IN THE UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

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OCTOBER 14, 2016

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WILLIAM E. HEYDORN, Ph.D.

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

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

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

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

Q. Okay. Do you know when he left?

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

Q. Do you know who took his place?

A. I don't know.

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

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

the study monitor.

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

MR. ABRAHAM: Objection.

THE WITNESS: I assume so.

BY MR. BAUM:

Q. You don't recall?

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

Q. What would you speculate?

A. I would think --

MR. ABRAHAM: Objection.

You can answer.

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

BY MR. BAUM:

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

A. Yes.

Q. Then you see Lawrence Olanoff?

A. Yes.

Q. What were their roles in MD-18?

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

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

Q. Did you interact with either of them?

A. Yes.

Q. And then Ivan Gergel?

A. Yes.

Q. Who is he?

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

Q. What happened to Charlie?

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

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

A. No.

Q. And who is Ed Lakatos?

A. Senior director of biostatistics and data management.

Q. Did you interact with him?

A. Very little, if at all.

MR. ABRAHAM: Objection.

THE WITNESS: Yes, I see that.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: That's my understanding.

BY MR. BAUM:

Q. Because it's greater than .05?

A. Yes, that's my understanding.

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

Q. For the primary endpoint?

A. For the primary endpoint.

MR. ABRAHAM: Object.

BY MR. BAUM:

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

scale after 8 weeks, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

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

MR. ABRAHAM: Objection.

THE WITNESS: That appears to be the

case.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

Do you see that?

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

MR. BAUM: You want to take a break.

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

(Brief recess.)

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

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

MR. ABRAHAM: Of which document?

MR. ABRAHAM: Objection.

THE WITNESS: No, not mine.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

A. Yes.

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

MR. ABRAHAM: Objection.

THE WITNESS: Assuming those patients were unblinded, yes.

BY MR. BAUM:

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

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

Do you see that?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. Did you write that section?

A. I don't recall.

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

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

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

A. Yes.

Q. And it's .167?

A. Yes.

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

MR. ABRAHAM: Objection.

THE WITNESS: I would say not.

BY MR. BAUM:

Q. And so the difference at Week 8 between

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

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

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

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. At Week 8 it was negative, correct?

were negative, correct?

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

Q. At Week 8, right.

And observed cases was negative at Week 8, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: At Week 8, yes.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Well, at Week 8, yes.

BY MR. BAUM:

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

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

THE WITNESS: Can we talk?

BY MR. BAUM:

Q. No, you can't.

A. Okay. Can you repeat the question.

MR. BAUM: Can you read it back.

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

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

BY MR. BAUM:

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

Can you answer my question?

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

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

THE WITNESS: I guess yes.

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

Q. And the investigators would know that?

MR. ABRAHAM: Objection.

BY MR. BAUM:

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

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

Q. So they were unblinded as well, correct?

MR. ABRAHAM: Objection.

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

BY MR. BAUM:

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

Q. Section 5.3.4.

A. Okay.

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

A. Yes, I see that.

Q. And that earlier statement that I read to you said that it was in first week, correct?

MS. KIEHN: Objection.

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. It's Section 7.0, Page 63.

A. It does say one week of medication, yes.

Q. So that's not actually true, right, with respect to patients 113 and 513, correct?

MR. ABRAHAM: Objection.

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

MR. BAUM: We can take a break now.

THE VIDEOGRAPHER: The time is now approximately 1:05 p.m. This is the end of Disk 2. We're off the record.

Q. So it's another letter -- it's addressed to Dr. Katz, correct?

A. Correct.

Q. At the FDA, and it's regarding this same problem of the eight randomized patients at two investigational sites who had a dispensing error, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. So we haven't seen any other earlier drafts of this e-mail?

A. No.

Q. I'm going to mark this as 7B.

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

BY MR. BAUM:

Q. I'm handing you what has been marked as Exhibit 7B, and this is a letter to the FDA draft dated March 8, 2000, Re: clinical supplies for the Pediatric Depression Study CIT-MD-18.

You see that?

A. Yes.

Q. Have you seen that before?

A. This particular exhibit?
Q. Yeah.
A. No.
Q. Do you see that handwriting on the upper part of it?
A. Yes.
Q. Do you recognize that handwriting? Is that Charlie Flicker's handwriting?
MR. ABRAHAM: Objection.
THE WITNESS: Yes, I recognize the handwriting.
BY MR. BAUM:
Q. Is it Charlie Flicker's?
A. Yes.
Q. Okay. So in the typed portion of the letter it says, "Dear Dr. Katz, the purpose of this letter is to inform the agency that an error was made during the packaging of the clinical supplies for the above-noted study."
Do you see that?
A. Yes.
Q. "Two of our investigational sites called in to report that some of their patients were receiving white tablets and others were receiving pink tablets."

colored tablets and that they wouldn't know which were the active and which were the placebo.

BY MR. BAUM:

Q. Well, by the time they got the March 2nd letter, they probably knew, didn't they?

MR. ABRAHAM: Objection.

THE WITNESS: Well, obviously, I don't know what any of the investigators were thinking, but that would not be an unreasonable conclusion.

BY MR. BAUM:

Q. Okay. If an investigator knows which patients are taking branded Celexa and which ones are taking white pills, doesn't that mean the integrity of the blind was mistakenly -- unmistakenly compromised?

MR. ABRAHAM: Objection.

THE WITNESS: It does raise questions about the integrity of the blind, yes.

BY MR. BAUM:

Q. Okay. So the letter continues, "On March 2nd, all sites were notified of this error by telephone and by fax."

Do you see that?

Q. You've got the Varner letter there in front of you, right?
A. Yes.
Q. That's Exhibit 7?
A. Seven, yes.
Q. Now, having seen this e-mail from Dr. Flicker and the fax from Dr. Tiseo, would you agree that the patients who were subject to the dispensing error were actually unblinded?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know for a fact, but that's the implication from these letters, yes.
BY MR. BAUM:
Q. Does it concern you that the clinical medical director at the time, Dr. Flicker, believes that the letter being sent to the FDA contains a masterful stroke of euphemism?
MR. ABRAHAM: Objection.
THE WITNESS: I don't know what his frame of mind was when he wrote that.
BY MR. BAUM:
Q. But they had the obligation to be upfront, truthful and honest with the FDA, correct?

BY MR. BAUM:

Q. Now, she doesn't say potentially unblinded, does she?

A. Unblinded, she said unblinded.

Q. And per the protocol, it would have been the correct procedure at that point to not include those patients for the efficacy measures, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes, if they were unblinded.

BY MR. BAUM:

Q. Well,this says unblinded, correct?

A. Yes.

Q. Charlie Flicker said they were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: What did he say? He said potentially unblinded.

BY MR. BAUM:

Q. No, go back to the other -- this 7D.

A. 7D. Yeah.

Q. He says, the blind was unmistakenly violated, correct?

A. Yes.

Q. And you have Dr. Tiseo saying they were automatically unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what he put in his fax, yes.

BY MR. BAUM:

Q. So these three people were closer to this than you were, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. And they said it was unblinded, correct?

MR. ABRAHAM: Objection.

BY MR. BAUM:

Q. Those patients were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: That's what they're saying here, yes.

BY MR. BAUM:

Q. And per the protocol, those patients should have been excluded because they were unblinded, correct?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

MS. KIEHN: Two pages.

MR. BAUM: I've got three. Can I see what you've got there?

THE WITNESS: Sure.

MR. BAUM: It's missing this page. All right. Sorry, I'm going to have to -- we're going to take a break. We're going to have to go get a copy of this.

THE VIDEOGRAPHER: The time is 3:44 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is 3:48 p.m. We're on the record.

BY MR. BAUM:

Q. Okay. So we're going to go back again to what we've marked as Exhibit 9. And now that you've had a chance to look this over, do you recognize it -- is your recollection refreshed as to your having drafted that?

A. Yes.

Q. Can you describe to me what this document summarizes?

A. This was a discussion among the attendees at the call on points that we were going to

make in the CIT-MD-18 study report.

Q. And the conversation was occurring between you and Charlie Flicker and James Jin, Jane Wu and then at PharmaNet Evelyn Kopke and Gundula LaBadie, right?

A. Yes.

Q. Does this refresh your recollection that maybe a first draft of the report was being written by PharmaNet?

MR. ABRAHAM: Objection.

THE WITNESS: Yes.

BY MR. BAUM:

Q. That's actually what you said in your prior deposition.

A. Okay.

Q. All right. So at this time, Natasha Mitchner was working for BSMG Communications, right?

A. Yes.

Q. Do you know why you were sending this e-mail to her?

A. I can't recall specifically, but I could venture a guess that it was probably in preparation for drafting the CIT-MD-18 manuscript.

Q. She did the first draft, right?

A. Right, that should be tablets.
Q. Some citalopram tablets were not blinded, right?
A. Correct.
Q. And that doesn't say potentially unblinded, right?
MR. ABRAHAM: Objection.
BY MR. BAUM:
Q. It says they were not blinded?
A. It says they were not blinded, yes.
Q. So per the protocol, they should not have been included in the efficacy measure, correct?
MR. ABRAHAM: Objection, asked and answered.
THE WITNESS: According to the protocol, patients who were unblinded should not have been included.
BY MR. BAUM:
Q. The 9 patients who received unblinded medication were included in the main analyses; a secondary post-hoc analysis of the ITT subpopulation was done. Refer to these analyses briefly in methods and results and reference the reader to the appendix table.

MR. ABRAHAM: Objection.

THE WITNESS: My opinion is the compound works in children and adolescents, in spite of the insignificant P-value.

BY MR. BAUM:

Q. It outperforms placebo?

A. Numerically outperforms placebo, we've been over this.

Q. But not statistically significantly?

A. It doesn't reach the .05 level.

Q. So it wouldn't have gotten an indication, correct?

MR. ABRAHAM: Objection.

THE WITNESS: It didn't.

BY MR. BAUM:

Q. Right, and it would not have gotten one by itself with a .052 P-value, correct?

MR. ABRAHAM: Objection.

THE WITNESS: No.

BY MR. BAUM:

Q. Do you have any regrets about your involvement with the CIT-MD-18 based on what I've shown you today?

A. I wish we had done things a little

differently.

Q. Like what?

A. I wish I had known for certain whether the patients, those nine patients were unblinded, but obviously I don't know. You showed me a lot of documents today suggesting that people knew the patients were unblinded. I don't know for a fact that they knew that. All I know is what they wrote on the paper. I wish I was aware of the correspondence with the FDA.

Q. Do you think, based on what I've shown you today, that Forest misled anyone about the results of MD-18?

A. It probably should have been more forthcoming.

Q. If you had known what I've shown you today, would you have changed anything in your first draft of the study report?

MR. ABRAHAM: Objection.

THE WITNESS: I don't believe I've seen my first draft of the study report. I saw the final draft of the study report.

BY MR. BAUM:

Q. Would you have changed anything in the

final study report?

MR. ABRAHAM: Objection, calls for speculation.

THE WITNESS: If I were the only one involved in writing it, I probably would have written it somewhat differently.

BY MR. BAUM:

Q. In what way?

MR. ABRAHAM: Objection.

THE WITNESS: Probably emphasizing more of the results at Week 8, clarifying some things, and I'm not sure how I would have handled the potential unblinding situation. I'd have to give that some thought.

BY MR. BAUM:

Q. Wouldn't you have had to have stated that they weren't potentially unblinded, they were actually unblinded?

MR. ABRAHAM: Objection.

THE WITNESS: I don't know that for a fact.

BY MR. BAUM:

Q. I just want to now --

A. But I would like to say that all of the

A. It was six years after the publication. I don't believe I responded. I had moved on in my career at that point, and I'd also like to object to the wording "ongoing suit to have been written and submitted to the Journal by a commercial medical writer on behalf of Forest Laboratories, Incorporated." It was not submitted on behalf of Forest by a commercial medical writer. It was submitted by the authors.

Q. Did Mary Prescott write the letter and have you guys sign it?

MR. ABRAHAM: Objection.

THE WITNESS: The cover letter?

BY MR. BAUM:

Q. Yeah.

A. I don't recall.

Q. If you go over to the second page of this, it continues, "The paper was submitted as a Brief Report, which the Journal's editors requested be resubmitted as a full-length article. Drs. Wagner, Robb and Findling report that they contributed with Dr. Heydorn to the resubmission and that they were not aware that Dr. Heydorn was working with a commercial writer. Dr. Heydorn did not respond to our request."

Is it true that neither Wagner, Robb or

Findling knew that you were communicating with a commercial writer?

MR. ABRAHAM: Objection.

THE WITNESS: I don't believe that to be a true statement.

BY MR. BAUM:

Q. Did you know that they were corresponding -- that they had information and e-mail correspondence with Mitchner and Prescott, right?

MR. ABRAHAM: Objection.

THE WITNESS: At the very least, by my recollection, Dr. Wagner didn't.

BY MR. BAUM:

Q. So this is a false statement?

MR. ABRAHAM: Objection.

THE WITNESS: I believe it's false, yes.

MR. BAUM: Take a break.

THE WITNESS: Yeah.

THE VIDEOGRAPHER: The time is now 5:25 p.m. We're off the record.

(Brief recess.)

THE VIDEOGRAPHER: The time is now 5:37 p.m. We're on the record.

MR. BAUM: We have no further questions.