

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24

IN THE UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE: CELEXA AND LEXAPRO :MDL NO. 2067
MARKETING AND SALES PRACTICES :Master Docket No.
LITIGATION :09-MD-2067-(NMG)

PAINTERS AND ALLIED TRADES :Case No. 13-CV-13113
DISTRICT COUNCIL 82 HEALTH :(NMG)
CARE FUND, A THIRD-PARTY :
HEALTHCARE PAYOR FUND, on :Hon. Nathaniel M. Gorton
behalf of itself and all :
others similarly situated, :Hon. Marianne B. Bowler
Plaintiffs, :
v. :
: :
FOREST PHARMACEUTICALS, INC. :
and FOREST LABORATORIES, INC., :
Defendants. :

IN RE: CELEXA AND LEXAPRO :MDL NO. 2067
MARKETING AND SALES PRACTICES :Master Docket No.
LITIGATION :09-MD-2067-(NMG)
DELANA S. KIOSSOVSKI and :Judge Nathaniel M Gorton
RENEE RAMIREZ, on behalf of :
themselves and all others :Case No.
similarly situated, :14-CV-13848 (NMG)
Plaintiffs, :
v. :Hon. Nathaniel M. Gorton
: :
FOREST PHARMACEUTICALS, INC. :Hon. Marianne B. Bowler
and FOREST LABORATORIES, INC., :
: :
Defendants. :

— — —
OCTOBER 14, 2016

— — —
WILLIAM E. HEYDORN, Ph.D.
— — —

GOLKOW TECHNOLOGIES, INC.
877.370.3377 ph/917.591.5672 fax
deps@golkow.com

1 A P P E A R A N C E S:

2 BAUM HEDLUND ARISTEI GOLDMAN PC

BY: MICHAEL L. BAUM, ESQUIRE

3 12100 Wilshire Boulevard

Los Angeles, California 90025

4 (310) 207-3233

mbaum@baumhedlundlaw.com

5 Co-counsel for Plaintiffs

6

LAW OFFICES OF S. SAMUEL GRIFFIN

7 BY: S. SAMUEL GRIFFIN, ESQUIRE

PO Box 77373

8 Atlanta, GA 30357

(404) 989-0665

9 attyinatl@gmail.com

10

DEBEVOISE & PLIMPTON, LLP

11 BY: KRISTIN D. KIEHN, ESQUIRE

J. ROBERT ABRAHAM, ESQUIRE

12 919 Third Avenue

New York, New York 10022

13 (212) 909-6000

kdkiehn@debevoise.com

14 jrabraham@debevoise.com

Counsel for Defendant

15

16 Also Present:

17 Charlie Bowman, Videotape Technician

18

19

20

21

22

23

24

1 APPEARING TELEPHONICALLY:
2 BAUM HEDLUND ARISTEI GOLDMAN PC
BY: R. BRENT WISNER, ESQUIRE
3 12100 Wilshire Boulevard
Los Angeles, California 90025
4 (310) 207-3233
bwisner@baumhedlundlaw.com
5 Co-counsel for Plaintiffs

6
PENDLEY BAUDIN & COFFIN, LLP
7 BY: TRACEY L. TURNER, ESQUIRE
P.O. Box 29492
8 Columbus, Ohio 43229
(614) 657-3454
9 tturner@pbclawfirm.com
Counsel for Plaintiffs

10

11

12

Also Present telephonically:

13

Leemon McHenry

14

15

16

17

18

19

20

21

22

23

24

1		I N D E X	
2	WITNESS:		Page
	WILLIAM E. HEYDORN, Ph.D.		
3	By Mr. Baum		7
	By Mr. Abraham		314
4		— — —	
5		E X H I B I T S	
6			
	HEYDORN DEPOSITION EXHIBITS		MARKED
7			
	No. 1	Curriculum Vitae of	
8		William E. Heydorn, Ph.D.	15
9	No. 2	U.S. Department of Justice	
		letter dated 9/15/10	22
10			
	No. 3	Forest Laboratories, "A Randomized,	
11		Double-Blind, Placebo-Controlled	
		Evaluation of the Safety and	
12		Efficacy of Citalopram in Children	
		and Adolescents with Depression"	
13		April 8, 2002, Version 1.0	28
14	No. 4	E-mail dated 8/15/01, with attached	
		draft contracts	67
15			
	No. 5	Forest Laboratories STUDY Report	
16		for Protocol No. CIT-MD-18	
		April 8, 2002, Version 1.0	71
17			
	No. 5A	Forest Laboratories, Inc. Study	
18		Report for Protocol CIT-MD-18	
		April 8, 2002	
19		[MDL-FORP0073423]	222
20	No. 6	E-mail dated 3/2/00, Subject:	
		CIT-18 FAX to Investigational	
21		sites	
		[MDL-FORP0175697 through 175701]	149
22			
	No. 7	Forest Laboratories, Inc. letter	
23		dated 3/20/00	
		[MDL-FORP0020561]	177
24			

1	No. 7A	E-mail dated 3/8/00, Subject: Letter to FDA for CIT-18	194
2			
3	No. 7B	Letter to FDA-Draft, March 8, 2000 [MDL-FORP0168118]	197
4	No. 7C	E-mail dated 3/9/00, with attached Letter to FDA for CIT-18	206
5			
6	No. 7D	E-mail dated 3/14/00, with attached letter to Dr. Katz	215
7	No. 7E	E-mail string, top one dated 3/15/00, with attached letter to	
8		Dr. Katz	221
9	No. 8	E-mail dated 12/6/00, with attached table	
10		[MDL-FORP0168046 and 168047]	222
11	No. 9	E-mail string, top one dated 10/24/01, with attached notes	
12		from conference call	233
13	No. 10	Memorandum dated 9/16/02 [MDL-FORP0016376 through 16382]	249
14			
15	No. 11	Letter dated 11/14/02 to Nancy Andreasen, MD, PhD	
16		[PRE 20400 through 20421]	260
17	No. 12	Article, "A Randomized, Placebo- controlled Trial of Citalopram for the Treatment of Major Depression in Children and Adolescents"	262
18			
19	No. 13	Letters to the Editor	281
20			
21	No. 14	Editor's Note, August 2009	310
22		---	
23			
24			

1 THE VIDEOGRAPHER: We are now on the
2 record. My name is Charlie Bowman, I'm a
3 videographer with Golkow Technologies. Today's
4 date is October 14th, 2016. The time is
5 9:40 a.m. This video deposition is being held
6 in Parsippany, New Jersey in the matter of In
7 Re: Celexa and Lexapro Marketing and Sales
8 Practices Litigation for the United States
9 District Court for the District of
10 Massachusetts.

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

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

18 BY MR. BAUM:

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

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

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

1 A. Good morning.

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

5 A. Okay.

6 Q. Are you familiar with that idea?

7 A. Yes.

8 Q. So what is your current address?

9 A. Home address?

10 Q. Yes.

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

13 Q. And are you represented by counsel
14 today?

15 A. Yes.

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

18 A. Well, counsel contacted me.

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

21 MR. ABRAHAM: Objection.

22 MS. KIEHN: That calls for privileged
23 information.

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

1 that's a privileged communication.

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

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

6 BY MR. BAUM:

7 Q. Who is representing you?

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

10 MR. ABRAHAM: Debevoise & Plimpton.

11 THE WITNESS: Okay. Thank you.

12 BY MR. BAUM:

13 Q. Are your attorneys being paid by Forest?

14 A. Yes, that's my understanding.

15 Q. Okay. Did you contact Forest?

16 A. No.

17 Q. And you've been deposed before?

18 A. Yes.

19 Q. How many times?

20 A. At least once.

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

23 A. That sounds about right.

24 Q. Okay. Did you have a chance to review

1 that deposition transcript?

2 A. Yes.

3 Q. When did you last look at it?

4 A. Yesterday.

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

8 A. Yes.

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

12 A. Not that I can recall, no.

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

15 A. Yes.

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

19 A. Yes.

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

22 A. Yes.

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

1 A. Okay.

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

5 A. I understand.

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

9 A. Okay.

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

12 A. All right.

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

18 A. Okay.

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

23 A. All right.

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

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

10 Does that make sense?

11 A. Yes.

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

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

16 A. No.

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

19 A. Yes.

20 Q. When did you meet?

21 A. Yesterday.

22 Q. For how long?

23 A. About five, five and a half hours.

24 Q. Okay. And did you meet with them again

1 today?

2 A. This morning for breakfast.

3 Q. About how long?

4 A. About 45 minutes.

5 Q. Okay. And you understand you're here

6 today in connection with lawsuits involving the drugs

7 Celexa and Lexapro, correct?

8 A. Yes.

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

11 A. In a broad sense, yes.

12 Q. What are they?

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

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

19 A. Yes.

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

23 A. Yes, that does sound familiar.

24 Q. Did you speak to any Forest employees

1 about those depositions?

2 A. No.

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

6 A. Yes.

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

9 A. Not in detail.

10 Q. What do you recall generally?

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

13 Q. Did you give them any documents?

14 A. I don't believe so.

15 Q. Did you sign any declarations?

16 A. I don't recall.

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

19 A. No, that I was not aware of.

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

22 A. No.

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

1 A. Yes.

2 Q. What documents did you review?

3 A. Well, we met yesterday, went over the
4 publication of the MD-18 study, the study report, some
5 e-mail communications regarding the ACNP poster from
6 2001, I believe it was.

7 Q. Anything else?

8 A. No. I saw a copy of the Lundbeck
9 publication, which I had not seen before, because that
10 was published after I left Forest, and that's about it.

11 Q. So you've brought with you today your
12 CV?

13 A. Yes.

14 Q. I'm going to mark that as Exhibit 1 and
15 hand that to you.

16 A. Yes.

17 (Document marked for identification as
18 Heydorn Deposition Exhibit No. 1.)

19 BY MR. BAUM:

20 Q. Is this your current CV?

21 A. Yes.

22 Q. And I see that since 2003 you've been
23 working for Lexicon?

24 A. Correct.

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

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

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

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

16 Q. What type of drugs are those?

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

22 Q. An orphan indication is for the same
23 compound?

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

1 small patient population.

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

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

6 Q. Any central nervous system type drugs?

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

10 Q. Was that an antidepressant?

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

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

16 A. Correct.

17 Q. Why did you leave?

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

23 Q. What was that position?

24 A. So I moved into internal medicine out of

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

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

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

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

13 A. No.

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

17 A. What do you mean by "prepared"?

18 Q. Being written up?

19 A. No, no, not that I recall.

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: When I stopped working.

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

4 BY MR. BAUM:

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

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

13 Q. What little projects were left?

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

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

20 A. I don't believe so.

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

24 A. No.

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection.

13 THE WITNESS: It was probably in the
14 2005 time frame, 2006.

15 BY MR. BAUM:

16 Q. How did you become aware of it?

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

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

23 A. No, not that I recall.

24 Q. With Forest lawyers?

1 A. Yes.

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

4 A. There were --

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

8 THE WITNESS: Okay, okay, yeah.

9 They were discussions relating to the
10 Department of Justice action.

11 BY MR. BAUM:

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

14 A. I believe --

15 MR. ABRAHAM: Objection.

16 THE WITNESS: I believe so.

17 BY MR. BAUM:

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

20 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

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

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

6 A. That does sound familiar to me, yes.

7 Q. Have you seen it?

8 A. No.

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

11 BY MR. BAUM:

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

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

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

17 A. Okay.

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

20 MR. ABRAHAM: Objection.

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

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

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

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

8 BY MR. BAUM:

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

16 Do you see that?

17 A. Yes.

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

21 A. Yes.

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

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

6 Do you see that?

7 A. Yes.

8 Q. Do you think that applies to you?

9 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

15 A. Yes.

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

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

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

1 MR. ABRAHAM: Objection.

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

8 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I guess you could call it
13 that.

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

18 MR. BAUM: Okay.

19 BY MR. BAUM:

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

22 A. I believe so.

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

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Yes, I would assume so.

3 BY MR. BAUM:

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

6 A. Yes.

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

10 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Yes.

21 BY MR. BAUM:

22 Q. What is a double-blind protocol?

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

1 being administered.

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

4 A. Yes.

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

7 A. I have not read it recently, no.

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

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

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

14 A. Yes.

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

20 MR. ABRAHAM: Objection.

21 THE WITNESS: Correct.

22 BY MR. BAUM:

23 Q. What is a control group?

24 A. A control group is the group that

1 receives the placebo.

2 Q. And MD-18 had a control group?

3 A. Yes.

4 Q. And they had a placebo group?

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

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

9 BY MR. BAUM:

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

13 A. Okay.

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

17 Do you see that?

18 A. Yes.

19 Q. Does this document look familiar to you?

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

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

24 A. That's fine.

1 Q. So do you recall that MD-18 was a
2 multisite clinical trial?

3 A. Yes.

4 Q. And each site was expected to follow the
5 study protocol; is that correct?

6 A. Correct.

7 Q. Did Dr. Karen Wagner run any of those
8 sites?

9 A. I believe she ran one of the sites, yes.

10 Q. Take a look at Page 309, which is the
11 next -- the second page here. You see this is signed
12 by a Paul Tiseo, September 1, 1999?

13 A. Yes.

14 Q. Do you know what Dr. Tiseo's role was in
15 the CIT-MD-18?

16 A. I believe he was the overall study
17 monitor.

18 Q. What does that mean?

19 A. He's the -- he would be the one person
20 at Forest ultimately responsible for the conduct of the
21 study.

22 Q. Did you interact with him with respect
23 to CIT-MD-18?

24 A. Not on a regular basis. During the

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

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

6 MR. ABRAHAM: Objection.

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

9 BY MR. BAUM:

10 Q. Okay. Do you know when he left?

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

13 Q. Do you know who took his place?

14 A. I don't know.

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

18 MR. ABRAHAM: Objection.

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

21 BY MR. BAUM:

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

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

1 the study monitor.

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: I assume so.

6 BY MR. BAUM:

7 Q. You don't recall?

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

9 Q. What would you speculate?

10 A. I would think --

11 MR. ABRAHAM: Objection.

12 You can answer.

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

15 BY MR. BAUM:

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

19 A. Yes.

20 Q. Then you see Lawrence Olanoff?

21 A. Yes.

22 Q. What were their roles in MD-18?

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

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

3 Q. Did you interact with either of them?

4 A. Yes.

5 Q. And then Ivan Gergel?

6 A. Yes.

7 Q. Who is he?

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

14 Q. What happened to Charlie?

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

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

19 A. No.

20 Q. And who is Ed Lakatos?

21 A. Senior director of biostatistics and
22 data management.

23 Q. Did you interact with him?

24 A. Very little, if at all.

1 Q. And what about Keith Rotenberg?

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

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

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

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

12 A. Yes.

13 Q. Were they people you dealt with more
14 directly?

15 A. Yes.

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

18 Do you see that?

19 A. Yes.

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

22 Do you see that?

23 A. Yes.

24 Q. And the "Primary Efficacy."

1 Do you see that?

2 A. Yes.

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

5 Do you see that?

6 A. Yes.

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

9 A. Yes.

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

13 Do you see that?

14 A. Yes.

15 Q. And "Severity and Improvement
16 subscales."

17 Do you see that?

18 A. Yes.

19 Q. And then you see the K-SADS?

20 A. Yes.

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

24 Do you see that?

1 A. Yes.

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

7 MR. ABRAHAM: Objection.

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

11 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

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

18 BY MR. BAUM:

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

22 MR. ABRAHAM: Objection.

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

1 BY MR. BAUM:

2 Q. Is it the result of a statistical
3 analysis?

4 A. Yes.

5 Q. Can you describe that?

6 A. Well, again --

7 Q. Generally.

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

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

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Yes.

16 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

23 Q. But from your perspective.

24 A. From my perspective, it's generally

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

4 Q. That's the P-value?

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

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

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes, that's my
10 understanding.

11 BY MR. BAUM:

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

14 A. Okay.

15 Q. You see there that it says that total of
16 160 patients will be randomized to double-blind
17 treatment.

18 Do you see that?

19 A. Yes.

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

22 MR. ABRAHAM: Objection.

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

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

3 BY MR. BAUM:

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

7 MR. ABRAHAM: Objection.

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

10 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I assume so.

23 BY MR. BAUM:

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

1 subheading "Study Procedures."

2 You see that?

3 A. Yes.

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

6 Do you see that?

7 A. Yes.

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

10 A. Yes.

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

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

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

24 MR. ABRAHAM: Objection.

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

5 BY MR. BAUM:

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

8 A. No, I do not.

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

11 A. That's correct.

12 MR. ABRAHAM: Objection.

13 THE WITNESS: I'm sorry.

14 BY MR. BAUM:

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

18 Do you see that?

19 A. Yes.

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

24 Do you see that?

1 A. Yes.

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

7 Do you see that?

8 A. Yes.

9 Q. And "Medication will be supplied in
10 bottles containing either 10 tablets for the lead-in
11 and the first four weeks of double-blind treatment, or
12 40 tablets of the remaining four weeks of the treatment
13 period."

14 Do you see that?

15 A. Yes.

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

18 A. Yes.

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

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

23 Q. What was that problem?

24 A. These patients received pink colored

1 tablets instead of white colored tablets.

2 Q. Do you know how many patients?

3 A. Somewhere up to nine patients is my
4 understanding.

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

7 A. That's my recollection, yes.

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

10 A. No, I do not.

11 Q. Let's go to Page 328. Under Section
12 "9.7 Unblinding Procedures."

13 Do you see that?

14 A. Yes.

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

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

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

22 A. That is --

23 MR. ABRAHAM: Objection.

24 THE WITNESS: That is correct.

1 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes, that's correct.

7 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

19 MS. KIEHN: If anything.

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

1 BY MR. BAUM:

2 Q. Have you ever had to do that?

3 A. Not that I can recall.

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

10 Do you see that?

11 A. Yes.

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

15 Do you see that?

16 A. Yes.

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

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I don't know.

21 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I don't know.

2 BY MR. BAUM:

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

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

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

10 A. I don't recall any, no.

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

13 A. I don't recall any discussions.

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

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

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

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

24 Q. When do you think you first heard about

1 it?

2 A. I couldn't say.

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

5 A. Yes.

6 Q. How often would you attend those?

7 A. I believe they were held weekly.

8 Q. Who ran them?

9 A. I don't recall.

10 Q. Was Ivan Gergel involved?

11 A. Yes.

12 Q. Charlie Flicker?

13 A. I believe so, yes.

14 Q. For a while Paul Tiseo?

15 A. Yes.

16 Q. Lawrence Olanoff?

17 A. Not on a regular basis, no.

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

20 MR. ABRAHAM: Objection.

21 THE WITNESS: I believe it did.

22 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

2 THE WITNESS: I don't recall.

3 BY MR. BAUM:

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

7 MR. ABRAHAM: Objection.

8 THE WITNESS: No, I don't recall.

9 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

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

16 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

1 Q. And who was that?

2 A. Well, it was Paul Tiseo in the
3 beginning.

4 Q. So then it devolved to Charlie Flicker?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I assume so. As I said, I
7 don't know for certain who took over after Paul
8 left.

9 BY MR. BAUM:

10 Q. Was Forest Laboratories notified of any
11 unblinding in CIT-MD-18?

12 A. They were certainly aware of the pink
13 tablets.

14 Q. How did Forest become aware of the pink
15 tablets?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: I don't know.

18 BY MR. BAUM:

19 Q. Do you know what Forest did in response
20 to learning about the pink tablets?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I reviewed some documents
23 yesterday so --

24 BY MR. BAUM:

1 Q. And what did they say?

2 A. I know they replaced the pink tablets
3 with white tablets.

4 Q. And what document did you review that
5 said that?

6 A. It was a fax that Paul Tiseo sent to the
7 investigator sites.

8 Q. That was a March 3rd, 2000 document?

9 A. I don't recall the date, but that would
10 probably be about right.

11 Q. Now, was it only nine bottles of pink
12 tablets that were sent out?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I don't know.

15 BY MR. BAUM:

16 Q. You don't know whether there were more
17 bottles sent to other sites that had to be retrieved?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: No, I don't know.

20 BY MR. BAUM:

21 Q. Do you know what information was sent
22 along with the bottles when they were sent to the
23 investigator sites?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: No, I do not.

2 BY MR. BAUM:

3 Q. Would there be information identifying
4 which drug or which medication they were receiving?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I -- what do you mean
7 by -- can you rephrase it?

8 BY MR. BAUM:

9 Q. Either active medication or placebo?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Well, the investigators
12 would be aware that it was a double-blind study
13 so that there -- the patients that they would
14 enroll into the study, some would be on the
15 active medication and some would be on placebo,
16 they would assume that that would be the case.

17 BY MR. BAUM:

18 Q. Now, these pink tablets, was it your
19 understanding they were actually active medication
20 Celexa?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I have no way of knowing
23 that, no.

24 BY MR. BAUM:

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

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

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

8 A. No.

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

11 A. They could have.

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

18 A. Okay.

19 Q. -- that clarify that, I think.

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

22 MR. ABRAHAM: Objection.

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

1 BY MR. BAUM:

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Not that I can recall, no.

6 BY MR. BAUM:

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

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

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

14 Do you see that?

15 A. Yes.

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: That's a statistical

23 question. I really can't -- I'm not an expert
24 in that area.

1 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

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

10 BY MR. BAUM:

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

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

18 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

1 Q. Then going on here it says, "Assuming an
2 effect size (treatment group difference relative to
3 pooled standard deviation) of 0.5, a sample size of 80
4 patients in each treatment group will provide at least
5 85% power at an alpha level of 0.05 (two-sided)."

6 Did I read that right?

7 A. Yes.

8 Q. Do you know what that means?

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

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

16 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

1 THE WITNESS: That is my understanding.

2 BY MR. BAUM:

3 Q. So as long as MD-18 had 160 patients'
4 results in the equations, that was enough to power
5 statistically significant results, right?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: That's my understanding,
8 given the assumptions that went into the sample
9 size consideration.

10 BY MR. BAUM:

11 Q. And you didn't need more than 160 to
12 power the study for statistical significance purposes,
13 right?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Again, yes, that's my
16 assumption, given that this -- given that this
17 assumption here is accurate.

18 BY MR. BAUM:

19 Q. And per this statement here, the
20 protocol endpoint for efficacy was Week 8, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. And measurements at Weeks 1, 2, 4 or 6

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

3 MR. ABRAHAM: Objection.

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

8 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes, that's my
15 understanding.

16 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

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

1 determine whether the study was efficacious or
2 not, whether the compound was efficacious or
3 not.

4 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: No, not in my opinion.

11 BY MR. BAUM:

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

15 MR. ABRAHAM: Objection.

16 THE WITNESS: You would have to include
17 both.

18 BY MR. BAUM:

19 Q. Otherwise you'd be misleading --

20 MR. ABRAHAM: Objection.

21 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Yes.

2 BY MR. BAUM:

3 Q. What is a study report?

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

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

9 A. Yes.

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

12 A. Yes.

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

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

17 Q. Did you write any of it?

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

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

21 Does that ring a bell?

22 MR. ABRAHAM: Objection.

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

1 BY MR. BAUM:

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

4 MR. ABRAHAM: Objection.

5 BY MR. BAUM:

6 Q. -- for MD-18?

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

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

13 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

18 Q. Who in particular edited it?

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

21 Q. Would he inform you of the comments?

22 A. Yes.

23 Q. How would he do that?

24 A. He would -- Charlie didn't use

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

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

6 A. Yes.

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

8 A. No.

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

13 Do you recall saying that?

14 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

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

20 A. I would assume I did, yes.

21 Q. What are case report forms?

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

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

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

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

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

10 MR. ABRAHAM: Objection.

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

16 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I don't know.

23 BY MR. BAUM:

24 Q. Do you know if anybody had the job of

1 doing that?

2 A. I don't know.

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: I would assume it was
8 accurate.

9 BY MR. BAUM:

10 Q. Why?

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

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

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Yes.

20 BY MR. BAUM:

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

23 A. Yes.

24 Q. Did you verify the accuracy of the

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: No, I did not.

6 BY MR. BAUM:

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

10 MR. ABRAHAM: Objection.

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

13 BY MR. BAUM:

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

17 Do you recall that?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Yes, I do recall that.

20 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

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

4 BY MR. BAUM:

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

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

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

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

17 Q. Did you review the efficacy related
18 appendices?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Probably not.

21 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I don't recall.

2 BY MR. BAUM:

3 Q. Did you review -- you weren't shown
4 something like that yesterday?

5 MR. ABRAHAM: Objection.

6 MS. KIEHN: Objection.

7 THE WITNESS: I don't recall seeing
8 Appendix 6.

9 BY MR. BAUM:

10 Q. Do you recall seeing a run that excluded
11 the patients that had the pink tablets dispensed to
12 them?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes, I do recall seeing
15 that.

16 BY MR. BAUM:

17 Q. When did you see it?

18 A. I saw that yesterday. If that was
19 Appendix 6, then I did see that yesterday.

20 Q. Had you seen that before?

21 A. I'm sure I had seen that when I was
22 working on the study report, but I can't recall
23 specifically.

24 Q. Do you recall any discussions when you

1 first -- let me strike that.

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

6 MR. ABRAHAM: Objection.

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

9 BY MR. BAUM:

10 Q. Who worked with you on the study report?

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

13 Q. Charlie Flicker for one, correct?

14 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

18 Q. Do you know who Paul Bukerait is?

19 A. Yes.

20 Q. Who is he?

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

23 Q. What did he do?

24 A. He worked on either study reports or

1 publications.

2 Q. What did he do on MD-18?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: I can't recall
5 specifically.

6 BY MR. BAUM:

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

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

12 MR. BAUM: Can we take a break now?

13 Good point.

14 MR. ABRAHAM: Sure.

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

17 (Brief recess.)

18 THE VIDEOGRAPHER: The time is now
19 10:52 a.m. This is the beginning of Disk 2.
20 We're on the record.

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

23 BY MR. BAUM:

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

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

3 Do you see that?

4 A. Yes.

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

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

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

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

17 Do you see that?

18 A. Yes.

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

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

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

24 A. I know we were considering working with

1 PharmaNet.

2 Q. And what's PIA?

3 A. I'm not sure who they are.

4 Q. Do you recall who PharmaNet was?

5 A. They were a contract research
6 organization.

7 Q. What did they do?

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

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

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

20 Do you see that?

21 A. Yes.

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

24 A. Yes, yes.

1 Q. So who are these guys?

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

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

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

9 Q. Okay. So looking at this e-mail it
10 looks like between Robert Exner and you on August 15,
11 2001.

12 Do you see that?

13 A. Yes.

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

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

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

22 A. No.

23 Q. Do you recall providing any information
24 to PharmaNet?

1 A. No.

2 Q. Do you recall that the MD-18 study
3 report was submitted to the FDA?

4 A. Yes.

5 Q. Do you recall approximately when?

6 A. I think we looked at that yesterday,
7 2002.

8 Q. Did Forest receive a six-month patent
9 extension for Celexa for doing clinical trials on
10 pediatric depression?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I believe so.

13 MR. BAUM: Let's go to the next exhibit.

14 Mark this as Exhibit 5.

15 (Document marked for identification as
16 Heydorn Deposition Exhibit No. 5.)

17 BY MR. BAUM:

18 Q. Okay. This appears to be a study report
19 for protocol CIT-MD-18?

20 A. Yes.

21 Q. Do you see that?

22 A. Yes.

23 Q. Do you recognize it?

24 A. Yes.

1 Q. Have you seen it before?

2 A. Yes.

3 MS. KIEHN: Michael, just to clarify, is
4 this a final copy?

5 MR. BAUM: I think this one is.

6 MS. KIEHN: It says Version 1 at the
7 bottom, that's why I asked.

8 MR. BAUM: As far as I know, this is the
9 final.

10 MS. KIEHN: The typeface looks weird on
11 the front too.

12 MR. BAUM: Well, if it's not the final,
13 it would be news to me.

14 MS. KIEHN: Okay, well, we'll just
15 proceed with it.

16 MR. BAUM: It's dated April 8, 2002.

17 MS. KIEHN: We'll proceed with the
18 reservation we're not sure that it's final.

19 MR. BAUM: Okay.

20 BY MR. BAUM:

21 Q. Well, looking at the front page of this
22 document, do you see that the initial date is
23 January 31, 2000.

24 Do you see that?

1 A. Yes.

2 Q. Is that the date that the trial started?

3 A. I don't know.

4 Q. You don't know what initiation date
5 means?

6 A. Different companies have different
7 definitions of that.

8 Q. Do you know what Forest's definition
9 was?

10 A. No, I do not.

11 Q. What is a -- do you think that might be
12 when patients first started being screened for entering
13 the CIT-MD-18?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: That would be one
16 definition companies use for initiation date.

17 BY MR. BAUM:

18 Q. And you see the completion date is
19 April 10, 2001?

20 A. Yes.

21 Q. And is that the date that the -- well,
22 what date would that have been?

23 A. That's -- my understanding is that's
24 generally last patient, last visit.

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: More efficacy data, yes.

7 BY MR. BAUM:

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

12 A. Yes.

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

17 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

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

3 BY MR. BAUM:

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

7 MR. ABRAHAM: Objection.

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

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

21 MR. BAUM: Yeah.

22 THE VIDEOGRAPHER: The time is now
23 11:03 a.m. We're off the record.

24 (Pause.)

1 THE VIDEOGRAPHER: The time is now
2 11:10 a.m. We're on the record.

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

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

14 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

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

21 BY MR. BAUM:

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

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

4 MR. BAUM: That's correct.

5 BY MR. BAUM:

6 Q. And have you found Page 69?

7 A. Yes, I have.

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

13 Do you see that?

14 A. Yes.

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

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

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

23 A. Yes.

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

1 says .038.

2 Do you see that?

3 A. Yes.

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: That's my understanding.

8 BY MR. BAUM:

9 Q. It's less than .05?

10 A. Yes.

11 Q. Which would be the cutoff for
12 statistical significance?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

19 THE WITNESS: That's my understanding.

20 BY MR. BAUM:

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

23 Do you see that?

24 A. Yes.

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

6 Did I read that correctly?

7 A. Yes.

8 Q. Did you write that sentence?

9 A. I don't recall.

10 Q. Do you know who wrote it?

11 A. No, I do not.

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

14 Did you find that?

15 A. Yes.

16 Q. And that's Appendix Table 6.

17 Do you see that?

18 A. Yes.

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

21 Do you see that?

22 A. Yes.

23 Q. So the change from baseline CDRS-R after
24 8 weeks was the primary efficacy measure for MD-18; is

1 that correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: Yes.

4 BY MR. BAUM:

5 Q. So this is an evaluation of CDRS-R after
6 8 weeks without the nine patients involved, correct?

7 A. Yes.

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

10 Do you see that?

11 A. Yes.

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

14 MR. ABRAHAM: Objection.

15 THE WITNESS: I don't know.

16 BY MR. BAUM:

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

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

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: Yes.

1 BY MR. BAUM:

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Not sure what you mean.

6 BY MR. BAUM:

7 Q. That's a bad question.

8 Do you know who generated this table?

9 A. No, I do not.

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

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

16 Q. Do you recall who the primary
17 biostatistician was?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Jin.

20 BY MR. BAUM:

21 Q. James Jin?

22 A. Yes, that sounds familiar.

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

1 A. Yes.

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

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

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

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

11 Q. Who would do that?

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

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

17 A. Not specifically.

18 Q. Do you know that it was done?

19 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

1 A. No.

2 Q. None were shown to you?

3 MS. KIEHN: Objection.

4 THE WITNESS: Well, this table was shown
5 to me yesterday, in very tiny print.

6 BY MR. BAUM:

7 Q. Any other vers -- in very tiny print?

8 A. Yes.

9 Q. Okay. Yes, it is tiny print.

10 A. No, this is much more readable, believe
11 me.

12 Q. Oh, great.

13 Okay. So the footnote at the bottom of
14 the page says "Report Generated by Program:

15 /sasprog/cit/citmdl8/programs/tables/apndx.6.sas."

16 Do you know what any of that stuff
17 means?

18 A. No.

19 Q. I would need to talk to someone like
20 James Jin to get that information?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I would assume so.

23 BY MR. BAUM:

24 Q. It wasn't in your wheelhouse to know

1 that?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: No, it was not.

4 BY MR. BAUM:

5 Q. Now, there is a note just above that
6 says, "Patients (105, 113, 114, 505, 506, 507, 509,
7 513, 514) with drug dispensing error are excluded."

8 Did I read that correctly?

9 A. Yes.

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

13 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

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

20 MR. ABRAHAM: Objection.

21 THE WITNESS: I don't know.

22 BY MR. BAUM:

23 Q. What do you think?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: There's a potential, yes.

2 BY MR. BAUM:

3 Q. Why?

4 A. They received different colored tablets.

5 Q. What would happen as a result of that?

6 MR. ABRAHAM: Objection.

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

11 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

15 THE WITNESS: I don't know.

16 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I don't know.

21 BY MR. BAUM:

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

24 Do you see that?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Yes, I see that.

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: That's my understanding.

8 BY MR. BAUM:

9 Q. Because it's greater than .05?

10 A. Yes, that's my understanding.

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

13 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

18 Q. For the primary endpoint?

19 A. For the primary endpoint.

20 MR. ABRAHAM: Object.

21 BY MR. BAUM:

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

1 scale after 8 weeks, correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: Yes.

4 BY MR. BAUM:

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

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

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

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: That appears to be the

1 case.

2 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

12 THE WITNESS: Yes.

13 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Yes.

18 BY MR. BAUM:

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

24 Do you see that?

1 A. Yes.

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: No, I don't recall.

7 BY MR. BAUM:

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

14 Did I read that correctly?

15 A. Yes.

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

20 MR. ABRAHAM: Objection.

21 THE WITNESS: Yes.

22 BY MR. BAUM:

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

1 patients incorrect?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: Potentially, yes.

4 BY MR. BAUM:

5 Q. It was, in fact, a shift from

6 statistically significant to statistically

7 insignificant, right?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

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

12 it?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

16 Q. Who was the target audience for the

17 MD-18 study report?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Target audience.

20 BY MR. BAUM:

21 Q. Who was intended to receive it?

22 A. Well, the Food and Drug Administration.

23 Q. And that would have been the FDA medical

24 reviewer and Tom Laughren deciding whether to approve

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

3 MR. ABRAHAM: Objection.

4 THE WITNESS: Yes.

5 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: I don't know.

11 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

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

4 BY MR. BAUM:

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

7 A. I do not know.

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know.

12 BY MR. BAUM:

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

17 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

21 Q. Do you know Tom Laughren?

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

24 Q. In what capacity did you work with him?

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

5 Q. What drug did you work on?

6 A. Primarily anti-depressants.

7 Q. Which anti-depressants?

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

10 Q. Was it Celexa?

11 A. No, I don't believe so.

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

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

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

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

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

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

3 BY MR. BAUM:

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

5 A. I don't believe so, no.

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

8 A. Not that I recall.

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

11 Let's go to Page 100, and this is "Table
12 3.1 Primary Efficacy."

13 Do you see that?

14 A. Yes.

15 Q. Change from baseline in CDRS after 8
16 weeks.

17 Do you see that?

18 A. Yes.

19 Q. ITT population - LOCF.

20 Do you see that?

21 A. Yes.

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

24 A. Yes.

1 Q. And this analysis included 174 patients,
2 85 patients in the placebo group and 89 patients in the
3 citalopram group.

4 Do you see that?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

8 Q. And that's a difference of eight
9 patients from the table -- Appendix Table 6, which had
10 166 patients.

11 Do you recall that?

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

17 MS. KIEHN: What is that?

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

20 THE WITNESS: Yeah, you're right.

21 BY MR. BAUM:

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

24 A. Yes.

1 Q. Do you know why there's a difference;
2 it's one patient short?

3 A. No, I do not.

4 Q. You don't recall that being discussed?

5 A. No.

6 Q. So looking over to like the middle right
7 section, you see the P-value is .038.

8 Do you see that?

9 A. Yes.

10 Q. And that's a statistically significant
11 P-value, correct?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: Yes.

14 BY MR. BAUM:

15 Q. And the P-value in Table 6 show the
16 citalopram versus placebo was not statistically
17 significant, but Table 3.1 shows that citalopram versus
18 placebo is statistically significant, correct?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Yes.

21 BY MR. BAUM:

22 Q. And do you know why the earlier
23 analysis -- well, first off, take a look at the date up
24 at the top right. It says October 30th, 2001.

1 Do you see that?

2 A. Yes.

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

6 A. September 12th, 2001.

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

9 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

15 MS. KIEHN: Objection.

16 MR. ABRAHAM: Objection.

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

19 BY MR. BAUM:

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

22 MR. ABRAHAM: Objection.

23 THE WITNESS: No, I do not.

24 BY MR. BAUM:

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

3 MR. ABRAHAM: Objection.

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

6 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: I do not know.

11 BY MR. BAUM:

12 Q. Would it have been Charlie Flicker?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: It may have been.

15 BY MR. BAUM:

16 Q. Ivan Gergel?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: It may have been.

19 BY MR. BAUM:

20 Q. Lawrence Olanoff?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: It may have been.

23 BY MR. BAUM:

24 Q. Were you involved in any discussions

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: I don't recall any
6 discussions.

7 BY MR. BAUM:

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

10 MS. KIEHN: Objection.

11 THE WITNESS: No.

12 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

21 Q. It wouldn't have been Solomon?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: I don't know.

24 BY MR. BAUM:

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

3 MR. ABRAHAM: Objection.

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

6 BY MR. BAUM:

7 Q. But it wasn't you?

8 MS. KIEHN: Objection.

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

12 BY MR. BAUM:

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

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Yes.

17 BY MR. BAUM:

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

21 Do you see that?

22 A. Yes.

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

1 procedure before database lock."

2 Do you see that?

3 A. Yes.

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

9 Do you see that?

10 A. Yes, yes.

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

16 Did I read that correctly?

17 A. Yes.

18 Q. So now if we go to Section 7.0 on Page
19 63, which I think is the next page over on the exhibit.

20 A. Yeah.

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

23 Do you see that?

24 A. Yes.

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

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

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

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

11 Q. Did you draft this section?

12 A. I don't remember.

13 Q. Okay. So the last paragraph it says,
14 Nine patients (Patients 105, 113, 114, 505, 506, 507,
15 509, 513, and 514) were mistakenly dispensed 1 week of
16 medication with potentially unblinding information
17 (tablets had an incorrect coating). Therefore, in
18 addition to the analysis specified in Section 6.4.1 for
19 the primary efficacy parameter, a post-hoc analysis was
20 performed on an ITT subpopulation that excluded these 9
21 patients.

22 Do you see that?

23 A. Yes.

24 Q. That post-hoc analysis was Table 6 in

1 the appendix, correct?

2 A. Yes, I believe that was the number.

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

7 MR. ABRAHAM: Objection.

8 THE WITNESS: I don't know.

9 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection.

13 THE WITNESS: Correct.

14 BY MR. BAUM:

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

17 MR. ABRAHAM: Objection.

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

21 BY MR. BAUM:

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

24 A. Because of the potential for unblinding,

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

4 Q. And it did, right?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: It appears to have, yes.

7 BY MR. BAUM:

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

15 Do you see that?

16 MS. KIEHN: Hold on.

17 BY MR. BAUM:

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

19 MS. KIEHN: Where is that?

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

21 Exhibit --

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

23 THE WITNESS: It's in the protocol.

24 MR. ABRAHAM: Are you referring to a

1 previous exhibit?

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

3 MR. ABRAHAM: 328, Page 16.

4 MR. BAUM: Or 328.

5 MR. ABRAHAM: Two page numbers.

6 BY MR. BAUM:

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

9 A. Yep, I've got, yep.

10 Q. So did I read that off correctly?

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

13 BY MR. BAUM:

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

16 A. Yes.

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

20 Do you see that?

21 A. Yes.

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

1 performed."

2 Do you see that?

3 A. Yes.

4 Q. That makes sense, right?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes, it makes sense.

7 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

12 THE WITNESS: This says unblinded, not
13 potential unblinded.

14 BY MR. BAUM:

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

17 MR. ABRAHAM: Objection.

18 THE WITNESS: That would be my
19 understanding, yes.

20 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

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

4 BY MR. BAUM:

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

6 MR. BAUM: You want to take a break.

7 THE VIDEOGRAPHER: The time is now
8 11:42 a.m. We're off the record.

9 (Brief recess.)

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

12 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

24 MR. ABRAHAM: Of which document?

1 THE WITNESS: Which document? Yes.

2 BY MR. BAUM:

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

4 MS. KIEHN: Exhibit 5.

5 BY MR. BAUM:

6 Q. -- the study report.

7 A. Okay.

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

10 A. Yep, yes.

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

13 A. Yes.

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

23 Did I read that correctly, more or less?

24 A. Yes.

1 Q. Did you write this part of the study
2 report?

3 A. I do not recall.

4 Q. Now, it says here "post-hoc analysis
5 excluding these patients supported the results from the
6 intent-to-treat analysis." That's actually untrue,
7 isn't it?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: I don't feel competent
10 enough to answer. That's a statistical
11 question.

12 BY MR. BAUM:

13 Q. Well, the post-hoc analysis had a
14 P-value of .052, correct?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Correct.

17 BY MR. BAUM:

18 Q. And it was not statistically
19 significant, correct?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: Correct.

22 BY MR. BAUM:

23 Q. So it's being not statistically
24 significant does not support the results of the intent

1 to treat analysis, does it?

2 MR. ABRAHAM: Objection.

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

5 BY MR. BAUM:

6 Q. It exceeds .050, correct?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Yes.

9 BY MR. BAUM:

10 Q. So it's not statistically significant?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: Yes.

13 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

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

19 BY MR. BAUM:

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: Yes.

1 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I don't know.

7 BY MR. BAUM:

8 Q. Do you recall any discussions about
9 that?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: No.

12 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

17 THE WITNESS: I don't know.

18 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. But not yours?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: No, not mine.

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

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

10 BY MR. BAUM:

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

13 A. Yes.

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

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Assuming those patients
20 were unblinded, yes.

21 BY MR. BAUM:

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

1 adolescents, correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: It appears to, yes.

4 BY MR. BAUM:

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

8 Would you agree that that's a
9 significant problem?

10 MR. ABRAHAM: Objection.

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

14 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

24 Q. Even if it was mischaracterized?

1 MR. ABRAHAM: Objection.

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

7 BY MR. BAUM:

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

10 MR. ABRAHAM: Objection.

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

14 BY MR. BAUM:

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

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

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

22 A. Similar, yes.

23 Q. Did you read them?

24 A. I would start with the data and the

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

3 Q. Did you ever encounter blinding
4 problems?

5 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

17 Do you see that?

18 A. Yes.

19 Q. What does that mean?

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

23 Q. That's what interpretable means?

24 A. Yes, to me.

1 Q. Do you think that statement was true?

2 A. Yes.

3 Q. If the -- if internally Forest had
4 concluded, in fact, that these patients were actually
5 unblinded, they should have been excluded; is that
6 correct?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: That would be my
9 interpretation from the wording in the
10 protocol.

11 BY MR. BAUM:

12 Q. And if those patients were excluded, the
13 conclusion regarding the citalopram outperformed
14 placebo with respect to the primary outcome measure
15 would have changed, correct?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Yes.

18 BY MR. BAUM:

19 Q. Do you know whether either Table 3.1 or
20 Table 6 evidenced clinical significance?

21 A. No.

22 Q. You don't know; is that what you're --

23 A. I don't know.

24 Q. Do you know whether there was clinical

1 significance measure administered with respect to
2 MD-18?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: I don't know.

5 BY MR. BAUM:

6 Q. Do you know how to do it?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: No, I don't.

9 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

15 THE WITNESS: No, I don't recall.

16 BY MR. BAUM:

17 Q. You don't recall the 2.9 number?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I saw that yesterday.

20 BY MR. BAUM:

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: No.

1 BY MR. BAUM:

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

4 A. Yes.

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

7 A. I don't recall.

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

10 A. Yes.

11 Q. And you reviewed it for accuracy?

12 A. Yes.

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

15 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

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

4 A. No.

5 Q. Whose job was that?

6 MR. ABRAHAM: Objection.

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

9 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Yes.

21 BY MR. BAUM:

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

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

2 MR. ABRAHAM: Objection.

3 THE WITNESS: Yes.

4 BY MR. BAUM:

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

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

11 Q. You saw the black box warning?

12 MR. ABRAHAM: Objection.

13 BY MR. BAUM:

14 Q. Have you read it?

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

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

19 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

1 Q. Okay. You are aware that there is a
2 suicidality problem with respect to Celexa from the
3 94404 study, correct?

4 MR. ABRAHAM: Objection.

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

7 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

12 THE WITNESS: Yes, that's my
13 recollection.

14 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Yes.

20 BY MR. BAUM:

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: I don't know.

1 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I don't know.

7 BY MR. BAUM:

8 Q. Do you know if -- okay.

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

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

14 A. I recall they did not at Week 8.

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

17 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

24 Q. They're kind of like cross-checks

1 against the main result?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I wouldn't quite put it

4 that way.

5 BY MR. BAUM:

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

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

11 Q. Are they important at all?

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

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

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

7 BY MR. BAUM:

8 Q. They were negative as well?

9 A. Yes.

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

12 A. No.

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

15 A. No, I don't know.

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

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I believe so.

20 BY MR. BAUM:

21 Q. What are observed cases?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: I'm not sure.

24 BY MR. BAUM:

1 Q. Do you know what LOCF is?

2 A. Yes.

3 Q. What is LOCF?

4 A. Last observation carried forward.

5 Q. What does that mean?

6 A. So if a patient drops out and you don't
7 have a measurement at Week 8, you take whatever the
8 last observation was and apply that to the Week 8
9 analysis.

10 Q. And observed cases is the people who
11 actually finished the trial; does that ring a bell?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: It may be, yes.

14 BY MR. BAUM:

15 Q. Do you know why studies wouldn't just
16 use the observed cases if people actually finished?
17 It's kind of artificial to use the last observations
18 carried forward, isn't it?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Again, not an expert in
21 the area, but my understanding is that you want
22 to -- you don't want to risk excluding
23 patients -- data from patients who maybe drop
24 out due to adverse events or for administrative

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

3 BY MR. BAUM:

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

7 MR. ABRAHAM: Objection.

8 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

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

14 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

24 Q. Used rating scales from earlier weeks,

1 right?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: Yes.

4 BY MR. BAUM:

5 Q. Rating scale results, rather?

6 A. Yeah.

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

12 MR. ABRAHAM: Objection.

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

15 THE WITNESS: Yeah, I think --

16 BY MR. BAUM:

17 Q. It's protocol, Page 2.

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

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

1 A. Yes.

2 Q. And what was the P-value there?

3 A. 0.257.

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Correct.

8 BY MR. BAUM:

9 Q. So citalopram failed to outperform
10 placebo with respect to -- significant -- let me say it
11 again.

12 Citalopram failed to significantly
13 outperform placebo on the CGI Improvement scale,
14 correct?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: That would appear to be
17 the case.

18 BY MR. BAUM:

19 Q. So it was negative for efficacy,
20 correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. Let's go to Page 102, which is, I

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

4 Do you see that?

5 A. Yes.

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

7 Do you see that?

8 A. Yes.

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

11 MR. ABRAHAM: Objection.

12 THE WITNESS: No, it is not.

13 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

17 THE WITNESS: At Week 8, yes.

18 BY MR. BAUM:

19 Q. At Week 8, correct.

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

22 Do you see that?

23 A. Yes.

24 Q. And this is another secondary efficacy

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

3 Do you see that?

4 A. Yes.

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

6 Do you see that?

7 A. Yes.

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: No, it was not.

12 BY MR. BAUM:

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

15 MR. ABRAHAM: Objection.

16 THE WITNESS: At Week 8, yes.

17 BY MR. BAUM:

18 Q. At Week 8, right.

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

23 Do you see that?

24 A. Yes.

1 Q. And the P-value there is .105; is that
2 correct?

3 A. Yes.

4 Q. And that's greater than .05 as well,
5 right?

6 A. Correct.

7 Q. So that's not statistically significant
8 either, right?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: At Week 8.

11 BY MR. BAUM:

12 Q. At Week 8, correct?

13 A. Correct.

14 Q. So the secondary endpoint of K-SADS
15 Depression Module was negative for efficacy at Week 8,
16 correct?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

20 Q. So isn't it true that all of the
21 prespecified secondary endpoints as listed in MD-18's
22 protocol were negative for efficacy, right, correct?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: At Week 8.

1 BY MR. BAUM:

2 Q. At Week 8, correct.

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

5 Do you see that?

6 A. Yes.

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

12 Do you see that?

13 A. Yes.

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

20 Do you see that?

21 A. Where are you?

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

1 A. Oh, I'm sorry, yes.

2 Q. So you see that first sentence that says
3 that the P value was .038?

4 A. Yes.

5 Q. And "the citalopram group exhibited
6 significantly greater improvement than the placebo
7 group at Week 1 and subsequent clinical visits."

8 Do you see that?

9 A. Yes.

10 Q. Then it shifts down to there were also
11 significant differences in the -- greater improvement
12 in the secondary outcome measures, right?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

16 Q. Then it says, statistically significant
17 effects were not found as consistently across study
18 time points for the secondary efficacy parameters as
19 for the primary efficacy parameter, but numerically
20 greater improvement in citalopram group was observed on
21 every efficacy parameter at every clinic visit in both
22 LOCF and OC analysis, correct?

23 A. Yes.

24 Q. So those two or three sentences there

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

3 MR. ABRAHAM: Objection.

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

6 BY MR. BAUM:

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Correct.

12 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

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

23 MR. ABRAHAM: Objection.

24 THE WITNESS: It obviously could have

1 been worded differently.

2 BY MR. BAUM:

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

6 A. No.

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

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

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Correct.

15 BY MR. BAUM:

16 Q. And do you know who drafted this
17 language?

18 A. I do not know.

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: No, I don't know.

23 BY MR. BAUM:

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

1 to focus on them; is that right?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I don't know.

4 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: No, I don't recall.

11 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I don't know.

15 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

1 the prior week's positive outcomes?

2 MR. ABRAHAM: Objection.

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

5 BY MR. BAUM:

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

8 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

17 Do you see that?

18 A. Yes.

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

21 A. Yes.

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

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

3 Do you see that?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Yes.

6 BY MR. BAUM:

7 Q. Did you write that section?

8 A. I don't recall.

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

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

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

16 A. Yes.

17 Q. And it's .167?

18 A. Yes.

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I would say not.

23 BY MR. BAUM:

24 Q. And so the difference at Week 8 between

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

4 MR. ABRAHAM: Objection.

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

7 BY MR. BAUM:

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

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

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. At Week 8 it was negative, correct?

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

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Well, we didn't go over
8 the data from all of the weeks, but I'm sure if
9 we did, we would find it was positive at Weeks
10 1, 4 and 6.

11 BY MR. BAUM:

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

15 MR. ABRAHAM: Objection.

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

18 BY MR. BAUM:

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

20 A. Correct.

21 Q. And so focusing on the positive 1, 4 and
22 6 weeks and not mentioning the negative Week 8 was a
23 material omission; don't you think?

24 MR. ABRAHAM: Objection.

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

6 BY MR. BAUM:

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

8 MR. ABRAHAM: Objection.

9 BY MR. BAUM:

10 Q. It's the endpoint, right?

11 A. Yes, it's the endpoint.

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

14 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

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

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

23 Q. Well, I appreciate that.

24 Why do you think that that's correct to

1 omit the Week 8 negative results in this section?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: It's implied here.

4 BY MR. BAUM:

5 Q. Okay.

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

7 Q. Okay. All right. So let's go to Page

8 84. This is the overall conclusion.

9 Do you see that?

10 A. Yes.

11 Q. The results of this study support the
12 conclusion that citalopram 2-4 -- oh, that's probably
13 20 to 40 milligrams a day?

14 A. Yeah.

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

18 Did I read that correctly?

19 A. Yes, you did.

20 Q. Is that actually true?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Certainly, in the primary
23 endpoint.

24 BY MR. BAUM:

1 Q. So that would be a result, correct?

2 A. Well, that was the prespecified primary
3 endpoint, the whatever --

4 Q. Including -- if you included the --

5 A. The nine patients.

6 Q. The nine patients, right?

7 A. Correct.

8 Q. So that's the only positive endpoint
9 amongst any of the endpoints measuring efficacy in
10 MD-18, correct?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: It was the primary
13 endpoint.

14 BY MR. BAUM:

15 Q. It was the only one? If you took out
16 the eight patients, it was negative, correct?

17 A. The P-value was greater than .5, yes.

18 MR. ABRAHAM: Objection.

19 BY MR. BAUM:

20 Q. And so that was negative, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. And all four of the secondary endpoints

1 were negative, correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: At Week 8, yes.

4 BY MR. BAUM:

5 Q. At Week 8, right.

6 And observed cases was negative at Week

7 8, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: At Week 8, yes.

15 BY MR. BAUM:

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

20 MR. ABRAHAM: Objection.

21 THE WITNESS: Well, at Week 8, yes.

22 BY MR. BAUM:

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

1 6 with them out made a difference in the outcome of the
2 MD-18s being negative or positive, correct?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: It appears to, yes.

5 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Yes.

18 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

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

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

5 A. The study met its primary endpoint.

6 Q. Overall?

7 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

15 MR. ABRAHAM: Objection.

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

18 On the secondary outcome measures.

19 BY MR. BAUM:

20 Q. At Weeks 1, 4, 6?

21 A. Yes, yeah.

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

24 MR. ABRAHAM: Objection.

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

3 BY MR. BAUM:

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

6 MR. ABRAHAM: Objection.

7 BY MR. BAUM:

8 Q. The endpoint was Week 8?

9 A. Yes.

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

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes, that's my
15 understanding.

16 BY MR. BAUM:

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

20 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

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

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

3 MR. ABRAHAM: Objection, asked and
4 answered.

5 THE WITNESS: Do I have to answer?

6 MR. ABRAHAM: You can answer.

7 THE WITNESS: Can you repeat it?

8 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection, asked and
13 answered.

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

17 BY MR. BAUM:

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

19 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

24 Q. Would you -- if you were responsible for

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

3 MR. ABRAHAM: Objection.

4 THE WITNESS: Potentially, yes.

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

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

9 BY MR. BAUM:

10 Q. Six, and this is MDL-FORP0175697, an
11 e-mail from Paul Tiseo to Joan Barton dated March 2nd,
12 2000, Re: CIT-18, and this is what we were discussing
13 earlier today.

14 You've seen this before, correct?

15 A. I saw it yesterday for the first time.

16 Q. Oh, you had never seen it before?

17 A. No.

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

20 A. Yes.

21 Q. Do you recall her position at Forest?

22 A. I believe she was in regulatory affairs.

23 Q. What does that mean?

24 A. Regulatory affairs is the group that's

1 responsible for interactions with the regulatory
2 authorities.

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

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Yes, I would say so.

8 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

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

18 BY MR. BAUM:

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

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

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

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

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

10 Did I read that right?

11 A. Yes.

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

13 A. Yes.

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

16 A. I believe so.

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

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

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

23 A. Just over a month, yeah.

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

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

3 A. Yes.

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

6 A. I have no idea.

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

10 Do you see that?

11 A. Yes.

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

13 A. Yes.

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

16 A. Yes.

17 Q. So that was an important message,
18 correct?

19 A. I would say so.

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

24 A. Yes.

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

6 Do you see that?

7 A. Yes.

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know.

12 BY MR. BAUM:

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

16 A. Yes, it does say that.

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

19 MR. ABRAHAM: Objection.

20 BY MR. BAUM:

21 Q. They were Celexa?

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

24 Q. Was there any other interpretation you

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

4 MR. ABRAHAM: Objection.

5 BY MR. BAUM:

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

9 MR. ABRAHAM: Objection.

10 THE WITNESS: It appears from this, yes.

11 BY MR. BAUM:

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

15 Do you see that?

16 A. Yes.

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

19 A. Yes, it says that.

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

22 MR. ABRAHAM: Objection.

23 THE WITNESS: It says would
24 automatically unblind the study.

1 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Can we talk?

7 BY MR. BAUM:

8 Q. No, you can't.

9 A. Okay. Can you repeat the question.

10 MR. BAUM: Can you read it back.

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

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

15 BY MR. BAUM:

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

19 Can you answer my question?

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

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

24 THE WITNESS: I guess yes.

1 BY MR. BAUM:

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

5 Did I read that correctly?

6 A. Yes.

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know.

12 BY MR. BAUM:

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

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Yes.

18 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

22 THE WITNESS: If they were unblinded,
23 yes.

24 BY MR. BAUM:

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

5 MR. ABRAHAM: Objection.

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

8 BY MR. BAUM:

9 Q. And the investigators would know that?

10 MR. ABRAHAM: Objection.

11 BY MR. BAUM:

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

14 MR. ABRAHAM: Objection.

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

17 BY MR. BAUM:

18 Q. So they were unblinded as well, correct?

19 MR. ABRAHAM: Objection.

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

22 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

2 THE WITNESS: I defer to the
3 statistician on that.

4 BY MR. BAUM:

5 Q. What do you think?

6 MR. ABRAHAM: Objection.

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

12 BY MR. BAUM:

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

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

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

22 A. Yes.

23 Q. Do you think they made pink placebo
24 tablets?

1 A. I don't know.

2 Q. It doesn't say that here, does it?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: No, it doesn't say that
5 here.

6 BY MR. BAUM:

7 Q. Okay. Do you know who Paul Tiseo was,
8 right?

9 A. Yes.

10 Q. Do you think he would have known more
11 about this than you?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: Yes, far more.

14 BY MR. BAUM:

15 Q. And he's saying right here that they
16 were conveyed active medication, pink-colored
17 commercial Celexa tablets, instead of the standard
18 white citalopram tablets used for blinded clinical
19 trials, that says that there was active medication,
20 commercial Celexa administered, correct?

21 MR. ABRAHAM: Objection.

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

23 BY MR. BAUM:

24 Q. So if it turned out that some of these

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

3 MR. ABRAHAM: Objection.

4 THE WITNESS: I have no way of knowing
5 that.

6 BY MR. BAUM:

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

10 MR. ABRAHAM: Objection.

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

13 BY MR. BAUM:

14 Q. Well, what do you think?

15 MR. ABRAHAM: Objection.

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

18 BY MR. BAUM:

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

21 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

1 Q. What do you think?

2 MR. ABRAHAM: Objection.

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

5 BY MR. BAUM:

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

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

12 Do you see that?

13 A. Yes.

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

17 A. Correct.

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

22 MR. ABRAHAM: Objection.

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

1 patient safety.

2 BY MR. BAUM:

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

7 MR. ABRAHAM: Objection.

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

11 BY MR. BAUM:

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

17 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

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

1 MR. ABRAHAM: Objection.

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

5 BY MR. BAUM:

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

9 A. No.

10 Q. Do you know how many came back?

11 A. No.

12 Q. Do you know who would know?

13 MR. ABRAHAM: Objection.

14 You can answer.

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

18 BY MR. BAUM:

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

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

24 Q. Did you interact with anybody in the

1 clinical supply unit at Forest?

2 A. No.

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

4 MR. ABRAHAM: Objection.

5 THE WITNESS: I do not know.

6 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

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

14 BY MR. BAUM:

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

17 MR. ABRAHAM: Objection.

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

20 BY MR. BAUM:

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

24 MR. ABRAHAM: Objection.

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

7 BY MR. BAUM:

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

12 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

18 MR. ABRAHAM: Objection.

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

21 BY MR. BAUM:

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

24 Do you see that?

1 A. Yes.

2 Q. So you know it went out to those
3 investigational sites, correct?

4 A. It went out --

5 MR. ABRAHAM: Objection.

6 BY MR. BAUM:

7 Q. You just don't know who read it?

8 A. Based on this e-mail, it says it went
9 out to the investigational sites. I have no idea who
10 at the site read the memo.

11 Q. So if the investigators who were
12 administering the pills and the CDRS rating scale with
13 these patients, if they had seen the pink tablets, they
14 would have been exposed to knowing that those patients
15 were receiving Celexa while they were conducting the
16 investigation, correct?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: There's a number of
19 assumptions built into that question.

20 BY MR. BAUM:

21 Q. Okay. But answer it anyway.

22 MR. ABRAHAM: Objection.

23 THE WITNESS: If the investigators knew
24 about the pink tablets, which is not a given,

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

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

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

16 BY MR. BAUM:

17 Q. Who would have seen it?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I don't know.

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

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

24 MS. KIEHN: Almost.

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

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

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

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

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

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

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

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

18 BY MR. BAUM:

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

21 A. Correct.

22 Q. 85 and 81, do you remember that?

23 A. Yep.

24 Q. So that was enough patients to power the

1 study without the unblinded patients having been
2 included, correct?

3 MR. ABRAHAM: Objection, asked and
4 answered.

5 THE WITNESS: Yes.

6 BY MR. BAUM:

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

11 MR. ABRAHAM: Objection.

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

15 BY MR. BAUM:

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

18 A. No.

19 MR. ABRAHAM: Objection.

20 BY MR. BAUM:

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

23 A. No, I do not.

24 Q. I suppose it was investigators told

1 Forest about some pink tablets that were being
2 administered?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: I don't know.

5 BY MR. BAUM:

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

9 Do you see that?

10 A. Yes.

11 Q. We went over that a little earlier. It
12 says -- it lists patients 105, 113, 114, 505, 506, 507,
13 509, 513 and 514 as the patients who were mistakenly
14 dispensed one week of medication with potentially
15 unblinding information.

16 Is that what it says?

17 A. Yes.

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

21 MR. ABRAHAM: Objection.

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

24 BY MR. BAUM:

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

3 MR. ABRAHAM: Objection.

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

6 BY MR. BAUM:

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

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yeah, I guess so.

12 BY MR. BAUM:

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

16 A. What page is this?

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

19 A. Do I have this?

20 MR. ABRAHAM: Yeah, it should be --

21 THE WITNESS: 1215, okay, yeah.

22 BY MR. BAUM:

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

1 Do you see that?

2 A. Yes.

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

5 Do you see that?

6 A. Yes, that sounds familiar.

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

10 You see that?

11 A. Correct.

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

15 A. Okay.

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

18 MR. ABRAHAM: Objection.

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

21 BY MR. BAUM:

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

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

1 MS. KIEHN: Page 63.

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

4 BY MR. BAUM:

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

7 Do you see that?

8 A. Yes.

9 Q. And his Week 4 visit was March 9.

10 Do you see that?

11 A. Yes.

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

15 MR. ABRAHAM: Objection.

16 THE WITNESS: It would appear to be,
17 yes.

18 BY MR. BAUM:

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

22 MR. ABRAHAM: Objection.

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

1 BY MR. BAUM:

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

4 A. Okay.

5 Q. If you look at patient 513.

6 A. Okay.

7 Q. That's one of the patients that's listed
8 as having been administered the pink tablets.

9 A. Okay.

10 MR. ABRAHAM: Objection.

11 BY MR. BAUM:

12 Q. This is a patient that was in the
13 citalopram group, and do you see the patient was
14 randomized on February 9th; that's baseline.

15 Do you see that?

16 A. Yes.

17 Q. And his Week 1 visit was February 16.

18 Do you see that?

19 A. Yes.

20 Q. And the Week 2 visit was February 23rd.

21 Do you see that?

22 A. Yes.

23 Q. And the Week 4 visit was March 9.

24 Do you see that?

1 A. Yes.

2 Q. So like patient 113, patient 513 was
3 nearly four weeks into the study when Dr. Tiseo sent
4 the March 2nd memo out, correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: That appears to be the
7 case, yes.

8 BY MR. BAUM:

9 Q. So patient 513 was dispensed more than
10 one week of medication at the point that the unblinding
11 was discovered, correct?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: Appears to be, yes.

14 BY MR. BAUM:

15 Q. So yet the study report says at Page 44,
16 Section 5.3.4, "When this error was identified at the
17 beginning of the study period, all study medication
18 shipments were replaced in full with tablets of
19 identical color to remove any potential for
20 unblinding."

21 Do you see that?

22 A. Where are you now?

23 Q. Page 44.

24 A. 44 of the study report.

1 Q. Section 5.3.4.

2 A. Okay.

3 Q. It says, when this error was identified
4 at the beginning of the study period, all medication
5 shipments were replaced in full with tablets of
6 identical color to remove any potential for unblinding,
7 correct?

8 A. Yes, I see that.

9 Q. And that earlier statement that I read
10 to you said that it was in first week, correct?

11 MS. KIEHN: Objection.

12 MR. ABRAHAM: Objection.

13 BY MR. BAUM:

14 Q. It's Section 7.0, Page 63.

15 A. It does say one week of medication, yes.

16 Q. So that's not actually true, right, with
17 respect to patients 113 and 513, correct?

18 MR. ABRAHAM: Objection.

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

21 MR. BAUM: We can take a break now.

22 THE VIDEOGRAPHER: The time is now

23 approximately 1:05 p.m. This is the end of

24 Disk 2. We're off the record.

1 (Luncheon recess.)

2 THE VIDEOGRAPHER: The time is now
3 approximately 2:19 p.m. This is the beginning
4 of Disk Number 3. We're on the record.

5 (Document marked for identification as
6 Heydorn Deposition Exhibit No. 7.)

7 BY MR. BAUM:

8 Q. So we're going to move on to the next
9 exhibit, which is Exhibit 7, MDL-FORP0020561, and this
10 is a letter from Forest employee Tracey Varner to
11 Russell Katz of the FDA dated March 20th, 2000, and
12 it's Re: IND 22,368, Serial No. 217, General
13 Correspondence.

14 Have you seen this letter before?

15 A. I saw it yesterday for the first time.

16 Q. Okay. And you see it's on Forest
17 letterhead?

18 A. Yes.

19 Q. And it's to Russell Katz.

20 Do you know who Russell Katz is?

21 A. Yes.

22 Q. Who is he?

23 A. Well, he's the director of division of
24 neuropharmacological drug products, and I worked with

1 him when I was at the FDA.

2 Q. And we saw in the previous Exhibit
3 Number 6, which I want you to keep handy, by the way.

4 A. Which one is 6?

5 Q. It's the -- yeah, that March 2nd one.

6 A. Right, the Tiseo fax, okay.

7 Q. Yeah, the Tiseo, yeah. That Ms. Varner
8 was on the e-mail correspondence about the unblinding
9 problem dated March 2nd, you see that?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yeah.

12 BY MR. BAUM:

13 Q. So and do you agree that Ms. Varner was
14 in the regulatory affairs department for Forest?

15 A. Yes.

16 Q. And a letter like this going to the FDA
17 to someone like Russell Katz from Forest would be
18 written with the knowledge of other Forest management,
19 right?

20 A. Yes.

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Sorry. Yes. That would
23 be my assumption.

24 BY MR. BAUM:

1 Q. She wouldn't do it on her own?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: No, I can't imagine that
4 to be the case.

5 BY MR. BAUM:

6 Q. This is an important communication,
7 right?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes, any communication
10 with the FDA is an important communication.

11 BY MR. BAUM:

12 Q. And needs to be truthful?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

16 Q. Need to be forthright?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

20 Q. Up front?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes.

23 BY MR. BAUM:

24 Q. So this says, Dear Dr. Katz, we are

1 taking this opportunity to notify the division of
2 clinical -- of a clinical supply packaging error for
3 study -- let me start over again, sorry.

4 Dear Dr. Katz, we are taking this
5 opportunity to notify the division of a clinical supply
6 packaging error for study CIT-MD-18 (site #2 -
7 Dr. Busner and site #16 - Dr. Wagner). Due to this
8 error, medication was dispensed to eight randomized
9 patients in a fashion that had the potential to cause
10 patient bias.

11 Do you see that?

12 A. Yes.

13 Q. Did I read that correctly?

14 A. Yes.

15 Q. In the next one says -- couple
16 paragraphs down, the third paragraph from the end
17 starting with "for reporting."

18 Do you see that?

19 A. Yes.

20 Q. It says, "For reporting purposes, the
21 primary efficacy analysis will exclude the eight
22 potentially unblinded patients, with a secondary
23 analysis including them also to be conducted."

24 Did I read that correctly?

1 A. Yes, you did.

2 Q. So according to Ms. Varner, the primary
3 analysis is the one excluding the potentially unblinded
4 patients, and the one including them is the secondary
5 analysis, right?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Yes.

8 BY MR. BAUM:

9 Q. And that's the scientifically correct
10 thing to do, right?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I would say the
13 appropriate thing to do would be to do both
14 analyses, which is what was apparently planned
15 here.

16 BY MR. BAUM:

17 Q. Which one should have been primary?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Well, she's committing to
20 the primary being done without the -- excluding
21 the potentially unblinded patients.

22 BY MR. BAUM:

23 Q. That's what she and Forest told the FDA
24 they were going to do, right?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Yes.

3 BY MR. BAUM:

4 Q. And this is before they had actually the
5 trial results, correct; this is before the clinical
6 trial was concluded?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Yes.

9 BY MR. BAUM:

10 Q. And it was consistent with the MD-18
11 protocols on blinding procedure too, to not include
12 them in any efficacy analysis, right?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes, if indeed they were
15 unblind.

16 BY MR. BAUM:

17 Q. But Forest didn't actually do what
18 Ms. Varner reported to the FDA here, right?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Well, they did an analysis
21 including and excluding the patients.

22 BY MR. BAUM:

23 Q. Which one was primary?

24 A. In the report it was one including

1 blinded -- potentially unblinded patients.

2 Q. So in the report to the FDA, they did
3 not do what they said they were going to do in this
4 letter here, did they?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

8 Q. So just to be clear, the analysis
9 excluding the potentially unblinded patients
10 reported -- was reported in the study report as the
11 primary, right?

12 A. Yes.

13 Q. And -- no, that's not right.

14 The study including the potentially
15 unblinded patients was reported as primary, which is
16 the opposite of what this letter said it would do?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

20 Q. Okay. Was the analysis excluding the
21 potentially unblinded patients reported as the primary
22 analysis as conveyed in this letter what was conveyed
23 to the general medical community in posters presented
24 at medical conferences?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: All of the patients were
3 included in the posters presented at medical
4 conferences.

5 BY MR. BAUM:

6 Q. So that again was the opposite of what
7 was done pursuant to what this letter said, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

11 Q. And was the analysis excluding the
12 potentially unblinded patients reported as the primary
13 analysis as conveyed to the general medical community
14 in articles published in medical journals like the HAP?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Can you rephrase the
17 question.

18 BY MR. BAUM:

19 Q. Was the analysis that was presented in
20 the manuscript publication in the American Journal of
21 Psychiatry based on the table that had the patients
22 included or the patients excluded?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: The table with the

1 patients included.

2 BY MR. BAUM:

3 Q. That's the opposite of what this letter
4 said they were going to do to with the FDA from March
5 2nd, 2000, correct?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: So reporting purposes
8 here, I would assume relates to reporting to
9 the FDA.

10 BY MR. BAUM:

11 Q. Okay. So here they said the primary
12 efficacy analysis was going to be the analysis without
13 the patients with the dispensing error, correct?

14 A. Correct.

15 Q. And that primary analysis with the
16 patients excluded was not what was conveyed in the
17 manuscript that was published in the American Journal
18 of Psychiatry, correct?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: Correct.

21 BY MR. BAUM:

22 Q. And any CME presentations that the
23 Dr. Wagner did, correct?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I don't have any knowledge
2 of what was presented in CME procedures --
3 or -- well, CME? Continuing medical education?

4 BY MR. BAUM:

5 Q. Yeah, continuing medical education.
6 Didn't you help prepare some slides with Natasha
7 Mitchner that were used in CME?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: I prepared slides, but my
10 recollection is that was for an internal
11 advisory board meeting. I don't recall if they
12 were used in CME presentations what I'm talking
13 about.

14 BY MR. BAUM:

15 Q. Well, let's just refer to those slides
16 that you do recall?

17 A. Yeah.

18 Q. In those slides, the primary efficacy
19 presentation that you used was based on the table that
20 had the patients with the dispensing error included,
21 correct?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: Yes, that's my
24 recollection.

1 BY MR. BAUM:

2 Q. And the posters that were presented at
3 ACNP, those had the primary efficacy analysis based on
4 Table 3.1 that had the dispensing error patients
5 excluded, correct?

6 MR. ABRAHAM: Objection.

7 MR. BAUM: Included, excuse me.

8 THE WITNESS: Included.

9 MR. BAUM: Let me start over. I need to
10 ask that question again.

11 BY MR. BAUM:

12 Q. The ACNP posters included as its primary
13 efficacy analysis data analyses that had included the
14 unblinded patients, correct?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Yes.

17 BY MR. BAUM:

18 Q. And that's also inconsistent with what
19 this letter to the FDA from Tracey Varner said,
20 correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Correct, but, as I said,
23 the reporting in here I would interpret as
24 reporting to the FDA.

1 BY MR. BAUM:

2 Q. But MD-18 Study Report, Appendix 6 was
3 not used as a primary efficacy outcome measure for
4 study MD-18, correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: That's the appendix
7 excluding the eight or nine patients, correct?

8 MR. BAUM: Right.

9 THE WITNESS: Then I would say yes.

10 MS. KIEHN: Can the phone people mute
11 themselves.

12 BY MR. BAUM:

13 Q. Using Table 3.1 with the unblinded
14 patients included made study MD-18 look positive so
15 Celexa and Lexapro could be marketed to children,
16 right?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: There's a big jump from
19 results from a study report to actually being
20 able to market compounds to that population.

21 BY MR. BAUM:

22 Q. Are you aware of Study 18's manuscript
23 and the posters being circulated to physicians and
24 shown to physicians?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Well, I certainly know the
3 manuscript and the poster were generated. I
4 don't have any specific knowledge of what was
5 done on the sales force as far as distribution
6 of those posters and manuscripts.

7 BY MR. BAUM:

8 Q. The posters were presented at
9 conventions?

10 MR. ABRAHAM: Objection.

11 BY MR. BAUM:

12 Q. Medical conventions?

13 A. Yeah, I would assume so, yes, yes.

14 Q. And so some physicians saw those there,
15 didn't they?

16 A. Yes.

17 MR. ABRAHAM: Objection.

18 BY MR. BAUM:

19 Q. And wasn't the purpose to convey the
20 positive results of CIT-MD-18 to them?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Well, the purpose was to
23 convey the results of the study, both the
24 efficacy and the safety results.

1 BY MR. BAUM:

2 Q. And that was intended to affect sales at
3 some point, correct?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: I really can't comment on
6 that. I don't know.

7 BY MR. BAUM:

8 Q. They weren't doing that, these studies
9 just for fun, were they?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: The studies -- in my
12 opinion, the studies were being done primarily
13 to educate physicians who were already using
14 Celexa in children, the appropriate dosing and
15 safety procedures.

16 BY MR. BAUM:

17 Q. To let them know whether there was
18 enough efficacy to justify prescribing it despite some
19 possible negative side effects, correct?

20 MR. ABRAHAM: Objection.

21 BY MR. BAUM:

22 Q. They had to be able to weigh the pros
23 and cons?

24 A. Correct.

1 Q. And this was conveying positive things
2 in order to outweigh the negative things to encourage
3 prescription, correct?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Right. It was conveying
6 the results of the study, including the
7 potentially unblinded patients.

8 BY MR. BAUM:

9 Q. So it gave a positive spin on the data,
10 correct?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: Yes, you could say that.

13 BY MR. BAUM:

14 Q. If the -- Appendix 6 had actually been
15 used as the primary efficacy measure, would that have
16 encouraged physicians to prescribe Celexa to children
17 and adolescents?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I don't know how
20 physicians make a decision on what medications
21 to use in their patients. I'm not a practicing
22 child psychiatrist.

23 BY MR. BAUM:

24 Q. But it was a negative outcome, correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: It was not statistically
3 significant.

4 BY MR. BAUM:

5 Q. And it was not negative, correct? I
6 mean, it was not positive, it was negative, correct?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Yeah, yes.

9 BY MR. BAUM:

10 Q. Do you know how much money Forest made
11 selling Celexa and Lexapro for use by kids based on the
12 allegedly positive outcome asserted in Table 3.1?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: No.

15 BY MR. BAUM:

16 Q. You know they did make money from it,
17 though, right?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I would assume so, yes.

20 BY MR. BAUM:

21 Q. Do you know why the primary and
22 secondary analyses -- so let me make sure I don't get
23 these confused.

24 A. Okay.

1 Q. So here the primary efficacy analysis
2 will be the one with the eight potentially unblinded
3 patients excluded, correct?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Yes.

6 BY MR. BAUM:

7 Q. And the secondary analysis would be the
8 one including them, correct?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

12 Q. Do you know why that got reversed in the
13 study report?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: No, I do not.

16 BY MR. BAUM:

17 Q. Do you know who would have made that
18 decision?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: No, I do not.

21 BY MR. BAUM:

22 Q. Do you know whose responsibility it
23 might have been to make that decision?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I could assume.

2 BY MR. BAUM:

3 Q. Who would you assume?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Either Dr. Flicker,
6 Dr. Gergel or Dr. Olanoff.

7 BY MR. BAUM:

8 Q. Dr. Olanoff?

9 A. Olanoff.

10 Q. Do you know whether or not reporting the
11 positive P-value with the patients included was part of
12 a corporate objective of Forest management?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I do not know.

15 BY MR. BAUM:

16 Q. That was above your pay grade?

17 A. Yes.

18 (Document marked for identification as
19 Heydorn Deposition Exhibit No. 7A.)

20 BY MR. BAUM:

21 Q. We're going to mark this as 7A. We're
22 going to have like three or four of these that are like
23 related to this Exhibit 7.

24 And so what I've handed you is

1 MDL-FOREM0030386; is that correct?

2 A. Yes.

3 Q. And it's from Paul Tiseo to Lawrence
4 Olanoff, Ivan Gergel, Amy Rubin, Anjana Bose, Tracey
5 Varner, Julie Kilbane and Charles Flicker.

6 Do you see that?

7 A. Yes.

8 Q. Okay. Have you seen this document
9 before?

10 A. No, I don't believe so.

11 Q. As you can see, this is an e-mail from
12 Tiseo to the group I just read off, and the subject of
13 the e-mail reads "Letter to FDA for CIT-18," right?

14 A. Yes.

15 Q. And it's dated March 8, 2000, which was
16 a few days after Dr. Tiseo sent the memorandum, in
17 fact, to the clinical trial investigators informing
18 them of the dispensing error?

19 A. Yes.

20 Q. So that letter was March 2nd, this is
21 March 8, about six days later, correct?

22 A. Yes.

23 Q. So in this e-mail dated March 8,
24 Dr. Tiseo states, "Attached please find the letter that

1 Charlie and I put together for the purpose of informing
2 the FDA of our packaging mishap in the citalopram
3 pediatric study."

4 Do you see that?

5 A. Yes.

6 Q. And then Dr. Tiseo was talking about
7 Charlie Flicker, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes, that would be my
10 assumption.

11 BY MR. BAUM:

12 Q. And then attached to the e-mail, if you
13 go to the other side, is a document titled letter to
14 FDA - draft, right?

15 A. Yes.

16 Q. And if you look through the letter, this
17 appears to be an early draft of the letter that was
18 ultimately sent to the FDA by Tracey Varner concerning
19 the dispensing error that we just read in a prior
20 exhibit, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: Yes, that's what I would
23 assume.

24 BY MR. BAUM:

1 Q. So it's another letter -- it's addressed
2 to Dr. Katz, correct?

3 A. Correct.

4 Q. At the FDA, and it's regarding this same
5 problem of the eight randomized patients at two
6 investigational sites who had a dispensing error,
7 correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes.

10 BY MR. BAUM:

11 Q. So we haven't seen any other earlier
12 drafts of this e-mail?

13 A. No.

14 Q. I'm going to mark this as 7B.

15 (Document marked for identification as
16 Heydorn Deposition Exhibit No. 7B.)

17 BY MR. BAUM:

18 Q. I'm handing you what has been marked as
19 Exhibit 7B, and this is a letter to the FDA draft dated
20 March 8, 2000, Re: clinical supplies for the Pediatric
21 Depression Study CIT-MD-18.

22 You see that?

23 A. Yes.

24 Q. Have you seen that before?

1 A. This particular exhibit?

2 Q. Yeah.

3 A. No.

4 Q. Do you see that handwriting on the upper
5 part of it?

6 A. Yes.

7 Q. Do you recognize that handwriting? Is
8 that Charlie Flicker's handwriting?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes, I recognize the
11 handwriting.

12 BY MR. BAUM:

13 Q. Is it Charlie Flicker's?

14 A. Yes.

15 Q. Okay. So in the typed portion of the
16 letter it says, "Dear Dr. Katz, the purpose of this
17 letter is to inform the agency that an error was made
18 during the packaging of the clinical supplies for the
19 above-noted study."

20 Do you see that?

21 A. Yes.

22 Q. "Two of our investigational sites called
23 in to report that some of their patients were receiving
24 white tablets and others were receiving pink tablets."

1 Do you see that?

2 A. Yes.

3 Q. "These reports were passed on to Forest
4 Clinical Packaging where it was discovered that a
5 number of bottles of 'active' medication were
6 mistakenly packed with the pink-colored commercial
7 Celexa tablets instead of the standard white citalopram
8 tablets used for blinded clinical studies."

9 Did I read that correctly?

10 A. Yes.

11 Q. So based on this letter, it appears the
12 dispensing error was discovered after two clinical
13 investigators called Forest inquiring about why some of
14 their patients were receiving white tablets and others
15 were receiving pink ones, right?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Well, two investigational
18 sites.

19 BY MR. BAUM:

20 Q. Okay. Does that provide a little bit
21 more information about how Forest found out about the
22 dispensing error?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: Yeah. I was not aware of

1 this, yeah, apparently a couple sites contacted
2 Forest about this.

3 BY MR. BAUM:

4 Q. The letter also indicates that a number
5 of bottles given to patients were mistakenly packed
6 with pink-colored commercial Celexa tablets, right?

7 A. Yes.

8 MS. KIEHN: Where is that?

9 BY MR. BAUM:

10 Q. It says, "Two of our investigational
11 sites called in to report that some of their patients
12 were receiving white tablets and others were receiving
13 pink tablets. These reports were passed on to Forest
14 Clinical Packaging where it was discovered that a
15 number of bottles of 'active' medication were
16 mistakenly packed with pink-colored commercial Celexa
17 tablets," so that's correct?

18 A. Yes.

19 Q. So they were provided pink-colored
20 commercial Celexa tablets, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: That's what it says here,
23 yeah.

24 BY MR. BAUM:

1 Q. So there was a question that we had a
2 little earlier whether they were pink placebo versus
3 pink Celexa; is that correct? Do you remember that?

4 A. Yes.

5 Q. This says it was pink Celexa, correct?

6 A. This would appear to say that, yes.

7 Q. So anybody who got those pink tablets
8 and consumed them received commercial Celexa at the
9 time, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Any patient that got a
12 pink tablet apparently got commercial Celexa
13 tablets, yes.

14 BY MR. BAUM:

15 Q. Okay. And if an investigator sees that
16 some patients are receiving white tablets and others
17 are receiving pink tablets, pink-colored commercial
18 Celexa tablets, wouldn't that, at the very least,
19 compromise the investigator's blind?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: I don't know what the
22 investigators were thinking. There's no
23 reason -- there's potential that they would
24 just notice that there were two different

1 colored tablets and that they wouldn't know
2 which were the active and which were the
3 placebo.

4 BY MR. BAUM:

5 Q. Well, by the time they got the March 2nd
6 letter, they probably knew, didn't they?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Well, obviously, I don't
9 know what any of the investigators were
10 thinking, but that would not be an unreasonable
11 conclusion.

12 BY MR. BAUM:

13 Q. Okay. If an investigator knows which
14 patients are taking branded Celexa and which ones are
15 taking white pills, doesn't that mean the integrity of
16 the blind was mistakenly -- unmistakably compromised?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: It does raise questions
19 about the integrity of the blind, yes.

20 BY MR. BAUM:

21 Q. Okay. So the letter continues, "On
22 March 2nd, all sites were notified of this error by
23 telephone and by fax."

24 Do you see that?

1 A. Yes.

2 Q. And that appears to be referring to
3 the -- you know, this other exhibit that we just were
4 talking about, correct?

5 A. Yes, Dr. Tiseo's fax.

6 Q. Dated March 2nd.

7 And in the fax memorandum, Dr. Tiseo
8 states that dispensing the pink-colored medication
9 would automatically unblind the study.

10 Do you recall that?

11 A. Yes.

12 Q. Now, if you look at the bottom of this
13 page, the last paragraph, next to last paragraph says,
14 "As only 8 of 160 patients had been randomized at the
15 time this error was discovered, the impact upon the
16 integrity of the study is suggested to be minimal. In
17 addition, these eight patients were restricted to only
18 two investigational sites (a total of 19 sites are
19 involved)."

20 Do you see that?

21 A. Yes.

22 Q. So in this draft there's no statement
23 that Forest will exclude unblinded patients from the
24 primary efficacy analysis, right?

1 A. Yes.

2 Q. Okay. Now, if you go up to the top
3 here, you see the handwriting?

4 A. Yes.

5 Q. Okay. So it says "reconsider, no
6 letter. Otherwise I recommend much less narrative,
7 more concise."

8 Do you see that?

9 A. Yes.

10 Q. And then colon, due to a packing error,
11 8 randomized patients at 3 investigational sites had
12 access to potentially unblinding information.

13 Do you see that?

14 A. Yes.

15 Q. Drug has been repackaged and a full
16 complement after 160 additional patients will be
17 enrolled under standard double-blind conditions. For
18 reporting purposes, the primary efficacy analysis will
19 exclude the potentially unblinded patients, and
20 secondary analysis including them will be conducted.
21 These patients will be included in all safety analyses.

22 Do you see that?

23 A. Yes.

24 Q. So it would appear that Dr. Flicker is

1 suggesting that the letter specify that the unblinded
2 patients will be excluded from the primary efficacy
3 analysis, correct?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: That would be a conclusion
6 from this letter, yes.

7 BY MR. BAUM:

8 Q. Okay. So let's go back to Deposition
9 Exhibit 7A, and if you look at the draft, do you see
10 that the language about excluding the 8 potentially
11 unblinded patients -- oh, wait a second.

12 Yes, if you look on this draft that's on
13 the back of Exhibit 7A.

14 A. Yes.

15 Q. If you look at the second paragraph,
16 "For reporting purposes, the primary efficacy analysis
17 will exclude the eight potentially unblinded patients,
18 with a secondary analysis including them also to be
19 conducted. All patients will be included in the safety
20 analysis."

21 Do you see that?

22 A. Yes.

23 Q. So that appears to be a typed-up version
24 of what Dr. Flicker was recommending, correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: It would appear to be
3 that, yes.

4 BY MR. BAUM:

5 Q. And so on 7A, the second paragraph where
6 it says, dear all, I mean it says, "Please review and
7 send your comments back to me within the next few days.
8 I will compile the corrections here and then send this
9 final letter to NJO for final regulatory review."

10 A. Yes.

11 Q. Do you know who -- what NJO refers to?

12 A. The New Jersey office.

13 (Document marked for identification as
14 Heydorn Deposition Exhibit No. 7C.)

15 BY MR. BAUM:

16 Q. Okay. I'm going to mark the next
17 exhibit as 7C, and this is Bates numbered
18 MDL-FOREM0030384, and it's from Amy Rubin to Lawrence
19 Olanoff, Ivan Gergel, Anjana Bose, Paul Tiseo, Tracey
20 Varner, Julie Kilbane and Charles Flicker, correct?

21 A. Yes.

22 Q. And you recognize all those names as
23 Forest employees?

24 A. Yes.

1 Q. Forest executives?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: They were not all Forest
4 executives.

5 BY MR. BAUM:

6 Q. Who were the Forest executives?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Well, Lawrence Olanoff was
9 the overall head of research and development.

10 BY MR. BAUM:

11 Q. Okay. Ivan Gergel?

12 A. Ivan Gergel was vice president of
13 clinical research, something like that, don't know,
14 don't remember.

15 Q. So he was a vice president?

16 A. I believe so. I am not sure.

17 Q. All right. So this one is dated
18 March 9th, 2000.

19 Do you see that?

20 A. Yes.

21 Q. And that's the day after this other one
22 that was sent out 7B, correct?

23 A. Correct.

24 Q. This appears to be an e-mail response to

1 Dr. Tiseo's e-mail from Amy Rubin, right?

2 A. Yes.

3 Q. So Dr. Tiseo was soliciting comments,
4 and then this is Amy Rubin's response to his request
5 for comments?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Yes, it appears to be that
8 way. Taking a step back, I have no idea when
9 Exhibit 7B was sent out.

10 BY MR. BAUM:

11 Q. Okay. 7A. Sorry.

12 A. 7A, okay, yes.

13 Q. 7A requested?

14 A. Yes, yes.

15 Q. Thanks for clarifying.

16 A. Okay, okay.

17 Q. So here Ms. Rubin states, "Paul, I have
18 taken the liberty of editing your letter as follows:
19 Please make any other changes you feel are necessary."

20 Do you see that?

21 A. Yes.

22 Q. So Amy Rubin was in regulatory affairs;
23 is that correct?

24 A. That's my recollection, yes.

1 Q. And that again was a person who was
2 involved with sending and receiving correspondence or
3 communicating with the FDA between Forest and the FDA,
4 correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Well, the regulatory
7 affairs group is responsible for that. What
8 each individual within the department did, I
9 don't specifically recall.

10 BY MR. BAUM:

11 Q. But they were responsible for making
12 sure that the information that was conveyed to the FDA
13 was accurate, truthful, forthcoming, up front, correct?

14 A. Yes.

15 MR. ABRAHAM: Objection.

16 BY MR. BAUM:

17 Q. And so as you look down, you see she
18 appears to have like pasted in some edits, and so it
19 starts with -- at the bottom of Page 1, it goes, "Dear
20 Dr. Katz, we are taking this opportunity to notify the
21 division of a clinical supply packaging error."

22 Do you see that?

23 A. Yes.

24 Q. Then below she appears -- and she leaves

1 the sites kind of blank, right; do you notice that?

2 A. Yes.

3 Q. And then it goes, due to this error,
4 medication was dispensed to eight randomized patients
5 in a fashion that had the potential to cause patient
6 bias.

7 Do you see that?

8 A. Yes.

9 Q. Now, if you compare that sentence with
10 the sentence that was in the first draft sent by
11 Dr. Tiseo, which is 7A?

12 A. Okay.

13 Q. It appears Ms. Rubin changed the
14 sentence from eight randomized patients at two
15 investigational sites were dispensed medication that
16 could have potentially unblinded the study, that's what
17 the 7A says, correct, the earlier Dr. Tiseo's draft?

18 A. Yes.

19 Q. And switched that to medication was
20 dispensed to eight randomized patients in a fashion
21 that had the potential to cause patient bias.

22 Do you see that?

23 A. Yes.

24 Q. That phrase "potential to cause patient

1 bias" is misleading; isn't it?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: No, I don't necessarily

4 think so. I'm not sure.

5 BY MR. BAUM:

6 Q. Well, isn't it true that the integrity

7 of the blind was unmistakably violated?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: I don't know.

10 BY MR. BAUM:

11 Q. Well, Dr. Tiseo's March 2nd letter said

12 it was automatically unblinded for those patients that

13 received those tablets, correct?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: That's what Dr. Tiseo

16 said, yes.

17 BY MR. BAUM:

18 Q. So by using the phrase potential to

19 cause patient bias, Forest is not exactly being up

20 front with the FDA, are they?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: No, I wouldn't agree

23 there. I think causing patient bias is

24 potentially an accurate description of what

1 happened here.

2 BY MR. BAUM:

3 Q. Well, that's quite a bit different than
4 saying it was automatically unblinded, right?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: If you compare it to the
7 facts, yes, that's a different statement.

8 BY MR. BAUM:

9 Q. So wouldn't a potential to cause patient
10 bias be a euphemism for automatically unblinded?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I don't know what Amy
13 meant when she wrote this.

14 BY MR. BAUM:

15 Q. It's quite a bit different than
16 automatically unblinded, correct?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: I don't know if it's quite
19 a bit different.

20 BY MR. BAUM:

21 Q. But it's different?

22 A. It's different.

23 Q. And it's different to say unmistakably
24 unblinded versus potentially unblinded, correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: I would say yes.

3 BY MR. BAUM:

4 Q. So if it was unmistakably unblinded,
5 that would mean that those patients should not be
6 included in an analysis for the primary efficacy
7 measure, correct?

8 MR. ABRAHAM: Objection.

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

11 BY MR. BAUM:

12 Q. Well, as a person of your background in
13 FDA review and your experience in the pharmaceutical
14 industry, what would be the right thing to do?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Well, the analysis should
17 be done both including and excluding those
18 patients.

19 BY MR. BAUM:

20 Q. And the primary efficacy measure should
21 exclude those patients, correct?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: I think you can make an
24 argument either way. I think you can make the

1 argument either way.

2 BY MR. BAUM:

3 Q. Well, they told the FDA they were going
4 to exclude them, correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

8 Q. Isn't that the appropriate thing to have
9 done?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Well, they were excluded
12 in the analysis that was done in the -- that
13 analysis was included in the CIT-MD-18 study
14 report.

15 BY MR. BAUM:

16 Q. But in the study report, it wasn't part
17 of the primary efficacy measure. They made the primary
18 efficacy measure include them; that's different, isn't
19 it?

20 A. Yes.

21 MR. ABRAHAM: Objection.

22 BY MR. BAUM:

23 Q. And if they followed what they said and
24 if they followed what should have been done with

1 unmistakenly unblinded patients, they ought not to have
2 included them in the primary efficacy measure, right?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: Yes, certainly what was
5 communicated to the FDA and what was done in
6 the study report are not consistent.

7 MR. BAUM: Let's go to the next exhibit,
8 7D.

9 (Document marked for identification as
10 Heydorn Deposition Exhibit No. 7D.)

11 BY MR. BAUM:

12 Q. And this is MDL Bates number
13 FOREM0030359 from Charles Flicker to Amy Rubin and cc'd
14 to Paul Tiseo. It's dated March 14, 2000.

15 You see that?

16 A. Yes.

17 Q. Have you seen that document before?

18 A. No, I have not.

19 Q. This is -- this looks to be Charlie
20 Flicker's response to Rubin's edits to the FDA letter.

21 Do you see that?

22 A. Yes.

23 Q. All right. So in this e-mail,
24 Dr. Flicker writes, "Although 'potential to cause bias'

1 is a masterful stroke of euphemism, I would be a little
2 more upfront about the fact that the integrity of the
3 blind was unmistakably violated."

4 Do you see that?

5 A. Yes.

6 Q. So Dr. Flicker has directly involved --
7 was directly involved in the resolving -- let me say
8 that again.

9 Dr. Flicker was directly involved in
10 resolving the dispensing error issue, wasn't he?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: What do you mean by
13 "resolving the dispensing error"?

14 BY MR. BAUM:

15 Q. He's helping write what's going to be
16 sent to the FDA, right?

17 A. Yes.

18 Q. And he was closer to the situation than
19 you were, right?

20 A. Yes.

21 Q. According to Dr. Flicker, using the
22 phrase potential to cause patient bias in the letter to
23 the FDA is a masterful stroke of euphemism, isn't it?

24 A. Yes.

1 Q. And according Dr. Flicker, use of the
2 phrase "potential to cause bias" is not being up front
3 with the FDA, is it?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: I don't know what he was
6 thinking, but that's what's written here, yes.

7 BY MR. BAUM:

8 Q. And, according to Dr. Flicker, Forest
9 should just be upfront about the fact that the
10 integrity of the blind was unmistakably violated,
11 right?

12 A. Yes.

13 Q. And, ultimately, the phrase "potential
14 to cause bias" ended up in the letter that Forest sent
15 to the FDA; isn't that true?

16 A. Yes.

17 Q. Now, if there was unmistakably -- if the
18 blind was unmistakably violated, those patients should
19 not have been included in the primary efficacy measure,
20 correct?

21 MR. ABRAHAM: Objection, asked and
22 answered.

23 THE WITNESS: Yes.

24 BY MR. BAUM:

1 Q. You've got the Varner letter there in
2 front of you, right?

3 A. Yes.

4 Q. That's Exhibit 7?

5 A. Seven, yes.

6 Q. Now, having seen this e-mail from
7 Dr. Flicker and the fax from Dr. Tiseo, would you agree
8 that the patients who were subject to the dispensing
9 error were actually unblinded?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know for a fact,
12 but that's the implication from these letters,
13 yes.

14 BY MR. BAUM:

15 Q. Does it concern you that the clinical
16 medical director at the time, Dr. Flicker, believes
17 that the letter being sent to the FDA contains a
18 masterful stroke of euphemism?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I don't know what his
21 frame of mind was when he wrote that.

22 BY MR. BAUM:

23 Q. But they had the obligation to be
24 upfront, truthful and honest with the FDA, correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Yes.

3 BY MR. BAUM:

4 Q. And this shows that they weren't,
5 correct?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: He apparently had some
8 concerns about this, yes.

9 BY MR. BAUM:

10 Q. Well, it was more than just concerns.
11 He said it was unmistakably unblinded, and they said it
12 had the potential for bias; that's a misrepresentation,
13 isn't it?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: It's a misrepresentation
16 of what Charlie Flicker thought should be
17 communicated to the FDA.

18 BY MR. BAUM:

19 Q. Did Dr. Flicker ever tell you directly
20 that the integrity of the blind was unmistakably
21 violated because of the dispensing error?

22 A. No.

23 Q. In all your interactions with him while
24 working on the study report, he never said that to you?

1 A. I don't recall him ever saying that to
2 me, no.

3 Q. Does it bother you that Forest never
4 told the FDA that the integrity of the blind was
5 unmistakenly violated because of the dispensing error?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: No, I think this is
8 nuances around words, to be perfectly honest.

9 BY MR. BAUM:

10 Q. Was it Amy Rubin's job to create
11 masterful euphemisms in letters to the FDA?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: I do not know Amy Rubin's
14 job description.

15 BY MR. BAUM:

16 Q. Well, she was in regulatory affairs,
17 right?

18 A. Yes.

19 Q. Isn't it true that she uses the phrase
20 potential to cause patient bias because it is her job
21 to protect marketing and medical using masterful
22 euphemisms?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: I don't know why she used

1 those terms.

2 MR. BAUM: I'm going to mark this as 7E.

3 (Document marked for identification as

4 Heydorn Deposition Exhibit No. 7E.)

5 BY MR. BAUM:

6 Q. And this is MDL-FOREM0030382, and it's
7 from Amy Rubin to Charlie Flicker and CC to Paul Tiseo.
8 It's dated March 15th, 2000, "Re[3]: Letter to FDA for
9 CIT-18."

10 Do you see that?

11 A. Yes.

12 Q. This appears to be Ms. Rubin's response
13 to Dr. Flicker's e-mail to her, right?

14 A. Yes.

15 Q. And she says -- it's dated right the
16 next day, actually, correct?

17 A. It's dated the 15th.

18 Q. I think the other was the 14th?

19 A. Fourteenth, okay, yes, all right.

20 Q. Ms. Rubin responds, "Thanks for the
21 compliment. Part of my job is to create 'masterful'
22 euphemisms to protect Medical and Marketing."

23 Do you see that?

24 A. Yes.

1 Q. In your opinion, do you think it is
2 appropriate for Ms. Rubin to be creating masterful
3 euphemisms to protect medical and marketing in her
4 communications with the FDA?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: No, it's not part of her
7 job.

8 BY MR. BAUM:

9 Q. Ms. Rubin is bragging about misleading
10 the FDA, isn't she?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I don't know what her
13 frame of mind was when she wrote this.

14 MR. BAUM: Just we have -- we're going
15 to put this version of the study report that
16 Kristin provided to us earlier, MDL-FORP0073423
17 into the record as 5A.

18 (Document marked for identification as
19 Heydorn Deposition Exhibit No. 5A.)

20 MR. BAUM: Okay. We're going to hand
21 you what we're going to mark as Exhibit 8.

22 (Document marked for identification as
23 Heydorn Deposition Exhibit No. 8.)

24 BY MR. BAUM:

1 Q. And this is MDL-FORP0168046.

2 Do you see that?

3 A. Yes.

4 Q. And this is an e-mail from Joan Barton
5 to Paul Tiseo, Charles Flicker, Joan Howard, Jane Wu,
6 Carlos Cobles, dated December 6, 2000, Re: CIT-MD-18
7 Study Drug.

8 Have you seen this document before?

9 A. I saw it yesterday.

10 Q. Who is Joan Barton?

11 A. I believe she was in clinical operations
12 at Forest.

13 Q. What was her job?

14 A. I don't know specifically what her job
15 was.

16 Q. She had something to do with MD-18
17 though?

18 A. Yes.

19 Q. Something to do with the statistics
20 related to MD-18 and reporting?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: If indeed she was in
23 operations, she was -- she would have played a
24 role in the overall management of the clinical

1 trial.

2 BY MR. BAUM:

3 Q. Okay.

4 A. I don't believe she was in statistics.

5 Q. Oh, okay. But overall management of the
6 conduct of the trial?

7 A. Yes.

8 Q. So unblinding would be a problem that
9 she would want to have to deal with, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know for a fact.

12 BY MR. BAUM:

13 Q. Or making sure that there were enough
14 patients to power the study, for instance?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Ensuring enrollment,
17 making sure appropriate supplies and study drug
18 were available.

19 BY MR. BAUM:

20 Q. Do you know who Joan Howard is?

21 A. The name is familiar, but I can't recall
22 what her exact role was.

23 Q. Jane Wu?

24 A. Again, the name is familiar. I can't

1 recall what her direct role was.

2 Q. Carlos Cobles?

3 A. That name is just very vaguely familiar.

4 Q. A statistician of some form?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I don't know.

7 BY MR. BAUM:

8 Q. Does this appear to have been a standard
9 or a routine e-mail produced in the ordinary course of
10 Forest business?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: It appears to be, yes.

13 BY MR. BAUM:

14 Q. Okay. So here this e-mail says,
15 "Attached is a table showing which patients were
16 randomized when the problem was discovered that the
17 study drug was unblinded. A total of 6 adolescents and
18 3 children had already been randomized. Please let me
19 know if this will alter the total number of children or
20 adolescent patients to be randomized for this trial."

21 Did I read that correctly?

22 A. Yes.

23 Q. Ms. Barton says that the study drug was
24 unblinded, not potentially unblinded, correct?

1 A. Yes.

2 Q. And when Ms. Barton asked if the
3 unblinded patients will alter the total number of child
4 or adolescent patients to be randomized for this trial,
5 she is questioning whether unblinded patients should be
6 excluded from the trial, correct?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: I don't know what she was
9 exactly asking.

10 BY MR. BAUM:

11 Q. Well, she's asking if it will alter the
12 total number of child or adolescent patients to be
13 randomized for this trial, correct?

14 A. Yes.

15 Q. What does that mean, to alter the total
16 number; that means that she's finding out whether we're
17 going to count these guys or not, right?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I don't know what she
20 meant by that. I could speculate that she
21 wanted to know whether the enrollment should be
22 increased to compensate for the -- here it's
23 apparently nine patients who were potentially
24 unblinded.

1 BY MR. BAUM:

2 Q. Now, she doesn't say potentially
3 unblinded, does she?

4 A. Unblinded, she said unblinded.

5 Q. And per the protocol, it would have been
6 the correct procedure at that point to not include
7 those patients for the efficacy measures, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Yes, if they were
10 unblinded.

11 BY MR. BAUM:

12 Q. Well, this says unblinded, correct?

13 A. Yes.

14 Q. Charlie Flicker said they were
15 unblinded, correct?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: What did he say? He said
18 potentially unblinded.

19 BY MR. BAUM:

20 Q. No, go back to the other -- this 7D.

21 A. 7D. Yeah.

22 Q. He says, the blind was unmistakably
23 violated, correct?

24 A. Yes.

1 Q. And you have Dr. Tiseo saying they were
2 automatically unblinded, correct?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: That's what he put in his
5 fax, yes.

6 BY MR. BAUM:

7 Q. So these three people were closer to
8 this than you were, correct?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

12 Q. And they said it was unblinded, correct?

13 MR. ABRAHAM: Objection.

14 BY MR. BAUM:

15 Q. Those patients were unblinded, correct?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: That's what they're saying
18 here, yes.

19 BY MR. BAUM:

20 Q. And per the protocol, those patients
21 should have been excluded because they were unblinded,
22 correct?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: Yes.

1 BY MR. BAUM:

2 Q. Now, when you helped draft the MD-18
3 study report, the MD-18 posters, any PowerPoints that
4 were used for CME and the publication in the American
5 Journal of Psychiatry on MD-18, were you aware that
6 Forest personnel like Tiseo and Joan Barton and Charlie
7 Flicker viewed these patients as unblinded as opposed
8 to potentially unblinded?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: No, not to my
11 recollection.

12 BY MR. BAUM:

13 Q. Do you think academics and physicians
14 exposed to the poster CME and the MD-18 journal article
15 ought to have been apprised of the unblinding issue in
16 order to fully weigh the pros and cons of prescribing
17 Celexa or Lexapro to kids?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Probably, yes.

20 BY MR. BAUM:

21 Q. The unblinding issue is at least a
22 factor a physician should weigh in evaluating whether
23 the questionable efficacy was worth the risks, right?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Yes.

2 BY MR. BAUM:

3 Q. If you turn to the attachment on the
4 next page, you will see that there's a listing of
5 patients there -- there's a listing of investigators
6 rather and then it's identifying which investigators
7 received study packaging error, right, and then how
8 many of them had randomized patients.

9 Do you see that?

10 A. Yes.

11 Q. Do you recall patients 113 and 513 that
12 we went over earlier were around three to four weeks
13 into the study when the dispensing error was
14 discovered?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: Yes.

17 BY MR. BAUM:

18 Q. And this list here is generated March 1,
19 2000.

20 Do you see that?

21 A. I see that's the date on here. I don't
22 know when it was generated.

23 Q. So the site tracking -- Study Drug
24 Packaging Error, Site Tracking - March 1, 2000.

1 Do you see that?

2 A. Right, so that was the status as of
3 March 1, 2000 is what I would interpret.

4 Q. And CIT-MD-18, according to the study
5 report we examined earlier began on January 31, 2000
6 and finished on April 10, 2001.

7 Do you recall that?

8 A. Yes.

9 Q. So Dr. Wagner knew that four patients
10 from her site were unblinded, didn't she?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I don't know what

13 Dr. Wagner knew.

14 BY MR. BAUM:

15 Q. Well, she's on this list, and her site
16 received the letter from Tiseo and shows here that two
17 adolescent patients, 513 and 514, and two children, 113
18 and 114, were amongst those that received the pink
19 Celexa tablets, correct?

20 A. Yes.

21 Q. Did she know about -- do you know
22 whether or not she knew about the five other patients
23 from the other sites who were unblinded?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: No. I don't know if she
2 knew about the four patients at her site. As
3 we discussed earlier, the investigators are not
4 necessarily involved in the day-to-day
5 activities of the study.

6 BY MR. BAUM:

7 Q. So a letter from Paul Tiseo to each of
8 the investigator sites with large, bolded urgent sent
9 to each of the investigator sites would not have gone
10 to someone like Dr. Wagner who ended up being the
11 primary author?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: I have no idea.

14 BY MR. BAUM:

15 Q. You think it's the type of thing she
16 ought to have known about?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: She should have known
19 about it, yeah.

20 BY MR. BAUM:

21 Q. Shouldn't all of the authors of the
22 publication for MD-18 in the American Journal of
23 Psychiatry known about this?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Yes.

2 BY MR. BAUM:

3 Q. And shouldn't they all have known that
4 Tiseo, Flicker and Barton considered the patients to
5 have been unblinded?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: I don't know if they
8 needed to know who within the organization
9 considered the patients unblinded.

10 BY MR. BAUM:

11 Q. Well, that some of the scientists
12 closest to the data considered it to have been
13 unblinded?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Yes.

16 MR. BAUM: Okay. Let's take a break.

17 THE VIDEOGRAPHER: The time is now
18 approximately 3:17 p.m. We're off the record.

19 (Brief recess.)

20 THE VIDEOGRAPHER: The time is now
21 3:41 p.m. This is the beginning of Disk Number
22 4. We're on the record.

23 (Document marked for identification as
24 Heydorn Deposition Exhibit No. 9.)

1 BY MR. BAUM:

2 Q. Okay. I'm handing to you what's marked
3 as Exhibit Heydorn-9, MDL-FOREM0028291, and it's an
4 e-mail exchange involving you and Natasha Mitchner and
5 Evelyn Kopke, Gundula LaBadie and then Charles Flicker,
6 James Jin, Jane Wu.

7 And there's -- the top e-mail says it's
8 from you to Natasha Mitchner.

9 Have you seen this before?

10 A. Since I wrote it, I assume I have.

11 Q. Does it appear to have been produced in
12 the ordinary course of Forest business?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: Yes.

15 BY MR. BAUM:

16 Q. Do you recall who Natasha Mitchner was?

17 A. She was one of the writers at BSMG, then
18 Prescott Communications, a medical communications firm
19 that we worked with.

20 Q. In her deposition she said she was a
21 ghost writer for the MD-18 drafts.

22 Would you agree with that
23 characterization?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I don't agree with the
2 term ghost writers. They assisted us in
3 drafting the first draft of the manuscript.

4 BY MR. BAUM:

5 Q. But if she characterized herself as
6 being a ghost writer, you would let her do that?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: I have no way of knowing
9 how she feels, but if that's how she feels, I
10 wouldn't argue with her.

11 BY MR. BAUM:

12 Q. So you're sending an e-mail to Natasha
13 Mitchner regarding notes from a conference call on
14 October 4, 2001, it looks like.

15 Do you recall having a telephone
16 conference with PharmaNet personnel and Forest
17 personnel regarding the MD-18 study report draft around
18 October of 2001?

19 A. Not specifically but --

20 Q. You want to look that over and
21 refamiliarize yourself with it.

22 A. (Witness reviews document.)

23 MR. BAUM: That doesn't look like he has
24 a complete exhibit. I have all this.

1 MS. KIEHN: Two pages.

2 MR. BAUM: I've got three. Can I see
3 what you've got there?

4 THE WITNESS: Sure.

5 MR. BAUM: It's missing this page. All
6 right. Sorry, I'm going to have to -- we're
7 going to take a break. We're going to have to
8 go get a copy of this.

9 THE VIDEOGRAPHER: The time is 3:44 p.m.
10 We're off the record.

11 (Brief recess.)

12 THE VIDEOGRAPHER: The time is 3:48 p.m.
13 We're on the record.

14 BY MR. BAUM:

15 Q. Okay. So we're going to go back again
16 to what we've marked as Exhibit 9. And now that you've
17 had a chance to look this over, do you recognize it --
18 is your recollection refreshed as to your having
19 drafted that?

20 A. Yes.

21 Q. Can you describe to me what this
22 document summarizes?

23 A. This was a discussion among the
24 attendees at the call on points that we were going to

1 make in the CIT-MD-18 study report.

2 Q. And the conversation was occurring
3 between you and Charlie Flicker and James Jin, Jane Wu
4 and then at PharmaNet Evelyn Kopke and Gundula LaBadie,
5 right?

6 A. Yes.

7 Q. Does this refresh your recollection that
8 maybe a first draft of the report was being written by
9 PharmaNet?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yes.

12 BY MR. BAUM:

13 Q. That's actually what you said in your
14 prior deposition.

15 A. Okay.

16 Q. All right. So at this time, Natasha
17 Mitchner was working for BSMG Communications, right?

18 A. Yes.

19 Q. Do you know why you were sending this
20 e-mail to her?

21 A. I can't recall specifically, but I could
22 venture a guess that it was probably in preparation for
23 drafting the CIT-MD-18 manuscript.

24 Q. She did the first draft, right?

1 A. That's my recollection, yes.

2 Q. And she wrote the poster?

3 MR. ABRAHAM: Objection.

4 BY MR. BAUM:

5 Q. For ACNP?

6 A. I can't recall specifically, but that
7 wouldn't surprise me.

8 Q. Okay. So you say, "Attached are my
9 notes from the conference call with the CRO on the peds
10 study," right? That's pediatric study?

11 A. Yes.

12 Q. And at the bottom of this page, you send
13 this to Evelyn Kopke and Gundula LaBadie, right?

14 A. Yes.

15 Q. And then Wu and Jin, they were Forest
16 statisticians; is that correct?

17 A. Certainly know Jin was, and I think Wu
18 was also.

19 Q. Okay. So if you go over to the next
20 page, you have the notes from the conference call with
21 PharmaNet, October 4, 2001.

22 Do you see that?

23 A. Yes.

24 Q. And you were an attendee to that

1 conference call, correct?

2 A. Yes.

3 Q. And this was produced in the ordinary
4 course of Forest business?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes. If my memory is
7 correct, I was primarily there as the scribe to
8 take notes.

9 BY MR. BAUM:

10 Q. But you wrote this, correct?

11 A. I believe so, yes.

12 Q. Do you recall how many conferences you
13 had with PharmaNet regarding CIT-MD-18?

14 A. No.

15 Q. And then you write, "Points of note in
16 the study report for CIT-MD-18."

17 Do you see that?

18 A. Yes.

19 Q. What did you mean by that?

20 A. This was a summary of the discussions
21 that we had on this conference call, and I was putting
22 together a summary of the high level points that Forest
23 felt should be included in the CIT-MD-18 study report.

24 Q. Okay. So if you look, there's a

1 paragraph that starts note that study, you see that,
2 was not powered?

3 A. Yes.

4 Q. And the second sentence there says, "The
5 sample size was calculated based on the anticipated
6 effect size for the primary efficacy variable."

7 Do you see that?

8 A. Yes.

9 Q. What does that mean?

10 A. Well, I'm not a statistician, but, in my
11 mind, that means the number of patients to be enrolled
12 in the study was calculated based on the anticipated
13 effect, the response that we would get for the primary
14 efficacy variable, that the study was powered
15 appropriately.

16 Q. What's an effect size?

17 A. At this point I'm not sure.

18 Q. Would it be something related to
19 clinical efficacy?

20 A. I believe so, yes.

21 MR. ABRAHAM: Objection.

22 BY MR. BAUM:

23 Q. So the next paragraph says, the results
24 from the CDRS-R looked strong at every visit.

1 Emphasize the positive effect early on; also emphasize
2 that the positive effect was seen early on with the 20
3 milligram a day dose. Include only the figure from the
4 primary endpoint; leave others as after text figures.

5 Do you see that?

6 A. Yes.

7 Q. What does that mean?

8 A. So the first sentence is pretty
9 self-explanatory, the results look strong at every
10 visit. Emphasizing the positive effect early on is
11 important because antidepressants generally take
12 several weeks before you see efficacy, and having
13 evidence that a compound worked early on was always
14 something that pharmaceutical companies were striving
15 for, trying to come up with compounds that work faster
16 than the six to eight weeks it generally takes for
17 antidepressants to show their effects.

18 Include only the figure from the primary
19 endpoint, that would be include only the figure in the
20 main body of the text. The only figure in the main
21 body of the text should be the primary endpoint, the
22 others would be -- you know, the secondary endpoints
23 would be after text figures or figures in the -- you
24 know, one of the appendices.

1 Q. Okay. So this reference to the strong
2 CDRS result was a reference to the analysis that
3 included the patients who were unblinded in the study,
4 correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I would assume so, yes.

7 BY MR. BAUM:

8 Q. And if they were excluded, it wouldn't
9 have been a strong result, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yes.

12 BY MR. BAUM:

13 Q. Let's look at the next paragraph. For
14 secondary efficacy measures, no significant difference
15 at the Week 8 LOCF analysis. It looks like there's --
16 probably they are.

17 A. There are.

18 Q. There are some significant findings
19 early on in treatment. Forest is looking at individual
20 patient listings to see if there are any clues as to
21 why Week 8 findings were not positive. For now,
22 emphasize the positive findings at earlier time points
23 for the secondary efficacy variables.

24 Did I read that correctly?

1 A. Yes.

2 Q. Now, the secondary endpoint efficacy
3 variables failed at Week 8, correct?

4 A. Yes.

5 Q. And none of them were positive?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Correct.

8 BY MR. BAUM:

9 Q. But this is suggesting emphasize the
10 positive and leave out the negative?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: No. It's saying Forest is
13 looking at patient listings to see if there are
14 any clues as to why the Week 8 findings were
15 not positive.

16 BY MR. BAUM:

17 Q. Then it says "emphasize the positive
18 findings at earlier time points."

19 Do you see that?

20 A. Yes.

21 Q. Okay. So let's go to the next one.

22 "Dosing error. Some citalopram tables
23 were not blinded."

24 Do you see that?

1 A. Right, that should be tablets.

2 Q. Some citalopram tablets were not
3 blinded, right?

4 A. Correct.

5 Q. And that doesn't say potentially
6 unblinded, right?

7 MR. ABRAHAM: Objection.

8 BY MR. BAUM:

9 Q. It says they were not blinded?

10 A. It says they were not blinded, yes.

11 Q. So per the protocol, they should not
12 have been included in the efficacy measure, correct?

13 MR. ABRAHAM: Objection, asked and
14 answered.

15 THE WITNESS: According to the protocol,
16 patients who were unblinded should not have
17 been included.

18 BY MR. BAUM:

19 Q. The 9 patients who received unblinded
20 medication were included in the main analyses; a
21 secondary post-hoc analysis of the ITT subpopulation
22 was done. Refer to these analyses briefly in methods
23 and results and reference the reader to the appendix
24 table.

1 Did I read that correctly?

2 A. Yes.

3 Q. Now, this is different than what they
4 told the FDA they were going to do back in March
5 of 2000, right?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: It would appear to be
8 inconsistent, yes.

9 BY MR. BAUM:

10 Q. And you didn't know about that letter
11 they sent to the FDA, did you?

12 A. No, I did not.

13 Q. So this paragraph here is essentially
14 some instructions of how to deal with the unblinding
15 problem in the study report, correct?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: I don't know for sure, but
18 that would be a reasonable conclusion.

19 BY MR. BAUM:

20 Q. Do you know if the instructions that
21 were decided upon were reached prior to this telephone
22 conference or this conference with -- this conference
23 call with PharmaNet on October 4th?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Can you repeat that. Not
2 sure I follow that.

3 BY MR. BAUM:

4 Q. These appear to be some instructions
5 that were being given to PharmaNet; is that correct?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: It was a summary of the
8 discussions at the meeting at the conference
9 call.

10 BY MR. BAUM:

11 Q. Do you recall having any meetings with
12 Charlie Flicker or James Jin or Jane Wu in advance of
13 this telephone conference?

14 A. I can't recall any, no.

15 Q. Do you recall having any conversations
16 with Charlie Flicker or Lawrence Olanoff or Ivan Gergel
17 about having PharmaNet draft this first draft to have
18 the nine unblinded patients included in the efficacy
19 analysis?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: I don't recall any
22 conversations about that, no.

23 BY MR. BAUM:

24 Q. Did anyone draw your attention to this

1 unblinding problem at this time?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I just don't remember.

4 BY MR. BAUM:

5 Q. Were you just acting as a scribe, as you
6 said?

7 A. At this meeting --

8 MR. ABRAHAM: Objection.

9 THE WITNESS: -- yes, I was acting as a
10 scribe.

11 BY MR. BAUM:

12 Q. But you were also kind of responsible
13 for the study report being accurate as well, correct?

14 MR. ABRAHAM: Objection, asked and
15 answered.

16 THE WITNESS: Yes.

17 BY MR. BAUM:

18 Q. If you had known about those -- the fax
19 from Tiseo to the investigation sites and Joan Barton's
20 e-mail saying that the patients were unblinded and
21 Charlie Flicker saying they were unmistakably
22 unblinded, would you have done anything differently
23 with respect to the study report?

24 MR. ABRAHAM: Objection, calls for

1 speculation.

2 THE WITNESS: I can't say at this point.

3 I don't know what I would have done.

4 BY MR. BAUM:

5 Q. You don't agree with its having been

6 including those unblinded patients in the primary

7 efficacy measure, do you?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: The study report included

10 both analyses.

11 BY MR. BAUM:

12 Q. Yeah, but it put the analyses with the

13 patients -- unblinded patients excluded in the appendix

14 and it called that a secondary, and it put the primary

15 with those patients in the Table 3.1, and that's

16 different than what the protocol said, different from

17 what they told the FDA they would do, correct?

18 MR. ABRAHAM: Objection, asked and

19 answered.

20 THE WITNESS: Yes, it appears to be

21 different.

22 BY MR. BAUM:

23 Q. And having worked for the FDA, you would

24 want to have upfront truthful and accurate data

1 provided to you, correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: As I've said, the review
4 starts at the data and works it way back.

5 BY MR. BAUM:

6 Q. So that you would expect the FDA to have
7 figured this out because they looked at the data and
8 worked up, correct?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

12 Q. And if they didn't actually look at the
13 data, they just relied on the study report conclusions,
14 that would explain possibly how they may have gone
15 along with it?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: I have no idea how the FDA
18 reviewed this study report.

19 (Document marked for identification as
20 Heydorn Deposition Exhibit No. 10.)

21 BY MR. BAUM:

22 Q. I'm going to mark this next exhibit as
23 Exhibit 10, and it's a letter dated September 16, 2002,
24 and it's MDL-FORP0016376, and it's from Tom Laughren

1 and -- who is a team leader, psychiatric drug products,
2 division of neuropharmacological drug products for the
3 FDA, correct?

4 A. Yes.

5 Q. And the subject is Recommendation for
6 Nonapproval Action for Pediatric Supplement for Celexa,
7 (Citalopram); negative results for Celexa in the
8 treatment of Major Depressive Disorder (MDD) in
9 pediatric patients.

10 Do you see that?

11 A. Yes.

12 Q. Have you seen this document before?

13 A. I saw it yesterday for the first time.

14 Q. Let's look at the last paragraph on the
15 first page. It says, "Since the proposal was to use
16 the currently approved Celexa formulations for this
17 expanded population, there was no need for chemistry or
18 pharmacology reviews."

19 Do you see that?

20 A. Yes.

21 Q. And then the next one goes, "The primary
22 review of the clinical efficacy and safety data was
23 done by Earl Hearst, M.D. from the clinical group."

24 Do you know him?

1 A. No, I do not.

2 Q. Okay. And then next it says, "Since
3 there was agreement between the sponsor and FDA that
4 these trials were negative, there was no need for a
5 statistics review of the efficacy data."

6 Do you see that?

7 A. Yes.

8 Q. What does that mean to you?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: I think it's pretty
11 self-explanatory. There was an agreement
12 between the sponsor and the FDA that -- I don't
13 know what they refer to as "these trials"
14 but...

15 BY MR. BAUM:

16 Q. 94404 and MD-18 were among those trials.

17 A. Okay.

18 MR. ABRAHAM: Objection.

19 MS. KIEHN: Objection.

20 BY MR. BAUM:

21 Q. And so but does it appear to you that
22 there was no need for a statistics review of the
23 efficacy data.

24 Do you see that?

1 A. Yes.

2 Q. So what does that mean to you?

3 MR. ABRAHAM: Objection, calls for
4 speculation.

5 THE WITNESS: That the statistician at
6 the FDA would not be looking at the efficacy
7 data.

8 BY MR. BAUM:

9 Q. That's what we were just talking about,
10 correct?

11 A. Yeah.

12 Q. So they didn't actually do a workup of
13 the statistics. They essentially looked at the summary
14 of the data, correct?

15 MR. ABRAHAM: Objection, calls for
16 speculation.

17 THE WITNESS: I don't know what they
18 looked at.

19 BY MR. BAUM:

20 Q. But they didn't do a statistics review
21 of the efficacy data, correct?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: That's what it says here.

24 BY MR. BAUM:

1 Q. Okay. So if you go to Page 2 here,
2 Section "5.0 Clinical Data" and then it has an
3 "Efficacy Data" section, and we go to -- actually, I
4 want to go to the next page over. At the top of the
5 page, the third page, it says, the total randomized
6 sample was n=174, 89 citalopram, 85 placebo.

7 Do you see that?

8 A. Yes.

9 Q. That's 174 patients. That's eight more
10 than the 166 that were not exposed to the pink tablets,
11 correct?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: Yes, that would appear to
14 be correct.

15 BY MR. BAUM:

16 Q. And this 174 includes the eight patients
17 who were exposed to the tablets the pink tablets, the
18 pink Celexa, correct?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I believe so, yes.

21 BY MR. BAUM:

22 Q. And then the efficacy results, it shows
23 that the P-value is .038.

24 Do you see that?

1 A. Yes.

2 Q. And that's the P-value for the analysis,
3 including the unblinded patients, correct?

4 MR. ABRAHAM: Objection, asked and
5 answered.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

8 Q. If you go to the section just below the
9 bold print, it starts with "thus."

10 Do you see that?

11 A. Yes.

12 Q. So it goes, thus, it appears that the
13 positive results for this trial are coming from the
14 adolescent subgroup. Note: There was a packaging
15 error resulting in tablets being distinguishable for
16 drug and placebo for 9 patients (although still
17 blinded). A reanalysis without these patients yielded
18 a P-value of 0.52 in favor of citalopram. Results also
19 significantly favor citalopram over placebo on most
20 secondary outcomes.

21 Did I read that correctly?

22 A. Yes.

23 Q. That's mostly false, correct?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Well, at Week 8 the
2 secondary outcomes were not in favor of
3 citalopram.

4 BY MR. BAUM:

5 Q. Okay. So and the results without the
6 dispensing error patients were not in favor of Celexa,
7 were they?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Well, of course, P-value
10 is a typo there.

11 BY MR. BAUM:

12 Q. That should be .052?

13 A. Right.

14 Q. So .052 is not statistically
15 significant, correct?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: No, it's not, but it's
18 still in favor of citalopram.

19 BY MR. BAUM:

20 Q. How is it in favor of citalopram? It's
21 negative -- if that were reported as the primary
22 efficacy measure, it would have been a negative
23 outcome, correct?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: But more patients -- the
2 scores improved in the patients on citalopram,
3 not statistically significant, but more so than
4 patients on placebo.

5 BY MR. BAUM:

6 Q. So it's a numerical improvement, but not
7 a statistically significant improvement, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: I think that would be one
10 way to put it, yes.

11 BY MR. BAUM:

12 Q. And can a drug be approved with a
13 statistically insignificant improvement?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: I'm not an expert on the
16 overall drug approval process, but I don't
17 believe so, no.

18 BY MR. BAUM:

19 Q. So it wouldn't have been approved for --
20 as an indication for adolescents or children with a
21 P-value of .052, correct?

22 MR. ABRAHAM: Objection, calls for
23 speculation.

24 THE WITNESS: That would be my guess.

1 BY MR. BAUM:

2 Q. Now, this paragraph of Dr. Laughren's
3 essentially echoes what was in the study report
4 language, not including -- well, essentially echoes
5 what was in the study report, correct?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: It appears to, yes.

8 BY MR. BAUM:

9 Q. And it essentially echoes what was in
10 the PharmaNet notes planning out what was going to be
11 put into the study report, correct?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: It's similar.

14 BY MR. BAUM:

15 Q. Are you aware that this analysis of
16 Study 18's results by Dr. Laughren was adopted by the
17 reviewers for Lexapro without further analysis as
18 providing evidence beyond Lexapro Study 32's isolated
19 positive outcome for adolescents?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: No.

22 BY MR. BAUM:

23 Q. Forest needed more than just a single
24 positive study, and this analysis by Laughren

1 mistakenly echoing the misleading language from the
2 MD-18 study report resulted in Lexapro getting an
3 indication for adolescent depression with only one
4 positive adolescent Lexapro trial.

5 Did you know that?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: No, I did not.

8 BY MR. BAUM:

9 Q. That's inconsistent with FDA standards
10 for approval of an indication, isn't it?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: There are instances where
13 a single positive study is used for drug
14 approval.

15 BY MR. BAUM:

16 Q. With additional evidence, though,
17 correct, not just one by itself?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Yes, one by itself.

20 BY MR. BAUM:

21 Q. That's not what the FDA regulations say?

22 A. That's not the standard, but there are
23 cases where a single positive study is considered
24 sufficient for approval.

1 Q. Okay. So we would need to ask
2 Dr. Laughren what he did and why with respect to this
3 analysis of MD-18 and how it was used with MD-32,
4 correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I certainly can't comment
7 on what Dr. Laughren was thinking.

8 BY MR. BAUM:

9 Q. Do you recall discussions with Forest
10 and GCI or Prescott referencing avoiding addressing the
11 negative secondary outcomes in the MD-18 manuscript
12 publication?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I know I've seen
15 communications about that, yes.

16 BY MR. BAUM:

17 Q. You were deposed about that in 2007?

18 A. Okay.

19 Q. So I don't want to go back and redo
20 that.

21 A. Okay.

22 Q. I just wanted to sort of refresh your
23 recollection that there was -- because there was going
24 to be a short or brief --

1 A. Brief communication.

2 Q. Brief communication, you wanted to avoid
3 communicating the negative outcomes for the Week 8
4 results for the secondary outcomes.

5 Do you recall that?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: If it's in my testimony.

8 It's been a long time.

9 (Document marked for identification as
10 Heydorn Deposition Exhibit No. 11.)

11 BY MR. BAUM:

12 Q. So I'm handing you what's been marked as
13 Exhibit 11; is that right?

14 A. Yes.

15 Q. And it's a letter dated November 14,
16 2002 to Nancy Andreasen, editor-in-chief at the
17 American Journal of Psychiatry.

18 Have you seen that before?

19 A. I don't recall, but I'm sure I have,
20 since my name is on it.

21 Q. It has attached to it a draft of the
22 manuscript that they want to publish, but it has, you
23 know, you as a signatory to the letter.

24 Do you see that?

1 A. Yes.

2 Q. Would this have been something that was
3 produced in the ordinary course of Forest business?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Yes.

6 BY MR. BAUM:

7 Q. Did Forest pay Prescott Medical
8 Communications to ghost write the submission draft?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes, I'm sure Forest paid
11 Prescott Medical Communications to generate the
12 initial draft of the manuscript.

13 BY MR. BAUM:

14 Q. Were you involved in the contract
15 between Forest and Prescott Medical Communications to
16 produce this manuscript of MD-18?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: I don't recall. Do you
19 mean the details of negotiating the contract, I
20 don't recall.

21 BY MR. BAUM:

22 Q. Okay. Have you been in contact with any
23 of your co-authors since the publication of MD-18?

24 A. No.

1 MR. BAUM: The next exhibit.

2 (Document marked for identification as
3 Heydorn Deposition Exhibit No. 12.)

4 BY MR. BAUM:

5 Q. So I'm handing you the manuscript
6 publication of -- in the American Journal of Psychiatry
7 dated June 2004, "A Randomized, Placebo-Controlled
8 Trial of Citalopram for the Treatment of Major
9 Depression in Children and Adolescents."

10 Do you see that?

11 A. Yes.

12 Q. Have you seen this before?

13 A. Yes.

14 Q. This is your -- you were amongst the
15 authors here, correct?

16 A. Yes.

17 Q. Why were you an author?

18 A. Due to the amount of work I put in on
19 the project, I was offered a chance to be named as an
20 author on the publication.

21 Q. I noticed that Charlie Flicker is not on
22 here.

23 Didn't he have a lot to do with it?

24 A. I'm sure he did.

1 Q. Why isn't he an author?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I don't know. I don't
4 remember.

5 BY MR. BAUM:

6 Q. What about Paul Tiseo; he had a lot to
7 do with it too, right?

8 A. I don't know. I know Paul left Forest a
9 number of years before this was published.

10 Q. But the actual deciding of what data was
11 in and what data was out was largely in the hands of
12 people like Charlie Flicker or Paul Tiseo or Lawrence
13 Olanoff; is that correct?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: It would not have been in
16 the hands of Paul Tiseo because he had left the
17 organization. Charlie had also left the
18 organization by then.

19 BY MR. BAUM:

20 Q. Well, by the time the study report was
21 generated and the initial drafts of this were
22 generated, wasn't Dr. Flicker involved?

23 A. Yes.

24 Q. And weren't the primary decisions about

1 what was going to be included as the primary efficacy
2 measure or the secondary results and the decision about
3 whether or not to include the unblinded patients in the
4 primary efficacy measure, did that all happen back then
5 when they were there?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: I believe so, yes.

8 BY MR. BAUM:

9 Q. Do you know why Dr. Wagner was listed as
10 the first author?

11 A. No, I don't. I don't remember.

12 Q. And so Dr. Robb and -- is it Findling,
13 how do you pronounce that?

14 A. I'm not sure.

15 Q. Do you know either of them?

16 A. No.

17 Q. Do you know whether or not either of
18 them knew that there were eight unblinded patients
19 included in the primary efficacy measure?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: No, I do not.

22 BY MR. BAUM:

23 Q. Do you think they ought to have known?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Yes, they probably should
2 have known.

3 BY MR. BAUM:

4 Q. Would that change the way this
5 publication was written?

6 MR. ABRAHAM: Objection, calls for
7 speculation.

8 THE WITNESS: Yeah, I don't know how.
9 It may have.

10 BY MR. BAUM:

11 Q. And Jianqing Jin, that's James Jin; is
12 that correct?

13 A. Yes.

14 Q. And Marcelo Gutierrez, who is Marcelo
15 Gutierrez?

16 A. He was the pharmacokineticist on the
17 program.

18 Q. So he -- what did he do,
19 pharmacokinetics?

20 A. Pharmacokinetics. I assume there's
21 plasma level data in here. I don't recall
22 specifically.

23 Q. Did you write any of the drafts of the
24 manuscripts for this publication?

1 A. I can't recall specifically.

2 Q. Do you recall editing them?

3 A. I can't specifically recall.

4 Q. Do you recall working with Natasha
5 Mitchner on some of the initial drafts?

6 A. Yes, that I can recall.

7 Q. And do you recall working with -- what's
8 Prescott's first name?

9 A. Mary.

10 Q. Mary Prescott, do you recall working
11 with Mary Prescott on some of the drafts for this
12 publication?

13 A. Yeah, I worked with Mary Prescott on a
14 number of projects.

15 Q. But on the drafts for this MD-18?

16 A. I can't specifically remember.

17 Q. But neither Natasha Mitchner nor Mary
18 Prescott appear as co-authors or any reference to them
19 at all in this publication, correct?

20 A. Correct. It was not common at that time
21 to recognize medical communications firms'
22 contributions to publications.

23 Q. And that was in order to hide that there
24 was some ghostwriting occurring, right?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: I would not characterize
3 it that way.

4 BY MR. BAUM:

5 Q. So let's go to Page 1080 and if you look
6 at the -- wait a second -- it's the Results section
7 starting at 1080, and I want to sort of direct your
8 attention to Figure 1 on Page 1081, the next page over.

9 A. Yes.

10 Q. And it has -- if you look at the
11 subjects receiving placebo, it's 85.

12 Do you see that?

13 A. Yes.

14 Q. And subjects receiving citalopram is 89?

15 A. Yes.

16 Q. And that adds up to 174?

17 A. Yes.

18 Q. That included the unblinded patients,
19 correct?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: It includes the
22 potentially unblinded patients, yes.

23 BY MR. BAUM:

24 Q. Were they potentially unblinded, or were

1 they unblinded?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I don't know.

4 BY MR. BAUM:

5 Q. Well, what did Paul Tiseo say?

6 MR. ABRAHAM: Objection, asked and
7 answered.

8 THE WITNESS: He wrote that they were
9 unblinded.

10 BY MR. BAUM:

11 Q. And Charlie Flicker?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: He wrote that they were
14 unblinded.

15 BY MR. BAUM:

16 Q. And Joan Barton?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: Yes.

19 BY MR. BAUM:

20 Q. And then in your notes from the
21 PharmaNet meeting on October 4, 2001, didn't you report
22 that they were unblinded?

23 MS. KIEHN: Objection.

24 MR. ABRAHAM: Objection.

1 BY MR. BAUM:

2 Q. Record that they were unblinded?

3 MS. KIEHN: No, objection, his report
4 refers to tablets, not patients.

5 MR. BAUM: Go ahead. And I'd like you
6 not to coach the witness.

7 THE WITNESS: It says some citalopram
8 tablets were not blinded.

9 BY MR. BAUM:

10 Q. All right. So were these patients
11 unblinded or potentially unblinded?

12 MR. ABRAHAM: Objection, asked and
13 answered.

14 THE WITNESS: I don't know.

15 BY MR. BAUM:

16 Q. The people closest to it thought they
17 were unblinded, correct?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: You should perhaps depose
20 them.

21 BY MR. BAUM:

22 Q. Well, based on the correspondence I've
23 shown you today, those people said it was unblinded,
24 correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Yes.

3 BY MR. BAUM:

4 Q. Now, this table on Page 1081 says that
5 citalopram achieved statistically significant
6 improvement over placebo amongst this group of subjects
7 of children and adolescents, correct, on the CDRS
8 rating scale?

9 A. You mean the figure?

10 Q. Yes.

11 A. Yes.

12 Q. That is only achieved with the unblinded
13 patients included, correct?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Yes.

16 BY MR. BAUM:

17 Q. And if the unblinded patients were
18 excluded, it would not show a statistically significant
19 difference, correct?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: No, it would not.

22 BY MR. BAUM:

23 Q. If you turn to -- back to the abstract
24 on Page 1079, it says that there -- if you look on the

1 Results section, it says effect size, 2.9.

2 Do you see that?

3 A. Yes.

4 Q. Does that refresh your recollection that
5 there is an effect size that was added to this
6 manuscript -- or included in this manuscript, sorry?

7 A. It's clearly included in the manuscript.

8 Q. Did you have anything to do with its
9 inclusion?

10 A. No.

11 Q. Do you know what it means?

12 A. No.

13 Q. Do you know whether or not it's a
14 correct figure?

15 A. No.

16 Q. All right. Is there anyplace in this
17 article where it references the unblinding issue?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: I have not read the
20 article recently, but I would guess probably
21 not.

22 BY MR. BAUM:

23 Q. Why is that?

24 A. I don't know.

1 Q. So shouldn't the prescribing physicians
2 who would be reading this article and academics who
3 might be reading this article have a right to know
4 there was an unblinding problem with CIT-MD-18?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Yes.

7 BY MR. BAUM:

8 Q. Let's go back to Page 1081. On the
9 right-hand side on the next to last paragraph there's
10 -- it starts with "citalopram treatment."

11 Do you see that?

12 A. Yes.

13 Q. The last sentence says, "For the CGI
14 severity rating, baseline values were 4.4 for the
15 citalopram group and 4.3 for the placebo group, and
16 endpoint values (last observation carried forward) were
17 3.1 for the citalopram group and 3.3 for the placebo
18 group."

19 Do you see that?

20 A. Yes.

21 Q. Does it say anything about those not
22 being statistically significant at Week 8?

23 A. It's not addressed either way.

24 Q. But at Week 8 those were negative,

1 correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I believe so, yes.

4 BY MR. BAUM:

5 Q. So instead of reporting the statistical
6 significance at Week 8, it reported the numerically
7 higher results without referencing the results that
8 were not statistically significant, right?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

12 Q. So this language here suggests that the
13 secondary outcome measures outperform placebo, correct?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Not adding the statistical
16 significance would suggest that they were not
17 statistically significant to someone who knew
18 -- knows the area.

19 BY MR. BAUM:

20 Q. But to physicians who are reading this,
21 does this clearly indicate that the secondary outcome
22 measures did not significantly outperform placebo?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: Yes.

1 BY MR. BAUM:

2 Q. It does?

3 A. Yes, to me it does.

4 Q. To a physician?

5 A. I don't know what physicians think.

6 Q. Okay.

7 A. But the lack of a clear statement about
8 statistical difference would suggest there is not a
9 statistically significant difference.

10 Q. It would be more clear if they had
11 stated there was a numerical --

12 A. Things can always be stated more
13 clearly. It's very clear to me.

14 Q. Okay. Let's go to 1082 in the
15 Discussion section. It says, "This randomized,
16 placebo-controlled, double-blind trial provides
17 evidence that citalopram produces a statistically and
18 clinically significant reduction in depressive symptoms
19 in children and adolescents."

20 Do you see that?

21 A. Yes.

22 Q. That's not actually true if you exclude
23 the unblinded patients, correct?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: Yes.

2 BY MR. BAUM:

3 Q. You agree with me; is that correct?

4 A. Yes.

5 Q. That's not a true statement if you
6 exclude the unblinded patients?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: It's not statistically
9 significant.

10 BY MR. BAUM:

11 Q. Do you know who wrote that statement?

12 A. No, I don't.

13 Q. Is there any reference in this
14 publication to the FDA's having rejected Forest's
15 request for a pediatric MDD indication for Celexa?

16 A. No.

17 Q. Isn't that an important piece of
18 information for physicians to weigh when deciding when
19 to prescribe Celexa to a child?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: Physicians should be aware
22 of what's in the package insert. That's what's
23 approved by the FDA.

24 BY MR. BAUM:

1 Q. Isn't this publication intended to
2 provide information to help physicians decide whether
3 to prescribe Celexa to children?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Yes.

6 BY MR. BAUM:

7 Q. And should it include all of the pros
8 and cons of doing that so that they're making an
9 informed decision?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yes.

12 BY MR. BAUM:

13 Q. And do you think it's important in
14 weighing the pros and cons to know that the FDA
15 rejected Forest's request for an MDD indication for
16 Celexa?

17 A. That's not the kind of information that
18 routinely appears in publications, and physicians have
19 access to the package insert that includes the approved
20 indications for every compound.

21 Q. Do you think it would have been
22 important for physicians to know that Forest had agreed
23 that Celexa -- the studies 94404 and MD-18 were
24 negative --

1 MR. ABRAHAM: Objection.

2 BY MR. BAUM:

3 Q. -- in their presentation to
4 Dr. Laughren?

5 MR. ABRAHAM: Objection, calls for
6 speculation.

7 THE WITNESS: Can you repeat the
8 question.

9 BY MR. BAUM:

10 Q. Do you remember the letter that went to
11 Dr. Laughren?

12 A. Right.

13 Q. You want to flip back to that. If you
14 look on the first page, bottom paragraph, it says that
15 the sponsor agreed that the studies were negative?

16 MS. KIEHN: Objection. Misquotes the
17 document.

18 THE WITNESS: Since there was an
19 agreement between the sponsor and FDA that
20 these trials were negative.

21 BY MR. BAUM:

22 Q. Right.

23 A. Yes.

24 Q. Do you think that would be an important

1 piece of information for physicians to know before
2 prescribing Celexa to children?

3 MR. ABRAHAM: Objection, calls for
4 speculation.

5 THE WITNESS: If the information is not
6 in the package insert, it suggests it shows
7 it's not approved by the agency for use in that
8 population.

9 BY MR. BAUM:

10 Q. Well, that's a little bit different than
11 actually conceding and concluding and telling the FDA
12 that they were negative, isn't it?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I'm not sure I follow.

15 BY MR. BAUM:

16 Q. All right. Well, there's no reference
17 to 94404 in this -- in this publication, correct?

18 A. Correct.

19 Q. And there's no reference to the FDA and
20 the sponsor agreeing that 94404 and MD-18 were
21 negative, correct?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: It's not information that
24 goes into a publication.

1 BY MR. BAUM:

2 Q. I'm just saying it's not here, is it?

3 A. It is not there, no.

4 Q. Okay. And there's no reference in here
5 that when the unblinded patients were excluded, it was
6 not a statistically significant outcome on the primary
7 efficacy measure, correct?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Correct.

10 BY MR. BAUM:

11 Q. And the observed cases, Week 8 outcome
12 being negative is not in here either, right?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: One generally doesn't
15 include all secondary outcomes in a
16 publication.

17 BY MR. BAUM:

18 Q. But there was plenty of space in this
19 brief to discuss the positive -- numerically positive
20 outcome versus secondary outcome measures, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: You mean the --

23 BY MR. BAUM:

24 Q. In the manuscript, at Page 1081, there's

1 a paragraph that discusses the improvements that were
2 made under the secondary outcomes, and there's no
3 reference to the Week 8 outcomes being negative, right?

4 A. Correct.

5 Q. And there's no reference to the observed
6 cases being negative at Week 8 either, correct?

7 A. Correct.

8 Q. And there's no reference to the
9 unblinded patients' results showing that it was
10 negative in the primary efficacy measure, correct?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: Correct.

13 BY MR. BAUM:

14 Q. Do you know if this Forest sponsored
15 medical journal article was used by Forest sales reps
16 in promoting Celexa use in the treatment of children
17 and adolescents?

18 A. I do not know. I had left Forest by the
19 time this was published.

20 Q. Do you know that the posters that were
21 based on the -- well, we've already covered that. Let
22 me go to the next exhibit.

23 MR. BAUM: We're almost done. Can I
24 take a break for a moment?

1 MS. KIEHN: Yep.

2 THE VIDEOGRAPHER: The time is 4:38 p.m.
3 We're off the record.

4 (Brief recess.)

5 THE VIDEOGRAPHER: The time is 4:49 p.m.
6 This is the beginning of Disk 5. We're on the
7 record.

8 MR. BAUM: So we're going to go to the
9 next Exhibit, which is 13.

10 (Document marked for identification as
11 Heydorn Deposition Exhibit No. 13.)

12 BY MR. BAUM:

13 Q. Which is some letters to the editor
14 regarding the American Journal of Psychiatry
15 publication dated April 2005.

16 Have you seen this before?

17 A. I saw it yesterday for the first time.

18 Q. You never saw this before?

19 A. No, not that I recall.

20 Q. Forest didn't contact you and let you
21 know that there was some criticism about the article
22 you published?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: I don't recall being

1 contacted.

2 BY MR. BAUM:

3 Q. All right. Well, let's take a look at
4 the first one on Page 817, which is from Drs. Andres
5 Martin, Walter Gilliam, Jeffrey Bostic and Joseph Rey.

6 Do you see that?

7 A. Yes.

8 Q. Do you know who Andres Martin is?

9 A. No.

10 Q. Do you know who Jeffrey Bostic is?

11 A. That name rings a bell.

12 Q. Do you recognize him as being a key
13 opinion leader spokesperson for Forest on pediatric use
14 of Celexa?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: The name rings a bell. I
17 wouldn't know what area he was an expert in.

18 BY MR. BAUM:

19 Q. You weren't aware that he was one of the
20 chief lecturers and got paid around \$750,000 by Forest
21 to present lectures on pediatric use of Celexa?

22 MR. ABRAHAM: Objection.

23 THE WITNESS: No, I was not aware of
24 that.

1 BY MR. BAUM:

2 Q. All right. So this is -- the only
3 reason I point that out is that you've got a guy who
4 was like a key opinion leader for Forest on the
5 pediatric use of Celexa writing a criticism of your
6 paper?

7 MR. ABRAHAM: Objection.

8 MS. KIEHN: Is there a question?

9 BY MR. BAUM:

10 Q. Did you notice that?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: I see his name is on the
13 letter to the editor, whatever this is.

14 BY MR. BAUM:

15 Q. Okay. So you weren't surprised to see
16 Dr. Bostic down there as a co-author on this critique?

17 A. I really had no opinion, no, one way or
18 the other. By the time this came out, I had left the
19 area and been doing something else for at least two
20 years.

21 Q. So this first one is titled "Child
22 Psychopharmacology, Effect Sizes and the Big Bang."

23 Do you see that?

24 A. Yes, I see that.

1 Q. And to the editor: we read with interest
2 the article by Karen Dineen Wagner, M.D., Ph.D., et.al.
3 We were surprised to find the authors reporting on an
4 overall effect size of 2.9.

5 Do you remember my pointing out to you
6 that 2.9 --

7 A. Yes.

8 Q. -- in the abstract?

9 With the commonly cited criteria set
10 forth by Cohen, effect sizes can be considered trivial,
11 that's less than .2 to -- greater than -- trivial is
12 less than -- how did I read this? I think it's less
13 than .2 is trivial. Greater than -- this is wrong
14 here.

15 It's considered trivial less than 0.2,
16 small 0.2 to 0.5, moderate 0.5 to 0.8 or large, greater
17 than .80.

18 Do you see that?

19 A. Yes.

20 Q. By these metrics, the reported effect
21 size can be characterized as gargantuan, big-bang
22 worthy. So they're being kind of facetious there,
23 right?

24 MR. ABRAHAM: Objection.

1 THE WITNESS: I don't know what their
2 frame of mind was, but I would think so.

3 BY MR. BAUM:

4 Q. The value does not appear to be a benign
5 typographical error for 0.29, given that 2.9 appears
6 twice. Only 36% -- going further down it says, only
7 36% of the patients treated with citalopram responded.
8 That means 64% didn't respond, right?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: I don't know.

11 BY MR. BAUM:

12 Q. Well, if only 36% responded, the rest
13 didn't, right?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: Seems reasonable, yes.

16 BY MR. BAUM:

17 Q. That's more than half, right; the
18 majority didn't respond?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: In antidepressant trials
21 that's not unusual.

22 BY MR. BAUM:

23 Q. But the majority didn't respond,
24 correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: Correct, not unusual in a
3 lot of clinical research.

4 BY MR. BAUM:

5 Q. Okay. So 24% of those -- compared to
6 24% of those with placebo (for a lukewarm number needed
7 to treat 8).

8 Do you know what that means?

9 A. No, I don't.

10 Q. "These results, while modest, are
11 respectable in their own right and nothing to sneeze at
12 in a clinical area that has been short on proven
13 therapeutic options. But a Majestic sequoia of 2.9
14 they are not."

15 Did I read that correctly?

16 A. Yes, you did.

17 Q. Now, they're criticizing the use of this
18 2.9, or their reference to this 2.9 as an effect size
19 for the article in which you're an author, correct?

20 A. Yes.

21 Q. And it's also interesting that they're
22 referring to this, these results, the 36% of the
23 patients responded compared to 24% on placebo, that
24 included the unblinded patients, correct?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: I don't know.

3 BY MR. BAUM:

4 Q. Well, the unblinded -- this is referring
5 to -- if you go back to the article itself, and if you
6 go to the abstract, that's the shortcut, and under
7 Results, it says, "The difference in response rate at
8 week 8 between placebo (24%) and citalopram (36%) was
9 also statistically significant."

10 And --

11 A. Okay.

12 Q. And the N numbers were 174, not 166,
13 correct?

14 A. Correct.

15 Q. So they included the unblinded patients
16 to arrive at this modest lukewarm effect size, correct?

17 MR. ABRAHAM: Objection.

18 BY MR. BAUM:

19 Q. Even with them in, it was modest?

20 MR. ABRAHAM: Objection.

21 THE WITNESS: In the opinion of these
22 authors, yes.

23 BY MR. BAUM:

24 Q. And Jeffrey Bostic was actually an

1 opinion leader for -- key opinion leader for Forest.

2 Did you know that?

3 MR. ABRAHAM: Objection.

4 THE WITNESS: You just mentioned that.

5 MR. ABRAHAM: Asked and answered.

6 BY MR. BAUM:

7 Q. So let's go up to the -- you don't know
8 whether or not that 2.9 was a mistake?

9 A. I don't know.

10 Q. Do you know who within Forest would know
11 that?

12 MR. ABRAHAM: Objection.

13 BY MR. BAUM:

14 Q. Probably Jin?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: I would speculate it would
17 be a statistician.

18 BY MR. BAUM:

19 Q. Okay. So on Page 819 of this exhibit,
20 it's Dr. Wagner and colleagues' reply.

21 Do you see that?

22 A. Yes.

23 Q. And the persons replying are Wagner,
24 Robb, Findling and Jin.

1 Do you see that?

2 A. Yes.

3 Q. You're not on that list?

4 A. No.

5 Q. Do you know why?

6 A. I don't know why. I wasn't aware that
7 they were -- I wasn't aware there were letters to the
8 editor and that a response was needed.

9 Q. Okay. And so on the last paragraph on
10 the first column that starts "Dr. Martin."

11 Do you see that?

12 A. Yes.

13 Q. It says, "Dr. Martin and colleagues
14 inquire about the value of 2.9, which was calculated as
15 the quotient of the least square mean, divided by the
16 common standard error of the mean for each treatment
17 group."

18 Do you understand any of that?

19 A. Barely.

20 Q. What do you barely understand of it?

21 A. The least squared mean is a
22 calculation -- some calculation of the mean score, and
23 the standard area is a measure of the variability in
24 the data across the population.

1 Q. Should I get Jin to explain that to me?

2 A. Yes, please too.

3 Q. Okay. And then "With Cohen's method,
4 the effect size was the 0.32."

5 Do you see that?

6 A. Yes.

7 Q. And then referring back to the letter to
8 the editor by Martin, Gilliam and Bostic on Page 817,
9 you've got these Cohen effect sizes?

10 A. Yes.

11 Q. Are you familiar with Cohen effect
12 sizes; have you ever heard of those before?

13 A. No.

14 Q. Well, where would .32 fit in on this
15 scale that's referenced here?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: Small.

18 BY MR. BAUM:

19 Q. So even with the unblinded patients
20 included, it was a small effect size, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: If the calculation of the
23 effect size was correct, yes, I have no way of
24 knowing.

1 BY MR. BAUM:

2 Q. That's a pretty big difference .32
3 versus 2.9, isn't it?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: Not knowing anything about
6 the area, I can't comment.

7 BY MR. BAUM:

8 Q. Okay. It looks like Drs. Martin and
9 Bostic kind of spotted an obvious problem?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I don't know.

12 BY MR. BAUM:

13 Q. Okay. Let's look at the second letter
14 then, the one from Remy Barbe, M.D.?

15 A. Okay.

16 Q. Do you know how to pronounce that?

17 A. Barbe -- I don't know, no.

18 Q. And it starts on the bottom of 817. At
19 the last part of that on the last paragraph of that
20 letter, it says, finally, it is somewhat surprising
21 that the authors do not compare their results with
22 those of another trial, involving 244 adolescents
23 (13-18 year olds), that showed no evidence of efficacy
24 of citalopram compared to placebo and a higher level of

1 self-harm, (16 [12.9%] of 124 versus nine [7.5%] of
2 120) in the citalopram group compared to the placebo
3 group. Although these data were not available to the
4 public until December of 2003, one would expect that
5 the authors, some of whom are employed by the company
6 that produces citalopram in the United States and
7 financed the study, had access to this information.

8 Did I read that correctly?

9 A. Yes.

10 Q. And the trial referred to by Dr. Barbe's
11 letter to the editor, that's the Lundbeck 94404 trial,
12 right?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: I assume so.

15 BY MR. BAUM:

16 Q. And you were aware of the 94404 results
17 as early as 2001; is that correct?

18 A. I was certainly --

19 MR. ABRAHAM: Objection.

20 THE WITNESS: -- aware of them. I don't
21 know exactly what date I was aware of them.

22 BY MR. BAUM:

23 Q. You testified regarding when you found
24 out about it in your prior deposition, and I'm just

1 going to like rely on that for the time period?

2 A. That's fine.

3 Q. But it predated the manuscript being
4 sent to Andreason and the American Journal of
5 Psychiatry, correct?

6 A. If it was 2001, then, yes, that was sent
7 in 2002.

8 Q. So you knew about the 94404 results and
9 so did Flicker, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: Yes.

12 BY MR. BAUM:

13 Q. And they weren't included in this study,
14 correct, in this manuscript, correct?

15 A. Yes.

16 Q. Now, if you go to Page 819 at the next
17 to the last paragraph, it goes -- they respond to
18 Dr. Barbe by saying, it may be considered premature to
19 compare the results of this trial with unpublished data
20 from the results of a study that was not -- has not
21 undergone the peer-review process. Once the
22 investigators involved in the European citalopram
23 adolescent depression study publish the results in a
24 peer-reviewed journal, it will be possible to compare

1 their study population, methods, and results with our
2 study with appropriate scientific rigor.

3 Do you see that?

4 A. Yes, I do.

5 Q. Now, that's not actually true, is it?

6 MR. ABRAHAM: Objection.

7 THE WITNESS: Well, yeah, I believe it
8 is true.

9 BY MR. BAUM:

10 Q. Well, the 94404 study report was done by
11 then, wasn't it?

12 A. I don't recall when it was done but --
13 by 2004?

14 Q. Yes.

15 A. Yes, it was done by them.

16 Q. And you participated in editing it,
17 didn't you?

18 A. Yes, I reviewed it and edited it.

19 Q. And so it did get some scientific review
20 by the scientists at Forest, correct?

21 MR. ABRAHAM: Objection.

22 THE WITNESS: I would hardly consider
23 myself an expert --

24 BY MR. BAUM:

1 Q. Well, it was people --

2 A. -- in pediatric depression.

3 Q. Yeah, but it was you and Flicker, and
4 who else?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I don't recall who else
7 reviewed it.

8 BY MR. BAUM:

9 Q. But it resulted in a study report that
10 you considered sufficiently accurate to convey to the
11 FDA, correct?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: It was conveyed to the
14 FDA, yes.

15 BY MR. BAUM:

16 Q. To get the pediatric indication or the
17 patent extension, correct?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: Well, we certainly didn't
20 get the pediatric indication.

21 BY MR. BAUM:

22 Q. But it was submitted to the FDA?

23 A. It was submitted to the FDA.

24 Q. So it had sufficient scientific rigor at

1 that point to have been submitted to the FDA, correct?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: It was submitted to the

4 FDA, yes.

5 BY MR. BAUM:

6 Q. And you guys had vetted it for you at
7 Forest, and Lundbeck had vetted it for accuracy before
8 it was submitted to the FDA, correct?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Yes.

11 BY MR. BAUM:

12 Q. So this statement here, "it may be
13 considered premature to compare the results," do you
14 see that?

15 A. Yes.

16 Q. It's trying to fend off why they didn't
17 convey it inaccurately, correct?

18 MR. ABRAHAM: Objection, calls for
19 speculation.

20 THE WITNESS: This was not our data.

21 This was Lundbeck's data.

22 BY MR. BAUM:

23 Q. Do you recall the e-mail correspondence
24 you had with Lundbeck where there was a discussion

1 about getting the positive data out before the negative
2 data?

3 A. Yes.

4 Q. Isn't that what happened?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: Certainly MD-18 was
7 published before 94404, yes.

8 BY MR. BAUM:

9 Q. And that was planned, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: That was a goal.

12 BY MR. BAUM:

13 Q. It was intended?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: We had no control over the
16 Lundbeck investigators.

17 BY MR. BAUM:

18 Q. Is that true? Because you had
19 correspondence with Lundbeck over whether or not to
20 have the positive data come out first and that there
21 was a benefit to Forest and Lundbeck who was profiting
22 as well from having the negative data come out after
23 the positive data, right?

24 MR. ABRAHAM: Objection.

1 MS. KIEHN: Objection. You're
2 completely mischaracterizing the
3 correspondence.

4 THE WITNESS: I believe my statement was
5 I had no contact with the Lundbeck
6 investigators.

7 BY MR. BAUM:

8 Q. Who did you have contact with at
9 Lundbeck?

10 A. I had contact with individuals at
11 Lundbeck, not their independent investigators.

12 Q. Okay. So you -- that Forest and
13 Lundbeck planned to have the positive data come out
14 before the negative data, correct?

15 MR. ABRAHAM: Objection.

16 THE WITNESS: That was the goal.

17 BY MR. BAUM:

18 Q. Okay.

19 A. They were clearly different patient
20 population that would help explain the different
21 results.

22 Q. Was it interpretable data?

23 A. In their population I believe it was.
24 It was published, so I'm assuming it was interpretable.

1 Q. And it was published as negative data,
2 correct?

3 A. Yes.

4 Q. And Forest told the FDA that it was
5 negative, right?

6 A. Yes.

7 Q. But it wasn't included in the manuscript
8 that was published in the American Journal of
9 Psychiatry?

10 A. That manuscript was on MD-18.

11 Q. Because you wanted to get the positive
12 data out regarding MD-18 before the negative data of
13 94404, right?

14 MR. ABRAHAM: Objection.

15 THE WITNESS: We didn't have the right
16 to refer to the Lundbeck data in our paper.

17 BY MR. BAUM:

18 Q. You had the right to refer to it to the
19 FDA, so it was good enough to refer to it to the FDA to
20 get the patent extension, it was good enough to report
21 to the FDA to get a pediatric indication, but it wasn't
22 good enough to give to the public or to academics who
23 would be reviewing this data to determine whether or
24 not to prescribe it to kids?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: That was Lundbeck's
3 decision, as I recall.

4 BY MR. BAUM:

5 Q. Wasn't Lundbeck Forest's partner in
6 getting this drug distributed and sold in the US?

7 MR. ABRAHAM: Objection.

8 THE WITNESS: Yes.

9 BY MR. BAUM:

10 Q. And both Lundbeck and Forest profited
11 from having the sales occur in the US?

12 MR. ABRAHAM: Objection.

13 THE WITNESS: I don't know what the
14 financial relationship was between Forest and
15 Lundbeck.

16 BY MR. BAUM:

17 Q. You know that there was a financial
18 relationship, though, right?

19 A. Yes.

20 Q. And that they both benefited or they
21 both received income from the sale of Celexa in the US,
22 correct?

23 MR. ABRAHAM: Objection.

24 THE WITNESS: That's my understanding,

1 yes.

2 BY MR. BAUM:

3 Q. And they both received income from
4 pediatric sales of Celexa in the US, correct?

5 MR. ABRAHAM: Objection.

6 THE WITNESS: I would assume so.

7 BY MR. BAUM:

8 Q. And they received income from pediatric
9 sales of Lexapro, correct?

10 MR. ABRAHAM: Objection.

11 THE WITNESS: I would assume so, but
12 we're not discussing Lexapro here.

13 BY MR. BAUM:

14 Q. Well, actually, we are, because MD-18
15 was used to justify and get an indication for Lexapro,
16 correct?

17 MR. ABRAHAM: Objection.

18 THE WITNESS: That's what I've been
19 told.

20 BY MR. BAUM:

21 Q. And if MD-18 was actually negative when
22 you take out the unblinded patients, then it wouldn't
23 actually justify a Lexapro indication for adolescents,
24 would it?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: That would be an FDA
3 decision.

4 BY MR. BAUM:

5 Q. If the FDA didn't actually look at the
6 statistics and just relied on the characterization of
7 the documentation, then they might have made a mistake,
8 huh?

9 MR. ABRAHAM: Objection, calls for
10 speculation.

11 THE WITNESS: I don't know.

12 BY MR. BAUM:

13 Q. Well, did --

14 A. I'm sorry. I'm looking for
15 Dr. Laughren's letter.

16 Q. Okay. That's it.

17 A. So this letter refers specifically to
18 the citalopram application. I don't know what sort of
19 review was done when MD-18 was submitted in support of
20 Lexapro.

21 Q. So if MD-18 were submitted in support of
22 Lexapro and they used the results that included the
23 unblinded patients, that would be a flawed use of MD-18
24 since it didn't outperform placebo with the unblinded

1 patients out, right?

2 MR. ABRAHAM: Objection.

3 THE WITNESS: I have no knowledge of
4 what the FDA did in its review of MD-18 in
5 support of the Lexapro pediatric indication.

6 BY MR. BAUM:

7 Q. Okay. Let's go to this next -- this
8 next letter is from Mathews, Adetunji and a bunch of
9 other people whose names I can barely pronounce. I can
10 pronounce Abraham.

11 A. Mathews there.

12 Q. Yeah, the rest of them are hard to
13 pronounce, but, in any case, you see this letter from
14 these doctors, correct?

15 A. Yes.

16 Q. And this says about halfway down the
17 second column on the right, "our greatest concern."

18 Do you see that?

19 A. Yes.

20 Q. "Our greatest concern is with the
21 results and conclusions drawn. There is no table
22 showing the results in detail. The authors have only
23 stated that 36% of citalopram-treated patients met the
24 criteria for response, compared to 24% of patients

1 receiving placebo. This response rate, while in itself
2 marginal compared to other studies of antidepressants,
3 does not in itself show that citalopram is better than
4 placebo."

5 Do you see that?

6 A. Yes.

7 Q. Then in the next paragraph, it goes
8 through -- they calculated the absolute benefit
9 increase of using citalopram as .12.

10 Do you see that?

11 A. Yes.

12 Q. Do you know what that means?

13 A. No.

14 Q. I should rely on a statistician like Jin
15 to tell me that, or maybe Flicker?

16 MR. ABRAHAM: Objection.

17 THE WITNESS: I would say a
18 statistician.

19 BY MR. BAUM:

20 Q. Okay. It goes that the odds ratio --
21 the odds of improving while taking citalopram compared
22 to placebo was 1.75.

23 You see that?

24 A. Yes.

1 Q. "The number needed to treat, i.e., the
2 number of children need to be treated for citalopram
3 for one additional positive outcome was eight."

4 Do you see that?

5 A. Yes.

6 Q. "None of these shows that citalopram is
7 any better than placebo."

8 Do you see that?

9 A. Yes.

10 Q. So even with the unblinded patients
11 included, these physicians are pointing out that the
12 clinical efficacy was not enough to show an improvement
13 over placebo, correct?

14 A. That appears --

15 MR. ABRAHAM: Objection.

16 THE WITNESS: That appears to be their
17 opinion.

18 BY MR. BAUM:

19 Q. Now, what do you think these physicians
20 would have thought if they had had the unblinded
21 patients' data excluded?

22 MR. ABRAHAM: Objection, calls for
23 speculation.

24 THE WITNESS: Yeah, I have no idea.

1 BY MR. BAUM:

2 Q. They would have had even more negative a
3 view of the results of MD-18, correct?

4 MR. ABRAHAM: Same objection.

5 THE WITNESS: I don't know.

6 BY MR. BAUM:

7 Q. What do you think?

8 MR. ABRAHAM: Objection.

9 THE WITNESS: Possibly.

10 BY MR. BAUM:

11 Q. Last line here of their letter says, "We
12 are surprised that the most respected psychiatric
13 journal in the world published a study that is
14 misleading to their readers in the extreme."

15 Do you see that?

16 A. Yes.

17 Q. It would be even more misleading if they
18 had known about the unblinding, correct?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I guess, yes.

21 BY MR. BAUM:

22 Q. Okay.

23 A. In their opinion.

24 Q. Your opinion?

1 MR. ABRAHAM: Objection.

2 THE WITNESS: My opinion is the compound
3 works in children and adolescents, in spite of
4 the insignificant P-value.

5 BY MR. BAUM:

6 Q. It outperforms placebo?

7 A. Numerically outperforms placebo, we've
8 been over this.

9 Q. But not statistically significantly?

10 A. It doesn't reach the .05 level.

11 Q. So it wouldn't have gotten an
12 indication, correct?

13 MR. ABRAHAM: Objection.

14 THE WITNESS: It didn't.

15 BY MR. BAUM:

16 Q. Right, and it would not have gotten one
17 by itself with a .052 P-value, correct?

18 MR. ABRAHAM: Objection.

19 THE WITNESS: No.

20 BY MR. BAUM:

21 Q. Do you have any regrets about your
22 involvement with the CIT-MD-18 based on what I've shown
23 you today?

24 A. I wish we had done things a little

1 differently.

2 Q. Like what?

3 A. I wish I had known for certain whether
4 the patients, those nine patients were unblinded, but
5 obviously I don't know. You showed me a lot of
6 documents today suggesting that people knew the
7 patients were unblinded. I don't know for a fact that
8 they knew that. All I know is what they wrote on the
9 paper. I wish I was aware of the correspondence with
10 the FDA.

11 Q. Do you think, based on what I've shown
12 you today, that Forest misled anyone about the results
13 of MD-18?

14 A. It probably should have been more
15 forthcoming.

16 Q. If you had known what I've shown you
17 today, would you have changed anything in your first
18 draft of the study report?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I don't believe I've seen
21 my first draft of the study report. I saw the
22 final draft of the study report.

23 BY MR. BAUM:

24 Q. Would you have changed anything in the

1 final study report?

2 MR. ABRAHAM: Objection, calls for
3 speculation.

4 THE WITNESS: If I were the only one
5 involved in writing it, I probably would have
6 written it somewhat differently.

7 BY MR. BAUM:

8 Q. In what way?

9 MR. ABRAHAM: Objection.

10 THE WITNESS: Probably emphasizing more
11 of the results at Week 8, clarifying some
12 things, and I'm not sure how I would have
13 handled the potential unblinding situation.
14 I'd have to give that some thought.

15 BY MR. BAUM:

16 Q. Wouldn't you have had to have stated
17 that they weren't potentially unblinded, they were
18 actually unblinded?

19 MR. ABRAHAM: Objection.

20 THE WITNESS: I don't know that for a
21 fact.

22 BY MR. BAUM:

23 Q. I just want to now --

24 A. But I would like to say that all of the

1 information was included in the study report.

2 Q. Okay. But it was mischaracterized in
3 the study report too, right?

4 MR. ABRAHAM: Objection.

5 THE WITNESS: It could have been
6 characterized differently.

7 BY MR. BAUM:

8 Q. Thank you.

9 So I'm going to hand you what we're
10 going to mark as Exhibit 14.

11 (Document marked for identification as
12 Heydorn Deposition Exhibit No. 14.)

13 BY MR. BAUM:

14 Q. And this is an Editors' Note from the
15 American Journal of Psychiatry dated August 2009.

16 Do you see that?

17 A. Yes.

18 Q. Have you ever seen that before?

19 A. Yes, I saw it this morning for the first
20 time.

21 Q. So here it says, The article "A
22 Randomized Placebo-Controlled Trial of Citalopram for
23 the Treatment of Major Depression in Children and
24 Adolescents," published in June 2004 in the American

1 Journal of Psychiatry is alleged by the United States
2 Department of Justice in an ongoing suit to have been
3 written and submitted to the Journal by a commercial
4 medical writer on behalf of Forest Laboratories.

5 Do you see that?

6 A. Yes.

7 Q. And then we requested responses from
8 Drs. Wagner, Robb, Findling (authors in their role as
9 investigators in the clinical trial at their respective
10 universities), Dr. William E. Heydorn, that's you,
11 correct?

12 A. Yes, that's me.

13 Q. The senior Forest laboratory study
14 director and Forest Laboratories.

15 A. I would like to point out that that
16 parenthetical is not correct.

17 Q. Okay. So it says they requested
18 responses from you.

19 Did you ever get a request from the
20 American Journal of Psychiatry for a response to these
21 letters, to this editors' note?

22 A. Yeah, you know, I vaguely recall getting
23 something a number of years ago.

24 Q. How did you respond?

1 A. It was six years after the publication.
2 I don't believe I responded. I had moved on in my
3 career at that point, and I'd also like to object to
4 the wording "ongoing suit to have been written and
5 submitted to the Journal by a commercial medical writer
6 on behalf of Forest Laboratories, Incorporated." It
7 was not submitted on behalf of Forest by a commercial
8 medical writer. It was submitted by the authors.

9 Q. Did Mary Prescott write the letter and
10 have you guys sign it?

11 MR. ABRAHAM: Objection.

12 THE WITNESS: The cover letter?

13 BY MR. BAUM:

14 Q. Yeah.

15 A. I don't recall.

16 Q. If you go over to the second page of
17 this, it continues, "The paper was submitted as a Brief
18 Report, which the Journal's editors requested be
19 resubmitted as a full-length article. Drs. Wagner,
20 Robb and Findling report that they contributed with
21 Dr. Heydorn to the resubmission and that they were not
22 aware that Dr. Heydorn was working with a commercial
23 writer. Dr. Heydorn did not respond to our request."

24 Is it true that neither Wagner, Robb or

1) Findling knew that you were communicating with a
2) commercial writer?

3) MR. ABRAHAM: Objection.

4) THE WITNESS: I don't believe that to be
5) a true statement.

6) BY MR. BAUM:

7) Q. Did you know that they were
8) corresponding -- that they had information and e-mail
9) correspondence with Mitchner and Prescott, right?

10) MR. ABRAHAM: Objection.

11) THE WITNESS: At the very least, by my
12) recollection, Dr. Wagner didn't.

13) BY MR. BAUM:

14) Q. So this is a false statement?

15) MR. ABRAHAM: Objection.

16) THE WITNESS: I believe it's false, yes.

17) MR. BAUM: Take a break.

18) THE WITNESS: Yeah.

19) THE VIDEOGRAPHER: The time is now
20) 5:25 p.m. We're off the record.

21) (Brief recess.)

22) THE VIDEOGRAPHER: The time is now
23) 5:37 p.m. We're on the record.

24) MR. BAUM: We have no further questions.

1 BY MR. ABRAHAM:

2 Q. Dr. Heydorn, you've answered a number of
3 questions regarding some patients who participated in
4 MD-18 who were potentially unblinded today, correct?

5 A. Yes.

6 Q. You don't actually know whether those
7 patients were, in fact, unblinded, do you?

8 A. No, I do not.

9 Q. To the extent in your testimony you
10 referred to, quote, unblinded patients, you don't
11 actually know that those patients were unblinded,
12 correct?

13 A. No, I do not know.

14 Q. To the extent you adopted Mr. Baum's use
15 of the term unblinded patients, you also don't know
16 that those patients were, in fact, unblinded, correct?

17 A. No, I do not.

18 MR. ABRAHAM: No further questions.

19 MR. BAUM: I think that's all.

20 THE VIDEOGRAPHER: The time is now
21 5:38 p.m. This is the end of Disk 5 and the
22 end of today's deposition. We're off the
23 record.

24 (Witness excused.)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24

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

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24

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.


(Signature)


(Date)

Subscribed and sworn before me this

 day of December, 2016



TERRI L. VERDERESE
Notary Public
State of New Jersey
My Commission Expires Apr 17, 2018