, and 31. Exactly, sir, exactly what your data was showing. Correct?

A In the whole group, yes.

Q Yeah. In the whole group. The one that was statistically significant.

And finally, you have 3357, a seven-year old whose prolactin started at eight. What's the normal limit, sir?

A Up to 18 or 19.

Q That's right, up to 18. And look at that. Do you see that, in the 8 to 12-week category? Conforming to the data. Bingo, at an elevated level at 8 to 12 weeks. Do you see that one?

A Yes.

Q Now I am not going to write them all out but let's look at a couple of these.

You have a nine-year-old girl, second from the bottom, with breast enlargement. Nine-year old girl. That's gynecomastia, too, isn't it?

A Again, that you need to ask the expert, because to which extent a physician in assessing adverse events calls it breast enlargement other than gynecomastia --

Q And that was elevated prolactin, correct?

A No, because the normal level for females is up to 30.

Q And you have a ten-year old at the bottom with vaginal hemorrhage, correct?

A Yes.

Q Whose prolactin went from five, which is less than one-third normal, to 33. Correct?

A That's correct.

Q And you have a girl who is 14, who doesn't get her period when her prolactin level goes from 7.4 to 36. Correct?

A Well --

Q Yes or no?

A No, that's wrong conclusion.

Q Is this girl 14.8 years old?

A Yes.

Q Did she have amenorrhea?

A Yes.

Q Is that lack of period?

A Yes.

Q And did she have a prolactin level which started at 7.4?

A Yes.

Q And ended -- and went up to 36.8?

A Yes.

Q And stayed up there above the normal limit in Weeks 8 to 12?

A No, because for girls the normal limit is 30.

Q No, there was a big debate, sir, and you darn well know that what happened was that the prolactin levels were set at 30 and your outside experts, and you know this to say under oath, your outside experts set it back down to 18?

MS. SULLIVAN: Objection to "darn well."

THE COURT: If we need to get into argument about this, we can do it --

MR. KLINE: We are almost done.

THE COURT: No rush. We are going to be here until 5 o'clock whether we finish this or not.

MR. KLINE: I will leave our usual 15 and 15, Your Honor, I promise.

Q And that's the tale of the children of the "real" SHAP, that you described as the real SHAP, is contained in this table, these are the faces behind the table, correct?

A Yes.

Q Each one is a little smiling face, correct?

A Yes. And I am glad you bring that up, because every adverse event that we see is one too many and I am fully aware of that. I --

Q Especially --

A Can I finish? I haven't found and nobody has found yet the way to find drugs without any adverse event. So the only thing we can do is we can identify them, we can write them down, and we can share this information with the prescribers. And that's the way the system works. And unfortunately, I would love to have a product without side effects.

Q Yes, and here, sir, respectfully, the problem, see if you agree: This was all not warned about and was all being used off-label to millions of prescriptions, correct? Yes or no?

A Incorrect.

Q There were millions of prescriptions?

A That's correct, but you had three questions. Go question by question then.

Q Now, to go further on this, you have Table 20, which is P-42(A), Table 20. Here is what this says.

I think we started way back when two days ago that you are not a statistician but you certainly know what these statistically significant values mean, correct?

A No, you told me that I don't know what the p-value means, but I think I do.

Q No, I didn't say that, sir.

A Yes, you did.

Q No, I said that you were not a statistician?

A That's correct.

Q And by the way, other witnesses have been asked the same question.

Now, on P-20, sir, let's go to Weeks 8 to 12, and I just need an interpretation of what this would mean.

This is nine of these kids, nine versus three. That is to say when they had an elevated prolactin level, nine of them went on to get

gynecomastia, correct?

THE COURT: Do you need a hard copy? Why don't you give him a hard copy.

A No, no, that's --

Q I can shorten this up, Your Honor.

A That's incorrect.

Q I will withdraw the question, I will shorten it up. I want to give time. Let's take it down. We will move on. I am going to try to get this finished.

Sir, we talked briefly about this label?

A Is it the 2006 label?

Q Yeah. By the way, 2006 label, when autism was changed, just to be clear, was not in effect when the drug was being used off-label for doctors in 2002 to 2006, correct?

A That is correct.

Q And by the way, sir, do you know of any effort Janssen took -- it's just a simple you know or you don't -- any effort Janssen took to send a Dear Doctor letter to doctors prescribing off-label, any time between 2002 and 2006, about this prolactin issue?

A No. We would not be even allowed to do so.

Q That's a different story, sir.

A Yeah.

Q Do you know -- it's just a do-you-know question -- do you know what the former Commissioner of the FDA told us about that?

A No, I was not here.

Q Yeah. And, sir, the label itself, the 2006 label, first of all, let's go to the proposal. This was with -- you did this with Ms. Sullivan, Exhibit 60(D). This would be JJRP00824752.

MR. GOMEZ: D-62.

Q Do you remember you were talking about the label markup?

A Yes.

Q This was in front of the jury earlier, it's D-234.23, it's D-60-D. It's a document previously marked, a defense Exhibit. I am told it's D-62.

Remember discussing it with counsel for the Janssen companies?

A What is the question? I am sorry.

Q Do you recall it, I want to put it in perspective so that I can ask you a few questions and hopefully sit down?

A Is this --

Q The label markup with the FDA?

A That the FDA sent us?

Q Yeah.

A Okay.

Q Because you see the first sentence, "As with other drugs that antagonize dopamine D2 receptors, risperidone elevates prolactin levels." Do you see that?

A Yes.

Q That was the language that Janssen suggested and it was crossed off by the FDA?

A No, no, this was the language that has been in since 1993.

Q Oh, and that's why it's crossed off. Got it. Okay, sir.

MR. KLINE: Nothing further right now, Your Honor. I want to be done today with our 15/15.

THE COURT: I guess this would be redirect.

MS. SULLIVAN: Thank you, Your Honor.

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REDIRECT EXAMINATION

- - -

BY MS. SULLIVAN:

Q Good afternoon, everyone. Good afternoon, Dr. Caers. Dr. Caers, I want to start by asking you about those events in the prepubertal kids that Mr. Kline was asking you about from the data tables? And I will get out the document and show you.

MS. SULLIVAN: If we could get Dr. Caers and Mr. Kline a copy of what's been marked as Dr. Caers' Exhibit 63, and that's where these tables that Mr. Kline was talking about came from.

Q Dr. Caers, Mr. Kline showed you -- if I could have the elmo -- showed you this table, and Dr. Caers, these are kids that are under the age of ten, right?

A The boys with gynecomastia, yes.

Q Yes. And one of the things that Mr. Kline didn't talk to you about was the fact that the company --

MR. KLINE: Objection to the form.

THE COURT: Sustained.

Q Was there also an analysis in this package that looked at whether or not these events were