IN THE UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE: CELEXA AND LEXAPRO MARKETING AND SALES PRACTICES LITIGATION	MDL NO. 2067 Master Docket No. 09-MD-2067-(NMG)
PAINTERS AND ALLIED TRADES DISTRICT COUNCIL 82 HEALTH CARE FUND, A THIRD-PARTY HEALTHCARE PAYOR FUND, on behalf of itself and all others similarly situated, Plaintiffs, v. FOREST PHARMACEUTICALS, INC. and FOREST LABORATORIES, INC., Defendants.	Case No. 13-CV-13113 (NMG) Hon. Nathaniel M. Gorton Hon. Marianne B. Bowler
IN RE: CELEXA AND LEXAPRO MARKETING AND SALES PRACTICES LITIGATION	MDL NO. 2067 Master Docket No. 09-MD-2067-(NMG)
DELANA S. KIOSSOVSKI and RENEE RAMIREZ, on behalf of themselves and all others similarly situated, Plaintiffs, v. FOREST PHARMACEUTICALS, INC. and FOREST LABORATORIES, INC., Defendants.	Judge Nathaniel M Gorton Case No. 14-CV-13848 (NMG) Hon. Nathaniel M. Gorton Hon. Marianne B. Bowler

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OCTOBER 14, 2016

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WILLIAM E. HEYDORN, Ph.D.

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Videotaped sworn deposition of WILLIAM E. HEYDORN, Ph.D., held at SHERATON PARSIPPANY HOTEL, 109 Smith Road, Parsippany, New Jersey, commencing at 9:40 a.m., before Margaret M. Reihl, a Registered Professional Reporter, Certified Court Reporter, Certified Realtime Reporter, and Notary Public.

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I N D E X

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E X H I B I T S

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THE VIDEOGRAPHER: We are now on the record. My name is Charlie Bowman, I'm a videographer with Golkow Technologies. Today's date is October 14th, 2016. The time is 9:40 a.m. This video deposition is being held in Parsippany, New Jersey in the matter of In Re: Celexa and Lexapro Marketing and Sales Practices Litigation for the United States District Court for the District of Massachusetts.

The deponent is William Heydorn. Counsel will be noted on the stenographic record. The court reporter is Peg Reihl and will now swear in the witness.

... WILLIAM E. HEYDORN, having been duly sworn as a witness, was examined and testified as follows ...

BY MR. BAUM:

Q. Can you please state and spell your full name for the record.

A. Sure, it's William E. Heydorn, H-e-y-d-o-r-n.

Q. Hi, I'm Michael Baum, I represent the plaintiffs in this action.

A. Good morning.

Q. And we brought a claim against Forest related to Celexa and Lexapro and its pediatric use and its promotion for pediatric use.

A. Okay.

Q. Are you familiar with that idea?

A. Yes.

Q. So what is your current address?

A. Home address?

Q. Yes.

A. Nine Eugene Circle in Lincoln Park, New Jersey.

Q. And are you represented by counsel today?

A. Yes.

Q. Did you seek counsel when you were originally served with a subpoena?

A. Well, counsel contacted me.

Q. Okay. How did you come to be being represented by this counsel that's here with you today?

MR. ABRAHAM: Objection.

MS. KIEHN: That calls for privileged information.

MR. BAUM: I'm not sure I understand how

that's a privileged communication.

MS. KIEHN: I'm not sure I understand the question.

MR. BAUM: Well, maybe that's a better objection.

BY MR. BAUM:

Q. Who is representing you?

A. Kristin and Rob here. I must admit, I forget the name of the firm.

MR. ABRAHAM: Debevoise & Plimpton.

THE WITNESS: Okay. Thank you.

BY MR. BAUM:

Q. Are your attorneys being paid by Forest?

A. Yes, that's my understanding.

Q. Okay. Did you contact Forest?

A. No.

Q. And you've been deposed before?

A. Yes.

Q. How many times?

A. At least once.

Q. And the one time that I am familiar with was in 2007?

A. That sounds about right.

Q. Okay. Did you have a chance to review

that deposition transcript?

A. Yes.

Q. When did you last look at it?

A. Yesterday.

Q. Were your answers to the questions in the 2007 deposition accurate and truthful, to the best of your ability at the time?

A. Yes.

Q. Are there any answers to the questions in your 2007 deposition that you would want to change now?

A. Not that I can recall, no.

Q. Now, you understand that you're here under oath, right?

A. Yes.

Q. And it's the same oath as if you were taking -- having your testimony being taken in front of a jury?

A. Yes.

Q. And the court reporter is here to take down everything we say?

A. Yes.

Q. And it's important that we don't talk over each other or she'll get mad at us.

A. Okay.

Q. So it's also important that you give oral responses that are instead of shaking your head or nodding your head for yes or no.

A. I understand.

Q. And you need to wait until I'm done rattling off my long-winded questions before you respond.

A. Okay.

Q. And I'll try not to step on your answers.

A. All right.

Q. If there is an objection, that means that they just don't like my question, they want the judge to review the way the question is asked, but I'm still entitled to your answer unless there's some privilege that's being asserted.

A. Okay.

Q. And they'll let you know when that happens, but, otherwise, they'll just object, and that's noted for the record and I will expect you to give a response?

A. All right.

Q. And then there will be a record made, a

transcript, and you'll be able to review that and make any changes. If you don't understand a question that I ask, ask and I'll rephrase the question, but, otherwise, if you respond I'll assume that you understood and that would be a -- your response that we would consider to be your valid response. You'll have a chance to make changes to your responses after you review the transcript, but I'll be able to comment on your having made changes.

Does that make sense?

A. Yes.

Q. So I would like you to give your best responses, if you can.

And is there anything that prevents you from giving accurate testimony today?

A. No.

Q. Okay. Did you meet with Forest attorneys before this deposition today?

A. Yes.

Q. When did you meet?

A. Yesterday.

Q. For how long?

A. About five, five and a half hours.

Q. Okay. And did you meet with them again

today?

A. This morning for breakfast.

Q. About how long?

A. About 45 minutes.

Q. Okay. And you understand you're here today in connection with lawsuits involving the drugs Celexa and Lexapro, correct?

A. Yes.

Q. Are you familiar with the allegations in our Complaint?

A. In a broad sense, yes.

Q. What are they?

A. It relates to inappropriate promotion of Celexa and Lexapro, off-label use in pediatric and adolescent patients.

Q. And you're aware that there have been legal actions against Forest for off-label marketing of Celexa to children and adolescents?

A. Yes.

Q. Are you aware that depositions of Forest employees were conducted in a securities case involving Celexa?

A. Yes, that does sound familiar.

Q. Did you speak to any Forest employees

about those depositions?

A. No.

Q. Were you interviewed by the Department of Justice lawyers in 2007 regarding the off-label promotion of Celexa in the pediatric population?

A. Yes.

Q. Do you recall the subjects matter of what you discussed?

A. Not in detail.

Q. What do you recall generally?

A. Relating to the promotion of the drug in pediatric and adolescent patients.

Q. Did you give them any documents?

A. I don't believe so.

Q. Did you sign any declarations?

A. I don't recall.

Q. Are you aware that Forest has pled guilty to misbranding in this case -- in that case?

A. No, that I was not aware of.

Q. Have you communicated with any Forest employees about their depositions?

A. No.

Q. Did you review any documents in preparation for your deposition today?

A. Yes.
Q. What documents did you review?
A. Well, we met yesterday, went over the publication of the MD-18 study, the study report, some e-mail communications regarding the ACNP poster from 2001, I believe it was.
Q. Anything else?
A. No. I saw a copy of the Lundbeck publication, which I had not seen before, because that was published after I left Forest, and that's about it.
Q. So you've brought with you today your CV?
A. Yes.
Q. I'm going to mark that as Exhibit 1 and hand that to you.
A. Yes.
(Document marked for identification as Heydorn Deposition Exhibit No. 1.)
BY MR. BAUM:
Q. Is this your current CV?
A. Yes.
Q. And I see that since 2003 you've been working for Lexicon?
A. Correct.

Q. Is that correct? And what is the general nature of the work you've been doing there?

A. So at Lexicon I've been involved in preclinical development, so studies in -- of our compounds in animals for efficacy and safety, also formulation development and clinical supplies distribution for clinical trials that are being conducted by Lexicon.

Q. What type of compounds have you been working on?

A. We've taken close to ten compounds into development based upon a genetic knockout technology that was developed by the founders of the company. We currently have two compounds in -- one compound in Phase III, one compound we've had an NDA filed.

Q. What type of drugs are those?

A. So the compound in Phase III is a diabetes compound with a unique mechanism of action. The other compound is for a condition called carcinoid syndrome, which is an orphan indication, and that's the compound we filed the NDA on.

Q. An orphan indication is for the same compound?

A. So an orphan indication, so it's a very

small patient population.

Q. Yeah, but using the same compound, the same drug?

A. Right, that drug is specifically for, yeah.

Q. Any central nervous system type drugs?

A. We took one into development earlier on in my career there, and then we moved away from the developing compounds for the CNS area.

Q. Was that an antidepressant?

A. No, it was actually a drug for mild to moderate -- we were hoping, targeting mild to moderate memory disorders.

Q. Okay. And you left Forest in 2003; is that right?

A. Correct.

Q. Why did you leave?

A. We had had a reorganization in 2002, and I was offered a position within the organization, but it was not something that I was particularly interested in doing or, you know, saw it as a good growth opportunity in the future.

Q. What was that position?

A. So I moved into internal medicine out of

the CNS area, and it was just a position I wasn't interested.

Q. Was there some sort of dissatisfaction with the work you were doing in the CNS area?

A. Not that I know of. And my understanding was the -- Larry Olanoff decided to reorganize. I headed up a medical writing and medical communications group, and he ended up splitting that such that the responsibility for that then fell within the specific therapeutic areas.

Q. Were there any disagreements that you had with any Forest personnel before you left?

A. No.

Q. And there was no disagreements you had with them regarding the way Celexa or Lexapro were being prepared?

A. What do you mean by "prepared"?

Q. Being written up?

A. No, no, not that I recall.

Q. Do you recall when you stopped working on the development of the pediatric use of Celexa or Lexapro?

MR. ABRAHAM: Objection.

THE WITNESS: When I stopped working.

Well, I was -- we were reorganized in the fall of 2002, so it would have been at that point I moved out of the CNS area.

BY MR. BAUM:

Q. Did you have any continuing responsibilities with regard to Celexa or Lexapro?

A. I continued to support Celexa. We had relatively few people left in the organization then who had any history with Celexa. People had moved on. The company was focusing its efforts on Lexapro, the single enantiomer compound, and so there were still a few small projects that I was involved with.

Q. What little projects were left?

A. I must admit, I don't remember specifically.

Q. When you left Forest, did you sign any Confidentiality Agreement that prevents you from discussing in this deposition the work that you did while at Forest?

A. I don't believe so.

Q. Are you subject to any agreement or requirement to not say anything negative about Forest or your work at Forest?

A. No.

Q. You've testified that you were interviewed as part of a Department of Justice investigation of Forest in connection with off-label marketing of Celexa and Lexapro; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. When did you first become aware of the department of justice investigation of Forest in connection with off-label marketing of Celexa and Lexapro?

MR. ABRAHAM: Objection.

THE WITNESS: It was probably in the 2005 time frame, 2006.

BY MR. BAUM:

Q. How did you become aware of it?

A. I was served a subpoena. I was contacted by Forest to inform me that this was -- this process was going to begin, and then I was served a subpoena.

Q. Did you have any interviews with Forest personnel at that time?

A. No, not that I recall.

Q. With Forest lawyers?

A. Yes.

Q. And what sort of meetings did you have with them?

A. There were --

MR. ABRAHAM: I would caution the witness not to discuss the subject matter of your conversations with Forest attorneys.

THE WITNESS: Okay, okay, yeah.

They were discussions relating to the Department of Justice action.

BY MR. BAUM:

Q. Were you given any sort of immunity in order to talk?

A. I believe --

MR. ABRAHAM: Objection.

THE WITNESS: I believe so.

BY MR. BAUM:

Q. Are you aware that Forest pled guilty and agreed to pay $313 million in that action?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I'm aware that they pled guilty. I didn't know the specific amount.

BY MR. BAUM:

Q. Are you aware of a plea agreement that the United States -- let me strike that.

Are you aware of a plea agreement between the United States and Forest that was entered in in around September of 2010?

A. That does sound familiar to me, yes.

Q. Have you seen it?

A. No.

(Document marked for identification as Heydorn Deposition Exhibit No. 2.)

BY MR. BAUM:

Q. So I'm going to mark as Exhibit 2, the plea agreement. I ask you to take a look at that.

A. Do you want me to read the whole thing?

Q. No, I don't. I'm going to point to a particular page.

A. Okay.

Q. Now, are you aware that Forest pled guilty to charges of illegal off-label promotion?

MR. ABRAHAM: Objection.

THE WITNESS: No, I must admit, you know, since I left the company, I haven't really followed the details of their legal issues, aside from maybe seeing something, you

know, in one of the online newsletters that I see, but it's not something I followed closely.

BY MR. BAUM:

Q. Were you ever concerned that you might have been drawn into it as a party to the charges?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't think so.

BY MR. BAUM:

Q. Okay. So let's take a look at Page 8. If you look at the bottom of that page it says, "Forest expressly and unequivocally further admits that it committed the offenses charged in the Information and is in fact guilty of those offenses. Forest agrees that it will not make any statements inconsistent with its explicit admission of guilt to these offenses."

Do you see that?

A. Yes.

Q. And then under -- up at the top here under "Cooperation," right under that Number 8, you see that?

A. Yes.

Q. It says, Forest shall cooperate completely and truthfully in any trial or other proceedings arising out of any ongoing civil, criminal

or administrative investigation or its current -- sorry -- criminal or administration investigation of its current and former officers, agents and employees and customers in connection with the matters described in the information.

Do you see that?

A. Yes.

Q. Do you think that applies to you?

MR. ABRAHAM: Objection.

THE WITNESS: I'm really not sure. I'm not a lawyer.

BY MR. BAUM:

Q. Okay. Do -- you intend to be truthful and forthcoming today, correct?

A. Yes.

Q. Can you tell me what a study protocol is?

A. So a study protocol is the preplanned plan that is developed prior to the initiation of any study that details what will be done, patient population, analyses. It's all kind of the preplanned information that is given to investigators.

Q. Why is a study protocol necessary for the conduct of a trial?

MR. ABRAHAM: Objection.

THE WITNESS: You want each site in a study to conduct the trial, you know, as similar a fashion as possible. So protocol is developed so that investigators have the -- you know, have the instructions basically to conduct the study as intended.

BY MR. BAUM:

Q. Is it kind of like a recipe for the clinical trial?

MR. ABRAHAM: Objection.

THE WITNESS: I guess you could call it that.

MS. KIEHN: I just want to clarify for the record, Dr. Heydorn is not here as an expert witness, so his testimony is in his personal capacity.

MR. BAUM: Okay.

BY MR. BAUM:

Q. Does a study protocol outline a procedure for the scientific integrity of the study?

A. I believe so.

Q. Was Forest expected to follow the study protocol for CIT-MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I would assume so.

BY MR. BAUM:

Q. And were you expected to follow the study protocol for study CIT-MD-18?

A. Yes.

Q. If you did not follow the study protocol, would that invalidate the results of the study?

MR. ABRAHAM: Objection.

THE WITNESS: Not necessarily. There are deviations in every protocol and every study, and those deviations should be noted as part of the final study report.

BY MR. BAUM:

Q. The placebo effect and observer bias require an experiment to use a double-blind protocol and a control group, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. What is a double-blind protocol?

A. So that is a protocol where neither the subject nor the investigator is aware of the treatment

being administered.

Q. Did the protocol for study CIT-MD-18 require a double-blind procedure?

A. Yes.

Q. You read the protocol for MD-18, correct?

A. I have not read it recently, no.

Q. But you read it at the time you were working there?

A. I assume I had read it, yes. I can't recall specifically, but that would be reasonable.

Q. So the -- and you recall that CIT-MD-18 had a double-blind procedure specified in the protocol?

A. Yes.

Q. And the double-blind procedure required that neither the experimenter nor the experimental subjects had knowledge of the identity of the treatments or the results until after the study is complete, right?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. What is a control group?

A. A control group is the group that

receives the placebo.

Q. And MD-18 had a control group?

A. Yes.

Q. And they had a placebo group?

A. That was the control group, the placebo group.

(Document marked for identification as Heydorn Deposition Exhibit No. 3.)

BY MR. BAUM:

Q. I'm going to hand you Exhibit 3, which is a subset of the study report for MD-18, which has the protocol in it.

A. Okay.

Q. And this is the section of the study report that is the protocol for MD-18 dated September 1, 1999.

Do you see that?

A. Yes.

Q. Does this document look familiar to you?

A. Vaguely. As I said, I have not seen it in many, many years.

Q. Do you recall this -- I'm just going to refer to it as MD-18?

A. That's fine.

Q. So do you recall that MD-18 was a multisite clinical trial?
A. Yes.
Q. And each site was expected to follow the study protocol; is that correct?
A. Correct.
Q. Did Dr. Karen Wagner run any of those sites?
A. I believe she ran one of the sites, yes.
Q. Take a look at Page 309, which is the next -- the second page here. You see this is signed by a Paul Tiseo, September 1, 1999?
A. Yes.
Q. Do you know what Dr. Tiseo's role was in the CIT-MD-18?
A. I believe he was the overall study monitor.
Q. What does that mean?
A. He's the -- he would be the one person at Forest ultimately responsible for the conduct of the study.
Q. Did you interact with him with respect to CIT-MD-18?
A. Not on a regular basis. During the

conduct of the study, I was not actively involved in, you know, any of the day-to-day details of the study.

Q. But when it came around to getting the poster, study reports, CME type stuff, did you work with him?

MR. ABRAHAM: Objection.

THE WITNESS: I believe at that point he had left the company.

BY MR. BAUM:

Q. Okay. Do you know when he left?

A. Maybe sometime in 2000. I don't recall exactly. I know we overlapped for just a few months.

Q. Do you know who took his place?

A. I don't know.

Q. Was there someone you answered to that was served in a similar role as the oversight -- overseer of MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not sure I understand the question.

BY MR. BAUM:

Q. Well, what did you say his role was with respect to MD-18?

A. He was the -- my recollection is he was

the study monitor.

Q. Okay. So did someone else step into the shoes of being study monitor for MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: I assume so.

BY MR. BAUM:

Q. You don't recall?

A. I don't recall. I could speculate.

Q. What would you speculate?

A. I would think --

MR. ABRAHAM: Objection.

You can answer.

THE WITNESS: Okay. I would think it was probably Dr. Flicker.

BY MR. BAUM:

Q. Okay. So you see in the next person down here on that page is Charles Flicker; is that right?

A. Yes.

Q. Then you see Lawrence Olanoff?

A. Yes.

Q. What were their roles in MD-18?

A. As I said, I believe Dr. Flicker took the role of study monitor after Paul Tiseo left the

organization. Larry Olanoff was overall head of research and development at Forest.

Q. Did you interact with either of them?

A. Yes.

Q. And then Ivan Gergel?

A. Yes.

Q. Who is he?

A. Well, he's the executive director of clinical research. When I first joined Forest my recollection is that, you know, I answered to Charlie Flicker. Charlie reported in to Ivan Gergel. And then after a reorganization in, I believe, 2000 I reported directly to Ivan.

Q. What happened to Charlie?

A. I know he left the organization, and I have lost touch with him.

Q. Okay. Have you talked to him since he left Forest?

A. No.

Q. And who is Ed Lakatos?

A. Senior director of biostatistics and data management.

Q. Did you interact with him?

A. Very little, if at all.

Q. And what about Keith Rotenberg?

A. Rotenberg, he's head of regulatory and quality. I interacted somewhat with him, but it's been many years, and I don't remember how often.

Q. What happened with regulatory affairs; what did they do with respect to MD-18?

A. Well, they're the ones that are responsible for filing the documents with the Food and Drug Administration.

Q. Do you recall an Amy Rubin or Tracey Varner working in that role?

A. Yes.

Q. Were they people you dealt with more directly?

A. Yes.

Q. Let's go to Page 313 of this document, which is a synopsis.

Do you see that?

A. Yes.

Q. And under the subheading below it says "Evaluations."

Do you see that?

A. Yes.

Q. And the "Primary Efficacy."

Do you see that?

A. Yes.

Q. And the "Children's Depression Rating Scale - Revised."

Do you see that?

A. Yes.

Q. Was that the primary outcome measure for determining efficacy in CIT-MD-18?

A. Yes.

Q. And then you see there's some Secondary Efficacy measures, the "Clinical Global Impression (CGI)."

Do you see that?

A. Yes.

Q. And "Severity and Improvement subscales."

Do you see that?

A. Yes.

Q. And then you see the K-SADS?

A. Yes.

Q. Which is depression module for K-SADS and then the "Children's Global Assessment Scale (CGAS)."

Do you see that?

A. Yes.

Q. These primary and secondary efficacy evaluations are the protocol specified outcome measures by which the study drug citalopram was determined to be successful or unsuccessful compared with placebo, right?

MR. ABRAHAM: Objection.

THE WITNESS: The primary efficacy endpoint was the primary determination of efficacy.

BY MR. BAUM:

Q. Okay. And what were the secondary endpoints there for?

MR. ABRAHAM: Objection.

THE WITNESS: Secondary endpoints are there to track -- generate additional information about the efficacy of the compound.

BY MR. BAUM:

Q. Can you explain how efficacy of the study drug versus a placebo is demonstrated by an outcome measure?

MR. ABRAHAM: Objection.

THE WITNESS: It's not really my area of expertise.

BY MR. BAUM:

Q. Is it the result of a statistical analysis?

A. Yes.

Q. Can you describe that?

A. Well, again --

Q. Generally.

A. I'm not a statistician, but there's a statistical test that is done to see if there is a difference between the active group and the control group.

Q. And the difference needs to be statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Can you explain what that means, statistical significance?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not a statistician.

BY MR. BAUM:

Q. But from your perspective.

A. From my perspective, it's generally

considered that the active and placebo are different if the probability of a random event is less than 5%, less than 8.25%.

Q. That's the P-value?

A. That's the P-value, yes.

Q. And that tells you that the difference didn't happen by chance?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's my understanding.

BY MR. BAUM:

Q. Let's go to Page 318, under the Study Design.

A. Okay.

Q. You see there that it says that total of 160 patients will be randomized to double-blind treatment.

Do you see that?

A. Yes.

Q. Was 160 patients the number needed to power the study?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not a statistician, but that would be my assumption

if that's what was selected for the -- you know, the N in the study population.

BY MR. BAUM:

Q. So they wanted to have at least 160 patients in the analysis in order to have statistically significant outcomes?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not a statistician, but my assumption would be yes.

BY MR. BAUM:

Q. Do you recall whether there was a problem with recruitment into this study?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall any specific problems with recruitment into the study.

BY MR. BAUM:

Q. Was the study powered to detect differences in the efficacy of citalopram in children and adolescents?

MR. ABRAHAM: Objection.

THE WITNESS: I assume so.

BY MR. BAUM:

Q. Let's a take a look at Page 321, it's

subheading "Study Procedures."

You see that?

A. Yes.

Q. And then if you look below, you see that there's some efficacy measures.

Do you see that?

A. Yes.

Q. And there's a description again of the primary, secondary efficacy measures?

A. Yes.

Q. Could you describe what the difference is between the primary and secondary efficacy measure?

A. So, in my experience, when you do a clinical study, a double-blind study for purposes of discussion you pick a single endpoint as your primary endpoint, and that defines whether the results, if you reached statistical significance on that primary endpoint, that defines whether the study was positive or not.

Q. So it was important for a study to have a positive outcome with a statistically significant number of P-value less than .05 in order to be positive?

MR. ABRAHAM: Objection.

THE WITNESS: Well, I wouldn't say it's important. I mean, that's the goal of the study. Some studies are done and no difference is shown between the two groups.

BY MR. BAUM:

Q. Do you know why the CRS-R was chosen as the primary measure?

A. No, I do not.

Q. You weren't involved with creating the protocol; is that correct?

A. That's correct.

MR. ABRAHAM: Objection.

THE WITNESS: I'm sorry.

BY MR. BAUM:

Q. Let's go to Page 326. And it has here under section "9. Study Drug" and "9.1 Study Medication."

Do you see that?

A. Yes.

Q. And it says there, "Citalopram (20 mg) and placebo medication will be supplied by Forest Laboratories as film-coated, white tablets of identical appearance."

Do you see that?

A. Yes.

Q. And "For the single-blind lead-in period, patients will be supplied with placebo tablets only. For the double-blind treatment period, identically appearing tablets will contain either 20 mg of citalopram or placebo."

Do you see that?

A. Yes.

Q. And "Medication will be supplied in bottles containing either 10 tablets for the lead-in and the first four weeks of double-blind treatment, or 40 tablets of the remaining four weeks of the treatment period."

Do you see that?

A. Yes.

Q. Were you familiar with that particular element of the protocol?

A. Yes.

Q. Do you know whether that protocol procedure was followed for CIT-MD-18?

A. I do know there was a problem with the first few patients that were enrolled in the study.

Q. What was that problem?

A. These patients received pink colored

tablets instead of white colored tablets.

Q. Do you know how many patients?

A. Somewhere up to nine patients is my understanding.

Q. Do you know how much -- they were pink colored tablets?

A. That's my recollection, yes.

Q. Do you know how many pink colored tablets they received?

A. No, I do not.

Q. Let's go to Page 328. Under Section "9.7 Unblinding Procedures."

Do you see that?

A. Yes.

Q. What does it mean for a study to be unblinded?

A. When a study is unblinded, then the subjects and the investigators know who was on active and who was on placebo.

Q. For it to be double-blinded, both have to be blind; is that correct?

A. That is --

MR. ABRAHAM: Objection.

THE WITNESS: That is correct.

BY MR. BAUM:

Q. And if the investigator knows, for instance, what patient is receiving, then it's not double-blind; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's correct.

BY MR. BAUM:

Q. Would you agree that if a study does not follow the unblinding procedures as specified in the study protocol, then the study cannot be a randomized, placebo-controlled trial?

MR. ABRAHAM: Objection.

THE WITNESS: I don't feel competent to answer that question.

BY MR. BAUM:

Q. What do you know about the effect of unblinding on a placebo-controlled trial?

MR. ABRAHAM: Objection.

MS. KIEHN: If anything.

THE WITNESS: Occasionally, one needs to unblind a particular patient in a study for safety issues, and there's always a mechanism built in to do that in the event of an adverse event.

BY MR. BAUM:

Q. Have you ever had to do that?

A. Not that I can recall.

Q. All right. So in this subsection "Unblinding Procedures," you see towards the bottom of that section it says, "Any patient for whom the blind has been broken will immediately be discontinued from the study and no further efficacy evaluations will be performed."

Do you see that?

A. Yes.

Q. And then if the blind is broken for any reason, Forest Laboratories must be notified immediately.

Do you see that?

A. Yes.

Q. Were any patients in study MD-18 unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Were you ever advised that the patients that were exposed to the pink tablets were unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Were you ever -- did you ever discuss the patients that had been exposed to the pink tablets as being unblinded?

A. I don't specifically recall any -- any discussions on that.

Q. You didn't have any discussions with Charlie Flicker about that?

A. I don't recall any, no.

Q. Did you have any discussions with Lawrence Olanoff about that?

A. I don't recall any discussions.

Q. You don't recall any discussions with anybody about the pink tablets?

A. It was -- I know it was discussed in the study report, and that's when I became really aware of the study. I was not directly involved in the study during the conduct of the study.

Q. When the study report was being drafted, you became aware of it?

A. At that point I know I was aware of it, yes. I may have heard about it prior to that.

Q. When do you think you first heard about

it?

A. I couldn't say.

Q. Did you participate in any citalopram clinical trial meetings?

A. Yes.

Q. How often would you attend those?

A. I believe they were held weekly.

Q. Who ran them?

A. I don't recall.

Q. Was Ivan Gergel involved?

A. Yes.

Q. Charlie Flicker?

A. I believe so, yes.

Q. For a while Paul Tiseo?

A. Yes.

Q. Lawrence Olanoff?

A. Not on a regular basis, no.

Q. Did the subject of the pink tablet dispensing get raised in those meetings?

MR. ABRAHAM: Objection.

THE WITNESS: I believe it did.

BY MR. BAUM:

Q. Do you recall whether they were referred to as unblinded patients in those meetings?

MR. ABRAHAM: Objection.

THE WITNESS: I don't recall.

BY MR. BAUM:

Q. Do you recall there being any discussions about there being a problem with these patients being unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall.

BY MR. BAUM:

Q. Do you recall any discussions about whether the investigators were unblinded with respect to those patients and the pink tablets?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall any specific discussions.

BY MR. BAUM:

Q. Who would have been in charge, you think, of monitoring whether or not the investigators or patients were unblinded with respect to those tablets?

MR. ABRAHAM: Objection.

THE WITNESS: What ultimately would be the in-house study monitor.

BY MR. BAUM:

Q. And who was that?
A. Well, it was Paul Tiseo in the beginning.
Q. So then it devolved to Charlie Flicker?
MR. ABRAHAM: Objection.
THE WITNESS: I assume so. As I said, I don't know for certain who took over after Paul left.
BY MR. BAUM:
Q. Was Forest Laboratories notified of any unblinding in CIT-MD-18?
A. They were certainly aware of the pink tablets.
Q. How did Forest become aware of the pink tablets?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know.
BY MR. BAUM:
Q. Do you know what Forest did in response to learning about the pink tablets?
MR. ABRAHAM: Objection.
THE WITNESS: I reviewed some documents yesterday so --
BY MR. BAUM:

Q. And what did they say?
A. I know they replaced the pink tablets with white tablets.
Q. And what document did you review that said that?
A. It was a fax that Paul Tiseo sent to the investigator sites.
Q. That was a March 3rd, 2000 document?
A. I don't recall the date, but that would probably be about right.
Q. Now, was it only nine bottles of pink tablets that were sent out?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know.
BY MR. BAUM:
Q. You don't know whether there were more bottles sent to other sites that had to be retrieved?
MR. ABRAHAM: Objection.
THE WITNESS: No, I don't know.
BY MR. BAUM:
Q. Do you know what information was sent along with the bottles when they were sent to the investigator sites?
MR. ABRAHAM: Objection.

THE WITNESS: No, I do not.
BY MR. BAUM:
Q. Would there be information identifying which drug or which medication they were receiving?
MR. ABRAHAM: Objection.
THE WITNESS: I -- what do you mean by -- can you rephrase it?
BY MR. BAUM:
Q. Either active medication or placebo?
MR. ABRAHAM: Objection.
THE WITNESS: Well, the investigators would be aware that it was a double-blind study so that there -- the patients that they would enroll into the study, some would be on the active medication and some would be on placebo, they would assume that that would be the case.
BY MR. BAUM:
Q. Now, these pink tablets, was it your understanding they were actually active medication Celexa?
MR. ABRAHAM: Objection.
THE WITNESS: I have no way of knowing that, no.
BY MR. BAUM:

Q. You didn't read anything that said that yesterday?

A. I don't recall reading anything yesterday that said that.

Q. Do you recall having read anything ever with respect to whether or not the pink pills were active medication or placebo?

A. No.

Q. They could have been placebo, as far as you knew?

A. They could have.

MR. ABRAHAM: Objection.

THE WITNESS: They could have been. I just -- I don't know.

BY MR. BAUM:

Q. We'll show you some documents in a little bit --

A. Okay.

Q. -- that clarify that, I think.

So what is your understanding of how Forest found out about the pink tablets?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know how they found out.

BY MR. BAUM:

Q. You haven't read anything that told you how they found out?

MR. ABRAHAM: Objection.

THE WITNESS: Not that I can recall, no.

BY MR. BAUM:

Q. There was no discussion of those at any of the citalopram clinical trial meetings?

A. There may have been. I just -- I don't recall. It was so long ago.

Q. Okay. Let's take a look at Page 331. And under the Section "12.7 Sample Size Considerations."

Do you see that?

A. Yes.

Q. For a clinical trial, in general, you need to have enough people in both sides of the placebo and medicated group to appropriately analyze whether or not there's going to be a significant performance of the drug versus placebo, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's a statistical question. I really can't -- I'm not an expert in that area.

BY MR. BAUM:

Q. Do you know enough to know that you need to have a certain number of people in order for it to be a valid trial?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I do know that. I know there are calculations that are done and assumptions that are done that drive the ultimate sample size.

BY MR. BAUM:

Q. Okay. So here we have Sample Size Considerations, and it says, "The primary efficacy variable is the change from baseline in CDRS-R score at Week 8."

Now, if they pick Week 8, that's important; is that correct, because that's the endpoint of that -- for the trial; is that right?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not an expert in clinical trial design, but my understanding is that you pick a specific measurement at a specific time as your endpoint to determine whether the compound is efficacious or not.

BY MR. BAUM:

Q. Then going on here it says, "Assuming an effect size (treatment group difference relative to pooled standard deviation) of 0.5, a sample size of 80 patients in each treatment group will provide at least 85% power at an alpha level of 0.05 (two-sided)."

Did I read that right?

A. Yes.

Q. Do you know what that means?

A. Honestly, no. I have read numerous protocols over my career, and not being a statistician, I assume the statisticians have done their job and that the statement on sample size consideration is accurate.

Q. Is the general concept of that that you needed at least 80 patients in each side of the trial in order for the trial to be sufficiently powered?

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding, given the expected response to the study medication.

BY MR. BAUM:

Q. So that 80 patients in each treatment group would be 160 patients needed to power that trial, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That is my understanding.
BY MR. BAUM:
Q. So as long as MD-18 had 160 patients' results in the equations, that was enough to power statistically significant results, right?
MR. ABRAHAM: Objection.
THE WITNESS: That's my understanding, given the assumptions that went into the sample size consideration.
BY MR. BAUM:
Q. And you didn't need more than 160 to power the study for statistical significance purposes, right?
MR. ABRAHAM: Objection.
THE WITNESS: Again, yes, that's my assumption, given that this -- given that this assumption here is accurate.
BY MR. BAUM:
Q. And per this statement here, the protocol endpoint for efficacy was Week 8, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. And measurements at Weeks 1, 2, 4 or 6

would not be considered efficacy endpoints for study MD-18, right?

MR. ABRAHAM: Objection.

THE WITNESS: They were useful information, but they would not determine whether the study showed a significant difference between the two treatment arms.

BY MR. BAUM:

Q. And so statistically significant improvement at Week 8, per this protocol, was the point at which efficacy was to be determined positive or negative, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's my understanding.

BY MR. BAUM:

Q. And it would be inconsistent with the protocol to suggest that positive results at weeks earlier than Week 8 indicated a positive trial outcome for MD-18, right?

MR. ABRAHAM: Objection.

THE WITNESS: These were interesting and important observations, but they in and of themselves would not, as I understand it,

determine whether the study was efficacious or not, whether the compound was efficacious or not.

BY MR. BAUM:

Q. Omitting the Week 8 result while highlighting positive results from the earlier weeks would be inconsistent with the protocol and misleading, right?

MR. ABRAHAM: Objection.

THE WITNESS: No, not in my opinion.

BY MR. BAUM:

Q. So it would be okay with you to talk about Weeks 1, 2, 4 and 6 results as positive but not mention that Week 8 was negative?

MR. ABRAHAM: Objection.

THE WITNESS: You would have to include both.

BY MR. BAUM:

Q. Otherwise you'd be misleading --

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. -- about the actual outcome of the trial, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. What is a study report?

A. The study report is the document that's generated at the conclusion of the study that summarizes all of the results of the study.

Q. You were a director of scientific communications at Forest; is that correct?

A. Yes.

Q. Was the creation of a study report part of your job?

A. Yes.

Q. Who created the study report for MD-18?

A. I don't recall specifically, but I'm assuming myself or someone in my group was responsible for that.

Q. Did you write any of it?

A. I believe I wrote the first draft of it.

Q. According to your 2007 deposition, you were the primary author of the final study report.

Does that ring a bell?

MR. ABRAHAM: Objection.

THE WITNESS: If that's what I testified then, I'm assuming that was the truth.

BY MR. BAUM:

Q. Do you consider yourself to have been the primary author of the final study report --

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. -- for MD-18?

A. No. The actual final report was a group effort within the organization. These reports are not written by a single individual without significant review within the organization.

Q. Who would you consider to have been the primary author?

MR. ABRAHAM: Objection.

THE WITNESS: As I said, I generated the first draft from my memory, and then it was edited by the clinical team.

BY MR. BAUM:

Q. Who in particular edited it?

A. I know Charlie Flicker had a number of comments on the report.

Q. Would he inform you of the comments?

A. Yes.

Q. How would he do that?

A. He would -- Charlie didn't use

computers. He handwrote on the first draft of the report and then handed it back to me.

Q. So he would handwrite on something, a draft of it, a copy of it, and then come to you and actually hand it to you?

A. Yes.

Q. He wouldn't e-mail it to you?

A. No.

Q. Also, according to your 2007 deposition, you were responsible for ensuring the study report for MD-18 was accurate and was available for submission to the FDA.

Do you recall saying that?

MR. ABRAHAM: Objection.

THE WITNESS: I assume I did, if it's in the deposition.

BY MR. BAUM:

Q. Did you review the MD-18 study report for accuracy?

A. I would assume I did, yes.

Q. What are case report forms?

A. Again, not my area of expertise, but they are the documentation that comes from the study site. It's a standard form that is filled out at the

study site. There's one for each patient that tracks the individual patient data.

Q. Did you look at case report forms for MD-18?

A. I don't recall ever looking at case report forms.

Q. How would you go about verifying the accuracy of statements that were in the study report without looking at the case report forms?

MR. ABRAHAM: Objection.

THE WITNESS: Summary tables are generated by statisticians that pool the data, pool all the data on a particular endpoint, and that's what's generally used to generate the study report.

BY MR. BAUM:

Q. Did anyone at Forest look at the case report forms to cross-check the case report form data against the summary data the statistician has generated?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you know if anybody had the job of

doing that?

A. I don't know.

Q. How do you know whether or not the summary of data that the statisticians provided was accurate?

MR. ABRAHAM: Objection.

THE WITNESS: I would assume it was accurate.

BY MR. BAUM:

Q. Why?

A. The data -- well, I'm assuming the data came from the case report forms. It was transferred into the computer systems that generated the summary tables that were used to generate the report.

Q. So, in effect, you were relying on the accuracy of the summary tables that were provided to you by the statisticians?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Did you review tables for the primary efficacy outcome data?

A. Yes.

Q. Did you verify the accuracy of the

CIT-MD-18 efficacy data by cross-checking the data summarized in MD-18's efficacy tables with the case report forms themselves?

MR. ABRAHAM: Objection.

THE WITNESS: No, I did not.

BY MR. BAUM:

Q. Did you look for inconsistencies between numbers of people who were assigned to placebo versus citalopram?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not sure I understand the question.

BY MR. BAUM:

Q. In the weekly citalopram clinical trial meetings, there was a report of how many people were participating in the trial.

Do you recall that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I do recall that.

BY MR. BAUM:

Q. And they kept track of how many people were on placebo and how many people were on Celexa; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: No, no, they would not have done that. They would keep track of the number of patients involved in the study.

BY MR. BAUM:

Q. So they kept track of the total number of patients as opposed to which ones were placebo and which ones were citalopram?

A. Correct. Studies are -- you know, generally we call them double-blind. They're actually triple-blind because neither the investigator, the patient nor the company knows who is on which medication.

Q. Did you review the appendices for the study, MD-18 study report?

A. Well, there were a significant number of appendices.

Q. Did you review the efficacy related appendices?

MR. ABRAHAM: Objection.

THE WITNESS: Probably not.

BY MR. BAUM:

Q. Did you review in particular one that was Appendix 6?

MR. ABRAHAM: Objection.

THE WITNESS: I don't recall.
BY MR. BAUM:
Q. Did you review -- you weren't shown something like that yesterday?
MR. ABRAHAM: Objection.
MS. KIEHN: Objection.
THE WITNESS: I don't recall seeing Appendix 6.
BY MR. BAUM:
Q. Do you recall seeing a run that excluded the patients that had the pink tablets dispensed to them?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, I do recall seeing that.
BY MR. BAUM:
Q. When did you see it?
A. I saw that yesterday. If that was Appendix 6, then I did see that yesterday.
Q. Had you seen that before?
A. I'm sure I had seen that when I was working on the study report, but I can't recall specifically.
Q. Do you recall any discussions when you

first -- let me strike that.

Do you recall any discussions while you were working on the study report as to whether or not the data that was in that Appendix 6 ought to have been used as the primary outcome measure?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall any discussions.

BY MR. BAUM:

Q. Who worked with you on the study report?

A. It's been so long, I don't recall who I worked with.

Q. Charlie Flicker for one, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Certainly Charlie was one of the reviewers of the report.

BY MR. BAUM:

Q. Do you know who Paul Bukerait is?

A. Yes.

Q. Who is he?

A. Paul was in my group. He was one of the writers in the group.

Q. What did he do?

A. He worked on either study reports or

publications.

Q. What did he do on MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: I can't recall specifically.

BY MR. BAUM:

Q. Did he have anything to do with helping you write it?

A. He may have. Again, these reports are group efforts. Multiple people contribute as either writers or reviewers.

MR. BAUM: Can we take a break now? Good point.

MR. ABRAHAM: Sure.

THE VIDEOGRAPHER: The time is now 10:41 a.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is now 10:52 a.m. This is the beginning of Disk 2. We're on the record.

(Document marked for identification as Heydorn Deposition Exhibit No. 4.)

BY MR. BAUM:

Q. I'm going to hand you what we're marking

as Exhibit 4, which is MDL-FOREM0002914. It's an August 15, 2001 memo from Exner to you.

Do you see that?

A. Yes.

Q. Do you recall this document? You might want to flip over.

A. No, I don't specifically recall this.

Q. So it says here that there's attached draft contracts that I sent to PIA, PharmaNet and Mary Cardinale. PharmaNet has agreed to their contract as proposed. Responses from PIA and Mary Cardinale are pending for this week.

And it says for you to take a -- "please take a look at all three draft contracts and let me know if you have any administrative changes that you want included in the final contracts."

Do you see that?

A. Yes.

Q. Do you recall entering into a contract with PharmaNet with respect to MD-18 study report?

A. No, I actually don't recall that.

Q. Do you recall having any interaction with PharmaNet with regard to the study report, MD-18?

A. I know we were considering working with

PharmaNet.

Q. And what's PIA?

A. I'm not sure who they are.

Q. Do you recall who PharmaNet was?

A. They were a contract research organization.

Q. What did they do?

A. Contract research organizations do work for what I'm familiar with is pharmaceutical companies.

Q. Do you recall working with PharmaNet to help draft the study report for MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't specifically recall that.

BY MR. BAUM:

Q. If you flip through a couple of pages here, you'll come to page -- the fourth page in. It has a consultant agreement between Pharmaceutical Information Associates Limited.

Do you see that?

A. Yes.

Q. Does that refresh your recollection with regard to what PIA might be?

A. Yes, yes.

Q. So who are these guys?

A. Again, they're a -- they were a smaller consulting firm that would do work for pharmaceutical companies.

Q. Do you recall what kind of work they did?

A. I know they -- I believe they specialized in writing.

Q. Okay. So looking at this e-mail it looks like between Robert Exner and you on August 15, 2001.

Do you see that?

A. Yes.

Q. Does that appear to have been something that was produced in the ordinary course of Forest business?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Do you recall working with anybody in particular at PharmaNet?

A. No.

Q. Do you recall providing any information to PharmaNet?

A. No.
Q. Do you recall that the MD-18 study report was submitted to the FDA?
A. Yes.
Q. Do you recall approximately when?
A. I think we looked at that yesterday, 2002.
Q. Did Forest receive a six-month patent extension for Celexa for doing clinical trials on pediatric depression?
MR. ABRAHAM: Objection.
THE WITNESS: I believe so.
MR. BAUM: Let's go to the next exhibit. Mark this as Exhibit 5.
(Document marked for identification as Heydorn Deposition Exhibit No. 5.)
BY MR. BAUM:
Q. Okay. This appears to be a study report for protocol CIT-MD-18?
A. Yes.
Q. Do you see that?
A. Yes.
Q. Do you recognize it?
A. Yes.

Q. Have you seen it before?
A. Yes.
MS. KIEHN: Michael, just to clarify, is this a final copy?
MR. BAUM: I think this one is.
MS. KIEHN: It says Version 1 at the bottom, that's why I asked.
MR. BAUM: As far as I know, this is the final.
MS. KIEHN: The typeface looks weird on the front too.
MR. BAUM: Well, if it's not the final, it would be news to me.
MS. KIEHN: Okay, well, we'll just proceed with it.
MR. BAUM: It's dated April 8, 2002.
MS. KIEHN: We'll proceed with the reservation we're not sure that it's final.
MR. BAUM: Okay.
BY MR. BAUM:
Q. Well, looking at the front page of this document, do you see that the initial date is January 31, 2000.
Do you see that?

A. Yes.
Q. Is that the date that the trial started?
A. I don't know.
Q. You don't know what initiation date means?
A. Different companies have different definitions of that.
Q. Do you know what Forest's definition was?
A. No, I do not.
Q. What is a -- do you think that might be when patients first started being screened for entering the CIT-MD-18?
MR. ABRAHAM: Objection.
THE WITNESS: That would be one definition companies use for initiation date.
BY MR. BAUM:
Q. And you see the completion date is April 10, 2001?
A. Yes.
Q. And is that the date that the -- well, what date would that have been?
A. That's -- my understanding is that's generally last patient, last visit.

Q. So that would be the point when the last patient comes in, gets their last evaluation, and then that would close off collecting more data; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: More efficacy data, yes.

BY MR. BAUM:

Q. Let's go to the next page, which is the synopsis. And you see again under the "criteria for evaluation" sort of repetition what we saw in the protocol for the efficacy measures?

A. Yes.

Q. So we've got some various efficacy measures. Can you explain how the efficacy of this study drug versus placebo is demonstrated by an outcome measure?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not an expert on the design of clinical studies.

BY MR. BAUM:

Q. But given what you do know with your work on a study report like MD-18, what would be your understanding?

MR. ABRAHAM: Objection.

THE WITNESS: So my understanding would be -- can you repeat the question, sorry.

BY MR. BAUM:

Q. Yeah. Can you explain how efficacy of the study drug versus placebo is demonstrated by an outcome measure?

MR. ABRAHAM: Objection.

THE WITNESS: So my understanding is one outcome measure is selected as the primary outcome measure and a specific time point following the initiation of treatment is selected as the time point at which that primary outcome measure is evaluated in all patients in the study, and then a statistical test is applied to evaluate whether there is a statistical difference between placebo and active patients, patients on active and patients on placebo.

MS. KIEHN: Michael, could we go off the record for one second.

MR. BAUM: Yeah.

THE VIDEOGRAPHER: The time is now 11:03 a.m. We're off the record.

(Pause.)

THE VIDEOGRAPHER: The time is now 11:10 a.m. We're on the record.

BY MR. BAUM:

Q. Can you explain the difference between statistical significance and clinical significance?

MR. ABRAHAM: Objection.

THE WITNESS: Statistical significance is a test that's done. Clinical significance is an assessment by individual patients or caregivers on whether any beneficial effect that is seen from the administering the compound is of value to the patient receiving the compound.

BY MR. BAUM:

Q. So it's whether there's -- clinical significance would be whether there's any observable difference?

MR. ABRAHAM: Objection.

THE WITNESS: Any difference that's meaningful to the patient.

BY MR. BAUM:

Q. Okay. So let's -- in this exhibit, which we've marked as Exhibit 5, let's take a look at Page 69.

MS. KIEHN: And, again, for the record, this is an excerpted document so it doesn't have all of the pages.

MR. BAUM: That's correct.

BY MR. BAUM:

Q. And have you found Page 69?

A. Yes, I have.

Q. Okay. And this is Section 10, Efficacy Evaluation, and under 10.1 you'll see that in this first paragraph where it says "Table 3.1 and Panel 11 presents the results from the LOCF analysis for the change from baseline to Week 8."

Do you see that?

A. Yes.

Q. So according to this page, CDRS is positive for efficacy; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Okay. So let's just go over to the next page, which is Page 70, and you see Panel 11 there at the top?

A. Yes.

Q. And for the P-value over on the right it

says .038.

Do you see that?

A. Yes.

Q. That's a statistically significant P-value; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding.

BY MR. BAUM:

Q. It's less than .05?

A. Yes.

Q. Which would be the cutoff for statistical significance?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. If it was over .05, it wouldn't be statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding.

BY MR. BAUM:

Q. Then further down on the page, you see below Panel 12 it says Appendix Table 6.

Do you see that?

A. Yes.

Q. And Appendix Table 6 presents the results from the LOCF analysis for the change from baseline to Week 8 excluding data from 9 patients for whom the study blind was potentially compromised (see Section 5.3.4).

Did I read that correctly?

A. Yes.

Q. Did you write that sentence?

A. I don't recall.

Q. Do you know who wrote it?

A. No, I do not.

Q. So let's turn to Page 244 in this exhibit.

Did you find that?

A. Yes.

Q. And that's Appendix Table 6.

Do you see that?

A. Yes.

Q. And it's entitled "Change from Baseline in CDRS-R after 8 weeks, ITT Sub-population - LOCF."

Do you see that?

A. Yes.

Q. So the change from baseline CDRS-R after 8 weeks was the primary efficacy measure for MD-18; is

that correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So this is an evaluation of CDRS-R after 8 weeks without the nine patients involved, correct?

A. Yes.

Q. And if you look at the upper right there, it says September 12, 2001.

Do you see that?

A. Yes.

Q. Would that have been the date that this table was run?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you know what any of these dates on these tables meant?

A. I could speculate that they were the dates on which the tables were run.

Q. Is that a reasonable speculation on your part, based on your experience?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. It would be like an estimate as opposed to a guess?

MR. ABRAHAM: Objection.

THE WITNESS: Not sure what you mean.

BY MR. BAUM:

Q. That's a bad question.

Do you know who generated this table?

A. No, I do not.

Q. Do you remember if it was a biostatistician for Forest?

MR. ABRAHAM: Objection.

THE WITNESS: There was a biostatistician who worked on the project.

BY MR. BAUM:

Q. Do you recall who the primary biostatistician was?

MR. ABRAHAM: Objection.

THE WITNESS: Jin.

BY MR. BAUM:

Q. James Jin?

A. Yes, that sounds familiar.

Q. Did you work with him on this study report?

A. Yes.

Q. And what sort of interaction did you have with him?

A. So it was a iterative interaction where data would be generated for inclusion in the report and then among the people reviewing the report, writing the report, additional analyses would be requested.

Q. Did you ever request additional analyses from James Jin on MD-18?

A. No, that's not something I would do.

Q. Who would do that?

A. That would be -- well, I don't know. I could speculate that it would be Charlie Flicker and/or Ivan Gergel.

Q. Do you recall Charlie Flicker or Ivan Gergel requesting additional analyses of MD-18 tables?

A. Not specifically.

Q. Do you know that it was done?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know. I don't know that it was done.

BY MR. BAUM:

Q. You haven't seen any draft tables or anything like that?

A. No.
Q. None were shown to you?
MS. KIEHN: Objection.
THE WITNESS: Well, this table was shown to me yesterday, in very tiny print.
BY MR. BAUM:
Q. Any other vers -- in very tiny print?
A. Yes.
Q. Okay. Yes, it is tiny print.
A. No, this is much more readable, believe me.
Q. Oh, great.
Okay. So the footnote at the bottom of the page says "Report Generated by Program: /sasprog/cit/citmd18/programs/tables/apndx.6.sas."
Do you know what any of that stuff means?
A. No.
Q. I would need to talk to someone like James Jin to get that information?
MR. ABRAHAM: Objection.
THE WITNESS: I would assume so.
BY MR. BAUM:
Q. It wasn't in your wheelhouse to know

that?

MR. ABRAHAM: Objection.

THE WITNESS: No, it was not.

BY MR. BAUM:

Q. Now, there is a note just above that says, "Patients (105, 113, 114, 505, 506, 507, 509, 513, 514) with drug dispensing error are excluded."

Did I read that correctly?

A. Yes.

Q. These were the nine patients in CIT-MD-18 who were unblinded in the study; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: These are the nine patients that received the pink colored tablets is my understanding.

BY MR. BAUM:

Q. Do you think there was actual or potential unblinding with respect to those patients?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. What do you think?

MR. ABRAHAM: Objection.

THE WITNESS: There's a potential, yes.

BY MR. BAUM:

Q. Why?

A. They received different colored tablets.

Q. What would happen as a result of that?

MR. ABRAHAM: Objection.

THE WITNESS: We don't know what the patients or the -- at least I'm not aware of what the patients or the physicians, the investigators knew.

BY MR. BAUM:

Q. Would the investigators have seen the pink tablets too?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Would the investigators have known which patients received pink tablets?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. So the P-value that results from excluding these nine unblinded patients is .052.

Do you see that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I see that.

BY MR. BAUM:

Q. And that P-value is not statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding.

BY MR. BAUM:

Q. Because it's greater than .05?

A. Yes, that's my understanding.

Q. So it was negative, not in favor of Celexa's efficacy, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not a statistician, but it shows there's not a statistical difference between the two groups.

BY MR. BAUM:

Q. For the primary endpoint?

A. For the primary endpoint.

MR. ABRAHAM: Object.

BY MR. BAUM:

Q. By excluding these nine patients, the P-value went from a statistically significant .038 to a statistically insignificant .052 on the CDRS-R rating

scale after 8 weeks, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So, in other words, this P-value shows citalopram versus placebo was negative for the primary outcome measure for MD-18, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And that's the difference between MD-18 being positive or negative, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So with the dispensing error, patients excluded from MD-18 -- excuse me. Let me read that again.

So with the dispensing error patients excluded from the MD-18 primary efficacy outcome measure, Celexa failed to significantly outperform placebo in treating pediatric depression, right?

MR. ABRAHAM: Objection.

THE WITNESS: That appears to be the

case.

BY MR. BAUM:

Q. That would be an important substantial difference, wouldn't it?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. That analysis was done on the subpopulation of 166 patients, 81 in the placebo group and 85 in the citalopram group, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And the 166 patients were greater than the 160 patients needed to power MD-18, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So let's go back to Page 70 of the study report. So it says that "Appendix Table 6 presents the results from the LOCF analysis for the change from baseline to Week 8 excluding data from the 9 patients for whom the study blind was potentially compromised."

Do you see that?

A. Yes.

Q. Going back over that, do you know whether you or Charlie Flicker drafted that, now that we've looked at it again?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall.

BY MR. BAUM:

Q. Okay. It says here, "The results from Week 8 LOCF analysis comparing mean change from baseline in CDRS-R in citalopram and placebo groups was not substantially affected by the exclusion of those patients; the LSM difference decreased from 4.6 to 4.3 and the P-value increased from 0.038 to 0.052."

Did I read that correctly?

A. Yes.

Q. And going from a P-value of .038 to .052 crosses the MD-18 protocol's prespecified and industry accepted statistical significance cutoff of .050, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So it wasn't suggesting that the result was not substantially affected by exclusion of those

patients incorrect?

MR. ABRAHAM: Objection.

THE WITNESS: Potentially, yes.

BY MR. BAUM:

Q. It was, in fact, a shift from statistically significant to statistically insignificant, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And that's a substantial shift, isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Who was the target audience for the MD-18 study report?

MR. ABRAHAM: Objection.

THE WITNESS: Target audience.

BY MR. BAUM:

Q. Who was intended to receive it?

A. Well, the Food and Drug Administration.

Q. And that would have been the FDA medical reviewer and Tom Laughren deciding whether to approve

Forest's request for a pediatric major depressive order indication; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. If they accepted this characterization of the P-value shift from .038 to .052 not being substantial, they would have been misled, right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. They would have drawn an incorrect conclusion, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Just based on this potentially, but I don't know. FDA reviewers don't rely on the -- what the company has written as a thorough review. I spent two years at the FDA. There's a thorough review of the data starting with the raw data and working their way up to the conclusions of the study.

BY MR. BAUM:

Q. When you say raw data, you mean case report forms?

MR. ABRAHAM: Objection.

THE WITNESS: They can go back as far as case report forms.

BY MR. BAUM:

Q. Do you know whether the FDA had the case report forms with respect to the MD-18?

A. I do not know.

Q. Do they have the case report forms for the nine patients that received the pink tablets?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. If the FDA reviewer and Dr. Laughren echoed this language from the study report in their evaluation, would that indicate that they accepted the characterization of Forest in the study report?

MR. ABRAHAM: Objection.

THE WITNESS: I wouldn't be able to comment on what they were thinking.

BY MR. BAUM:

Q. Do you know Tom Laughren?

A. I worked with him many years ago. I doubt he would remember me.

Q. In what capacity did you work with him?

A. I started my career after my post-doctoral training as a reviewer at the neuropharmacology division of FDA, and he was the team leader for, I believe, the psychopharmacology products.

Q. What drug did you work on?

A. Primarily anti-depressants.

Q. Which anti-depressants?

A. I'm not sure I'm able to reveal that information.

Q. Was it Celexa?

A. No, I don't believe so.

Q. Why aren't you able to reveal that information?

A. I'm not sure whether the drugs I worked on at the FDA is confidential information or not.

Q. If I go to the FDA website on most drugs, I think I can get most of the medical reviewer reports, and if I do FOIAs, I can get most of those. I don't think that's confidential.

MS. KIEHN: If he's not comfortable giving the information, he's not going to give the information.

THE WITNESS: No, you might be right. I just wasn't sure, but you make a good point,

and I don't remember which drugs I worked on specifically. Again, that was 30 years ago.

BY MR. BAUM:

Q. All right. So but it wasn't citalopram?

A. I don't believe so, no.

Q. Did you ever have any interaction with Forest while you were working at the FDA?

A. Not that I recall.

Q. Okay. So let's take a look at Page 71, and -- I'm going to come back to that in a little bit.

Let's go to Page 100, and this is "Table 3.1 Primary Efficacy."

Do you see that?

A. Yes.

Q. Change from baseline in CDRS after 8 weeks.

Do you see that?

A. Yes.

Q. ITT population - LOCF.

Do you see that?

A. Yes.

Q. All right. So this Table 3.1 is also for change in baseline CDRS after 8 weeks, correct?

A. Yes.

Q. And this analysis included 174 patients, 85 patients in the placebo group and 89 patients in the citalopram group.

Do you see that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And that's a difference of eight patients from the table -- Appendix Table 6, which had 166 patients.

Do you recall that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, apparently. I didn't do the math, but I'll trust you on that.

BY MR. BAUM:

Q. Here, I'll just pull that out.

MS. KIEHN: What is that?

MR. BAUM: That's the same one. That's Table 6, Appendix Table 6.

THE WITNESS: Yeah, you're right.

BY MR. BAUM:

Q. So that's eight patient difference, not nine patient difference?

A. Yes.

Q. Do you know why there's a difference; it's one patient short?
A. No, I do not.
Q. You don't recall that being discussed?
A. No.
Q. So looking over to like the middle right section, you see the P-value is .038.
Do you see that?
A. Yes.
Q. And that's a statistically significant P-value, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. And the P-value in Table 6 show the citalopram versus placebo was not statistically significant, but Table 3.1 shows that citalopram versus placebo is statistically significant, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. And do you know why the earlier analysis -- well, first off, take a look at the date up at the top right. It says October 30th, 2001.

Do you see that?

A. Yes.

Q. And if you look at the date on Table 6, I'll just hand you this, it's quicker for you, what's the date?

A. September 12th, 2001.

Q. So this Table 6 appears to have been run earlier; is that right?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to have been run earlier, yes.

BY MR. BAUM:

Q. Do you know why the earlier run wasn't used?

MS. KIEHN: Objection.

MR. ABRAHAM: Objection.

THE WITNESS: Well, what do you mean "used"?

BY MR. BAUM:

Q. Why it was placed in the appendix and not used as Table 3.1 for the primary efficacy measure?

MR. ABRAHAM: Objection.

THE WITNESS: No, I do not.

BY MR. BAUM:

Q. Was that a judgment call you didn't make?

MR. ABRAHAM: Objection.

THE WITNESS: No, that's not a judgment call I would have made.

BY MR. BAUM:

Q. Do you know who would have made that judgment call?

MR. ABRAHAM: Objection.

THE WITNESS: I do not know.

BY MR. BAUM:

Q. Would it have been Charlie Flicker?

MR. ABRAHAM: Objection.

THE WITNESS: It may have been.

BY MR. BAUM:

Q. Ivan Gergel?

MR. ABRAHAM: Objection.

THE WITNESS: It may have been.

BY MR. BAUM:

Q. Lawrence Olanoff?

MR. ABRAHAM: Objection.

THE WITNESS: It may have been.

BY MR. BAUM:

Q. Were you involved in any discussions

with them about whether or not to use 3.1 as the -- the present 3.1 as the primary efficacy measure versus the Appendix Table 6?

MR. ABRAHAM: Objection.

THE WITNESS: I don't recall any discussions.

BY MR. BAUM:

Q. Can you think of anyone else that might have been responsible for making that decision?

MS. KIEHN: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. Those three guys that we just went through, Charlie Flicker, Ivan Gergel, Lawrence Olanoff?

MR. ABRAHAM: Objection.

THE WITNESS: I can't think of anyone else besides one of those three that would have made that decision.

BY MR. BAUM:

Q. It wouldn't have been Solomon?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Amy Rubin or Tracey Varner, they wouldn't have anything to do with that?

MR. ABRAHAM: Objection.

THE WITNESS: I wouldn't think so, but I have no direct knowledge of that.

BY MR. BAUM:

Q. But it wasn't you?

MS. KIEHN: Objection.

THE WITNESS: It was not me. I was responsible for writing the study report given the data that was generated.

BY MR. BAUM:

Q. You were responsible for its being accurate too, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. All right. So let's go to Page 44 of the study report excerpt we have here, and we have Section 5.34 blinding.

Do you see that?

A. Yes.

Q. And in that last paragraph it says, "No double-blind treatment assignment was unblinded by this

procedure before database lock."

Do you see that?

A. Yes.

Q. And then it says, because of a drug packaging error, the citalopram or placebo tablets initially dispensed to 9 patients at 3 study centers were distinguishable in color, although otherwise unblinded -- otherwise blinded (see section 7.0).

Do you see that?

A. Yes, yes.

Q. And "when this error was identified at the beginning of the study period, all study medication shipments were replaced in full with tablets of identical color to remove any potential for unblinding."

Did I read that correctly?

A. Yes.

Q. So now if we go to Section 7.0 on Page 63, which I think is the next page over on the exhibit.

A. Yeah.

Q. It says, "Changes in the Conduct of the Study and Planned Analyses."

Do you see that?

A. Yes.

Q. Okay. So what is -- do you know what that section is about?

A. Well, as the title says, it's -- well, it appears to focus on changes in the planned analysis.

Q. We mentioned earlier or you mentioned earlier that sometimes there might be variations in a protocol. Is that -- is this where those variations would be entered?

A. Right, yes, that would be my understanding.

Q. Did you draft this section?

A. I don't remember.

Q. Okay. So the last paragraph it says, Nine patients (Patients 105, 113, 114, 505, 506, 507, 509, 513, and 514) were mistakenly dispensed 1 week of medication with potentially unblinding information (tablets had an incorrect coating). Therefore, in addition to the analysis specified in Section 6.4.1 for the primary efficacy parameter, a post-hoc analysis was performed on an ITT subpopulation that excluded these 9 patients.

Do you see that?

A. Yes.

Q. That post-hoc analysis was Table 6 in

the appendix, correct?

A. Yes, I believe that was the number.

Q. Was the analysis in Table 6 actually a post-hoc analysis, or was the analysis in Table 6 actually the first analysis that was done by Forest statisticians?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. The date on the Table 6 was earlier than the date on Table 3.1, wasn't it?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. Would that suggest that it was not a post-hoc analysis at all?

MR. ABRAHAM: Objection.

THE WITNESS: I would have no way of knowing. These analyses are run -- can be run multiple times.

BY MR. BAUM:

Q. Do you know why Forest conducted the post-hoc analysis at all?

A. Because of the potential for unblinding,

they wanted to evaluate whether inclusion of those patients had any impact on the overall outcome of the study.

Q. And it did, right?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to have, yes.

BY MR. BAUM:

Q. Okay. Do you recall that the study protocol stated in Paragraph 9.7 on Page 16, "If the blind is broken for any reason, Forest Laboratories must be notified immediately. Any patient for whom the blind has been broken will immediately be discontinued from the study and no further efficacy evaluations will be performed."

Do you see that?

MS. KIEHN: Hold on.

BY MR. BAUM:

Q. Sorry, seeing that, do you recall that?

MS. KIEHN: Where is that?

MR. BAUM: That's at Page 16 I think of Exhibit --

MS. KIEHN: We don't have Page 16.

THE WITNESS: It's in the protocol.

MR. ABRAHAM: Are you referring to a

previous exhibit?

MR. BAUM: Protocol. It's Page 16.

MR. ABRAHAM: 328, Page 16.

MR. BAUM: Or 328.

MR. ABRAHAM: Two page numbers.

BY MR. BAUM:

Q. It has all sorts of page numbers on here. Of Exhibit 3. Do you have it there?

A. Yep, I've got, yep.

Q. So did I read that off correctly?

MS. KIEHN: I think you'll need to read it again.

BY MR. BAUM:

Q. Okay. So in the middle, third paragraph that's bolded, do you see that?

A. Yes.

Q. And the last sentence of that starts -- says, "If the blind is broken for any reason, Forest Laboratories must be notified immediately."

Do you see that?

A. Yes.

Q. And "Any patient for whom the blind has been broken will immediately be discontinued from the study and no further efficacy evaluations will be

performed."

Do you see that?

A. Yes.

Q. That makes sense, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, it makes sense.

BY MR. BAUM:

Q. It shouldn't include patients that have potential unblinding problems in efficacy measures, correct?

MR. ABRAHAM: Objection.

THE WITNESS: This says unblinded, not potential unblinded.

BY MR. BAUM:

Q. Shouldn't include patients who are unblinded in efficacy measures, right?

MR. ABRAHAM: Objection.

THE WITNESS: That would be my understanding, yes.

BY MR. BAUM:

Q. And if these nine patients were, in fact, unblinded or the investigators were unblinded, you should not include those patients in the efficacy measures, correct?

MR. ABRAHAM: Objection.

THE WITNESS: From what I've seen, we don't know if those patients were unblinded.

BY MR. BAUM:

Q. So -- okay. We'll come back to that.

MR. BAUM: You want to take a break.

THE VIDEOGRAPHER: The time is now 11:42 a.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is now 11:54 a.m. We're on the record.

BY MR. BAUM:

Q. So if these eight patients or nine patients were unblinded or if the investigators working with them were unblinded, the efficacy scores for those individuals should not have been included in the primary outcome measure, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah, apparently from the wording in the protocol, if they were indeed unblinded.

BY MR. BAUM:

Q. Okay. So let's go to Page 83.

MR. ABRAHAM: Of which document?

THE WITNESS: Which document? Yes.

BY MR. BAUM:

Q. All right. So let's go back to --

MS. KIEHN: Exhibit 5.

BY MR. BAUM:

Q. -- the study report.

A. Okay.

Q. And we're in Section "13.0 Discussion and Overall Conclusions."

A. Yep, yes.

Q. And under the subheading "Validity," do you see that?

A. Yes.

Q. "The study was designed to provide a valid, prospectively randomized, double-blind comparison of the treatment effects of citalopram and placebo. A medication packaging error partially compromised the study blind for 9 of the 174 patients. Post-hoc analysis excluding these patients supported the results from the intent-to-treat analysis. It is concluded that the study results are valid and interpretable."

Did I read that correctly, more or less?

A. Yes.

Q. Did you write this part of the study report?
A. I do not recall.
Q. Now, it says here "post-hoc analysis excluding these patients supported the results from the intent-to-treat analysis." That's actually untrue, isn't it?
MR. ABRAHAM: Objection.
THE WITNESS: I don't feel competent enough to answer. That's a statistical question.
BY MR. BAUM:
Q. Well, the post-hoc analysis had a P-value of .052, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Correct.
BY MR. BAUM:
Q. And it was not statistically significant, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Correct.
BY MR. BAUM:
Q. So it's being not statistically significant does not support the results of the intent

to treat analysis, does it?

MR. ABRAHAM: Objection.

THE WITNESS: The trend is still in the same direction.

BY MR. BAUM:

Q. It exceeds .050, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So it's not statistically significant?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. It's negative for the primary outcome measure, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear to be negative, yes.

BY MR. BAUM:

Q. And its being negative for the primary outcome measure does not support its being positive for the primary input, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Do you think that's why the results reported in Appendix 6 were relegated to the appendix and were not reported as the primary outcome results?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you recall any discussions about that?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. Again, the people that would have made those decisions would have been Flicker or Olanoff or Gergel?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. It would have been their responsibility to make that type of decision?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. But not yours?

MR. ABRAHAM: Objection.

THE WITNESS: No, not mine.

BY MR. BAUM:

Q. What was your responsibility with respect to something like that?

MR. ABRAHAM: Objection.

THE WITNESS: My role was to generate the study report based upon the data that was generated in the study.

BY MR. BAUM:

Q. Was it part of your job to make sure the statements in here were true?

A. Yes.

Q. Appendix Table 6's results undermine the assertions that Study 18's outcome was positive for showing Celexa significantly improved major depression disorder in children and adolescents, right?

MR. ABRAHAM: Objection.

THE WITNESS: Assuming those patients were unblinded, yes.

BY MR. BAUM:

Q. But Table 6's results undermined the assertion that citalopram outperformed placebo with respect to major depression disorder among children and

adolescents, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to, yes.

BY MR. BAUM:

Q. Would you agree that if a study was partially compromised -- it says here a medication packager partially compromised the study blind.

Would you agree that that's a significant problem?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not an expert from a statistical perspective, if that's how you're asking the question.

BY MR. BAUM:

Q. Well, from your perspective as a person responsible for truthful communications to the FDA regarding the outcome of a study, do you think that's a significant statement?

MR. ABRAHAM: Objection.

THE WITNESS: As long as all of the information was included in the study report, I would be comfortable.

BY MR. BAUM:

Q. Even if it was mischaracterized?

MR. ABRAHAM: Objection.

THE WITNESS: As I said, the agency, to be perfectly honest, probably doesn't even read this. They start with the data and work their way forward from there. At least that's how I was taught to do my reviews.

BY MR. BAUM:

Q. So it didn't matter what you said in the study report?

MR. ABRAHAM: Objection.

THE WITNESS: In many respects, it doesn't, it's the truth, if the review was done appropriately.

BY MR. BAUM:

Q. Did you review study reports when you were working at the FDA?

A. I was on the nonclinical side, so I reviewed nonclinical study reports, results from animal studies.

Q. And those would be written up kind of like this?

A. Similar, yes.

Q. Did you read them?

A. I would start with the data and the

tables, the summary tables, come to my conclusion and then read what the company wrote.

Q. Did you ever encounter blinding problems?

MR. ABRAHAM: Objection.

THE WITNESS: Well, we -- it's different in animal studies. It's impossible to unblind -- everyone knows who is getting what. It's not a blinding. We don't blind nonclinical studies. They're a lot easier to do, too.

BY MR. BAUM:

Q. Okay. Now, it says here that the conclusion of the study results are valid -- rather is the -- here it says that the study results are valid and interpretable.

Do you see that?

A. Yes.

Q. What does that mean?

A. Basically, it means what it says, that the results are valid and you're able to draw a conclusion from the study results.

Q. That's what interpretable means?

A. Yes, to me.

Q. Do you think that statement was true?
A. Yes.
Q. If the -- if internally Forest had concluded, in fact, that these patients were actually unblinded, they should have been excluded; is that correct?
MR. ABRAHAM: Objection.
THE WITNESS: That would be my interpretation from the wording in the protocol.
BY MR. BAUM:
Q. And if those patients were excluded, the conclusion regarding the citalopram outperformed placebo with respect to the primary outcome measure would have changed, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Do you know whether either Table 3.1 or Table 6 evidenced clinical significance?
A. No.
Q. You don't know; is that what you're --
A. I don't know.
Q. Do you know whether there was clinical

significance measure administered with respect to MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you know how to do it?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't.

BY MR. BAUM:

Q. Do you recall that a clinical significance metric was added to the manuscript for MD-18 that was published in the American Journal of Psychiatry?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall.

BY MR. BAUM:

Q. You don't recall the 2.9 number?

MR. ABRAHAM: Objection.

THE WITNESS: I saw that yesterday.

BY MR. BAUM:

Q. Did you have anything to do with having that number added to the manuscript?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. But you're an author of the manuscript, correct?

A. Yes.

Q. Did you have to approve that being added to the manuscript?

A. I don't recall.

Q. You reviewed it before it got sent in for publication?

A. Yes.

Q. And you reviewed it for accuracy?

A. Yes.

Q. Wouldn't you have wanted to know whether that 2.9 was accurate or not?

MR. ABRAHAM: Objection.

THE WITNESS: I must admit, I don't remember the context in which the 2.9 was discussed. I know we discussed it yesterday. It was a statistical measure, I believe, and if that's the case, I relied on the statistician to accurately present the data.

BY MR. BAUM:

Q. So independent of discussions you had with counsel yesterday, back when the manuscripts were

being prepared and the manuscripts were being submitted for publication, do you recall having discussions about clinical significance?

A. No.

Q. Whose job was that?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know whose job that was.

BY MR. BAUM:

Q. It would be important to know whether a drug actually had a clinical effect, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would say so to the individual patient, yes.

BY MR. BAUM:

Q. It's not important enough just for it to slightly outperform placebo on a scale. It needs to be something that actually makes a difference, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And you want to have something that makes a difference because there might be side effects that are negative that you have to weigh as a physician

whether you're going to prescribe it to someone, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And you're aware that there was a suicidality problem with respect to antidepressants being administered to children, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. You saw the black box warning?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Have you read it?

A. I don't know if I've ever seen the black box warning.

Q. You know that there is a black box warning regarding suicidality?

MR. ABRAHAM: Objection.

THE WITNESS: I know there is an issue with suicidality and depression in children. I don't know for a fact whether there's a black box warning in the package insert.

BY MR. BAUM:

Q. Okay. You are aware that there is a suicidality problem with respect to Celexa from the 94404 study, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That was -- it was a different population.

BY MR. BAUM:

Q. But there was an elevated rate -- an elevated number of suicidal behavior or suicidality in the patients exposed to citalopram, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's my recollection.

BY MR. BAUM:

Q. So this is all coming back to you had wanted to make sure that you had a clinical benefit to outweighing any of these potential risks, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Do you know whether or not Celexa had a small or large or trivial clinical significance?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you know whether or not someone observing children who were given citalopram or placebo would have been able to tell the difference?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you know if -- okay.

A. I'm not a child psychologist or psychiatrist.

Q. What is the -- well, do you recall whether the secondary outcome measures for MD-18 demonstrated statistical significance?

A. I recall they did not at Week 8.

Q. What is the purpose of secondary outcome measures in a clinical trial?

MR. ABRAHAM: Objection.

THE WITNESS: Again, I'm not -- I'm not an expert in the design of clinical trials, but my understanding is it's additional measures that are looked at to evaluate the overall efficacy of the compound.

BY MR. BAUM:

Q. They're kind of like cross-checks

against the main result?

MR. ABRAHAM: Objection.

THE WITNESS: I wouldn't quite put it that way.

BY MR. BAUM:

Q. Helpful information, I guess? How would you characterize it?

A. You know, it's, as I said, additional information that helps you interpret the overall efficacy of the compound.

Q. Are they important at all?

MR. ABRAHAM: Objection.

THE WITNESS: They're certainly less important than the primary efficacy endpoint.

BY MR. BAUM:

Q. Would it be important that they were all negative at Week 8?

MR. ABRAHAM: Objection.

THE WITNESS: If the primary efficacy is demonstrated at Week 8, then it's irrelevant is my understanding.

BY MR. BAUM:

Q. Okay. So but the outcome with the eight patients was negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: The P-value is .052, yes.

BY MR. BAUM:

Q. And that's more or less consistent with the secondary outcome measures, right?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. They were negative as well?

A. Yes.

Q. Do you know what the observed cases outcome was for the CDRS-R?

A. No.

Q. Do you know whether or not it was negative?

A. No, I don't know.

Q. You know that observed cases was also evaluated for MD-18, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I believe so.

BY MR. BAUM:

Q. What are observed cases?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not sure.

BY MR. BAUM:

Q. Do you know what LOCF is?
A. Yes.
Q. What is LOCF?
A. Last observation carried forward.
Q. What does that mean?
A. So if a patient drops out and you don't have a measurement at Week 8, you take whatever the last observation was and apply that to the Week 8 analysis.
Q. And observed cases is the people who actually finished the trial; does that ring a bell?
MR. ABRAHAM: Objection.
THE WITNESS: It may be, yes.
BY MR. BAUM:
Q. Do you know why studies wouldn't just use the observed cases if people actually finished? It's kind of artificial to use the last observations carried forward, isn't it?
MR. ABRAHAM: Objection.
THE WITNESS: Again, not an expert in the area, but my understanding is that you want to -- you don't want to risk excluding patients -- data from patients who maybe drop out due to adverse events or for administrative

reasons. Patients have a number of reasons why they drop out of studies.

BY MR. BAUM:

Q. If you use an LOCF, that's not actually what the patients' reports were at -- and results were at the endpoint for the study, correct?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. It's an artificially imposed set of numbers from Weeks 2 or 3 or 4, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would have to defer to a statistician.

BY MR. BAUM:

Q. Well, they are artificially imposed numbers. They're not the actual results from the patient having been administered the rating scales at Week 8, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, it's correct that the patients were not administered the rating scales at Week 8.

BY MR. BAUM:

Q. Used rating scales from earlier weeks,

right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Rating scale results, rather?

A. Yeah.

Q. Now, with respect to MD-18, secondary endpoints, you recall that per the protocol, the secondary endpoints were the CGI improvement score change from baseline and CGI severity, K-SADS, depression module, CGI score at Week 8, correct?

MR. ABRAHAM: Objection.

MS. KIEHN: If he needs to look at a document to confirm that.

THE WITNESS: Yeah, I think --

BY MR. BAUM:

Q. It's protocol, Page 2.

A. Yeah, CGI-S, CGI-I, CGAS, Kiddie schedule and the K-SADS depression module, yes, those appear to be the secondary endpoints.

Q. And in Exhibit 5, the study report, let's turn to Page 101. And this is a statistical table reflecting the secondary endpoint of CGI Improvement after 8 weeks, correct?

A. Yes.
Q. And what was the P-value there?
A. 0.257.
Q. And that's not statistically significant, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Correct.
BY MR. BAUM:
Q. So citalopram failed to outperform placebo with respect to -- significant -- let me say it again.
Citalopram failed to significantly outperform placebo on the CGI Improvement scale, correct?
MR. ABRAHAM: Objection.
THE WITNESS: That would appear to be the case.
BY MR. BAUM:
Q. So it was negative for efficacy, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Let's go to Page 102, which is, I

believe, Table 3.3 from the study report, and it's again secondary efficacy measure, change from baseline in CGI Severity after 8 weeks.

Do you see that?

A. Yes.

Q. And it has P-value of .266.

Do you see that?

A. Yes.

Q. And that's not statistically significant, is it?

MR. ABRAHAM: Objection.

THE WITNESS: No, it is not.

BY MR. BAUM:

Q. So the secondary endpoint of CGI Severity was negative for efficacy, correct?

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

Q. At Week 8, correct.

Let's go to the next table in the exhibit, and it's Table 3.4 on Page 103.

Do you see that?

A. Yes.

Q. And this is another secondary efficacy

measure, change from baseline in CGAS after 8 weeks in the intent-to-treat population - LOCF.

Do you see that?

A. Yes.

Q. And the P-value there is .309.

Do you see that?

A. Yes.

Q. And that wasn't statistically significant either, right?

MR. ABRAHAM: Objection.

THE WITNESS: No, it was not.

BY MR. BAUM:

Q. So the secondary endpoint for CGAS was negative for efficacy as well, right?

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

Q. At Week 8, right.

And going to the next one, Table 3.5 on Page 104, which is another secondary efficacy measure, change from baseline in K-SADS-P Depression Module after 8 weeks.

Do you see that?

A. Yes.

Q. And the P-value there is .105; is that correct?
A. Yes.
Q. And that's greater than .05 as well, right?
A. Correct.
Q. So that's not statistically significant either, right?
MR. ABRAHAM: Objection.
THE WITNESS: At Week 8.
BY MR. BAUM:
Q. At Week 8, correct?
A. Correct.
Q. So the secondary endpoint of K-SADS Depression Module was negative for efficacy at Week 8, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. So isn't it true that all of the prespecified secondary endpoints as listed in MD-18's protocol were negative for efficacy, right, correct?
MR. ABRAHAM: Objection.
THE WITNESS: At Week 8.

BY MR. BAUM:

Q. At Week 8, correct.

Let's go to Page 72 of the study report, under "10.5 Efficacy Conclusions."

Do you see that?

A. Yes.

Q. And it says in the second paragraph, significant differences (P less than 0.05), indicative of greater improvement in citalopram patients than placebo patients, were also observed in the CGI-I CGI-S, and CGAS.

Do you see that?

A. Yes.

Q. Now, you see above there the first paragraph it says that the primary efficacy parameter change from baseline CDRS at Week 8, citalopram produced significantly greater improvement than placebo, P value -- P equals 0.038 in the LOCF analysis.

Do you see that?

A. Where are you?

Q. In the first paragraph under Efficacy Conclusions, just above the one we were just talking about?

A. Oh, I'm sorry, yes.
Q. So you see that first sentence that says that the P value was .038?
A. Yes.
Q. And "the citalopram group exhibited significantly greater improvement than the placebo group at Week 1 and subsequent clinical visits."
Do you see that?
A. Yes.
Q. Then it shifts down to there were also significant differences in the -- greater improvement in the secondary outcome measures, right?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Then it says, statistically significant effects were not found as consistently across study time points for the secondary efficacy parameters as for the primary efficacy parameter, but numerically greater improvement in citalopram group was observed on every efficacy parameter at every clinic visit in both LOCF and OC analysis, correct?
A. Yes.
Q. So those two or three sentences there

suggests that the outcomes for the secondary outcome measures were positive as opposed to negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, we know they were positive at the earlier time points.

BY MR. BAUM:

Q. But there's no reference here that it was negative at the Week 8, which is the endpoint, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. And so this suggests, you know, that there were positive results, but, in fact, there was actually a negative result at the endpoint, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, but this should not be read in isolation, because I know this was discussed earlier in the study report.

BY MR. BAUM:

Q. Well, this is the conclusions. Shouldn't the conclusions say what happened at Week 8?

MR. ABRAHAM: Objection.

THE WITNESS: It obviously could have

been worded differently.

BY MR. BAUM:

Q. As a reviewer for the FDA, did sometimes you just looked at the conclusions to see what the outcomes were?

A. No.

Q. You wouldn't have done that, okay?

A. That's not what I would do, no.

Q. All right. So, in any case, there's no reference here in the conclusions to the Week 8 outcomes being negative for the secondary endpoints, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. And do you know who drafted this language?

A. I do not know.

Q. Do you know why the Week 8 outcomes were left out?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't know.

BY MR. BAUM:

Q. They were negative, so they didn't want

to focus on them; is that right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you recall a plan that there was discussed to have the secondary outcome measures for the earlier weeks emphasized, in the Week 8 outcomes de-emphasized?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't recall.

BY MR. BAUM:

Q. That would be improper, wouldn't it?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Do you think it's appropriate to focus on the positive and deflect attention from the negative if the negative is the week eight outcome?

MR. ABRAHAM: Objection.

THE WITNESS: These were secondary outcomes, so the emphasis on them is less.

BY MR. BAUM:

Q. So is it appropriate to exclude the actual Week 8 outcome which was negative and focus on

the prior week's positive outcomes?

MR. ABRAHAM: Objection.

THE WITNESS: As I said, it could have been worded differently.

BY MR. BAUM:

Q. And by that you mean that it -- how would you -- do you think it ought to have been worded?

MR. ABRAHAM: Objection.

THE WITNESS: The Week 8 negative outcomes on the secondary endpoints should have been mentioned in the efficacy conclusions.

BY MR. BAUM:

Q. Okay. Let's go to Page 69 and it's under Section 10.1, which is part of the efficacy evaluations again. Part way down, like the next to the last paragraph says "analyses using."

Do you see that?

A. Yes.

Q. It says, analyses using the OC, that would be observed cases?

A. Yes.

Q. Approach likewise demonstrated significantly greater improvement in the citalopram group compared to the placebo group, with significant

citalopram differences (pn0.05) observed at Weeks 1, 4 and 6, (Table 4.1B).

Do you see that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Did you write that section?

A. I don't recall.

Q. You don't recall whether the OC data was negative or positive?

A. To be honest, no, I don't. I did not recall that.

Q. Okay. So let's take a look at Page 110, Table 4.1B. It's actually Page 111, the next page down for the Week 8. You see the P-value there for Week 8?

A. Yes.

Q. And it's .167?

A. Yes.

Q. And so that's not statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would say not.

BY MR. BAUM:

Q. And so the difference at Week 8 between

Celexa and placebo for the primary endpoint using observed cases is not statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear not to be, yes.

BY MR. BAUM:

Q. So referring back to Page 69 of the study report, if you'd like, you want to take the stapler out of those.

A. No, no, I'll get them all mixed up then. I don't like the double-sided, I know, trying to save the environment. Okay.

Q. So let's go back to Page 69 on the efficacy evaluation. So that says, analysis using the OC approach likewise demonstrated significantly greater improvement in the citalopram group compared to the placebo group, and it leaves -- with significant citalopram differences .05 observed at 1, 4 and 6, weeks 1, 4 and 6, leaves out Week 8, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. At Week 8 it was negative, correct?

A. I would conclude that from reading this paragraph, yes.

Q. And so this phrase here suggesting that the OC -- the observed cases results were positive is misleading because it leaves out Week 8, right?

MR. ABRAHAM: Objection.

THE WITNESS: Well, we didn't go over the data from all of the weeks, but I'm sure if we did, we would find it was positive at Weeks 1, 4 and 6.

BY MR. BAUM:

Q. But it suggests that the Week 8 endpoint for observed cases demonstrated significantly greater improvement, when it actually didn't, right?

MR. ABRAHAM: Objection.

THE WITNESS: No, it doesn't suggest that at all.

BY MR. BAUM:

Q. Doesn't even mention Week 8, right?

A. Correct.

Q. And so focusing on the positive 1, 4 and 6 weeks and not mentioning the negative Week 8 was a material omission; don't you think?

MR. ABRAHAM: Objection.

THE WITNESS: In this case, no. I think a competent reviewer would read this paragraph and would say it was positive at Weeks 1, 4 and 6 and, therefore, was not positive at Weeks 2 and 8.

BY MR. BAUM:

Q. But isn't Week 8 the important week?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. It's the endpoint, right?

A. Yes, it's the endpoint.

Q. And that's where you determine whether it's positive or negative for the trial, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, but this was the observed cases analysis, not the LOCF.

BY MR. BAUM:

Q. Yeah, but the Week 8 is the endpoint, correct?

A. I have no problem with the way this paragraph is worded, I'll be perfectly honest. I've been honest all along.

Q. Well, I appreciate that.

Why do you think that that's correct to

omit the Week 8 negative results in this section?

MR. ABRAHAM: Objection.

THE WITNESS: It's implied here.

BY MR. BAUM:

Q. Okay.

A. I mean, it's obvious to me.

Q. Okay. All right. So let's go to Page 84. This is the overall conclusion.

Do you see that?

A. Yes.

Q. The results of this study support the conclusion that citalopram 2-4 -- oh, that's probably 20 to 40 milligrams a day?

A. Yeah.

Q. Is safe and efficacious in the treatment of major depressive disorder in children and adolescents.

Did I read that correctly?

A. Yes, you did.

Q. Is that actually true?

MR. ABRAHAM: Objection.

THE WITNESS: Certainly, in the primary endpoint.

BY MR. BAUM:

Q. So that would be a result, correct?
A. Well, that was the prespecified primary endpoint, the whatever --
Q. Including -- if you included the --
A. The nine patients.
Q. The nine patients, right?
A. Correct.
Q. So that's the only positive endpoint amongst any of the endpoints measuring efficacy in MD-18, correct?
MR. ABRAHAM: Objection.
THE WITNESS: It was the primary endpoint.
BY MR. BAUM:
Q. It was the only one? If you took out the eight patients, it was negative, correct?
A. The P-value was greater than .5, yes.
MR. ABRAHAM: Objection.
BY MR. BAUM:
Q. And so that was negative, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. And all four of the secondary endpoints

were negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

Q. At Week 8, right.

And observed cases was negative at Week 8, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So five, six of the results were negative, and one was positive, correct?

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

Q. And here it says the results of this study support the conclusion -- there's only one result that was positive, and it was the Table 3.1 that included the eight unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, at Week 8, yes.

BY MR. BAUM:

Q. So I guess, in other words, whether one used Table 3.1 with the unblinded patients in or Table

6 with them out made a difference in the outcome of the MD-18s being negative or positive, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to, yes.

BY MR. BAUM:

Q. And even with those patients included, all four of the secondary outcome measures were negative at Week 8, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And with them included, with those eight patients included, the observed cases at Week 8 had a nonsignificant P-value as well, correct, so it was negative?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And Lundbeck's 94404 study was negative for efficacy as well, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So do you think it's accurate to say,

overall, the results of study MD-18 support the conclusion that Celexa is efficacious in the treatment of the major depressive disorder in children and adolescents?

A. The study met its primary endpoint.

Q. Overall?

MR. ABRAHAM: Objection.

THE WITNESS: There was positive effects at earlier weeks on multiple secondary endpoints, the observed cases were positive at earlier weeks.

BY MR. BAUM:

Q. Multiple endpoints? There was only one endpoint that was positive, right?

MR. ABRAHAM: Objection.

THE WITNESS: I'm sorry. Let me rephrase.

On the secondary outcome measures.

BY MR. BAUM:

Q. At Weeks 1, 4, 6?

A. Yes, yeah.

Q. And Weeks 1, 4, 6 are not the endpoint, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Those are secondary endpoints, those are secondary measures.

BY MR. BAUM:

Q. They're secondary measures, but they're not endpoints, are they?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. The endpoint was Week 8?

A. Yes.

Q. And determining whether or not a trial is positive or negative occurs at the endpoint, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's my understanding.

BY MR. BAUM:

Q. And there was only one measure that was positive at Week 8, and the rest were all negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, the primary outcome measure was positive at Week 8.

BY MR. BAUM:

Q. So is it accurate to say, overall, the

results were positive when, you know, most of them were negative?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Do I have to answer?

MR. ABRAHAM: You can answer.

THE WITNESS: Can you repeat it?

BY MR. BAUM:

Q. Is it accurate to say that, overall, the results were positive, when most of them were actually negative?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Across all of the time points, there was multiple positive indications of efficacy with the compound.

BY MR. BAUM:

Q. But not overall, what's overall mean?

MR. ABRAHAM: Objection.

THE WITNESS: Multiple measures were taken at multiple time points. The secondary measures were positive at Weeks 1, 2, 4 and 6.

BY MR. BAUM:

Q. Would you -- if you were responsible for

drafting this all by yourself, would you change the way that was worded?

MR. ABRAHAM: Objection.

THE WITNESS: Potentially, yes.

MR. BAUM: Okay. So let's move on to the next exhibit.

(Document marked for identification as Heydorn Deposition Exhibit No. 6.)

BY MR. BAUM:

Q. Six, and this is MDL-FORP0175697, an e-mail from Paul Tiseo to Joan Barton dated March 2nd, 2000, Re: CIT-18, and this is what we were discussing earlier today.

You've seen this before, correct?

A. I saw it yesterday for the first time.

Q. Oh, you had never seen it before?

A. No.

Q. Do you see in the CC line the name Tracey Varner?

A. Yes.

Q. Do you recall her position at Forest?

A. I believe she was in regulatory affairs.

Q. What does that mean?

A. Regulatory affairs is the group that's

responsible for interactions with the regulatory authorities.

Q. They're responsible for making sure that there's accurate and truthful communications between the company and the FDA?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I would say so.

BY MR. BAUM:

Q. So this -- did you see e-mails and correspondence like this while you were working at Forest regarding like interactions between staff regarding correspondence to investigators in the conduct of trials?

MR. ABRAHAM: Objection.

THE WITNESS: I'm sure I saw some, but it was not the primary focus of my job so -- but I'm sure I saw some.

BY MR. BAUM:

Q. So you never saw this in your preparation of the study report?

A. I don't recall seeing this, no.

Q. Okay. So the e-mail says, "Dear all, for your information, a copy of the fax that went out to all CIT-MD-18 Pediatric Investigational sites this

morning is attached. All sites have also been contacted by telephone and given verbal instructions on how to proceed with both drug shipment, as well as their patients who have been screened and/or randomized.

I would also like to that everyone involved in this process for their input and their assistance in rectifying this situation in such a timely manner."

Did I read that right?

A. Yes.

Q. So this is March 2nd, 2000, right?

A. Yes.

Q. And that's before the trial concluded, correct?

A. I believe so.

Q. Do you want to look at the study report? Look at the start dates.

A. Okay, started January 31st and completed April 10th, this is March 2000, yes, so it's --

Q. So it's a couple months into the initiation date, following the initiation?

A. Just over a month, yeah.

Q. So let's -- Dr. Tiseo says, this went

out to all the CIT-MD-18 investigational sites, correct?

A. Yes.

Q. Do you know who would have received the fax at the sites?

A. I have no idea.

Q. Okay. So let's go to the next page, which says transmission -- a fax transmission cover sheet.

Do you see that?

A. Yes.

Q. And it's dated March 2nd, 2000?

A. Yes.

Q. And it says "Urgent Message," do you see that, and it's in bold, large with asterisks around it?

A. Yes.

Q. So that was an important message, correct?

A. I would say so.

Q. It says, "It has come to our attention that an error was made during the packaging of the clinical supplies for the above-noted study," which is CIT-MD-18, right?

A. Yes.

Q. A number of bottles of active medication were mistakenly packed with the pink-colored commercial Celexa tablets instead of the standard white citalopram tablets used for blinded clinical trials -- clinical studies.

Do you see that?

A. Yes.

Q. So that's saying they were actually given the active medication, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. It says, a number of bottles of active medication were mistakenly packed with the pink-colored commercial Celexa tablets, correct?

A. Yes, it does say that.

Q. So the pink tablets weren't placebo, they were active medication?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. They were Celexa?

A. I don't know. I guess that's one interpretation of this, yes.

Q. Was there any other interpretation you

can make from the language a number of bottles of active medication were mistakenly packed with the pink-colored commercial Celexa tablets?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Pink-colored Celexa -- pink-colored commercial Celexa tablets active medication means they were given Celexa, right?

MR. ABRAHAM: Objection.

THE WITNESS: It appears from this, yes.

BY MR. BAUM:

Q. So it goes on and says, "as a result, dispensing these tablets would automatically unblind the study."

Do you see that?

A. Yes.

Q. So that says it was dispensing those tablets would automatically unblind the study?

A. Yes, it says that.

Q. That's pretty clear, isn't it? Didn't say potentially unblind, does it?

MR. ABRAHAM: Objection.

THE WITNESS: It says would automatically unblind the study.

BY MR. BAUM:

Q. So with respect to the nine patients who received the pink tablets, the study was unblinded with respect to them automatically, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Can we talk?

BY MR. BAUM:

Q. No, you can't.

A. Okay. Can you repeat the question.

MR. BAUM: Can you read it back.

(The court reporter read back the record as requested.)

THE WITNESS: This is inconsistent with what is in the data tables.

BY MR. BAUM:

Q. Okay. So that's -- I like your saying that, I think that's true, that's not exactly an answer to my question.

Can you answer my question?

THE WITNESS: Can you repeat the question one more time.

(The court reporter read back the record as requested.)

THE WITNESS: I guess yes.

BY MR. BAUM:

Q. So then it says, "This medication needs to be replaced with the appropriate white tablets immediately to maintain the study blind."

Did I read that correctly?

A. Yes.

Q. Do you agree with this memo's statement that it was important to replace these tablets immediately?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Now, at this point the investigators have been advised that the tablets that were pink that they received were active medication, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So they would know which patients were actually assigned active medication, wouldn't they?

MR. ABRAHAM: Objection.

THE WITNESS: If they were unblinded, yes.

BY MR. BAUM:

Q. Well, if they received the pink tablets and they're being told just now that they were active medication, those patients were being given active medication, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I would assume so, yeah.

BY MR. BAUM:

Q. And the investigators would know that?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. They would know which patients received them, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would have no direct knowledge, but I would assume so.

BY MR. BAUM:

Q. So they were unblinded as well, correct?

MR. ABRAHAM: Objection.

THE WITNESS: With respect to those patients, I would assume so.

BY MR. BAUM:

Q. So those patients should have been counted in the efficacy measures, should they?

MR. ABRAHAM: Objection.

THE WITNESS: I defer to the statistician on that.

BY MR. BAUM:

Q. What do you think?

MR. ABRAHAM: Objection.

THE WITNESS: You can make arguments either way on this one. As I said, this appears to be inconsistent with the data tables that suggest there were pink placebo tablets that were also out there.

BY MR. BAUM:

Q. So you think there might have been pink placebo tablets?

A. Based on the data tables you showed me, there were four patients in each of the active and placebo group that were excluded in the reanalysis.

Q. So here it says that they received active medication packed with pink-colored commercial Celexa tablets instead of the standard white citalopram tablets?

A. Yes.

Q. Do you think they made pink placebo tablets?

A. I don't know.
Q. It doesn't say that here, does it?
MR. ABRAHAM: Objection.
THE WITNESS: No, it doesn't say that here.
BY MR. BAUM:
Q. Okay. Do you know who Paul Tiseo was, right?
A. Yes.
Q. Do you think he would have known more about this than you?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, far more.
BY MR. BAUM:
Q. And he's saying right here that they were conveyed active medication, pink-colored commercial Celexa tablets, instead of the standard white citalopram tablets used for blinded clinical trials, that says that there was active medication, commercial Celexa administered, correct?
MR. ABRAHAM: Objection.
THE WITNESS: That's what it says, yes.
BY MR. BAUM:
Q. So if it turned out that some of these

patients were randomized to placebo, they would have been placebo patients given active medication, right?

MR. ABRAHAM: Objection.

THE WITNESS: I have no way of knowing that.

BY MR. BAUM:

Q. It kind of messes up with the protocol of the trials, so it's better just not to count them, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would defer to a statistician on that.

BY MR. BAUM:

Q. Well, what do you think?

MR. ABRAHAM: Objection.

THE WITNESS: There are concerns about these nine patients, yes.

BY MR. BAUM:

Q. And they shouldn't have been counted, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I think you can make arguments both ways.

BY MR. BAUM:

Q. What do you think?

MR. ABRAHAM: Objection.

THE WITNESS: The analysis was done both with and without those patients.

BY MR. BAUM:

Q. Okay. And the one without those patients -- well, let's go to the next paragraph down.

"For those sites that have already randomized patients, please be advised that this error in packaging does not affect the safety of your patients in any way."

Do you see that?

A. Yes.

Q. And then "The medication used in both the white and the pink tablets is exactly the same. Only the color of the tablets is different," correct?

A. Correct.

Q. So it's essentially advising them that even though they were pink tablets, it was safe because they were the same old Celexa that's used on -- only the color of the tablets is different, correct?

MR. ABRAHAM: Objection.

THE WITNESS: The first concern with any medication error during a clinical trial is

patient safety.

BY MR. BAUM:

Q. And so they were saying, you know, they weren't given a poison, they were given Celexa, so don't worry about it; is that essentially what it's saying?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah, essentially what it's saying is they were given an FDA approved medication.

BY MR. BAUM:

Q. Okay. Now, there was -- appears that there were bottles of pink tablets that had been assigned to patients who had not actually started taking them yet, and they want those bottles sent back, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know from this memo, I can't tell.

BY MR. BAUM:

Q. Well, they sent this to a whole bunch of sites to every single investigator, and it wasn't just the three that had the nine unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: When there's a concern about a medication error in a clinical study, all of the medication is routinely replaced.

BY MR. BAUM:

Q. Okay. Do you know how many bottles of active medication were actually sent out to the investigator sites?

A. No.

Q. Do you know how many came back?

A. No.

Q. Do you know who would know?

MR. ABRAHAM: Objection.

You can answer.

THE WITNESS: There should be a clinical supply group at Forest that would track this information.

BY MR. BAUM:

Q. Do you know who was in the clinical supply -- what did you call it again?

A. Well, companies call it different things. In our company it's called the clinical supply unit.

Q. Did you interact with anybody in the

clinical supply unit at Forest?

A. No.

Q. Do you know if Dr. Flicker or Tiseo did?

MR. ABRAHAM: Objection.

THE WITNESS: I do not know.

BY MR. BAUM:

Q. When the investigators sent back the bottles of pink pills, weren't they aware at that point that specific patients of theirs received active medication, Celexa?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what the investigators knew.

BY MR. BAUM:

Q. Well, they would know they had bottles assigned to patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: They had bottles assigned to patients -- I'm not sure I follow.

BY MR. BAUM:

Q. They had bottles of tablets that had been assigned to their particular patients and then they had to return some that were pink, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, as patients come into a trial, they get assigned to a specific -- they get a patient number and they get assigned to a specific treatment group, so the ones that had the nine patients had already been assigned to a treatment group.

BY MR. BAUM:

Q. Well, with respect to those nine patients, the investigators returning those pink pills that weren't used with them would have known then that their patients were receiving pink pills, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what the investigators knew.

BY MR. BAUM:

Q. Well, they knew what was in this memo, correct, because they were all sent it, right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know who read this memo at the sites.

BY MR. BAUM:

Q. It says, this fax went out to all CIT-MD-18 Pediatric Investigational sites.

Do you see that?

A. Yes.
Q. So you know it went out to those investigational sites, correct?
A. It went out --
MR. ABRAHAM: Objection.
BY MR. BAUM:
Q. You just don't know who read it?
A. Based on this e-mail, it says it went out to the investigational sites. I have no idea who at the site read the memo.
Q. So if the investigators who were administering the pills and the CDRS rating scale with these patients, if they had seen the pink tablets, they would have been exposed to knowing that those patients were receiving Celexa while they were conducting the investigation, correct?
MR. ABRAHAM: Objection.
THE WITNESS: There's a number of assumptions built into that question.
BY MR. BAUM:
Q. Okay. But answer it anyway.
MR. ABRAHAM: Objection.
THE WITNESS: If the investigators knew about the pink tablets, which is not a given,

the investigators are oftentimes removed from the actual day-to-day administration of the trial. Study coordinators are the ones that interact with the patients. The pharmacy is the group, of course, that handles the medication.

So I have no idea of whether the investigators even knew this was an issue. This could have been handled -- I'm speculating now, but this is real clinical research, these investigators oftentimes rely on their study coordinators and nurses to handle the day-to-day operations of the clinical trial.

So I do not know what the investigators knew. They may not have even seen this fax.

BY MR. BAUM:

Q. Who would have seen it?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

MS. KIEHN: Michael, it's almost 1:00, whenever you think it's appropriate to break for lunch.

MR. BAUM: It's 1:00 already?

MS. KIEHN: Almost.

MR. BAUM: Time flies when you're having fun.

I've probably got another 20 questions or so related to this document before we move on to the next one.

MS. KIEHN: Is that okay, Mr. Heydorn?

THE WITNESS: Yes, that's okay, yeah.

MR. BAUM: If you want to go through and finish off like my addressing this particular document, then go do lunch, does that sound good?

THE WITNESS: Yep, that would be fine, yeah.

THE VIDEOGRAPHER: I've only got about 15 minutes left on this disk.

MR. BAUM: That's probably about -- sounds about right.

BY MR. BAUM:

Q. When we looked at that Table Appendix 6 and you saw there were 166 patients?

A. Correct.

Q. 85 and 81, do you remember that?

A. Yep.

Q. So that was enough patients to power the

study without the unblinded patients having been included, correct?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And based on the date of this memo, March 2nd, 2000, is it fair to assume that the dispensing error was discovered by Forest near March 2nd, 2000?

MR. ABRAHAM: Objection.

THE WITNESS: I don't have any firsthand knowledge of that, but that would be a reasonable assumption.

BY MR. BAUM:

Q. Forest wouldn't have delayed notifying the investigators of the dispensing error?

A. No.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. And you don't know how Forest found out about the dispensing error?

A. No, I do not.

Q. I suppose it was investigators told

Forest about some pink tablets that were being administered?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. If you look back at the study report at Page 63, that's the Section "7.0 Changes in the Conduct of the Study and Plan Analysis."

Do you see that?

A. Yes.

Q. We went over that a little earlier. It says -- it lists patients 105, 113, 114, 505, 506, 507, 509, 513 and 514 as the patients who were mistakenly dispensed one week of medication with potentially unblinding information.

Is that what it says?

A. Yes.

Q. Is it your understanding that these patients only received one week of medication with potentially unblinding information?

MR. ABRAHAM: Objection.

THE WITNESS: That's what it says here, yes.

BY MR. BAUM:

Q. If it were more than one week, that would be inaccurate, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah, it would be inaccurate, yeah.

BY MR. BAUM:

Q. So if some of these patients received two or three or four weeks of medication by March 2nd, this paragraph would be inaccurate, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah, I guess so.

BY MR. BAUM:

Q. In the study report section, let's turn to Page 1214, this is a listing, it's towards the back here.

A. What page is this?

Q. It says -- wait a second. Oh, crud, copied off the wrong page. It's Page 1215.

A. Do I have this?

MR. ABRAHAM: Yeah, it should be --

THE WITNESS: 1215, okay, yeah.

BY MR. BAUM:

Q. So this says "Listing 8 Efficacy Parameters."

Do you see that?

A. Yes.

Q. And patient 105 was one of the patients who was subject to the dispensing error.

Do you see that?

A. Yes, that sounds familiar.

Q. And there's 105 is listed here, he was at Center 2, he was on citalopram, and he was in the children age group.

You see that?

A. Correct.

Q. And his date of assessment -- so stop dealing with 105 for a second, let's move to next patient down, 113.

A. Okay.

Q. 113 was one of the patients that were dispensed the pink tablets, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I assume so. I don't remember specifically.

BY MR. BAUM:

Q. If you look at Table 6, it lists them out.

A. I know there is a list in section --

MS. KIEHN: Page 63.

THE WITNESS: Page 63. Okay, yes, 113 was one of the patients.

BY MR. BAUM:

Q. Okay. And this patient's Week 2 visit was February 23rd, 2000.

Do you see that?

A. Yes.

Q. And his Week 4 visit was March 9.

Do you see that?

A. Yes.

Q. So this patient was nearly four weeks into the study when Dr. Tiseo's memo was sent out, right?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear to be, yes.

BY MR. BAUM:

Q. So patient 13 was not dispensed just one week of medication, they had about four weeks, nearly four weeks at that point, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, it would appear to be that way.

BY MR. BAUM:

Q. Let's go to the Page 1237 of the study report, which is the next one over.

A. Okay.

Q. If you look at patient 513.

A. Okay.

Q. That's one of the patients that's listed as having been administered the pink tablets.

A. Okay.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. This is a patient that was in the citalopram group, and do you see the patient was randomized on February 9th; that's baseline.

Do you see that?

A. Yes.

Q. And his Week 1 visit was February 16.

Do you see that?

A. Yes.

Q. And the Week 2 visit was February 23rd.

Do you see that?

A. Yes.

Q. And the Week 4 visit was March 9.

Do you see that?

A. Yes.

Q. So like patient 113, patient 513 was nearly four weeks into the study when Dr. Tiseo sent the March 2nd memo out, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That appears to be the case, yes.

BY MR. BAUM:

Q. So patient 513 was dispensed more than one week of medication at the point that the unblinding was discovered, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Appears to be, yes.

BY MR. BAUM:

Q. So yet the study report says at Page 44, Section 5.3.4, "When this error was identified at the beginning of the study period, all study medication shipments were replaced in full with tablets of identical color to remove any potential for unblinding."

Do you see that?

A. Where are you now?

Q. Page 44.

A. 44 of the study report.

Q. Section 5.3.4.

A. Okay.

Q. It says, when this error was identified at the beginning of the study period, all medication shipments were replaced in full with tablets of identical color to remove any potential for unblinding, correct?

A. Yes, I see that.

Q. And that earlier statement that I read to you said that it was in first week, correct?

MS. KIEHN: Objection.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. It's Section 7.0, Page 63.

A. It does say one week of medication, yes.

Q. So that's not actually true, right, with respect to patients 113 and 513, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear not to be true, yes.

MR. BAUM: We can take a break now.

THE VIDEOGRAPHER: The time is now approximately 1:05 p.m. This is the end of Disk 2. We're off the record.

(Luncheon recess.)

THE VIDEOGRAPHER: The time is now approximately 2:19 p.m. This is the beginning of Disk Number 3. We're on the record.

(Document marked for identification as Heydorn Deposition Exhibit No. 7.)

BY MR. BAUM:

Q. So we're going to move on to the next exhibit, which is Exhibit 7, MDL-FORP0020561, and this is a letter from Forest employee Tracey Varner to Russell Katz of the FDA dated March 20th, 2000, and it's Re: IND 22,368, Serial No. 217, General Correspondence.

Have you seen this letter before?

A. I saw it yesterday for the first time.

Q. Okay. And you see it's on Forest letterhead?

A. Yes.

Q. And it's to Russell Katz.

Do you know who Russell Katz is?

A. Yes.

Q. Who is he?

A. Well, he's the director of division of neuropharmacological drug products, and I worked with

him when I was at the FDA.

Q. And we saw in the previous Exhibit Number 6, which I want you to keep handy, by the way.

A. Which one is 6?

Q. It's the -- yeah, that March 2nd one.

A. Right, the Tiseo fax, okay.

Q. Yeah, the Tiseo, yeah. That Ms. Varner was on the e-mail correspondence about the unblinding problem dated March 2nd, you see that?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah.

BY MR. BAUM:

Q. So and do you agree that Ms. Varner was in the regulatory affairs department for Forest?

A. Yes.

Q. And a letter like this going to the FDA to someone like Russell Katz from Forest would be written with the knowledge of other Forest management, right?

A. Yes.

MR. ABRAHAM: Objection.

THE WITNESS: Sorry. Yes. That would be my assumption.

BY MR. BAUM:

Q. She wouldn't do it on her own?
MR. ABRAHAM: Objection.
THE WITNESS: No, I can't imagine that to be the case.
BY MR. BAUM:
Q. This is an important communication, right?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, any communication with the FDA is an important communication.
BY MR. BAUM:
Q. And needs to be truthful?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Need to be forthright?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Up front?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. So this says, Dear Dr. Katz, we are

taking this opportunity to notify the division of clinical -- of a clinical supply packaging error for study -- let me start over again, sorry.

Dear Dr. Katz, we are taking this opportunity to notify the division of a clinical supply packaging error for study CIT-MD-18 (site #2 - Dr. Busner and site #16 - Dr. Wagner). Due to this error, medication was dispensed to eight randomized patients in a fashion that had the potential to cause patient bias.

Do you see that?

A. Yes.

Q. Did I read that correctly?

A. Yes.

Q. In the next one says -- couple paragraphs down, the third paragraph from the end starting with "for reporting."

Do you see that?

A. Yes.

Q. It says, "For reporting purposes, the primary efficacy analysis will exclude the eight potentially unblinded patients, with a secondary analysis including them also to be conducted."

Did I read that correctly?

A. Yes, you did.

Q. So according to Ms. Varner, the primary analysis is the one excluding the potentially unblinded patients, and the one including them is the secondary analysis, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And that's the scientifically correct thing to do, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would say the appropriate thing to do would be to do both analyses, which is what was apparently planned here.

BY MR. BAUM:

Q. Which one should have been primary?

MR. ABRAHAM: Objection.

THE WITNESS: Well, she's committing to the primary being done without the -- excluding the potentially unblinded patients.

BY MR. BAUM:

Q. That's what she and Forest told the FDA they were going to do, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And this is before they had actually the trial results, correct; this is before the clinical trial was concluded?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And it was consistent with the MD-18 protocols on blinding procedure too, to not include them in any efficacy analysis, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, if indeed they were unblind.

BY MR. BAUM:

Q. But Forest didn't actually do what Ms. Varner reported to the FDA here, right?

MR. ABRAHAM: Objection.

THE WITNESS: Well, they did an analysis including and excluding the patients.

BY MR. BAUM:

Q. Which one was primary?

A. In the report it was one including

blinded -- potentially unblinded patients.

Q. So in the report to the FDA, they did not do what they said they were going to do in this letter here, did they?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So just to be clear, the analysis excluding the potentially unblinded patients reported -- was reported in the study report as the primary, right?

A. Yes.

Q. And -- no, that's not right.

The study including the potentially unblinded patients was reported as primary, which is the opposite of what this letter said it would do?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Okay. Was the analysis excluding the potentially unblinded patients reported as the primary analysis as conveyed in this letter what was conveyed to the general medical community in posters presented at medical conferences?

MR. ABRAHAM: Objection.

THE WITNESS: All of the patients were included in the posters presented at medical conferences.

BY MR. BAUM:

Q. So that again was the opposite of what was done pursuant to what this letter said, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And was the analysis excluding the potentially unblinded patients reported as the primary analysis as conveyed to the general medical community in articles published in medical journals like the HAP?

MR. ABRAHAM: Objection.

THE WITNESS: Can you rephrase the question.

BY MR. BAUM:

Q. Was the analysis that was presented in the manuscript publication in the American Journal of Psychiatry based on the table that had the patients included or the patients excluded?

MR. ABRAHAM: Objection.

THE WITNESS: The table with the

patients included.

BY MR. BAUM:

Q. That's the opposite of what this letter said they were going to do to with the FDA from March 2nd, 2000, correct?

MR. ABRAHAM: Objection.

THE WITNESS: So reporting purposes here, I would assume relates to reporting to the FDA.

BY MR. BAUM:

Q. Okay. So here they said the primary efficacy analysis was going to be the analysis without the patients with the dispensing error, correct?

A. Correct.

Q. And that primary analysis with the patients excluded was not what was conveyed in the manuscript that was published in the American Journal of Psychiatry, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. And any CME presentations that the Dr. Wagner did, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't have any knowledge of what was presented in CME procedures -- or -- well, CME? Continuing medical education?

BY MR. BAUM:

Q. Yeah, continuing medical education. Didn't you help prepare some slides with Natasha Mitchner that were used in CME?

MR. ABRAHAM: Objection.

THE WITNESS: I prepared slides, but my recollection is that was for an internal advisory board meeting. I don't recall if they were used in CME presentations what I'm talking about.

BY MR. BAUM:

Q. Well, let's just refer to those slides that you do recall?

A. Yeah.

Q. In those slides, the primary efficacy presentation that you used was based on the table that had the patients with the dispensing error included, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's my recollection.

BY MR. BAUM:

Q. And the posters that were presented at ACNP, those had the primary efficacy analysis based on Table 3.1 that had the dispensing error patients excluded, correct?

MR. ABRAHAM: Objection.

MR. BAUM: Included, excuse me.

THE WITNESS: Included.

MR. BAUM: Let me start over. I need to ask that question again.

BY MR. BAUM:

Q. The ACNP posters included as its primary efficacy analysis data analyses that had included the unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And that's also inconsistent with what this letter to the FDA from Tracey Varner said, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct, but, as I said, the reporting in here I would interpret as reporting to the FDA.

BY MR. BAUM:

Q. But MD-18 Study Report, Appendix 6 was not used as a primary efficacy outcome measure for study MD-18, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's the appendix excluding the eight or nine patients, correct?

MR. BAUM: Right.

THE WITNESS: Then I would say yes.

MS. KIEHN: Can the phone people mute themselves.

BY MR. BAUM:

Q. Using Table 3.1 with the unblinded patients included made study MD-18 look positive so Celexa and Lexapro could be marketed to children, right?

MR. ABRAHAM: Objection.

THE WITNESS: There's a big jump from results from a study report to actually being able to market compounds to that population.

BY MR. BAUM:

Q. Are you aware of Study 18's manuscript and the posters being circulated to physicians and shown to physicians?

MR. ABRAHAM: Objection.

THE WITNESS: Well, I certainly know the manuscript and the poster were generated. I don't have any specific knowledge of what was done on the sales force as far as distribution of those posters and manuscripts.

BY MR. BAUM:

Q. The posters were presented at conventions?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Medical conventions?

A. Yeah, I would assume so, yes, yes.

Q. And so some physicians saw those there, didn't they?

A. Yes.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. And wasn't the purpose to convey the positive results of CIT-MD-18 to them?

MR. ABRAHAM: Objection.

THE WITNESS: Well, the purpose was to convey the results of the study, both the efficacy and the safety results.

BY MR. BAUM:

Q. And that was intended to affect sales at some point, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I really can't comment on that. I don't know.

BY MR. BAUM:

Q. They weren't doing that, these studies just for fun, were they?

MR. ABRAHAM: Objection.

THE WITNESS: The studies -- in my opinion, the studies were being done primarily to educate physicians who were already using Celexa in children, the appropriate dosing and safety procedures.

BY MR. BAUM:

Q. To let them know whether there was enough efficacy to justify prescribing it despite some possible negative side effects, correct?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. They had to be able to weigh the pros and cons?

A. Correct.

Q. And this was conveying positive things in order to outweigh the negative things to encourage prescription, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Right. It was conveying the results of the study, including the potentially unblinded patients.

BY MR. BAUM:

Q. So it gave a positive spin on the data, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, you could say that.

BY MR. BAUM:

Q. If the -- Appendix 6 had actually been used as the primary efficacy measure, would that have encouraged physicians to prescribe Celexa to children and adolescents?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know how physicians make a decision on what medications to use in their patients. I'm not a practicing child psychiatrist.

BY MR. BAUM:

Q. But it was a negative outcome, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It was not statistically significant.

BY MR. BAUM:

Q. And it was not negative, correct? I mean, it was not positive, it was negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah, yes.

BY MR. BAUM:

Q. Do you know how much money Forest made selling Celexa and Lexapro for use by kids based on the allegedly positive outcome asserted in Table 3.1?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. You know they did make money from it, though, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would assume so, yes.

BY MR. BAUM:

Q. Do you know why the primary and secondary analyses -- so let me make sure I don't get these confused.

A. Okay.

Q. So here the primary efficacy analysis will be the one with the eight potentially unblinded patients excluded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And the secondary analysis would be the one including them, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Do you know why that got reversed in the study report?

MR. ABRAHAM: Objection.

THE WITNESS: No, I do not.

BY MR. BAUM:

Q. Do you know who would have made that decision?

MR. ABRAHAM: Objection.

THE WITNESS: No, I do not.

BY MR. BAUM:

Q. Do you know whose responsibility it might have been to make that decision?

MR. ABRAHAM: Objection.

THE WITNESS: I could assume.

BY MR. BAUM:

Q. Who would you assume?

MR. ABRAHAM: Objection.

THE WITNESS: Either Dr. Flicker, Dr. Gergel or Dr. Olanoff.

BY MR. BAUM:

Q. Dr. Olanoff?

A. Olanoff.

Q. Do you know whether or not reporting the positive P-value with the patients included was part of a corporate objective of Forest management?

MR. ABRAHAM: Objection.

THE WITNESS: I do not know.

BY MR. BAUM:

Q. That was above your pay grade?

A. Yes.

(Document marked for identification as Heydorn Deposition Exhibit No. 7A.)

BY MR. BAUM:

Q. We're going to mark this as 7A. We're going to have like three or four of these that are like related to this Exhibit 7.

And so what I've handed you is

MDL-FOREM0030386; is that correct?

A. Yes.

Q. And it's from Paul Tiseo to Lawrence Olanoff, Ivan Gergel, Amy Rubin, Anjana Bose, Tracey Varner, Julie Kilbane and Charles Flicker.

Do you see that?

A. Yes.

Q. Okay. Have you seen this document before?

A. No, I don't believe so.

Q. As you can see, this is an e-mail from Tiseo to the group I just read off, and the subject of the e-mail reads "Letter to FDA for CIT-18," right?

A. Yes.

Q. And it's dated March 8, 2000, which was a few days after Dr. Tiseo sent the memorandum, in fact, to the clinical trial investigators informing them of the dispensing error?

A. Yes.

Q. So that letter was March 2nd, this is March 8, about six days later, correct?

A. Yes.

Q. So in this e-mail dated March 8, Dr. Tiseo states, "Attached please find the letter that

Charlie and I put together for the purpose of informing the FDA of our packaging mishap in the citalopram pediatric study."

Do you see that?

A. Yes.

Q. And then Dr. Tiseo was talking about Charlie Flicker, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that would be my assumption.

BY MR. BAUM:

Q. And then attached to the e-mail, if you go to the other side, is a document titled letter to FDA - draft, right?

A. Yes.

Q. And if you look through the letter, this appears to be an early draft of the letter that was ultimately sent to the FDA by Tracey Varner concerning the dispensing error that we just read in a prior exhibit, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that's what I would assume.

BY MR. BAUM:

Q. So it's another letter -- it's addressed to Dr. Katz, correct?

A. Correct.

Q. At the FDA, and it's regarding this same problem of the eight randomized patients at two investigational sites who had a dispensing error, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So we haven't seen any other earlier drafts of this e-mail?

A. No.

Q. I'm going to mark this as 7B.

(Document marked for identification as Heydorn Deposition Exhibit No. 7B.)

BY MR. BAUM:

Q. I'm handing you what has been marked as Exhibit 7B, and this is a letter to the FDA draft dated March 8, 2000, Re: clinical supplies for the Pediatric Depression Study CIT-MD-18.

You see that?

A. Yes.

Q. Have you seen that before?

A. This particular exhibit?
Q. Yeah.
A. No.
Q. Do you see that handwriting on the upper part of it?
A. Yes.
Q. Do you recognize that handwriting? Is that Charlie Flicker's handwriting?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, I recognize the handwriting.
BY MR. BAUM:
Q. Is it Charlie Flicker's?
A. Yes.
Q. Okay. So in the typed portion of the letter it says, "Dear Dr. Katz, the purpose of this letter is to inform the agency that an error was made during the packaging of the clinical supplies for the above-noted study."
Do you see that?
A. Yes.
Q. "Two of our investigational sites called in to report that some of their patients were receiving white tablets and others were receiving pink tablets."

Do you see that?

A. Yes.

Q. "These reports were passed on to Forest Clinical Packaging where it was discovered that a number of bottles of 'active' medication were mistakenly packed with the pink-colored commercial Celexa tablets instead of the standard white citalopram tablets used for blinded clinical studies."

Did I read that correctly?

A. Yes.

Q. So based on this letter, it appears the dispensing error was discovered after two clinical investigators called Forest inquiring about why some of their patients were receiving white tablets and others were receiving pink ones, right?

MR. ABRAHAM: Objection.

THE WITNESS: Well, two investigational sites.

BY MR. BAUM:

Q. Okay. Does that provide a little bit more information about how Forest found out about the dispensing error?

MR. ABRAHAM: Objection.

THE WITNESS: Yeah. I was not aware of

this, yeah, apparently a couple sites contacted Forest about this.

BY MR. BAUM:

Q. The letter also indicates that a number of bottles given to patients were mistakenly packed with pink-colored commercial Celexa tablets, right?

A. Yes.

MS. KIEHN: Where is that?

BY MR. BAUM:

Q. It says, "Two of our investigational sites called in to report that some of their patients were receiving white tablets and others were receiving pink tablets. These reports were passed on to Forest Clinical Packaging where it was discovered that a number of bottles of 'active' medication were mistakenly packed with pink-colored commercial Celexa tablets," so that's correct?

A. Yes.

Q. So they were provided pink-colored commercial Celexa tablets, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what it says here, yeah.

BY MR. BAUM:

Q. So there was a question that we had a little earlier whether they were pink placebo versus pink Celexa; is that correct? Do you remember that?

A. Yes.

Q. This says it was pink Celexa, correct?

A. This would appear to say that, yes.

Q. So anybody who got those pink tablets and consumed them received commercial Celexa at the time, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Any patient that got a pink tablet apparently got commercial Celexa tablets, yes.

BY MR. BAUM:

Q. Okay. And if an investigator sees that some patients are receiving white tablets and others are receiving pink tablets, pink-colored commercial Celexa tablets, wouldn't that, at the very least, compromise the investigator's blind?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what the investigators were thinking. There's no reason -- there's potential that they would just notice that there were two different

colored tablets and that they wouldn't know which were the active and which were the placebo.

BY MR. BAUM:

Q. Well, by the time they got the March 2nd letter, they probably knew, didn't they?

MR. ABRAHAM: Objection.

THE WITNESS: Well, obviously, I don't know what any of the investigators were thinking, but that would not be an unreasonable conclusion.

BY MR. BAUM:

Q. Okay. If an investigator knows which patients are taking branded Celexa and which ones are taking white pills, doesn't that mean the integrity of the blind was mistakenly -- unmistakenly compromised?

MR. ABRAHAM: Objection.

THE WITNESS: It does raise questions about the integrity of the blind, yes.

BY MR. BAUM:

Q. Okay. So the letter continues, "On March 2nd, all sites were notified of this error by telephone and by fax."

Do you see that?

A. Yes.

Q. And that appears to be referring to the -- you know, this other exhibit that we just were talking about, correct?

A. Yes, Dr. Tiseo's fax.

Q. Dated March 2nd.

And in the fax memorandum, Dr. Tiseo states that dispensing the pink-colored medication would automatically unblind the study.

Do you recall that?

A. Yes.

Q. Now, if you look at the bottom of this page, the last paragraph, next to last paragraph says, "As only 8 of 160 patients had been randomized at the time this error was discovered, the impact upon the integrity of the study is suggested to be minimal. In addition, these eight patients were restricted to only two investigational sites (a total of 19 sites are involved)."

Do you see that?

A. Yes.

Q. So in this draft there's no statement that Forest will exclude unblinded patients from the primary efficacy analysis, right?

A. Yes.

Q. Okay. Now, if you go up to the top here, you see the handwriting?

A. Yes.

Q. Okay. So it says "reconsider, no letter. Otherwise I recommend much less narrative, more concise."

Do you see that?

A. Yes.

Q. And then colon, due to a packing error, 8 randomized patients at 3 investigational sites had access to potentially unblinding information.

Do you see that?

A. Yes.

Q. Drug has been repackaged and a full complement after 160 additional patients will be enrolled under standard double-blind conditions. For reporting purposes, the primary efficacy analysis will exclude the potentially unblinded patients, and secondary analysis including them will be conducted. These patients will be included in all safety analyses.

Do you see that?

A. Yes.

Q. So it would appear that Dr. Flicker is

suggesting that the letter specify that the unblinded patients will be excluded from the primary efficacy analysis, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That would be a conclusion from this letter, yes.

BY MR. BAUM:

Q. Okay. So let's go back to Deposition Exhibit 7A, and if you look at the draft, do you see that the language about excluding the 8 potentially unblinded patients -- oh, wait a second.

Yes, if you look on this draft that's on the back of Exhibit 7A.

A. Yes.

Q. If you look at the second paragraph, "For reporting purposes, the primary efficacy analysis will exclude the eight potentially unblinded patients, with a secondary analysis including them also to be conducted. All patients will be included in the safety analysis."

Do you see that?

A. Yes.

Q. So that appears to be a typed-up version of what Dr. Flicker was recommending, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear to be that, yes.

BY MR. BAUM:

Q. And so on 7A, the second paragraph where it says, dear all, I mean it says, "Please review and send your comments back to me within the next few days. I will compile the corrections here and then send this final letter to NJO for final regulatory review."

A. Yes.

Q. Do you know who -- what NJO refers to?

A. The New Jersey office.

(Document marked for identification as Heydorn Deposition Exhibit No. 7C.)

BY MR. BAUM:

Q. Okay. I'm going to mark the next exhibit as 7C, and this is Bates numbered MDL-FOREM0030384, and it's from Amy Rubin to Lawrence Olanoff, Ivan Gergel, Anjana Bose, Paul Tiseo, Tracey Varner, Julie Kilbane and Charles Flicker, correct?

A. Yes.

Q. And you recognize all those names as Forest employees?

A. Yes.

Q. Forest executives?

MR. ABRAHAM: Objection.

THE WITNESS: They were not all Forest executives.

BY MR. BAUM:

Q. Who were the Forest executives?

MR. ABRAHAM: Objection.

THE WITNESS: Well, Lawrence Olanoff was the overall head of research and development.

BY MR. BAUM:

Q. Okay. Ivan Gergel?

A. Ivan Gergel was vice president of clinical research, something like that, don't know, don't remember.

Q. So he was a vice president?

A. I believe so. I am not sure.

Q. All right. So this one is dated March 9th, 2000.

Do you see that?

A. Yes.

Q. And that's the day after this other one that was sent out 7B, correct?

A. Correct.

Q. This appears to be an e-mail response to

Dr. Tiseo's e-mail from Amy Rubin, right?

A. Yes.

Q. So Dr. Tiseo was soliciting comments, and then this is Amy Rubin's response to his request for comments?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, it appears to be that way. Taking a step back, I have no idea when Exhibit 7B was sent out.

BY MR. BAUM:

Q. Okay. 7A. Sorry.

A. 7A, okay, yes.

Q. 7A requested?

A. Yes, yes.

Q. Thanks for clarifying.

A. Okay, okay.

Q. So here Ms. Rubin states, "Paul, I have taken the liberty of editing your letter as follows: Please make any other changes you feel are necessary."

Do you see that?

A. Yes.

Q. So Amy Rubin was in regulatory affairs; is that correct?

A. That's my recollection, yes.

Q. And that again was a person who was involved with sending and receiving correspondence or communicating with the FDA between Forest and the FDA, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, the regulatory affairs group is responsible for that. What each individual within the department did, I don't specifically recall.

BY MR. BAUM:

Q. But they were responsible for making sure that the information that was conveyed to the FDA was accurate, truthful, forthcoming, up front, correct?

A. Yes.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. And so as you look down, you see she appears to have like pasted in some edits, and so it starts with -- at the bottom of Page 1, it goes, "Dear Dr. Katz, we are taking this opportunity to notify the division of a clinical supply packaging error."

Do you see that?

A. Yes.

Q. Then below she appears -- and she leaves

the sites kind of blank, right; do you notice that?

A. Yes.

Q. And then it goes, due to this error, medication was dispensed to eight randomized patients in a fashion that had the potential to cause patient bias.

Do you see that?

A. Yes.

Q. Now, if you compare that sentence with the sentence that was in the first draft sent by Dr. Tiseo, which is 7A?

A. Okay.

Q. It appears Ms. Rubin changed the sentence from eight randomized patients at two investigational sites were dispensed medication that could have potentially unblinded the study, that's what the 7A says, correct, the earlier Dr. Tiseo's draft?

A. Yes.

Q. And switched that to medication was dispensed to eight randomized patients in a fashion that had the potential to cause patient bias.

Do you see that?

A. Yes.

Q. That phrase "potential to cause patient

bias" is misleading; isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: No, I don't necessarily think so. I'm not sure.

BY MR. BAUM:

Q. Well, isn't it true that the integrity of the blind was unmistakenly violated?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Well, Dr. Tiseo's March 2nd letter said it was automatically unblinded for those patients that received those tablets, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what Dr. Tiseo said, yes.

BY MR. BAUM:

Q. So by using the phrase potential to cause patient bias, Forest is not exactly being up front with the FDA, are they?

MR. ABRAHAM: Objection.

THE WITNESS: No, I wouldn't agree there. I think causing patient bias is potentially an accurate description of what

happened here.

BY MR. BAUM:

Q. Well, that's quite a bit different than saying it was automatically unblinded, right?

MR. ABRAHAM: Objection.

THE WITNESS: If you compare it to the facts, yes, that's a different statement.

BY MR. BAUM:

Q. So wouldn't a potential to cause patient bias be a euphemism for automatically unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what Amy meant when she wrote this.

BY MR. BAUM:

Q. It's quite a bit different than automatically unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know if it's quite a bit different.

BY MR. BAUM:

Q. But it's different?

A. It's different.

Q. And it's different to say unmistakenly unblinded versus potentially unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would say yes.

BY MR. BAUM:

Q. So if it was unmistakenly unblinded, that would mean that those patients should not be included in an analysis for the primary efficacy measure, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would defer to a statistician on that.

BY MR. BAUM:

Q. Well, as a person of your background in FDA review and your experience in the pharmaceutical industry, what would be the right thing to do?

MR. ABRAHAM: Objection.

THE WITNESS: Well, the analysis should be done both including and excluding those patients.

BY MR. BAUM:

Q. And the primary efficacy measure should exclude those patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I think you can make an argument either way. I think you can make the

argument either way.

BY MR. BAUM:

Q. Well, they told the FDA they were going to exclude them, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Isn't that the appropriate thing to have done?

MR. ABRAHAM: Objection.

THE WITNESS: Well, they were excluded in the analysis that was done in the -- that analysis was included in the CIT-MD-18 study report.

BY MR. BAUM:

Q. But in the study report, it wasn't part of the primary efficacy measure. They made the primary efficacy measure include them; that's different, isn't it?

A. Yes.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. And if they followed what they said and if they followed what should have been done with

unmistakenly unblinded patients, they ought not to have included them in the primary efficacy measure, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, certainly what was communicated to the FDA and what was done in the study report are not consistent.

MR. BAUM: Let's go to the next exhibit, 7D.

(Document marked for identification as Heydorn Deposition Exhibit No. 7D.)

BY MR. BAUM:

Q. And this is MDL Bates number FOREM0030359 from Charles Flicker to Amy Rubin and cc'd to Paul Tiseo. It's dated March 14, 2000.

You see that?

A. Yes.

Q. Have you seen that document before?

A. No, I have not.

Q. This is -- this looks to be Charlie Flicker's response to Rubin's edits to the FDA letter.

Do you see that?

A. Yes.

Q. All right. So in this e-mail, Dr. Flicker writes, "Although 'potential to cause bias'

is a masterful stroke of euphemism, I would be a little more upfront about the fact that the integrity of the blind was unmistakenly violated."

Do you see that?

A. Yes.

Q. So Dr. Flicker has directly involved -- was directly involved in the resolving -- let me say that again.

Dr. Flicker was directly involved in resolving the dispensing error issue, wasn't he?

MR. ABRAHAM: Objection.

THE WITNESS: What do you mean by "resolving the dispensing error"?

BY MR. BAUM:

Q. He's helping write what's going to be sent to the FDA, right?

A. Yes.

Q. And he was closer to the situation than you were, right?

A. Yes.

Q. According to Dr. Flicker, using the phrase potential to cause patient bias in the letter to the FDA is a masterful stroke of euphemism, isn't it?

A. Yes.

Q. And according Dr. Flicker, use of the phrase "potential to cause bias" is not being up front with the FDA, is it?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what he was thinking, but that's what's written here, yes.

BY MR. BAUM:

Q. And, according to Dr. Flicker, Forest should just be upfront about the fact that the integrity of the blind was unmistakenly violated, right?

A. Yes.

Q. And, ultimately, the phrase "potential to cause bias" ended up in the letter that Forest sent to the FDA; isn't that true?

A. Yes.

Q. Now, if there was unmistakenly -- if the blind was unmistakenly violated, those patients should not have been included in the primary efficacy measure, correct?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Yes.

BY MR. BAUM:

Q. You've got the Varner letter there in front of you, right?
A. Yes.
Q. That's Exhibit 7?
A. Seven, yes.
Q. Now, having seen this e-mail from Dr. Flicker and the fax from Dr. Tiseo, would you agree that the patients who were subject to the dispensing error were actually unblinded?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know for a fact, but that's the implication from these letters, yes.
BY MR. BAUM:
Q. Does it concern you that the clinical medical director at the time, Dr. Flicker, believes that the letter being sent to the FDA contains a masterful stroke of euphemism?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know what his frame of mind was when he wrote that.
BY MR. BAUM:
Q. But they had the obligation to be upfront, truthful and honest with the FDA, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And this shows that they weren't, correct?

MR. ABRAHAM: Objection.

THE WITNESS: He apparently had some concerns about this, yes.

BY MR. BAUM:

Q. Well, it was more than just concerns. He said it was unmistakenly unblinded, and they said it had the potential for bias; that's a misrepresentation, isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: It's a misrepresentation of what Charlie Flicker thought should be communicated to the FDA.

BY MR. BAUM:

Q. Did Dr. Flicker ever tell you directly that the integrity of the blind was unmistakenly violated because of the dispensing error?

A. No.

Q. In all your interactions with him while working on the study report, he never said that to you?

A. I don't recall him ever saying that to me, no.

Q. Does it bother you that Forest never told the FDA that the integrity of the blind was unmistakenly violated because of the dispensing error?

MR. ABRAHAM: Objection.

THE WITNESS: No, I think this is nuances around words, to be perfectly honest.

BY MR. BAUM:

Q. Was it Amy Rubin's job to create masterful euphemisms in letters to the FDA?

MR. ABRAHAM: Objection.

THE WITNESS: I do not know Amy Rubin's job description.

BY MR. BAUM:

Q. Well, she was in regulatory affairs, right?

A. Yes.

Q. Isn't it true that she uses the phrase potential to cause patient bias because it is her job to protect marketing and medical using masterful euphemisms?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know why she used

those terms.

MR. BAUM: I'm going to mark this as 7E.

(Document marked for identification as Heydorn Deposition Exhibit No. 7E.)

BY MR. BAUM:

Q. And this is MDL-FOREM0030382, and it's from Amy Rubin to Charlie Flicker and CC to Paul Tiseo. It's dated March 15th, 2000, "Re[3]: Letter to FDA for CIT-18."

Do you see that?

A. Yes.

Q. This appears to be Ms. Rubin's response to Dr. Flicker's e-mail to her, right?

A. Yes.

Q. And she says -- it's dated right the next day, actually, correct?

A. It's dated the 15th.

Q. I think the other was the 14th?

A. Fourteenth, okay, yes, all right.

Q. Ms. Rubin responds, "Thanks for the compliment. Part of my job is to create 'masterful' euphemisms to protect Medical and Marketing."

Do you see that?

A. Yes.

Q. In your opinion, do you think it is appropriate for Ms. Rubin to be creating masterful euphemisms to protect medical and marketing in her communications with the FDA?

MR. ABRAHAM: Objection.

THE WITNESS: No, it's not part of her job.

BY MR. BAUM:

Q. Ms. Rubin is bragging about misleading the FDA, isn't she?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what her frame of mind was when she wrote this.

MR. BAUM: Just we have -- we're going to put this version of the study report that Kristin provided to us earlier, MDL-FORP0073423 into the record as 5A.

(Document marked for identification as Heydorn Deposition Exhibit No. 5A.)

MR. BAUM: Okay. We're going to hand you what we're going to mark as Exhibit 8.

(Document marked for identification as Heydorn Deposition Exhibit No. 8.)

BY MR. BAUM:

Q. And this is MDL-FORP0168046.

Do you see that?

A. Yes.

Q. And this is an e-mail from Joan Barton to Paul Tiseo, Charles Flicker, Joan Howard, Jane Wu, Carlos Cobles, dated December 6, 2000, Re: CIT-MD-18 Study Drug.

Have you seen this document before?

A. I saw it yesterday.

Q. Who is Joan Barton?

A. I believe she was in clinical operations at Forest.

Q. What was her job?

A. I don't know specifically what her job was.

Q. She had something to do with MD-18 though?

A. Yes.

Q. Something to do with the statistics related to MD-18 and reporting?

MR. ABRAHAM: Objection.

THE WITNESS: If indeed she was in operations, she was -- she would have played a role in the overall management of the clinical

trial.

BY MR. BAUM:

Q. Okay.

A. I don't believe she was in statistics.

Q. Oh, okay. But overall management of the conduct of the trial?

A. Yes.

Q. So unblinding would be a problem that she would want to have to deal with, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know for a fact.

BY MR. BAUM:

Q. Or making sure that there were enough patients to power the study, for instance?

MR. ABRAHAM: Objection.

THE WITNESS: Ensuring enrollment, making sure appropriate supplies and study drug were available.

BY MR. BAUM:

Q. Do you know who Joan Howard is?

A. The name is familiar, but I can't recall what her exact role was.

Q. Jane Wu?

A. Again, the name is familiar. I can't

recall what her direct role was.

Q. Carlos Cobles?

A. That name is just very vaguely familiar.

Q. A statistician of some form?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Does this appear to have been a standard or a routine e-mail produced in the ordinary course of Forest business?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to be, yes.

BY MR. BAUM:

Q. Okay. So here this e-mail says, "Attached is a table showing which patients were randomized when the problem was discovered that the study drug was unblinded. A total of 6 adolescents and 3 children had already been randomized. Please let me know if this will alter the total number of children or adolescent patients to be randomized for this trial."

Did I read that correctly?

A. Yes.

Q. Ms. Barton says that the study drug was unblinded, not potentially unblinded, correct?

A. Yes.

Q. And when Ms. Barton asked if the unblinded patients will alter the total number of child or adolescent patients to be randomized for this trial, she is questioning whether unblinded patients should be excluded from the trial, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what she was exactly asking.

BY MR. BAUM:

Q. Well, she's asking if it will alter the total number of child or adolescent patients to be randomized for this trial, correct?

A. Yes.

Q. What does that mean, to alter the total number; that means that she's finding out whether we're going to count these guys or not, right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what she meant by that. I could speculate that she wanted to know whether the enrollment should be increased to compensate for the -- here it's apparently nine patients who were potentially unblinded.

BY MR. BAUM:

Q. Now, she doesn't say potentially unblinded, does she?

A. Unblinded, she said unblinded.

Q. And per the protocol, it would have been the correct procedure at that point to not include those patients for the efficacy measures, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, if they were unblinded.

BY MR. BAUM:

Q. Well,this says unblinded, correct?

A. Yes.

Q. Charlie Flicker said they were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: What did he say? He said potentially unblinded.

BY MR. BAUM:

Q. No, go back to the other -- this 7D.

A. 7D. Yeah.

Q. He says, the blind was unmistakenly violated, correct?

A. Yes.

Q. And you have Dr. Tiseo saying they were automatically unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what he put in his fax, yes.

BY MR. BAUM:

Q. So these three people were closer to this than you were, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And they said it was unblinded, correct?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Those patients were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what they're saying here, yes.

BY MR. BAUM:

Q. And per the protocol, those patients should have been excluded because they were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Now, when you helped draft the MD-18 study report, the MD-18 posters, any PowerPoints that were used for CME and the publication in the American Journal of Psychiatry on MD-18, were you aware that Forest personnel like Tiseo and Joan Barton and Charlie Flicker viewed these patients as unblinded as opposed to potentially unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: No, not to my recollection.

BY MR. BAUM:

Q. Do you think academics and physicians exposed to the poster CME and the MD-18 journal article ought to have been apprised of the unblinding issue in order to fully weigh the pros and cons of prescribing Celexa or Lexapro to kids?

MR. ABRAHAM: Objection.

THE WITNESS: Probably, yes.

BY MR. BAUM:

Q. The unblinding issue is at least a factor a physician should weigh in evaluating whether the questionable efficacy was worth the risks, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. If you turn to the attachment on the next page, you will see that there's a listing of patients there -- there's a listing of investigators rather and then it's identifying which investigators received study packaging error, right, and then how many of them had randomized patients.

Do you see that?

A. Yes.

Q. Do you recall patients 113 and 513 that we went over earlier were around three to four weeks into the study when the dispensing error was discovered?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And this list here is generated March 1, 2000.

Do you see that?

A. I see that's the date on here. I don't know when it was generated.

Q. So the site tracking -- Study Drug Packaging Error, Site Tracking - March 1, 2000.

Do you see that?

A. Right, so that was the status as of March 1, 2000 is what I would interpret.

Q. And CIT-MD-18, according to the study report we examined earlier began on January 31, 2000 and finished on April 10, 2001.

Do you recall that?

A. Yes.

Q. So Dr. Wagner knew that four patients from her site were unblinded, didn't she?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what Dr. Wagner knew.

BY MR. BAUM:

Q. Well, she's on this list, and her site received the letter from Tiseo and shows here that two adolescent patients, 513 and 514, and two children, 113 and 114, were amongst those that received the pink Celexa tablets, correct?

A. Yes.

Q. Did she know about -- do you know whether or not she knew about the five other patients from the other sites who were unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: No. I don't know if she knew about the four patients at her site. As we discussed earlier, the investigators are not necessarily involved in the day-to-day activities of the study.

BY MR. BAUM:

Q. So a letter from Paul Tiseo to each of the investigator sites with large, bolded urgent sent to each of the investigator sites would not have gone to someone like Dr. Wagner who ended up being the primary author?

MR. ABRAHAM: Objection.

THE WITNESS: I have no idea.

BY MR. BAUM:

Q. You think it's the type of thing she ought to have known about?

MR. ABRAHAM: Objection.

THE WITNESS: She should have known about it, yeah.

BY MR. BAUM:

Q. Shouldn't all of the authors of the publication for MD-18 in the American Journal of Psychiatry known about this?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And shouldn't they all have known that Tiseo, Flicker and Barton considered the patients to have been unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know if they needed to know who within the organization considered the patients unblinded.

BY MR. BAUM:

Q. Well, that some of the scientists closest to the data considered it to have been unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

MR. BAUM: Okay. Let's take a break.

THE VIDEOGRAPHER: The time is now approximately 3:17 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is now 3:41 p.m. This is the beginning of Disk Number 4. We're on the record.

(Document marked for identification as Heydorn Deposition Exhibit No. 9.)

BY MR. BAUM:

Q. Okay. I'm handing to you what's marked as Exhibit Heydorn-9, MDL-FOREM0028291, and it's an e-mail exchange involving you and Natasha Mitchner and Evelyn Kopke, Gundula LaBadie and then Charles Flicker, James Jin, Jane Wu.

And there's -- the top e-mail says it's from you to Natasha Mitchner.

Have you seen this before?

A. Since I wrote it, I assume I have.

Q. Does it appear to have been produced in the ordinary course of Forest business?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Do you recall who Natasha Mitchner was?

A. She was one of the writers at BSMG, then Prescott Communications, a medical communications firm that we worked with.

Q. In her deposition she said she was a ghost writer for the MD-18 drafts.

Would you agree with that characterization?

MR. ABRAHAM: Objection.

THE WITNESS: I don't agree with the term ghost writers. They assisted us in drafting the first draft of the manuscript.

BY MR. BAUM:

Q. But if she characterized herself as being a ghost writer, you would let her do that?

MR. ABRAHAM: Objection.

THE WITNESS: I have no way of knowing how she feels, but if that's how she feels, I wouldn't argue with her.

BY MR. BAUM:

Q. So you're sending an e-mail to Natasha Mitchner regarding notes from a conference call on October 4, 2001, it looks like.

Do you recall having a telephone conference with PharmaNet personnel and Forest personnel regarding the MD-18 study report draft around October of 2001?

A. Not specifically but --

Q. You want to look that over and refamiliarize yourself with it.

A. (Witness reviews document.)

MR. BAUM: That doesn't look like he has a complete exhibit. I have all this.

MS. KIEHN: Two pages.

MR. BAUM: I've got three. Can I see what you've got there?

THE WITNESS: Sure.

MR. BAUM: It's missing this page. All right. Sorry, I'm going to have to -- we're going to take a break. We're going to have to go get a copy of this.

THE VIDEOGRAPHER: The time is 3:44 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is 3:48 p.m. We're on the record.

BY MR. BAUM:

Q. Okay. So we're going to go back again to what we've marked as Exhibit 9. And now that you've had a chance to look this over, do you recognize it -- is your recollection refreshed as to your having drafted that?

A. Yes.

Q. Can you describe to me what this document summarizes?

A. This was a discussion among the attendees at the call on points that we were going to

make in the CIT-MD-18 study report.

Q. And the conversation was occurring between you and Charlie Flicker and James Jin, Jane Wu and then at PharmaNet Evelyn Kopke and Gundula LaBadie, right?

A. Yes.

Q. Does this refresh your recollection that maybe a first draft of the report was being written by PharmaNet?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. That's actually what you said in your prior deposition.

A. Okay.

Q. All right. So at this time, Natasha Mitchner was working for BSMG Communications, right?

A. Yes.

Q. Do you know why you were sending this e-mail to her?

A. I can't recall specifically, but I could venture a guess that it was probably in preparation for drafting the CIT-MD-18 manuscript.

Q. She did the first draft, right?

A. That's my recollection, yes.
Q. And she wrote the poster?
MR. ABRAHAM: Objection.
BY MR. BAUM:
Q. For ACNP?
A. I can't recall specifically, but that wouldn't surprise me.
Q. Okay. So you say, "Attached are my notes from the conference call with the CRO on the peds study," right? That's pediatric study?
A. Yes.
Q. And at the bottom of this page, you send this to Evelyn Kopke and Gundula LaBadie, right?
A. Yes.
Q. And then Wu and Jin, they were Forest statisticians; is that correct?
A. Certainly know Jin was, and I think Wu was also.
Q. Okay. So if you go over to the next page, you have the notes from the conference call with PharmaNet, October 4, 2001.
Do you see that?
A. Yes.
Q. And you were an attendee to that

conference call, correct?

A. Yes.

Q. And this was produced in the ordinary course of Forest business?

MR. ABRAHAM: Objection.

THE WITNESS: Yes. If my memory is correct, I was primarily there as the scribe to take notes.

BY MR. BAUM:

Q. But you wrote this, correct?

A. I believe so, yes.

Q. Do you recall how many conferences you had with PharmaNet regarding CIT-MD-18?

A. No.

Q. And then you write, "Points of note in the study report for CIT-MD-18."

Do you see that?

A. Yes.

Q. What did you mean by that?

A. This was a summary of the discussions that we had on this conference call, and I was putting together a summary of the high level points that Forest felt should be included in the CIT-MD-18 study report.

Q. Okay. So if you look, there's a

paragraph that starts note that study, you see that, was not powered?

A. Yes.

Q. And the second sentence there says, "The sample size was calculated based on the anticipated effect size for the primary efficacy variable."

Do you see that?

A. Yes.

Q. What does that mean?

A. Well, I'm not a statistician, but, in my mind, that means the number of patients to be enrolled in the study was calculated based on the anticipated effect, the response that we would get for the primary efficacy variable, that the study was powered appropriately.

Q. What's an effect size?

A. At this point I'm not sure.

Q. Would it be something related to clinical efficacy?

A. I believe so, yes.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. So the next paragraph says, the results from the CDRS-R looked strong at every visit.

Emphasize the positive effect early on; also emphasize that the positive effect was seen early on with the 20 milligram a day dose. Include only the figure from the primary endpoint; leave others as after text figures.

Do you see that?

A. Yes.

Q. What does that mean?

A. So the first sentence is pretty self-explanatory, the results look strong at every visit. Emphasizing the positive effect early on is important because antidepressants generally take several weeks before you see efficacy, and having evidence that a compound worked early on was always something that pharmaceutical companies were striving for, trying to come up with compounds that work faster than the six to eight weeks it generally takes for antidepressants to show their effects.

Include only the figure from the primary endpoint, that would be include only the figure in the main body of the text. The only figure in the main body of the text should be the primary endpoint, the others would be -- you know, the secondary endpoints would be after text figures or figures in the -- you know, one of the appendices.

Q. Okay. So this reference to the strong CDRS result was a reference to the analysis that included the patients who were unblinded in the study, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would assume so, yes.

BY MR. BAUM:

Q. And if they were excluded, it wouldn't have been a strong result, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Let's look at the next paragraph. For secondary efficacy measures, no significant difference at the Week 8 LOCF analysis. It looks like there's -- probably they are.

A. There are.

Q. There are some significant findings early on in treatment. Forest is looking at individual patient listings to see if there are any clues as to why Week 8 findings were not positive. For now, emphasize the positive findings at earlier time points for the secondary efficacy variables.

Did I read that correctly?

A. Yes.
Q. Now, the secondary endpoint efficacy variables failed at Week 8, correct?
A. Yes.
Q. And none of them were positive?
MR. ABRAHAM: Objection.
THE WITNESS: Correct.
BY MR. BAUM:
Q. But this is suggesting emphasize the positive and leave out the negative?
MR. ABRAHAM: Objection.
THE WITNESS: No. It's saying Forest is looking at patient listings to see if there are any clues as to why the Week 8 findings were not positive.
BY MR. BAUM:
Q. Then it says "emphasize the positive findings at earlier time points."
Do you see that?
A. Yes.
Q. Okay. So let's go to the next one.
"Dosing error. Some citalopram tables were not blinded."
Do you see that?

A. Right, that should be tablets.
Q. Some citalopram tablets were not blinded, right?
A. Correct.
Q. And that doesn't say potentially unblinded, right?
MR. ABRAHAM: Objection.
BY MR. BAUM:
Q. It says they were not blinded?
A. It says they were not blinded, yes.
Q. So per the protocol, they should not have been included in the efficacy measure, correct?
MR. ABRAHAM: Objection, asked and answered.
THE WITNESS: According to the protocol, patients who were unblinded should not have been included.
BY MR. BAUM:
Q. The 9 patients who received unblinded medication were included in the main analyses; a secondary post-hoc analysis of the ITT subpopulation was done. Refer to these analyses briefly in methods and results and reference the reader to the appendix table.

Did I read that correctly?

A. Yes.

Q. Now, this is different than what they told the FDA they were going to do back in March of 2000, right?

MR. ABRAHAM: Objection.

THE WITNESS: It would appear to be inconsistent, yes.

BY MR. BAUM:

Q. And you didn't know about that letter they sent to the FDA, did you?

A. No, I did not.

Q. So this paragraph here is essentially some instructions of how to deal with the unblinding problem in the study report, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know for sure, but that would be a reasonable conclusion.

BY MR. BAUM:

Q. Do you know if the instructions that were decided upon were reached prior to this telephone conference or this conference with -- this conference call with PharmaNet on October 4th?

MR. ABRAHAM: Objection.

THE WITNESS: Can you repeat that. Not sure I follow that.

BY MR. BAUM:

Q. These appear to be some instructions that were being given to PharmaNet; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: It was a summary of the discussions at the meeting at the conference call.

BY MR. BAUM:

Q. Do you recall having any meetings with Charlie Flicker or James Jin or Jane Wu in advance of this telephone conference?

A. I can't recall any, no.

Q. Do you recall having any conversations with Charlie Flicker or Lawrence Olanoff or Ivan Gergel about having PharmaNet draft this first draft to have the nine unblinded patients included in the efficacy analysis?

MR. ABRAHAM: Objection.

THE WITNESS: I don't recall any conversations about that, no.

BY MR. BAUM:

Q. Did anyone draw your attention to this

unblinding problem at this time?

MR. ABRAHAM: Objection.

THE WITNESS: I just don't remember.

BY MR. BAUM:

Q. Were you just acting as a scribe, as you said?

A. At this meeting --

MR. ABRAHAM: Objection.

THE WITNESS: -- yes, I was acting as a scribe.

BY MR. BAUM:

Q. But you were also kind of responsible for the study report being accurate as well, correct?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Yes.

BY MR. BAUM:

Q. If you had known about those -- the fax from Tiseo to the investigation sites and Joan Barton's e-mail saying that the patients were unblinded and Charlie Flicker saying they were unmistakenly unblinded, would you have done anything differently with respect to the study report?

MR. ABRAHAM: Objection, calls for

speculation.

THE WITNESS: I can't say at this point. I don't know what I would have done.

BY MR. BAUM:

Q. You don't agree with its having been including those unblinded patients in the primary efficacy measure, do you?

MR. ABRAHAM: Objection.

THE WITNESS: The study report included both analyses.

BY MR. BAUM:

Q. Yeah, but it put the analyses with the patients -- unblinded patients excluded in the appendix and it called that a secondary, and it put the primary with those patients in the Table 3.1, and that's different than what the protocol said, different from what they told the FDA they would do, correct?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Yes, it appears to be different.

BY MR. BAUM:

Q. And having worked for the FDA, you would want to have upfront truthful and accurate data

provided to you, correct?

MR. ABRAHAM: Objection.

THE WITNESS: As I've said, the review starts at the data and works it way back.

BY MR. BAUM:

Q. So that you would expect the FDA to have figured this out because they looked at the data and worked up, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And if they didn't actually look at the data, they just relied on the study report conclusions, that would explain possibly how they may have gone along with it?

MR. ABRAHAM: Objection.

THE WITNESS: I have no idea how the FDA reviewed this study report.

(Document marked for identification as Heydorn Deposition Exhibit No. 10.)

BY MR. BAUM:

Q. I'm going to mark this next exhibit as Exhibit 10, and it's a letter dated September 16, 2002, and it's MDL-FORP0016376, and it's from Tom Laughren

and -- who is a team leader, psychiatric drug products, division of neuropharmacological drug products for the FDA, correct?

A. Yes.

Q. And the subject is Recommendation for Nonapproval Action for Pediatric Supplement for Celexa, (Citalopram); negative results for Celexa in the treatment of Major Depressive Disorder (MDD) in pediatric patients.

Do you see that?

A. Yes.

Q. Have you seen this document before?

A. I saw it yesterday for the first time.

Q. Let's look at the last paragraph on the first page. It says, "Since the proposal was to use the currently approved Celexa formulations for this expanded population, there was no need for chemistry or pharmacology reviews."

Do you see that?

A. Yes.

Q. And then the next one goes, "The primary review of the clinical efficacy and safety data was done by Earl Hearst, M.D. from the clinical group."

Do you know him?

A. No, I do not.

Q. Okay. And then next it says, "Since there was agreement between the sponsor and FDA that these trials were negative, there was no need for a statistics review of the efficacy data."

Do you see that?

A. Yes.

Q. What does that mean to you?

MR. ABRAHAM: Objection.

THE WITNESS: I think it's pretty self-explanatory. There was an agreement between the sponsor and the FDA that -- I don't know what they refer to as "these trials" but...

BY MR. BAUM:

Q. 94404 and MD-18 were among those trials.

A. Okay.

MR. ABRAHAM: Objection.

MS. KIEHN: Objection.

BY MR. BAUM:

Q. And so but does it appear to you that there was no need for a statistics review of the efficacy data.

Do you see that?

A. Yes.
Q. So what does that mean to you?
MR. ABRAHAM: Objection, calls for speculation.
THE WITNESS: That the statistician at the FDA would not be looking at the efficacy data.
BY MR. BAUM:
Q. That's what we were just talking about, correct?
A. Yeah.
Q. So they didn't actually do a workup of the statistics. They essentially looked at the summary of the data, correct?
MR. ABRAHAM: Objection, calls for speculation.
THE WITNESS: I don't know what they looked at.
BY MR. BAUM:
Q. But they didn't do a statistics review of the efficacy data, correct?
MR. ABRAHAM: Objection.
THE WITNESS: That's what it says here.
BY MR. BAUM:

Q. Okay. So if you go to Page 2 here, Section "5.0 Clinical Data" and then it has an "Efficacy Data" section, and we go to -- actually, I want to go to the next page over. At the top of the page, the third page, it says, the total randomized sample was n=174, 89 citalopram, 85 placebo.

Do you see that?

A. Yes.

Q. That's 174 patients. That's eight more than the 166 that were not exposed to the pink tablets, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, that would appear to be correct.

BY MR. BAUM:

Q. And this 174 includes the eight patients who were exposed to the tablets the pink tablets, the pink Celexa, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I believe so, yes.

BY MR. BAUM:

Q. And then the efficacy results, it shows that the P-value is .038.

Do you see that?

A. Yes.

Q. And that's the P-value for the analysis, including the unblinded patients, correct?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: Yes.

BY MR. BAUM:

Q. If you go to the section just below the bold print, it starts with "thus."

Do you see that?

A. Yes.

Q. So it goes, thus, it appears that the positive results for this trial are coming from the adolescent subgroup. Note: There was a packaging error resulting in tablets being distinguishable for drug and placebo for 9 patients (although still blinded). A reanalysis without these patients yielded a P-value of 0.52 in favor of citalopram. Results also significantly favor citalopram over placebo on most secondary outcomes.

Did I read that correctly?

A. Yes.

Q. That's mostly false, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Well, at Week 8 the secondary outcomes were not in favor of citalopram.

BY MR. BAUM:

Q. Okay. So and the results without the dispensing error patients were not in favor of Celexa, were they?

MR. ABRAHAM: Objection.

THE WITNESS: Well, of course, P-value is a typo there.

BY MR. BAUM:

Q. That should be .052?

A. Right.

Q. So .052 is not statistically significant, correct?

MR. ABRAHAM: Objection.

THE WITNESS: No, it's not, but it's still in favor of citalopram.

BY MR. BAUM:

Q. How is it in favor of citalopram? It's negative -- if that were reported as the primary efficacy measure, it would have been a negative outcome, correct?

MR. ABRAHAM: Objection.

THE WITNESS: But more patients -- the scores improved in the patients on citalopram, not statistically significant, but more so than patients on placebo.

BY MR. BAUM:

Q. So it's a numerical improvement, but not a statistically significant improvement, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I think that would be one way to put it, yes.

BY MR. BAUM:

Q. And can a drug be approved with a statistically insignificant improvement?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not an expert on the overall drug approval process, but I don't believe so, no.

BY MR. BAUM:

Q. So it wouldn't have been approved for -- as an indication for adolescents or children with a P-value of .052, correct?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: That would be my guess.

BY MR. BAUM:

Q. Now, this paragraph of Dr. Laughren's essentially echoes what was in the study report language, not including -- well, essentially echoes what was in the study report, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It appears to, yes.

BY MR. BAUM:

Q. And it essentially echoes what was in the PharmaNet notes planning out what was going to be put into the study report, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It's similar.

BY MR. BAUM:

Q. Are you aware that this analysis of Study 18's results by Dr. Laughren was adopted by the reviewers for Lexapro without further analysis as providing evidence beyond Lexapro Study 32's isolated positive outcome for adolescents?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. Forest needed more than just a single positive study, and this analysis by Laughren

mistakenly echoing the misleading language from the MD-18 study report resulted in Lexapro getting an indication for adolescent depression with only one positive adolescent Lexapro trial.

Did you know that?

MR. ABRAHAM: Objection.

THE WITNESS: No, I did not.

BY MR. BAUM:

Q. That's inconsistent with FDA standards for approval of an indication, isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: There are instances where a single positive study is used for drug approval.

BY MR. BAUM:

Q. With additional evidence, though, correct, not just one by itself?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, one by itself.

BY MR. BAUM:

Q. That's not what the FDA regulations say?

A. That's not the standard, but there are cases where a single positive study is considered sufficient for approval.

Q. Okay. So we would need to ask Dr. Laughren what he did and why with respect to this analysis of MD-18 and how it was used with MD-32, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I certainly can't comment on what Dr. Laughren was thinking.

BY MR. BAUM:

Q. Do you recall discussions with Forest and GCI or Prescott referencing avoiding addressing the negative secondary outcomes in the MD-18 manuscript publication?

MR. ABRAHAM: Objection.

THE WITNESS: I know I've seen communications about that, yes.

BY MR. BAUM:

Q. You were deposed about that in 2007?

A. Okay.

Q. So I don't want to go back and redo that.

A. Okay.

Q. I just wanted to sort of refresh your recollection that there was -- because there was going to be a short or brief --

A. Brief communication.

Q. Brief communication, you wanted to avoid communicating the negative outcomes for the Week 8 results for the secondary outcomes.

Do you recall that?

MR. ABRAHAM: Objection.

THE WITNESS: If it's in my testimony. It's been a long time.

(Document marked for identification as Heydorn Deposition Exhibit No. 11.)

BY MR. BAUM:

Q. So I'm handing you what's been marked as Exhibit 11; is that right?

A. Yes.

Q. And it's a letter dated November 14, 2002 to Nancy Andreasen, editor-in-chief at the American Journal of Psychiatry.

Have you seen that before?

A. I don't recall, but I'm sure I have, since my name is on it.

Q. It has attached to it a draft of the manuscript that they want to publish, but it has, you know, you as a signatory to the letter.

Do you see that?

A. Yes.
Q. Would this have been something that was produced in the ordinary course of Forest business?
MR. ABRAHAM: Objection.
THE WITNESS: Yes.
BY MR. BAUM:
Q. Did Forest pay Prescott Medical Communications to ghost write the submission draft?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, I'm sure Forest paid Prescott Medical Communications to generate the initial draft of the manuscript.
BY MR. BAUM:
Q. Were you involved in the contract between Forest and Prescott Medical Communications to produce this manuscript of MD-18?
MR. ABRAHAM: Objection.
THE WITNESS: I don't recall. Do you mean the details of negotiating the contract, I don't recall.
BY MR. BAUM:
Q. Okay. Have you been in contact with any of your co-authors since the publication of MD-18?
A. No.

MR. BAUM: The next exhibit.

(Document marked for identification as Heydorn Deposition Exhibit No. 12.)

BY MR. BAUM:

Q. So I'm handing you the manuscript publication of -- in the American Journal of Psychiatry dated June 2004, "A Randomized, Placebo-Controlled Trial of Citalopram for the Treatment of Major Depression in Children and Adolescents."

Do you see that?

A. Yes.

Q. Have you seen this before?

A. Yes.

Q. This is your -- you were amongst the authors here, correct?

A. Yes.

Q. Why were you an author?

A. Due to the amount of work I put in on the project, I was offered a chance to be named as an author on the publication.

Q. I noticed that Charlie Flicker is not on here.

Didn't he have a lot to do with it?

A. I'm sure he did.

Q. Why isn't he an author?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know. I don't remember.

BY MR. BAUM:

Q. What about Paul Tiseo; he had a lot to do with it too, right?

A. I don't know. I know Paul left Forest a number of years before this was published.

Q. But the actual deciding of what data was in and what data was out was largely in the hands of people like Charlie Flicker or Paul Tiseo or Lawrence Olanoff; is that correct?

MR. ABRAHAM: Objection.

THE WITNESS: It would not have been in the hands of Paul Tiseo because he had left the organization. Charlie had also left the organization by then.

BY MR. BAUM:

Q. Well, by the time the study report was generated and the initial drafts of this were generated, wasn't Dr. Flicker involved?

A. Yes.

Q. And weren't the primary decisions about

what was going to be included as the primary efficacy measure or the secondary results and the decision about whether or not to include the unblinded patients in the primary efficacy measure, did that all happen back then when they were there?

MR. ABRAHAM: Objection.

THE WITNESS: I believe so, yes.

BY MR. BAUM:

Q. Do you know why Dr. Wagner was listed as the first author?

A. No, I don't. I don't remember.

Q. And so Dr. Robb and -- is it Findling, how do you pronounce that?

A. I'm not sure.

Q. Do you know either of them?

A. No.

Q. Do you know whether or not either of them knew that there were eight unblinded patients included in the primary efficacy measure?

MR. ABRAHAM: Objection.

THE WITNESS: No, I do not.

BY MR. BAUM:

Q. Do you think they ought to have known?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, they probably should have known.

BY MR. BAUM:

Q. Would that change the way this publication was written?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: Yeah, I don't know how. It may have.

BY MR. BAUM:

Q. And Jianqing Jin, that's James Jin; is that correct?

A. Yes.

Q. And Marcelo Gutierrez, who is Marcelo Gutierrez?

A. He was the pharmacokineticist on the program.

Q. So he -- what did he do, pharmacokinetics?

A. Pharmacokinetics. I assume there's plasma level data in here. I don't recall specifically.

Q. Did you write any of the drafts of the manuscripts for this publication?

A. I can't recall specifically.
Q. Do you recall editing them?
A. I can't specifically recall.
Q. Do you recall working with Natasha Mitchner on some of the initial drafts?
A. Yes, that I can recall.
Q. And do you recall working with -- what's Prescott's first name?
A. Mary.
Q. Mary Prescott, do you recall working with Mary Prescott on some of the drafts for this publication?
A. Yeah, I worked with Mary Prescott on a number of projects.
Q. But on the drafts for this MD-18?
A. I can't specifically remember.
Q. But neither Natasha Mitchner nor Mary Prescott appear as co-authors or any reference to them at all in this publication, correct?
A. Correct. It was not common at that time to recognize medical communications firms' contributions to publications.
Q. And that was in order to hide that there was some ghostwriting occurring, right?

MR. ABRAHAM: Objection.

THE WITNESS: I would not characterize it that way.

BY MR. BAUM:

Q. So let's go to Page 1080 and if you look at the -- wait a second -- it's the Results section starting at 1080, and I want to sort of direct your attention to Figure 1 on Page 1081, the next page over.

A. Yes.

Q. And it has -- if you look at the subjects receiving placebo, it's 85.

Do you see that?

A. Yes.

Q. And subjects receiving citalopram is 89?

A. Yes.

Q. And that adds up to 174?

A. Yes.

Q. That included the unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It includes the potentially unblinded patients, yes.

BY MR. BAUM:

Q. Were they potentially unblinded, or were

they unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Well, what did Paul Tiseo say?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: He wrote that they were unblinded.

BY MR. BAUM:

Q. And Charlie Flicker?

MR. ABRAHAM: Objection.

THE WITNESS: He wrote that they were unblinded.

BY MR. BAUM:

Q. And Joan Barton?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And then in your notes from the PharmaNet meeting on October 4, 2001, didn't you report that they were unblinded?

MS. KIEHN: Objection.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Record that they were unblinded?

MS. KIEHN: No, objection, his report refers to tablets, not patients.

MR. BAUM: Go ahead. And I'd like you not to coach the witness.

THE WITNESS: It says some citalopram tablets were not blinded.

BY MR. BAUM:

Q. All right. So were these patients unblinded or potentially unblinded?

MR. ABRAHAM: Objection, asked and answered.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. The people closest to it thought they were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: You should perhaps depose them.

BY MR. BAUM:

Q. Well, based on the correspondence I've shown you today, those people said it was unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Now, this table on Page 1081 says that citalopram achieved statistically significant improvement over placebo amongst this group of subjects of children and adolescents, correct, on the CDRS rating scale?

A. You mean the figure?

Q. Yes.

A. Yes.

Q. That is only achieved with the unblinded patients included, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And if the unblinded patients were excluded, it would not show a statistically significant difference, correct?

MR. ABRAHAM: Objection.

THE WITNESS: No, it would not.

BY MR. BAUM:

Q. If you turn to -- back to the abstract on Page 1079, it says that there -- if you look on the

Results section, it says effect size, 2.9.

Do you see that?

A. Yes.

Q. Does that refresh your recollection that there is an effect size that was added to this manuscript -- or included in this manuscript, sorry?

A. It's clearly included in the manuscript.

Q. Did you have anything to do with its inclusion?

A. No.

Q. Do you know what it means?

A. No.

Q. Do you know whether or not it's a correct figure?

A. No.

Q. All right. Is there anyplace in this article where it references the unblinding issue?

MR. ABRAHAM: Objection.

THE WITNESS: I have not read the article recently, but I would guess probably not.

BY MR. BAUM:

Q. Why is that?

A. I don't know.

Q. So shouldn't the prescribing physicians who would be reading this article and academics who might be reading this article have a right to know there was an unblinding problem with CIT-MD-18?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Let's go back to Page 1081. On the right-hand side on the next to last paragraph there's -- it starts with "citalopram treatment."

Do you see that?

A. Yes.

Q. The last sentence says, "For the CGI severity rating, baseline values were 4.4 for the citalopram group and 4.3 for the placebo group, and endpoint values (last observation carried forward) were 3.1 for the citalopram group and 3.3 for the placebo group."

Do you see that?

A. Yes.

Q. Does it say anything about those not being statistically significant at Week 8?

A. It's not addressed either way.

Q. But at Week 8 those were negative,

correct?

MR. ABRAHAM: Objection.

THE WITNESS: I believe so, yes.

BY MR. BAUM:

Q. So instead of reporting the statistical significance at Week 8, it reported the numerically higher results without referencing the results that were not statistically significant, right?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So this language here suggests that the secondary outcome measures outperform placebo, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Not adding the statistical significance would suggest that they were not statistically significant to someone who knew -- knows the area.

BY MR. BAUM:

Q. But to physicians who are reading this, does this clearly indicate that the secondary outcome measures did not significantly outperform placebo?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. It does?

A. Yes, to me it does.

Q. To a physician?

A. I don't know what physicians think.

Q. Okay.

A. But the lack of a clear statement about statistical difference would suggest there is not a statistically significant difference.

Q. It would be more clear if they had stated there was a numerical --

A. Things can always be stated more clearly. It's very clear to me.

Q. Okay. Let's go to 1082 in the Discussion section. It says, "This randomized, placebo-controlled, double-blind trial provides evidence that citalopram produces a statistically and clinically significant reduction in depressive symptoms in children and adolescents."

Do you see that?

A. Yes.

Q. That's not actually true if you exclude the unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.
BY MR. BAUM:
Q. You agree with me; is that correct?
A. Yes.
Q. That's not a true statement if you exclude the unblinded patients?
MR. ABRAHAM: Objection.
THE WITNESS: It's not statistically significant.
BY MR. BAUM:
Q. Do you know who wrote that statement?
A. No, I don't.
Q. Is there any reference in this publication to the FDA's having rejected Forest's request for a pediatric MDD indication for Celexa?
A. No.
Q. Isn't that an important piece of information for physicians to weigh when deciding when to prescribe Celexa to a child?
MR. ABRAHAM: Objection.
THE WITNESS: Physicians should be aware of what's in the package insert. That's what's approved by the FDA.
BY MR. BAUM:

Q. Isn't this publication intended to provide information to help physicians decide whether to prescribe Celexa to children?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And should it include all of the pros and cons of doing that so that they're making an informed decision?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And do you think it's important in weighing the pros and cons to know that the FDA rejected Forest's request for an MDD indication for Celexa?

A. That's not the kind of information that routinely appears in publications, and physicians have access to the package insert that includes the approved indications for every compound.

Q. Do you think it would have been important for physicians to know that Forest had agreed that Celexa -- the studies 94404 and MD-18 were negative --

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. -- in their presentation to Dr. Laughren?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: Can you repeat the question.

BY MR. BAUM:

Q. Do you remember the letter that went to Dr. Laughren?

A. Right.

Q. You want to flip back to that. If you look on the first page, bottom paragraph, it says that the sponsor agreed that the studies were negative?

MS. KIEHN: Objection. Misquotes the document.

THE WITNESS: Since there was an agreement between the sponsor and FDA that these trials were negative.

BY MR. BAUM:

Q. Right.

A. Yes.

Q. Do you think that would be an important

piece of information for physicians to know before prescribing Celexa to children?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: If the information is not in the package insert, it suggests it shows it's not approved by the agency for use in that population.

BY MR. BAUM:

Q. Well, that's a little bit different than actually conceding and concluding and telling the FDA that they were negative, isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: I'm not sure I follow.

BY MR. BAUM:

Q. All right. Well, there's no reference to 94404 in this -- in this publication, correct?

A. Correct.

Q. And there's no reference to the FDA and the sponsor agreeing that 94404 and MD-18 were negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It's not information that goes into a publication.

BY MR. BAUM:

Q. I'm just saying it's not here, is it?

A. It is not there, no.

Q. Okay. And there's no reference in here that when the unblinded patients were excluded, it was not a statistically significant outcome on the primary efficacy measure, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. And the observed cases, Week 8 outcome being negative is not in here either, right?

MR. ABRAHAM: Objection.

THE WITNESS: One generally doesn't include all secondary outcomes in a publication.

BY MR. BAUM:

Q. But there was plenty of space in this brief to discuss the positive -- numerically positive outcome versus secondary outcome measures, correct?

MR. ABRAHAM: Objection.

THE WITNESS: You mean the --

BY MR. BAUM:

Q. In the manuscript, at Page 1081, there's

a paragraph that discusses the improvements that were made under the secondary outcomes, and there's no reference to the Week 8 outcomes being negative, right?

A. Correct.

Q. And there's no reference to the observed cases being negative at Week 8 either, correct?

A. Correct.

Q. And there's no reference to the unblinded patients' results showing that it was negative in the primary efficacy measure, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct.

BY MR. BAUM:

Q. Do you know if this Forest sponsored medical journal article was used by Forest sales reps in promoting Celexa use in the treatment of children and adolescents?

A. I do not know. I had left Forest by the time this was published.

Q. Do you know that the posters that were based on the -- well, we've already covered that. Let me go to the next exhibit.

MR. BAUM: We're almost done. Can I take a break for a moment?

MS. KIEHN: Yep.

THE VIDEOGRAPHER: The time is 4:38 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is 4:49 p.m. This is the beginning of Disk 5. We're on the record.

MR. BAUM: So we're going to go to the next Exhibit, which is 13.

(Document marked for identification as Heydorn Deposition Exhibit No. 13.)

BY MR. BAUM:

Q. Which is some letters to the editor regarding the American Journal of Psychiatry publication dated April 2005.

Have you seen this before?

A. I saw it yesterday for the first time.

Q. You never saw this before?

A. No, not that I recall.

Q. Forest didn't contact you and let you know that there was some criticism about the article you published?

MR. ABRAHAM: Objection.

THE WITNESS: I don't recall being

contacted.

BY MR. BAUM:

Q. All right. Well, let's take a look at the first one on Page 817, which is from Drs. Andres Martin, Walter Gilliam, Jeffrey Bostic and Joseph Rey.

Do you see that?

A. Yes.

Q. Do you know who Andres Martin is?

A. No.

Q. Do you know who Jeffrey Bostic is?

A. That name rings a bell.

Q. Do you recognize him as being a key opinion leader spokesperson for Forest on pediatric use of Celexa?

MR. ABRAHAM: Objection.

THE WITNESS: The name rings a bell. I wouldn't known what area he was an expert in.

BY MR. BAUM:

Q. You weren't aware that he was one of the chief lecturers and got paid around $750,000 by Forest to present lectures on pediatric use of Celexa?

MR. ABRAHAM: Objection.

THE WITNESS: No, I was not aware of that.

BY MR. BAUM:

Q. All right. So this is -- the only reason I point that out is that you've got a guy who was like a key opinion leader for Forest on the pediatric use of Celexa writing a criticism of your paper?

MR. ABRAHAM: Objection.

MS. KIEHN: Is there a question?

BY MR. BAUM:

Q. Did you notice that?

MR. ABRAHAM: Objection.

THE WITNESS: I see his name is on the letter to the editor, whatever this is.

BY MR. BAUM:

Q. Okay. So you weren't surprised to see Dr. Bostic down there as a co-author on this critique?

A. I really had no opinion, no, one way or the other. By the time this came out, I had left the area and been doing something else for at least two years.

Q. So this first one is titled "Child Psychopharmacology, Effect Sizes and the Big Bang."

Do you see that?

A. Yes, I see that.

Q. And to the editor: we read with interest the article by Karen Dineen Wagner, M.D., Ph.D., et.al. We were surprised to find the authors reporting on an overall effect size of 2.9.

Do you remember my pointing out to you that 2.9 --

A. Yes.

Q. -- in the abstract?

With the commonly cited criteria set forth by Cohen, effect sizes can be considered trivial, that's less than .2 to -- greater than -- trivial is less than -- how did I read this? I think it's less than .2 is trivial. Greater than -- this is wrong here.

It's considered trivial less than 0.2, small 0.2 to 0.5, moderate 0.5 to 0.8 or large, greater than .80.

Do you see that?

A. Yes.

Q. By these metrics, the reported effect size can be characterized as gargantuan, big-bang worthy. So they're being kind of facetious there, right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what their frame of mind was, but I would think so.

BY MR. BAUM:

Q. The value does not appear to be a benign typographical error for 0.29, given that 2.9 appears twice. Only 36% -- going further down it says, only 36% of the patients treated with citalopram responded. That means 64% didn't respond, right?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Well, if only 36% responded, the rest didn't, right?

MR. ABRAHAM: Objection.

THE WITNESS: Seems reasonable, yes.

BY MR. BAUM:

Q. That's more than half, right; the majority didn't respond?

MR. ABRAHAM: Objection.

THE WITNESS: In antidepressant trials that's not unusual.

BY MR. BAUM:

Q. But the majority didn't respond, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Correct, not unusual in a lot of clinical research.

BY MR. BAUM:

Q. Okay. So 24% of those -- compared to 24% of those with placebo (for a lukewarm number needed to treat 8).

Do you know what that means?

A. No, I don't.

Q. "These results, while modest, are respectable in their own right and nothing to sneeze at in a clinical area that has been short on proven therapeutic options. But a Majestic sequoia of 2.9 they are not."

Did I read that correctly?

A. Yes, you did.

Q. Now, they're criticizing the use of this 2.9, or their reference to this 2.9 as an effect size for the article in which you're an author, correct?

A. Yes.

Q. And it's also interesting that they're referring to this, these results, the 36% of the patients responded compared to 24% on placebo, that included the unblinded patients, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Well, the unblinded -- this is referring to -- if you go back to the article itself, and if you go to the abstract, that's the shortcut, and under Results, it says, "The difference in response rate at week 8 between placebo (24%) and citalopram (36%) was also statistically significant."

And --

A. Okay.

Q. And the N numbers were 174, not 166, correct?

A. Correct.

Q. So they included the unblinded patients to arrive at this modest lukewarm effect size, correct?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Even with them in, it was modest?

MR. ABRAHAM: Objection.

THE WITNESS: In the opinion of these authors, yes.

BY MR. BAUM:

Q. And Jeffrey Bostic was actually an

opinion leader for -- key opinion leader for Forest.

Did you know that?

MR. ABRAHAM: Objection.

THE WITNESS: You just mentioned that.

MR. ABRAHAM: Asked and answered.

BY MR. BAUM:

Q. So let's go up to the -- you don't know whether or not that 2.9 was a mistake?

A. I don't know.

Q. Do you know who within Forest would know that?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Probably Jin?

MR. ABRAHAM: Objection.

THE WITNESS: I would speculate it would be a statistician.

BY MR. BAUM:

Q. Okay. So on Page 819 of this exhibit, it's Dr. Wagner and colleagues' reply.

Do you see that?

A. Yes.

Q. And the persons replying are Wagner, Robb, Findling and Jin.

Do you see that?

A. Yes.

Q. You're not on that list?

A. No.

Q. Do you know why?

A. I don't know why. I wasn't aware that they were -- I wasn't aware there were letters to the editor and that a response was needed.

Q. Okay. And so on the last paragraph on the first column that starts "Dr. Martin."

Do you see that?

A. Yes.

Q. It says, "Dr. Martin and colleagues inquire about the value of 2.9, which was calculated as the quotient of the least square mean, divided by the common standard error of the mean for each treatment group."

Do you understand any of that?

A. Barely.

Q. What do you barely understand of it?

A. The least squared mean is a calculation -- some calculation of the mean score, and the standard area is a measure of the variability in the data across the population.

Q. Should I get Jin to explain that to me?
A. Yes, please too.
Q. Okay. And then "With Cohen's method, the effect size was the 0.32."
Do you see that?
A. Yes.
Q. And then referring back to the letter to the editor by Martin, Gilliam and Bostic on Page 817, you've got these Cohen effect sizes?
A. Yes.
Q. Are you familiar with Cohen effect sizes; have you ever heard of those before?
A. No.
Q. Well, where would .32 fit in on this scale that's referenced here?
MR. ABRAHAM: Objection.
THE WITNESS: Small.
BY MR. BAUM:
Q. So even with the unblinded patients included, it was a small effect size, correct?
MR. ABRAHAM: Objection.
THE WITNESS: If the calculation of the effect size was correct, yes, I have no way of knowing.

BY MR. BAUM:

Q. That's a pretty big difference .32 versus 2.9, isn't it?

MR. ABRAHAM: Objection.

THE WITNESS: Not knowing anything about the area, I can't comment.

BY MR. BAUM:

Q. Okay. It looks like Drs. Martin and Bostic kind of spotted an obvious problem?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Okay. Let's look at the second letter then, the one from Remy Barbe, M.D.?

A. Okay.

Q. Do you know how to pronounce that?

A. Barbe -- I don't know, no.

Q. And it starts on the bottom of 817. At the last part of that on the last paragraph of that letter, it says, finally, it is somewhat surprising that the authors do not compare their results with those of another trial, involving 244 adolescents (13-18 year olds), that showed no evidence of efficacy of citalopram compared to placebo and a higher level of

self-harm, (16 [12.9%] of 124 versus nine [7.5%] of 120) in the citalopram group compared to the placebo group. Although these data were not available to the public until December of 2003, one would expect that the authors, some of whom are employed by the company that produces citalopram in the United States and financed the study, had access to this information.

Did I read that correctly?

A. Yes.

Q. And the trial referred to by Dr. Barbe's letter to the editor, that's the Lundbeck 94404 trial, right?

MR. ABRAHAM: Objection.

THE WITNESS: I assume so.

BY MR. BAUM:

Q. And you were aware of the 94404 results as early as 2001; is that correct?

A. I was certainly --

MR. ABRAHAM: Objection.

THE WITNESS: -- aware of them. I don't know exactly what date I was aware of them.

BY MR. BAUM:

Q. You testified regarding when you found out about it in your prior deposition, and I'm just

going to like rely on that for the time period?

A. That's fine.

Q. But it predated the manuscript being sent to Andreason and the American Journal of Psychiatry, correct?

A. If it was 2001, then, yes, that was sent in 2002.

Q. So you knew about the 94404 results and so did Flicker, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And they weren't included in this study, correct, in this manuscript, correct?

A. Yes.

Q. Now, if you go to Page 819 at the next to the last paragraph, it goes -- they respond to Dr. Barbe by saying, it may be considered premature to compare the results of this trial with unpublished data from the results of a study that was not -- has not undergone the peer-review process. Once the investigators involved in the European citalopram adolescent depression study publish the results in a peer-reviewed journal, it will be possible to compare

their study population, methods, and results with our study with appropriate scientific rigor.

Do you see that?

A. Yes, I do.

Q. Now, that's not actually true, is it?

MR. ABRAHAM: Objection.

THE WITNESS: Well, yeah, I believe it is true.

BY MR. BAUM:

Q. Well, the 94404 study report was done by then, wasn't it?

A. I don't recall when it was done but -- by 2004?

Q. Yes.

A. Yes, it was done by them.

Q. And you participated in editing it, didn't you?

A. Yes, I reviewed it and edited it.

Q. And so it did get some scientific review by the scientists at Forest, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would hardly consider myself an expert --

BY MR. BAUM:

Q. Well, it was people --
A. -- in pediatric depression.
Q. Yeah, but it was you and Flicker, and who else?
MR. ABRAHAM: Objection.
THE WITNESS: I don't recall who else reviewed it.
BY MR. BAUM:
Q. But it resulted in a study report that you considered sufficiently accurate to convey to the FDA, correct?
MR. ABRAHAM: Objection.
THE WITNESS: It was conveyed to the FDA, yes.
BY MR. BAUM:
Q. To get the pediatric indication or the patent extension, correct?
MR. ABRAHAM: Objection.
THE WITNESS: Well, we certainly didn't get the pediatric indication.
BY MR. BAUM:
Q. But it was submitted to the FDA?
A. It was submitted to the FDA.
Q. So it had sufficient scientific rigor at

that point to have been submitted to the FDA, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It was submitted to the FDA, yes.

BY MR. BAUM:

Q. And you guys had vetted it for you at Forest, and Lundbeck had vetted it for accuracy before it was submitted to the FDA, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So this statement here, "it may be considered premature to compare the results," do you see that?

A. Yes.

Q. It's trying to fend off why they didn't convey it inaccurately, correct?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: This was not our data. This was Lundbeck's data.

BY MR. BAUM:

Q. Do you recall the e-mail correspondence you had with Lundbeck where there was a discussion

about getting the positive data out before the negative data?

A. Yes.

Q. Isn't that what happened?

MR. ABRAHAM: Objection.

THE WITNESS: Certainly MD-18 was published before 94404, yes.

BY MR. BAUM:

Q. And that was planned, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That was a goal.

BY MR. BAUM:

Q. It was intended?

MR. ABRAHAM: Objection.

THE WITNESS: We had no control over the Lundbeck investigators.

BY MR. BAUM:

Q. Is that true? Because you had correspondence with Lundbeck over whether or not to have the positive data come out first and that there was a benefit to Forest and Lundbeck who was profiting as well from having the negative data come out after the positive data, right?

MR. ABRAHAM: Objection.

MS. KIEHN: Objection. You're completely mischaracterizing the correspondence.

THE WITNESS: I believe my statement was I had no contact with the Lundbeck investigators.

BY MR. BAUM:

Q. Who did you have contact with at Lundbeck?

A. I had contact with individuals at Lundbeck, not their independent investigators.

Q. Okay. So you -- that Forest and Lundbeck planned to have the positive data come out before the negative data, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That was the goal.

BY MR. BAUM:

Q. Okay.

A. They were clearly different patient population that would help explain the different results.

Q. Was it interpretable data?

A. In their population I believe it was. It was published, so I'm assuming it was interpretable.

Q. And it was published as negative data, correct?

A. Yes.

Q. And Forest told the FDA that it was negative, right?

A. Yes.

Q. But it wasn't included in the manuscript that was published in the American Journal of Psychiatry?

A. That manuscript was on MD-18.

Q. Because you wanted to get the positive data out regarding MD-18 before the negative data of 94404, right?

MR. ABRAHAM: Objection.

THE WITNESS: We didn't have the right to refer to the Lundbeck data in our paper.

BY MR. BAUM:

Q. You had the right to refer to it to the FDA, so it was good enough to refer to it to the FDA to get the patent extension, it was good enough to report to the FDA to get a pediatric indication, but it wasn't good enough to give to the public or to academics who would be reviewing this data to determine whether or not to prescribe it to kids?

MR. ABRAHAM: Objection.

THE WITNESS: That was Lundbeck's decision, as I recall.

BY MR. BAUM:

Q. Wasn't Lundbeck Forest's partner in getting this drug distributed and sold in the US?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And both Lundbeck and Forest profited from having the sales occur in the US?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know what the financial relationship was between Forest and Lundbeck.

BY MR. BAUM:

Q. You know that there was a financial relationship, though, right?

A. Yes.

Q. And that they both benefited or they both received income from the sale of Celexa in the US, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding,

yes.

BY MR. BAUM:

Q. And they both received income from pediatric sales of Celexa in the US, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would assume so.

BY MR. BAUM:

Q. And they received income from pediatric sales of Lexapro, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I would assume so, but we're not discussing Lexapro here.

BY MR. BAUM:

Q. Well, actually, we are, because MD-18 was used to justify and get an indication for Lexapro, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what I've been told.

BY MR. BAUM:

Q. And if MD-18 was actually negative when you take out the unblinded patients, then it wouldn't actually justify a Lexapro indication for adolescents, would it?

MR. ABRAHAM: Objection.

THE WITNESS: That would be an FDA decision.

BY MR. BAUM:

Q. If the FDA didn't actually look at the statistics and just relied on the characterization of the documentation, then they might have made a mistake, huh?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. Well, did --

A. I'm sorry. I'm looking for Dr. Laughren's letter.

Q. Okay. That's it.

A. So this letter refers specifically to the citalopram application. I don't know what sort of review was done when MD-18 was submitted in support of Lexapro.

Q. So if MD-18 were submitted in support of Lexapro and they used the results that included the unblinded patients, that would be a flawed use of MD-18 since it didn't outperform placebo with the unblinded

patients out, right?

MR. ABRAHAM: Objection.

THE WITNESS: I have no knowledge of what the FDA did in its review of MD-18 in support of the Lexapro pediatric indication.

BY MR. BAUM:

Q. Okay. Let's go to this next -- this next letter is from Mathews, Adetunji and a bunch of other people whose names I can barely pronounce. I can pronounce Abraham.

A. Mathews there.

Q. Yeah, the rest of them are hard to pronounce, but, in any case, you see this letter from these doctors, correct?

A. Yes.

Q. And this says about halfway down the second column on the right, "our greatest concern."

Do you see that?

A. Yes.

Q. "Our greatest concern is with the results and conclusions drawn. There is no table showing the results in detail. The authors have only stated that 36% of citalopram-treated patients met the criteria for response, compared to 24% of patients

receiving placebo. This response rate, while in itself marginal compared to other studies of antidepressants, does not in itself show that citalopram is better than placebo."

Do you see that?

A. Yes.

Q. Then in the next paragraph, it goes through -- they calculated the absolute benefit increase of using citalopram as .12.

Do you see that?

A. Yes.

Q. Do you know what that means?

A. No.

Q. I should rely on a statistician like Jin to tell me that, or maybe Flicker?

MR. ABRAHAM: Objection.

THE WITNESS: I would say a statistician.

BY MR. BAUM:

Q. Okay. It goes that the odds ratio -- the odds of improving while taking citalopram compared to placebo was 1.75.

You see that?

A. Yes.

Q. "The number needed to treat, i.e., the number of children need to be treated for citalopram for one additional positive outcome was eight."

Do you see that?

A. Yes.

Q. "None of these shows that citalopram is any better than placebo."

Do you see that?

A. Yes.

Q. So even with the unblinded patients included, these physicians are pointing out that the clinical efficacy was not enough to show an improvement over placebo, correct?

A. That appears --

MR. ABRAHAM: Objection.

THE WITNESS: That appears to be their opinion.

BY MR. BAUM:

Q. Now, what do you think these physicians would have thought if they had had the unblinded patients' data excluded?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: Yeah, I have no idea.

BY MR. BAUM:

Q. They would have had even more negative a view of the results of MD-18, correct?

MR. ABRAHAM: Same objection.

THE WITNESS: I don't know.

BY MR. BAUM:

Q. What do you think?

MR. ABRAHAM: Objection.

THE WITNESS: Possibly.

BY MR. BAUM:

Q. Last line here of their letter says, "We are surprised that the most respected psychiatric journal in the world published a study that is misleading to their readers in the extreme."

Do you see that?

A. Yes.

Q. It would be even more misleading if they had known about the unblinding, correct?

MR. ABRAHAM: Objection.

THE WITNESS: I guess, yes.

BY MR. BAUM:

Q. Okay.

A. In their opinion.

Q. Your opinion?

MR. ABRAHAM: Objection.

THE WITNESS: My opinion is the compound works in children and adolescents, in spite of the insignificant P-value.

BY MR. BAUM:

Q. It outperforms placebo?

A. Numerically outperforms placebo, we've been over this.

Q. But not statistically significantly?

A. It doesn't reach the .05 level.

Q. So it wouldn't have gotten an indication, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It didn't.

BY MR. BAUM:

Q. Right, and it would not have gotten one by itself with a .052 P-value, correct?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. Do you have any regrets about your involvement with the CIT-MD-18 based on what I've shown you today?

A. I wish we had done things a little

differently.

Q. Like what?

A. I wish I had known for certain whether the patients, those nine patients were unblinded, but obviously I don't know. You showed me a lot of documents today suggesting that people knew the patients were unblinded. I don't know for a fact that they knew that. All I know is what they wrote on the paper. I wish I was aware of the correspondence with the FDA.

Q. Do you think, based on what I've shown you today, that Forest misled anyone about the results of MD-18?

A. It probably should have been more forthcoming.

Q. If you had known what I've shown you today, would you have changed anything in your first draft of the study report?

MR. ABRAHAM: Objection.

THE WITNESS: I don't believe I've seen my first draft of the study report. I saw the final draft of the study report.

BY MR. BAUM:

Q. Would you have changed anything in the

final study report?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: If I were the only one involved in writing it, I probably would have written it somewhat differently.

BY MR. BAUM:

Q. In what way?

MR. ABRAHAM: Objection.

THE WITNESS: Probably emphasizing more of the results at Week 8, clarifying some things, and I'm not sure how I would have handled the potential unblinding situation. I'd have to give that some thought.

BY MR. BAUM:

Q. Wouldn't you have had to have stated that they weren't potentially unblinded, they were actually unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know that for a fact.

BY MR. BAUM:

Q. I just want to now --

A. But I would like to say that all of the

information was included in the study report.

Q. Okay. But it was mischaracterized in the study report too, right?

MR. ABRAHAM: Objection.

THE WITNESS: It could have been characterized differently.

BY MR. BAUM:

Q. Thank you.

So I'm going to hand you what we're going to mark as Exhibit 14.

(Document marked for identification as Heydorn Deposition Exhibit No. 14.)

BY MR. BAUM:

Q. And this is an Editors' Note from the American Journal of Psychiatry dated August 2009.

Do you see that?

A. Yes.

Q. Have you ever seen that before?

A. Yes, I saw it this morning for the first time.

Q. So here it says, The article "A Randomized Placebo-Controlled Trial of Citalopram for the Treatment of Major Depression in Children and Adolescents," published in June 2004 in the American

Journal of Psychiatry is alleged by the United States Department of Justice in an ongoing suit to have been written and submitted to the Journal by a commercial medical writer on behalf of Forest Laboratories.

Do you see that?

A. Yes.

Q. And then we requested responses from Drs. Wagner, Robb, Findling (authors in their role as investigators in the clinical trial at their respective universities), Dr. William E. Heydorn, that's you, correct?

A. Yes, that's me.

Q. The senior Forest laboratory study director and Forest Laboratories.

A. I would like to point out that that parenthetical is not correct.

Q. Okay. So it says they requested responses from you.

Did you ever get a request from the American Journal of Psychiatry for a response to these letters, to this editors' note?

A. Yeah, you know, I vaguely recall getting something a number of years ago.

Q. How did you respond?

A. It was six years after the publication. I don't believe I responded. I had moved on in my career at that point, and I'd also like to object to the wording "ongoing suit to have been written and submitted to the Journal by a commercial medical writer on behalf of Forest Laboratories, Incorporated." It was not submitted on behalf of Forest by a commercial medical writer. It was submitted by the authors.

Q. Did Mary Prescott write the letter and have you guys sign it?

MR. ABRAHAM: Objection.

THE WITNESS: The cover letter?

BY MR. BAUM:

Q. Yeah.

A. I don't recall.

Q. If you go over to the second page of this, it continues, "The paper was submitted as a Brief Report, which the Journal's editors requested be resubmitted as a full-length article. Drs. Wagner, Robb and Findling report that they contributed with Dr. Heydorn to the resubmission and that they were not aware that Dr. Heydorn was working with a commercial writer. Dr. Heydorn did not respond to our request."

Is it true that neither Wagner, Robb or

Findling knew that you were communicating with a commercial writer?

MR. ABRAHAM: Objection.

THE WITNESS: I don't believe that to be a true statement.

BY MR. BAUM:

Q. Did you know that they were corresponding -- that they had information and e-mail correspondence with Mitchner and Prescott, right?

MR. ABRAHAM: Objection.

THE WITNESS: At the very least, by my recollection, Dr. Wagner didn't.

BY MR. BAUM:

Q. So this is a false statement?

MR. ABRAHAM: Objection.

THE WITNESS: I believe it's false, yes.

MR. BAUM: Take a break.

THE WITNESS: Yeah.

THE VIDEOGRAPHER: The time is now 5:25 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is now 5:37 p.m. We're on the record.

MR. BAUM: We have no further questions.

BY MR. ABRAHAM:

Q. Dr. Heydorn, you've answered a number of questions regarding some patients who participated in MD-18 who were potentially unblinded today, correct?

A. Yes.

Q. You don't actually know whether those patients were, in fact, unblinded, do you?

A. No, I do not.

Q. To the extent in your testimony you referred to, quote, unblinded patients, you don't actually know that those patients were unblinded, correct?

A. No, I do not know.

Q. To the extent you adopted Mr. Baum's use of the term unblinded patients, you also don't know that those patients were, in fact, unblinded, correct?

A. No, I do not.

MR. ABRAHAM: No further questions.

MR. BAUM: I think that's all.

THE VIDEOGRAPHER: The time is now 5:38 p.m. This is the end of Disk 5 and the end of today's deposition. We're off the record.

(Witness excused.)

C E R T I F I C A T I O N

I, MARGARET M. REIHL, a Registered Professional Reporter, Certified Realtime Reporter, Certified Shorthand Reporter, Certified LiveNote Reporter and Notary Public, do hereby certify that the foregoing is a true and accurate transcript of the testimony as taken stenographically by and before me at the time, place, and on the date hereinbefore set forth.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

Margaret M. Reihl, RPR, CRR, CLR
CSR #XI01497 Notary Public

ACKNOWLEDGMENT OF DEPONENT

I, WILLIAM E. HEYDORN, Ph.D., do hereby certify that I have read the foregoing pages, and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

_____

WILLIAM E. HEYDORN, Ph.D. DATE

Subscribed and sworn to before me this

_____ day of _____, 2016.

My commission expires:_____

_____

Notary Public

In Re: Celexa and Lexapro Marketing and Sales Practices Litigation, MDL No. 2067, No. 09-MD-2067 (NMG) (D. Mass.)

Errata Sheet to the Deposition of William E. Heydorn, Ph.D.
Deposition Date: October 14, 2016

Page	Line(s)	Now Reads	Should Read	Reason
25	3-5	conduct the trial, you know, as similar a fashion as possible. So protocol is developed	conduct the trial, you know, in as similar a fashion as possible. So a protocol is developed	Stenographic error
143	17	The P-value was greater than .5, yes.	The P-value was greater than .05, yes.	Stenographic error
151	6	I would also like to that everyone	I would also like to thank everyone	Stenographic error
290	2	Yes, please too.	Yes, please do.	Stenographic error

I, the undersigned, declare under penalty of perjury that I have read the deposition transcript; that I have made any corrections, additions, or deletions that I was desirous of making in the errata sheet above; and that the deposition transcript is otherwise a true and correct transcript of my testimony contained therein.

William E Heydorn
(Signature)

5 Dec 2016
(Date)

Subscribed and sworn before me this

5th day of December, 2016

Terri L Verderese

TERRI L. VERDERESE
Notary Public
State of New Jersey
My Commission Expires Apr 17, 2018