

IN THE SUPERIOR COURT FOR THE STATE OF ALASKA
THIRD JUDICIAL DISTRICT AT ANCHORAGE

STATE OF ALASKA,)
)
 Plaintiff,)
)
 vs.)
)
 ELI LILLY AND COMPANY,)
)
 Defendant.)
)
 _____)
 Case No. 3AN-06-05630 CI

VOLUME 15

TRANSCRIPT OF PROCEEDINGS

March 21, 2008 - Pages 1 through 199

BEFORE THE HONORABLE MARK RINDNER
Superior Court Judge

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

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1 PROCEEDINGS
 2 THE COURT: Please be seated.
 3 We're on the record in State of Alaska versus Eli
 4 Lilly and Company, 3AN-06-5630. We're outside
 5 the presence of the jury. Counsel are present.
 6 I understand there are some issues to take up.
 7 MR. LEHNER: Good morning,
 8 Your Honor. We just wanted to -- I think we
 9 filed our motion with respect to Patrizia
 10 Cavazzoni, and we wish to be heard on that.
 11 THE COURT: Okay. Does the State
 12 need an opportunity to respond in writing or --
 13 MR. SUGGS: I don't think we need
 14 to in writing, Your Honor.
 15 MR. JAMIESON: Good morning,
 16 Your Honor. Please feel free to cut me off.
 17 We're going to take a little trip down memory
 18 lane as to what happened, I guess.
 19 THE COURT: I'm going to cut you
 20 off, Mr. Jamieson. I read your brief and I would
 21 really like to hear from is the State.
 22 MR. JAMIESON: Very good, Your
 23 Honor. Lilly would like to participate to the
 24 same degree the State has been able to
 25 participate and benefit from the MDL proceedings.

1 A-P-P-E-A-R-A-N-C-E-S, continued

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1 MR. SUGGS: Your Honor, Dr.
 2 Cavazzoni's deposition --
 3 THE COURT: Well, let me just ask
 4 you, Mr. Suggs: Hasn't the whole sort of history
 5 of how this litigation been done, been predicated
 6 on the idea particularly coming from the State
 7 is we've got all these MDL depositions; we're
 8 going to use all these MDL depositions; we'll
 9 bifurcate the trial and we don't need to take a
 10 lot of depositions. All we need is a few State
 11 depositions; limited discovery, ten, let's move
 12 this along. We've got the whole MDL going.
 13 Isn't sort of the whole idea being
 14 that everybody was going to use all the MDL --
 15 hasn't that been kind of what -- the
 16 depositions -- hasn't that been the whole flavor
 17 of the arguments for the State to move this along
 18 faster, to get this done quicker, to get this
 19 case bifurcated.
 20 Don't all the transcripts and the
 21 motions that the State made in regard to that
 22 seem to suggest that everybody was going to use
 23 the MDL? And there were all these depositions in
 24 the MDL that could be taken and we would
 25

1 predicate the management of this case based on
2 that?

3 MR. SUGGS: Your Honor, I don't
4 ever remembering that we were going to waive the
5 rules. The rules are that a deposition can be
6 used against any party who was given notice of it
7 and who was present and attended there. When
8 Mr. Fibich issued the notice of the deposition,
9 he did that as part of the MDL, not the State of
10 Alaska.

11 THE COURT: That would certainly be
12 the rules, and if we didn't have this history, I
13 would say those were the rules and there wasn't
14 notice. But the history seems to be that
15 regardless of whether or not Ms. Cavazzoni or
16 someone was noticed on this case -- and I
17 recognize also that there have been depositions
18 in this case that were taken by lots of different
19 people. And -- but to the extent that there
20 would have been an argument that Dr. Cavazzoni
21 wasn't noticed particularly for this case, hasn't
22 it been waived by all the arguments that the
23 State has made? I guess that's the guts of the
24 issue.

25 MR. SUGGS: I don't think so. None

1 of the attorneys who were representing the State
2 of Alaska were there in that capacity at that
3 deposition to represent Alaska's interest.
4 Moreover, they told us that they were going to
5 bring Dr. Cavazzoni here to testify live. They
6 were going to bring her here in our case in chief
7 and we were perfectly happy with it. And now all
8 of a sudden --

9 THE COURT: And you told them that
10 you weren't going to call Dr. Hopson in your case
11 in chief, and you did. So there's been some
12 changes, and my question has been all along, just
13 as it is with Dr. Hopson, what's really fair
14 given the history and those kinds of things? And
15 given that I mean, you got ten extra depositions
16 and if Dr. Cavazzoni had been really important
17 for you to take, you could have retook her as
18 part of your ten, correct?

19 MR. SUGGS: We could have --

20 THE COURT: And you didn't do that.

21 MR. SUGGS: We chose not to.

22 THE COURT: What I'm saying is,
23 isn't everybody on notice that all the
24 depositions in the MDL were going to be used
25 here, particularly if people were listed as

1 witnesses along the way?

2 MR. SUGGS: As I read the
3 transcripts and the materials submitted with
4 their brief, Your Honor, I don't see anything
5 about we were somehow waiving the rules here. I
6 think the rule is very clear. I just don't see
7 that there's any waiver of it. I mean, I've
8 looked at the transcripts that they've attached
9 there. I have not seen anything that says we're
10 waiving the rules here.

11 THE COURT: Wasn't there a whole
12 bunch of discussion about the need to redepose
13 witnesses and whether you should have to ask
14 permission to redepose witnesses or whether you
15 should be able to designate your ten. I mean,
16 wasn't the whole suggestion of this --

17 MR. SUGGS: There was lots of
18 discussion about that, Your Honor, and lots of
19 other things but I don't see anything in there
20 that we were waiving Rule 32 in this case.

21 MR. JAMIESON: Your Honor, on that
22 point my I be heard? It wasn't a waiver -- it
23 was a waiver, we think. But in addition, it was
24 the order of this Court. If you look at the
25 transcript from the January 8th status

1 conference, at page 67, which we've attached to
2 this brief as Exhibit C, I believe.

3 The Court: You'll participate in
4 the discovery that's part of the MDL.

5 Mr. Sanders: Is that an order or a
6 question?

7 And the Court: Both, I think. And
8 then you went on.

9 And the concern of the State at
10 that time was not that they wouldn't be able to
11 use the MDL, but that they needed to redo some
12 MDL depositions that they didn't like the way
13 that those MDL depositions were taken for -- for
14 the Alaska-specific issues or any issue at all.

15 They were free to go redepose ten.
16 They got the ten freebie rule, which is what
17 Your Honor ordered. And they could -- and
18 Mr. Sanders came back to this Court a couple
19 months later and said, you know, Your Honor,
20 we're -- if somebody from Texas -- he actually
21 said if somebody from Texas does this deposition
22 and I don't like it and Your Honor said, that's
23 what you got the ten freebies for.

24 And that was the order of this
25 Court. It wasn't something that happened by

1 accident; it happened on purpose and tremendous
2 benefits have flowed to the Plaintiffs as a
3 result of the discovery in the MDL.

4 MR. SUGGS: Your Honor, you said --
5 he points to language that you said on January
6 8th, 2007. You'll -- you will -- participate in
7 the discovery that's part of the MDL. That
8 statement was six months after the deposition of
9 Dr. Cavazzoni was taken. We have an unqualified
10 right to use depositions of their folks where
11 they were represented. They do not -- under Rule
12 32, they don't have the right to use depositions
13 unless the party was represented and I don't see
14 any order --

15 THE COURT: What's Dr. Cavazzoni's
16 status?

17 MR. JAMIESON: Her status?

18 THE COURT: Yeah.

19 MR. JAMIESON: She's not going to
20 be here at trial.

21 THE COURT: Where is she?

22 MR. JAMIESON: She's an employee of
23 Eli Lilly.

24 THE COURT: Where is she?

25 MR. LEHNER: She's in Indianapolis,

1 Your Honor. She is a single mother. She's had a
2 lot of trouble sort of scheduling. She has a
3 very difficult family situation. We thought we
4 had her for a day. It didn't work out.

5 THE COURT: What I'm asking really,
6 to front is there a way to do a telephonic
7 deposition of her to fill in this alleged gap?

8 MR. LEHNER: I'm not sure what the
9 gap is, Your Honor, because -- I mean -- it seems
10 to me either we are able to use the material of
11 the MDL. I mean if you want to take time from
12 the Court to do a telephonic deposition --

13 THE COURT: I mean if the question
14 is notice. If that's a problem I can cure that.

15 MR. LEHNER: I don't think it's
16 really notice, Your Honor. She was deposed twice
17 on all of the generic issues that have been at
18 issue in this court. She has no Alaska-specific
19 information.

20 THE COURT: If she had
21 Alaska-specific information and it was important
22 for the State to depose, I assume that the State
23 would have listed her as one of your ten? I
24 mean, you didn't use your full ten, did you?

25 MR. SUGGS: No, we didn't, Your

1 Honor.

2 THE COURT: So, I mean --

3 MR. SUGGS: I'm sorry, what's your
4 question, sir?

5 THE COURT: So my question is, I
6 mean, to the extent that the question is we
7 didn't get to use her for Alaska purposes because
8 she wasn't noticed to Alaska purposes. You could
9 have used her for Alaska purposes. You chose not
10 to.

11 MR. SUGGS: Your Honor, I wasn't
12 there. Mr. Allen wasn't there representing the
13 State of Alaska. This was June of 2006.

14 THE COURT: Right. But we ended
15 up -- what you just pointed out to me is we ended
16 up with the ten freebie rule if I that's what I
17 can shorthand call it after she was deposed;
18 correct?

19 MR. SUGGS: Yes.

20 THE COURT: So you could have gone
21 back if it was critical to redepose her and --

22 MR. SUGGS: Your Honor, we didn't
23 think we needed to redepose her because we didn't
24 think she was going to be coming here because of
25 Rule 32. I mean, Rule 32 says they can't use

1 it unless they retook it.

2 THE COURT: Wasn't she on the
3 witness list from Day One? Wasn't she talked
4 about in the opening statement?

5 MR. SUGGS: Yeah, and they were
6 entitled to bring her live. They could have
7 brought her live. This is a person who's--

8 THE COURT: I mean, haven't we had
9 a lot of talk about documents authored by
10 Dr. Cavazzoni? I'm sorry, Mr. Suggs, but if you
11 tell me you didn't think she was going to be here
12 or wasn't going to be a witness in this case I
13 have some problems with that.

14 MR. SUGGS: Your Honor, I have no
15 problem with her coming here at all. I would
16 love to have her on that witness stand, Your
17 Honor. I would love to have her live.

18 THE COURT: I understand that and I
19 understand what's really going on here, but --

20 MR. SUGGS: Your Honor, this lady
21 is head, I think, of global safety.

22 MR. FIBICH: Can we call a time
23 out? We need to talk. Let's call a time out.

24 MR. ALLEN: Can we talk? Can we
25 talk?

1 THE COURT: Yeah. We'll be off
 2 record.
 3 THE CLERK: Off record.
 4 (Discussion off the record.)
 5 THE COURT: Mr. Suggs.
 6 MR. SUGGS: Your Honor, we have our
 7 objection, but we will withdraw it and let them
 8 play Ms. Cavazzoni's deposition.
 9 THE COURT: Okay. Then what we
 10 need to do is designate those portions and deal
 11 with objections and all of those kinds of things
 12 and deal with counterdesignations of which I'm
 13 sure there's going to be a few.
 14 MS. GUSSACK: I believe they've
 15 been submitted to the Plaintiffs.
 16 MR. ALLEN: Unfortunately, Your
 17 Honor, there's not much.
 18 MS. GUSSACK: It's relatively brief
 19 on both -- I think both sides, Your Honor. But
 20 we'll make sure that you have whatever is in
 21 dispute.
 22 THE COURT: Okay.
 23 What's the plan for today?
 24 MR. LEHNER: Your Honor, we're
 25 going to play depositions of Dr. Beasley and then

1 perhaps a brief deposition of 20 minutes, maybe
 2 30 minutes of Dr. Toleffson and then bring
 3 Dr. Baker on as our live witness.
 4 THE COURT: Okay. And again, I'll
 5 remind everybody, jury instructions.
 6 MR. ALLEN: We do -- trust me, even
 7 I had to learn that yesterday.
 8 MS. GUSSACK: Your Honor, on that
 9 subject, do you have in your schedule of you as
 10 to when next week you would want to have a
 11 conference on those?
 12 THE COURT: Well, part of that will
 13 depend on -- what I need to know is -- I'm
 14 tempted to have fun with you, Ms. Gussack and I
 15 guess I'll say this --
 16 MS. GUSSACK: It's Friday, Judge,
 17 you're allowed.
 18 THE COURT: -- so a noncoy answer
 19 about when Lilly thinks they'll be done with
 20 their case and then a noncoy answer --
 21 MR. ALLEN: Judge, I'm not coy. We
 22 can say a lot of things about me; coy is not one.
 23 THE COURT: That's what Ms. Gussack
 24 said too.
 25 MR. ALLEN: Yeah, but she wasn't

1 telling the truth.
 2 THE COURT: I need to get a sense
 3 from the State as to what it's going to do on
 4 rebuttal. What I'll try to do is plan this and
 5 even if I have to send the jury home for a day
 6 while we take this up, but I want to do it at a
 7 point that it makes sense, and that will depend
 8 on when Lilly is likely to rest and how much
 9 rebuttal the State's going to have, because that
 10 will let me figure out when this case might
 11 actually be going to the jury and when you will
 12 be doing -- I'm assuming at this point, and
 13 please correct me if I'm wrong, that we'll have a
 14 whole day jointly for closing arguments and then
 15 if we have time that day, we'll instruct the jury
 16 and they can start deliberating.
 17 If not, we'll bring them back in
 18 the morning and they can be instructed and start
 19 deliberating. I'll also consider, and you can
 20 all tell me what your views on this is.
 21 Sometimes people have -- given jury instructions
 22 before the closings and I'm willing to do that
 23 if -- I'm willing to think about that. I haven't
 24 done that in a case, but I understand why it
 25 might be a useful thing for everybody.

1 MR. ALLEN: We prefer it.
 2 THE COURT: I'll let everybody
 3 think about it for a day or so. If that's the
 4 case, we'll figure that -- what I don't want to
 5 do is split somebody's -- split the closing
 6 arguments in any way at all. But if -- if we
 7 know we're going to do jury instructions and then
 8 closings and then they deliberate, start
 9 deliberating, I'll let them know that on that day
 10 they're going to start deliberating, they can
 11 expect to be here the whole day. So, as soon as
 12 you know and let me know when you are likely to
 13 be resting or what your plan is, you can let me
 14 know how much you've got in rebuttal.
 15 MR. ALLEN: I have 12 minutes.
 16 MS. GUSSACK: Your Honor, we -- in
 17 large measure informed by the length of
 18 cross-examination of our witnesses, we think
 19 realistically it looks like it could be Wednesday
 20 but, you know, that's really just an estimate
 21 right now. We'll certainly let you know as soon
 22 as we know more.
 23 THE COURT: Well, again --
 24 MR. FIBICH: Your Honor, I do not
 25 expect at this time that the State is going to

1 call any live witnesses in rebuttal. Obviously,
2 I can be just as coy and say, well, that may
3 change. But it's unlikely. Mr. Allen has 12
4 minutes that I think you are familiar with that
5 is going to be offered in rebuttal. But we do
6 not anticipate a lot of rebuttal testimony.
7 There may be some short offers, but from our
8 standpoint, we're not going to have --

9 THE COURT: So what I'm sort of
10 hearing is it's possible that the case -- the
11 evidentiary portion of the case may conclude on
12 Wednesday subject to how long the
13 cross-examination is. If you take a day and a
14 half to cross-examine somebody --

15 MR. ALLEN: Did somebody do that?

16 THE COURT: -- I would anticipate
17 that any live witnesses the State goes on -- that
18 Lilly puts on might take that long, but the State
19 will have to decide how vigorous their
20 cross-examinations are going to be.

21 MR. FIBICH: Well, Your Honor, we
22 appreciate the Court's questioning on this issue.
23 And we don't want to get into what we've been
24 told in the hall, but we need some definiteness
25 about when they think they're going to rest.

1 THE COURT: Well, again, I
2 understand how what they say is somewhat
3 dependent on what you do on your cross. And I
4 don't know how many live witnesses we have, and
5 I've got to deal hopefully sooner rather than
6 later with any of the Cavazzoni objections and
7 cross-designations and those things before they
8 can cut their tape.

9 MR. ALLEN: I think --

10 MS. GUSSACK: I think we have --

11 A SPEAKER: They've given us their
12 designations.

13 MR. ALLEN: Objections? It's
14 unlikely I would object.

15 MR. LEHNER: Counterdesignations.

16 MS. GUSSACK: I'm sorry,
17 counterdesignations.

18 MR. ALLEN: I've instructed
19 Mr. Suggs because I told him I wanted him to be
20 brief like me with Dr. Baker today. He promised
21 me he would.

22 MR. SUGGS: Your Honor, when he
23 told me that, I laughed.

24 MS. GUSSACK: Your Honor, and I
25 take it also about the issue about 12 minutes on

1 rebuttal is something that is still being held in
2 reserve by the Court.

3 THE COURT: I assume that that was
4 a comment sort of directed on the information in
5 the Eski deposition that I haven't let in.

6 MR. ALLEN: That was exactly what
7 it was.

8 MS. GUSSACK: So we could be
9 finished much earlier then -- by 12 minutes?

10 MR. ALLEN: Twelve minutes early.

11 MS. GUSSACK: Thank you, sir.

12 THE COURT: I'll take a look at my
13 calendar with this sort of generalized schedule,
14 recognizing we're going to have to be flexible
15 and try to figure out where I may have some time.
16 What I'll do if I can, but I kind of doubt it, is
17 if I can move something in an afternoon, we can
18 take this up in the afternoon. I have a feeling
19 I'm going to have to move a lot of things and
20 that's a little more problematic. So we may just
21 take a morning and not have the jury come in that
22 day.

23 Anything else before we bring in
24 the jury?

25 Then we'll give the jury a heads up

1 and we'll get started. We'll be off record.

2 THE CLERK: Please rise. Superior
3 Court now stands in recess.

4 Off record.

5 (Break.)

6 (Jury in.)

7 THE COURT: Please be seated.

8 We're back on the record and all
9 members of the jury are present. Good morning,
10 ladies and gentlemen.

11 Eli Lilly is ready to call its next
12 witness?

13 MR. LEHNER: Yes, Your Honor.

14 Thank you.

15 Good morning.

16 Eli Lilly and Company calls as its
17 witness Dr. Charles Beasley, the distinguished
18 Lilly scholar and chief scientific officer in the
19 Global Patient Safety Group.

20 VIDEOTAPED TESTIMONY OF CHARLES M. BEASLEY, JR.
21 Q. Would you state your full name for the
22 record, please?

23 A. Yes. My name is Charles M. Beasley.

24 THE COURT: Are we going to put
25 this screen up?

1 MR. LEHNER: Yes.
 2 Q. Good morning, Dr. Beasley.
 3 Would you state your full name for
 4 the record, please?
 5 A. Yes, my name is Charles M. Beasley, Jr.
 6 Q. And how old are you, sir?
 7 A. I am 56.
 8 Q. And are you married?
 9 A. Yes, I am.
 10 Q. And do you have any children?
 11 A. No, I do not.
 12 Q. Okay. And are you currently employed by
 13 Eli Lilly?
 14 A. Yes, I am.
 15 Q. And what's your current job title?
 16 A. My current job title is distinguished
 17 Lilly scholar and chief scientific officer for
 18 Global Product Safety.
 19 Q. And how long have you held that
 20 position?
 21 A. I've held that position since the spring
 22 of 2003.
 23 Q. Okay. And do you currently have any
 24 responsibilities regarding the drug Zyprexa?
 25 A. No, sir, not directly. I -- my current

1 function is a consultant within Global Product
 2 Safety across a number of compounds as people
 3 would come and consult to me.
 4 Q. Thank you. I'd like to go over some of
 5 your background. I believe you were born in 1950
 6 in Tokyo, Japan; is that correct?
 7 A. That's correct.
 8 Q. And I assume your father was stationed
 9 there in the military?
 10 A. That's correct.
 11 Q. Okay. And then you received your
 12 undergraduate degree in psychology at Yale
 13 University in 1977?
 14 A. That's correct.
 15 Q. And you received your medical degree in
 16 1983 from the University of Kentucky College of
 17 Medicine; is that correct?
 18 A. That's correct.
 19 Q. And then I believe you did an internship
 20 at Yale University in the Department of
 21 Psychiatry for a year?
 22 A. That's correct.
 23 Q. So that would take us up to 1984?
 24 A. That's correct.
 25 Q. Okay. And then you did a three-year

1 residency in psychiatry at the University of
 2 Cincinnati in Ohio between 1984 and 1987; is that
 3 correct?
 4 A. That would be correct. I completed the
 5 residency in June of 1987.
 6 Q. Okay. And I believe you became
 7 board-certified in psychiatry in 1988; is that
 8 correct?
 9 A. That would have been correct. It's a
 10 two-step process, and I believe that I completed
 11 the second part in, I believe it was October of
 12 1988.
 13 Q. Okay. And you joined Eli Lilly as an
 14 associate research physician in July of 1987; is
 15 that correct?
 16 A. That's correct.
 17 Q. Okay. And can you briefly describe, in
 18 general terms, the positions you've held at Eli
 19 Lilly since joining the company in 1987?
 20 A. Well, there's -- there's been about a
 21 19-year evolution --
 22 Q. I understand that?
 23 A. -- evolution here. I joined with the
 24 title of associate research physician. And my
 25 first work in the company was with fluoxetine,

1 trade name of Prozac --
 2 Q. Okay.
 3 A. -- the antidepressant. And I managed
 4 and developed, supervised a number of clinical
 5 trials for Prozac. I don't remember the specific
 6 number. I believe it was someplace in the order
 7 of eight or ten.
 8 Q. And then, continue, if you would,
 9 describing the positions you've held.
 10 A. Okay. While I was working on
 11 fluoxetine, I also had responsibilities as the
 12 trial designer and -- for the molecule that was
 13 then referred to as atomoxetine. It was being
 14 developed as an antidepressant. This molecule
 15 was not taken completely through development at
 16 the time as an antidepressant. And this work
 17 occurred simultaneously with my work on
 18 fluoxetine, and took me -- takes me up to
 19 approximately 1991.
 20 Q. Okay.
 21 A. I did receive a promotion during that
 22 time from associate research physician to
 23 research physician. And 1991 was the point where
 24 I was assigned responsibilities for the continued
 25 development of olanzapine for trade name Zyprexa.

1 And I worked in this program on a global basis,
 2 both in the United States and in coordination
 3 with other physicians outside of the United
 4 States, up through 1997 as part of the olanzapine
 5 team. And there was an -- there was an evolution
 6 from the drug being developed as part of the
 7 general neuroscience team to a team focused
 8 specifically on the development of that molecule.
 9 So I took part in both of those.

10 Q. And during that period, were you
 11 developing and monitoring clinical trials that
 12 were in support of the new drug application?

13 A. Yes, I was.

14 Q. Okay.

15 A. In 1997, there occurred a significant
 16 organizational change. I also had been promoted
 17 in that period twice to senior research physician
 18 and then to Lilly adviser.

19 In -- in 1997 there was a -- a
 20 reorganization. The team leader for the Zyprexa
 21 team, Dr. Gary Toleffson, was promoted to
 22 president of the entire central nervous system
 23 unit. Dr. Breier was placed in charge of the
 24 team, and I transitioned off the team to report
 25 directly to Dr. Toleffson in a consultative role.

1 I was still rather much involved with olanzapine,
 2 but in this different organizational system.

3 It was in about, I think, 1998 or
 4 '99 that I was assigned to be team leader for the
 5 development of a -- we call it a transition team
 6 for another molecule. Again, a central nervous
 7 system molecule intended for the treatment of
 8 anxiety disorders.

9 Q. Let me interrupt for a second.

10 What year was it that happened?

11 A. I believe that was either 1998 or 1999.
 12 I don't recall the specific date. And this was a
 13 molecule that did not come to NDA, and, in fact,
 14 I was transitioned off that team prior to -- the
 15 completion of that -- of that project.

16 In 2001, I transitioned completely
 17 out of the neuroscience area. I was requested to
 18 take the position of medical director for our
 19 compound tadalafil, also known as Cialis, in the
 20 cardiovascular area.

21 In 2003, I transitioned back to
 22 a -- a consultative position, pretty much across
 23 all the therapeutic areas within Lilly, although
 24 I reported directly to Dr. Gary Toleffson. So,
 25 my home organizational base was within central

1 nervous system, but worked across a broad number
 2 of compounds.

3 And then in 2004, was -- during
 4 another company reorganization, was asked to take
 5 the -- a position in global product safety.
 6 Dr. Toleffson had retired, and I was both, once
 7 again, promoted to my current position and given
 8 my current functional organizational
 9 responsibilities.

10 Q. Okay. And it indicates there that the
 11 molecule olanzapine, which was later marketed
 12 under the trade name Zyprexa, was first
 13 synthesized in April of 1982.

14 Does that square with your
 15 understanding?

16 A. That would be my understanding.

17 Q. Okay. And then the investigational new
 18 drug application was filed in 1986; is that
 19 correct?

20 A. To the best of my knowledge, yes, that
 21 would be correct.

22 Q. And that's sometimes referred to as an
 23 IND, correct?

24 A. That's correct. That's how it is
 25 abbreviated here.

1 Q. And an IND is something that a drug
 2 company has to file with the FDA in order to
 3 begin testing on human subjects; is that correct?

4 A. Yes. And, of course, that would be
 5 within the United States --

6 Q. Correct.

7 A. -- since it's filed with the FDA.

8 Q. And the document also indicates that the
 9 first human dose was in September of 1986; is
 10 that correct?

11 A. Yes, it does.

12 Q. Okay. And the first open-label clinical
 13 dose was in December of 1988, correct?

14 A. December of 1988, yes.

15 Q. Okay. And that phrase first open-label
 16 clinical dose, refers to a type of study where
 17 the drug is given to -- to subjects in a clinical
 18 setting, correct?

19 A. Yes. This would also be what we would
 20 call an uncontrolled clinical trial. It is a
 21 very preliminary observation of the medication
 22 in -- in patients with the disease that is --
 23 that the drug hopefully treats or is intended to
 24 treat.

25 Q. Okay. And in order to receive approval

1 from the FDA to market a drug, drug companies
2 have to perform various clinical trials,
3 typically, involving placebo-controlled and
4 double-blind studies; is that correct?

5 A. That's correct.

6 Q. And in this case, the first double-blind
7 placebo-controlled dose was given in November of
8 1991; is that correct?

9 A. That's correct.

10 Q. And I believe you said you started
11 working with Zyprexa in 1991. Were you involved
12 in that very first clinical testing?

13 A. Yes, I was. Although I did not design
14 those -- those clinical trials, I took over
15 responsibility for the supervision of the
16 molecule as those trials were beginning.

17 Q. Okay. And then the document indicates
18 that the completion of core studies occurred in
19 February of 1995. And can you describe for us
20 what is meant by the term "core studies"?

21 A. Yes. These would have been the studies
22 that would have been included in both the new
23 drug application, the NDA in the United States,
24 as well as the regulatory submissions in other
25 countries.

1 Q. Okay. And the document also indicates
2 that worldwide regulatory submission was filed in
3 September of 1995; is that correct?

4 A. That's correct.

5 Q. And was there more than one regulatory
6 submission filed at that time?

7 A. The two submissions that were filed
8 almost simultaneously were the U.S. submission
9 and the European submission.

10 Q. Okay. And in Europe it was submitted to
11 what agency?

12 A. It was submitted to the European
13 Medicine Agency.

14 Q. Okay. Is that sometimes referred to as
15 EMEA?

16 A. EMEA.

17 Q. Okay. And am I correct that the largest
18 of the core studies that was done was a study
19 that was referred to as HGAJ?

20 A. That was the largest.

21 Q. And it had approximately how many
22 subjects in it?

23 A. It had 1,996 subjects.

24 Q. Okay. And was it the largest, by far,
25 of the various clinical studies that were done in

1 connection with the drug?

2 A. It was.

3 Q. Okay. Fair to say that the vast
4 majority of the data that you had from clinical
5 trials regarding Zyprexa was the data from HGAJ?

6 A. Given the four other trials, I think it
7 remained the -- probably the majority. Again, I
8 don't have a precise number, but I think it was
9 probably just slightly over the majority.

10 Q. Okay.

11 A. In fact, if I can just -- in thinking, I
12 think there were a total of -- of 2500 patients
13 treated in clinical trials that were included in
14 the NDA, and I believe there were 1300 in --
15 treated with olanzapine, Zyprexa in that trial.
16 So I think that is slightly more than half.

17 Q. Okay. And in the HGAJ study, am I
18 correct that patients were treated in that study
19 for up to a year with Zyprexa?

20 A. Well, if I may, it actually had a rather
21 complex design from a -- from a time perspective.
22 There was an acute treatment period of six weeks.
23 So all patients were treated up for -- for six
24 weeks. If patients were not doing well, either
25 because of tolerance or efficacy, and they

1 remained in the trial for three weeks, they could
2 discontinue and be placed on open-label
3 olanzapine. But that would have continued to be
4 within this trial.

5 There was then a -- what we call an
6 extension that, actually, ran past a year. It
7 ran until the time that the drug was actually
8 approved. So, there was no definite terminal
9 period. The option available to patients was for
10 them to actually be continued for longer than a
11 year.

12 Q. Okay. And the other studies that were
13 done in connection with the NDA, were they as
14 long-term as HGAJ?

15 A. Yes. They were, in fact, longer term.
16 We had placed for patients the -- within all of
17 the studies -- the ability to take medication
18 until the time that we either discontinued the --
19 the development project or the medication was
20 approved in their specific countries. Obviously,
21 for the patients that were doing well on the
22 medication, that was viewed as an appropriate
23 opportunity for them to continue to receive
24 treatment.

25 Q. Am I correct that in that gap of time,

1 between February and September of 1995, the data
2 was essentially cut off, collection data was cut
3 off, and that there was then a period of time
4 where the data was written up for submission?

5 A. That's -- that's partially correct. As
6 I said, we allowed the studies to run until the
7 drug was approved. So, there was a time when we
8 declared the -- the collection of data for
9 submission to the NDA to be finalized. And that
10 was a period where those data were unblinded, a
11 term that we refer to as locked. Those data were
12 finalized, they were developed and written up.

13 Although, again, patients were
14 continued and data were continued to be collected
15 in these -- in these studies that were ongoing.

16 Q. Okay. And at the time that the data was
17 locked up or cut off for write-up purposes, if I
18 can use that phrase, page 6 of this exhibit
19 indicates that there were about 3,000 people who
20 had received more than one dose; is that correct?

21 A. That's correct.

22 Q. But only about 2,000 had received more
23 than one month?

24 A. That's correct.

25 Q. And only about 875 had received more

1 than six months?

2 A. That's correct.

3 Q. And only slightly more than 300 had
4 actually used the drug for more than a year; is
5 that correct?

6 A. That's correct.

7 Q. Didn't your clinical trials show that
8 there was increased cholesterol and also type 2
9 diabetes?

10 A. I do not recall the -- the specifics of
11 the results of all the analyses of cholesterol.
12 My recollection is that taking all of the data in
13 total, we did not see an association between the
14 drug and cholesterol. And with respect to
15 diabetes, the same.

16 Clearly, cases were observed in
17 what we would call temporal association when
18 individuals in clinical trials did develop
19 diabetes, a small number, and we did not, in
20 looking at all the data, see the compound as --
21 given the date that we had, as there being an
22 increased or excessive development within our
23 clinical trial database.

24 Q. And the labeling that was in effect at
25 that time when the product came out in the market

1 did not warn physicians that your clinical
2 studies had found statistically significant
3 increased incidence of high glucose in Zyprexa
4 users, correct?

5 A. That is correct. But my recollection of
6 the data as you have -- have asked your question,
7 is that we would not have found that. We would
8 have -- and what we did was we analyzed both the
9 placebo-controlled data and the
10 haloperidol-controlled data. There were three
11 studies that include haloperidol on what we call
12 an integrated basis. And my recollection is that
13 those integrated analyses did not show or support
14 the finding that we'd been discussing in J.

15 Q. Do you recall that the FDA approved
16 Zyprexa for marketing in September of 1996?

17 A. I don't recall whether it was late
18 September or early October.

19 Q. Okay. And am I correct that one of the
20 last things that happens before a drug is
21 marketed is the drafting of labeling for
22 prescribing physicians?

23 A. Well, there is, actually a draft that is
24 prepared as part of the new drug application.

25 Q. And it's submitted to the FDA as part of

1 the new drug application. The FDA then comes
2 back and says whether they approve that language
3 or not, correct?

4 A. That's correct.

5 Q. And oftentimes -- and there is
6 interchange between the company and the FDA as to
7 what's going to be in the content of the
8 language, correct?

9 A. That's correct.

10 Q. And when the FDA saw the data, the
11 FDA -- well, let me back up for a second.

12 When we talk about the labeling,
13 that's the package insert material, correct?

14 A. That's correct.

15 Q. It's also contained in the Physicians'
16 Desk Reference, which is a big, thick book which
17 contains the labeling for all prescription
18 products, correct?

19 A. I think for the majority. It's not all.
20 And those are copies of -- obviously, intended to
21 be kept current -- the prescribing information or
22 the package insert.

23 Q. Okay. And that information, the
24 prescribing information that is contained in the
25 labeling is very critical for doctors to have;

1 isn't that correct?

2 A. It is intended to be a summary of the
3 data that would allow the effective and safe use
4 of the medication. That is correct.

5 Q. And it's absolutely necessary that the
6 information in there is complete and accurate,
7 correct?

8 A. Again, it's important that it -- that it
9 allow for the safe and effective use of the
10 medication. From a concept of complete, again,
11 all 1.5 million pages can't be contained. So,
12 the intent is that it is a summary of the most
13 pertinent information that will allow the drug to
14 be prescribed appropriately.

15 Q. And do you know who Dr. Ken Hornbuckle
16 was?

17 A. Yes.

18 Q. And who is he?

19 A. He is a veterinarian and epidemiologist.
20 He's our chief epidemiologist --

21 Q. Okay.

22 A. -- at Lilly.

23 Q. And is he still in that capacity?

24 A. Yes, he is.

25 Q. And who is Dr. Man Fung?

1 A. He was --

2 Q. By the way, am I pronouncing his name
3 correctly?

4 A. Yes. that's correct. Man Fung.
5 Dr. Fung was the physician responsible for
6 Zyprexa, olanzapine in the pharmacovigilance and
7 epidemiology division within the company.

8 Q. And what is the worldwide
9 pharmacovigilance and epidemiology division?

10 A. This is a unit that serves a number of
11 functions in terms of monitoring the safety of
12 products, both drugs and administration
13 instruments. They deal with the collection of
14 the spontaneous adverse event reports, their
15 organization, their analysis. They -- it's been
16 an evolving organization.

17 They're also involved in
18 potentially setting up epidemiological studies,
19 intentionally suggesting prospective studies and
20 then interfacing with regulatory. They sit as
21 part of regulatory. This is, actually where,
22 with a different name, my current position
23 resides within this -- within this organization.

24 Q. Do you know who, back in 1998,
25 Dr. Hornbuckle and Dr. Fung would have reported

1 to?

2 A. No, I'm not certain at this -- at this
3 time.

4 Q. Okay. Would you -- did you have
5 interaction with either of those gentlemen back
6 in '98?

7 A. Yes, I would have.

8 Q. With respect to Zyprexa?

9 A. Yes.

10 Q. Okay. And describe the nature of your
11 interaction with those folks back in '98.

12 A. Well, again, although I was not part of
13 the olanzapine team, I did review aspects of
14 safety from a product team perspective. So, I
15 would have interacted with these individuals who
16 also served to review safety data. So it was
17 a -- we, in essence, formed a -- a larger team
18 across several components of the corporation.

19 Q. And who is the "we" that you're
20 referring to there?

21 A. Would have been Dr. Hornbuckle,
22 Dr. Fung, other members of the product team,
23 medical members of the U.S. affiliate, members of
24 their -- additional members of the worldwide
25 pharmacovigilance and epidemiology staff.

1 Q. And did that collection of individuals
2 you've just described, did they have a name or
3 a -- for that team or group?

4 A. No, there was no specific name for that
5 group of individuals.

6 Q. Is there -- was there anyone who sort of
7 led or headed up that group?

8 A. It was driven, I think, as sort of a
9 joint effort with Dr. Fung, Dr. Hornbuckle, and
10 myself.

11 Q. Okay. And I've seen reference to a
12 Dr. Kenneth Kwong. Was he part of that
13 pharmacovigilance and epidemiology group as well?

14 A. When Dr. Fung moved on to other
15 assignments, Dr. Kwong took his place.

16 Q. Okay. Am I correct that one of the --
17 well, let's talk about these spontaneous reports
18 and what they are. These are sometimes referred
19 to as adverse reaction reports, or adverse event
20 reports, correct?

21 A. Adverse event reports, yes.

22 Q. Okay. And they can come into the
23 company from doctors or from consumers?

24 A. Among other people. There are a lot of
25 sources. They can also come in from literature,

1 for example, as well as -- as well as other
2 sources.

3 Q. Okay. You referred several times to a
4 group known as the product team that was led by
5 Alan Breier; am I correct?

6 A. That's correct.

7 Q. And can you describe for us what that
8 product team consisted of or who was on that
9 team?

10 A. That was a very large team of
11 individuals that was responsible for this
12 molecule exclusively from a worldwide and
13 corporate perspective, primarily directed at
14 doing research, but also with a global marketing
15 component.

16 And that is in contrast to the --
17 the -- I guess, 190 international affiliates who
18 actually did -- also did research and actually
19 directly marketed the compound. So this is a --
20 this is a group that did general work with the
21 compound. And I hope that's an adequate
22 explanation.

23 Q. I'd like to probe a bit more in terms
24 of -- you said it's a large team, and I don't
25 expect you to remember all the particular

1 individuals, but were there different departments
2 that comprised the components of that team?

3 A. Yes. There would have been a medical
4 component. So, there were a number of physicians
5 that were on the -- on the team.

6 Q. And you mentioned Dr. Breier. He's,
7 obviously, a physician.

8 A. He was a physician -- but he was the
9 head of the whole organization.

10 Q. Do you recall whether Drs. Kinon and
11 Dr. Robert Baker were members of that product
12 team?

13 A. I think they were actually members of
14 the U.S. affiliate, so they would not have been
15 members of the product team at least at this
16 point in time. I don't think -- I think
17 Dr. Kinon was briefly a member of the product
18 team early when he came to the company, but then
19 moved to the -- to the U.S. affiliate. And I
20 don't think -- I think Dr. Baker when he came
21 was -- came directly into the U.S. affiliate.

22 Q. Okay. I interrupted you. You were
23 telling me that part of the product team was a
24 medical -- well, it was led by Dr. Breier. There
25 was a medical component. And that's when I

1 interrupted you.

2 A. There would have been a medical
3 component -- I hope I get most of these. There
4 would have been a statistical component. There
5 would have been a very large component -- there
6 would have been a systems component, people that
7 actually worked with the computers in contrast to
8 the statistical individuals.

9 There would have been what we call,
10 for instance, medical plans. These are the
11 individuals, usually with bachelor's or master's
12 degree training that actually support physicians
13 in the conduct and the interface with doing
14 research. There would have been a medical
15 writing component. Those are the ones that I'm
16 familiar with. I may be missing a component or
17 two -- a component or two.

18 Q. Let me direct your attention back to
19 Exhibit 6890, and this agenda for Zyprexa medical
20 marketing in December of 1998. Do you recall
21 this particular meeting?

22 A. No. Almost seven and a half years ago,
23 I don't recall the specific meeting.

24 Q. Okay. Do you see under the agenda,
25 there's several bullet points. The middle one

1 is: Weight gain and link to diabetes, question
2 mark. What does the data say and what is our
3 action plan, question mark.

4 Do you see that reference?

5 A. Yes, I do.

6 Q. And then there's a handwritten note at
7 the bottom relating to weight gain, correct?

8 A. Yes, there is.

9 Q. By the way, do you recognize that
10 handwriting?

11 A. No, I don't.

12 Q. The handwritten note says: Weight gain
13 and genetic vulnerability lead to hyperglycemia,
14 correct?

15 A. Yes, it does.

16 Q. And do you agree with that medical
17 concept?

18 A. I would characterize this as being not
19 correct.

20 Q. Okay. In what way do you say it's not
21 correct?

22 A. I would view both weight gain and
23 genetic variability as risk factors for the
24 development of hyperglycemia. Individuals who
25 have these risk factors may or may not go on to

1 develop hyperglycemia. A lot of people gain
2 weight who don't become diabetic, as with
3 people -- there are people who become diabetic
4 who don't gain weight.

5 Presumably, there is this element
6 of genetic variability. Certainly, a strong
7 hypothesis built on epidemiologic studies noting
8 that it runs in families, but we have not
9 identified the -- the gene abnormality that
10 invariably leads to hyperglycemia or developing.

11 Q. And if someone has a risk factor, that
12 means that they may develop that problem,
13 correct?

14 A. That -- that puts them at increased
15 risk. To be very precise, that puts them at
16 increased risk relative to patients or
17 individuals without that risk factor.

18 Q. And if, in fact, you have a group of
19 people who are at increased risk, then those
20 people -- some of them -- you may not be able to
21 tell who, but some of them will, indeed, come
22 down with the -- with the adverse event at the
23 end of the day, right?

24 A. I -- I can't absolutely conclude that
25 because, again, these things remain risk factors.

1 Some of them actually having a relatively low
2 incidence of increased risk. So I cannot
3 automatically know that because someone has risk
4 or that a large group of individuals has risk
5 factors, that somebody will definitely develop
6 the condition within that --

7 Q. Let me restate the question.

8 Would you agree, sir, that if you
9 have a group of people who are at increased risk
10 of having some adverse event occur that it is
11 more probable than not, at the end of the day,
12 that some of those people will, in fact, develop
13 the adverse event as a result of using the drug
14 that increased their risk?

15 A. All I can say is that there is increased
16 probability among those individuals with that
17 risk factor of developing the condition if
18 they -- than if they did not have the risk
19 factor.

20 That would be correct.

21 Q. And, in fact, as we saw earlier, your
22 clinical trials back in 1995 showed a
23 statistically significant increased incidence of
24 hyperglycemia with use of Zyprexa, correct?

25 A. And I disagree with that. As we

1 discussed, there was one finding in one clinical
2 trial of many analysis showing that finding.

3 Q. And by -- strike that.

4 When the clinical trials for
5 Zyprexa was done before it was marketed, was the
6 evaluation of the risk of diabetes with Zyprexa a
7 specific goal of those clinical studies?

8 A. Although it was not a -- stated as a
9 primary outcome in the protocol, it was clearly
10 one of the many aspects of safety that was
11 evaluated.

12 Q. If diabetes or hyperglycemia had been
13 the specific goal of the study, would you have
14 recommended that fasting glucose blood tests be
15 taken as opposed to random blood glucose testing?

16 A. Actually, I would not have made that
17 recommendation.

18 Q. And why is that?

19 A. My concern is with the compliance of
20 patients that suffer severe mental disease, and
21 knowing that you could get the possibility of
22 really significant noncompliance in this patient
23 population, so that if you thought you had
24 fasting glucoses, in many instances you may well
25 not have fasting glucoses.

1 Q. Okay.

2 A. That was -- that was my opinion at the
3 time.

4 Q. Okay. And in item C in this e-mail it
5 states: Charles Beasley reassures that
6 regulators have felt satisfied with Lilly's
7 explanations and Lilly's commitment to conduct
8 new clinical trials and to continue to do
9 proactive post-marketing safety surveillance.

10 Did I read that correctly?

11 A. Yes, you did.

12 Q. And who did you work with on that
13 project?

14 A. There were a number of people that
15 I worked with -- and this actually represents a
16 number of projects. And, again, I don't recall
17 specific conversation with Edmundo, but there
18 were several activities that were going on at the
19 time.

20 I worked with the pharmacovigilance
21 individuals and the -- the team -- the product
22 team to produce a review, very detailed review of
23 both the spontaneous data and the -- and the
24 clinical trial data that -- substantial amount of
25 which had accumulated since the drug had been

1 released. We had also made the decision to
2 conduct -- and this was in part of agreeing with
3 this senior leadership cross-functional team, to
4 conduct some studies of potential mechanisms of
5 inducing hyperglycemia. So that we -- we had
6 intended to study ways in which the medication
7 might cause patients to become hyperglycemic, if
8 it did.

9 Q. This -- as you referred to it, detailed
10 review of the spontaneous data and clinical trial
11 data in 1999, was that for the purpose of
12 addressing the hyperglycemia issue?

13 A. The -- the topic of hyperglycemia, yes.

14 Q. Okay. And who was it that directed you
15 to undertake that review?

16 A. No one, actually directed that review to
17 be undertaken, to the best of my recollection.
18 It was Dr. Kwong in pharmacovigilance, his group,
19 and myself that felt it would be appropriate to
20 conduct a very, very thorough --

21 Q. Okay.

22 A. -- and comprehensive review. I believe
23 that it began in early 1999.

24 Q. Okay. And would it be fair to say that
25 you and Kenneth Kwong were the principal drivers

1 for undertaking that review?

2 A. Yes, directly. But, again, Dr. Breier
3 had put together this team that, I believe, he
4 actually convened earlier than 1999. I'm not
5 sure when he actually convened this team to look
6 at clinical data, preclinical data for both
7 weight gain, which was -- which there was
8 recognized data of an association, and
9 potentially develop treatment methods,
10 potentially do studies to investigate potential
11 treatment methods, and that this piece of work
12 that Dr. Kwong and I decided to undertake, we
13 actually viewed as a component of this overall
14 activity.

15 Q. And, Dr. Beasley, if I could refer you
16 to the second physical page of the document.

17 A. Uh-huh.

18 Q. There's a heading towards the top of the
19 page below the confidential label that says:
20 Olanzapine labeling change on hyperglycemia for
21 the February 21, 2000, GPLC meeting.

22 Do you see that?

23 And regardless of whether you
24 personally drafted the text that's in here, would
25 it be fair to say that you not only reviewed but

1 approved this language?

2 A. Yes.

3 Q. Okay. And by approving it, you believed
4 that what was stated in there was accurate and
5 truthful, correct?

6 A. At -- at the time --

7 Q. Sure. That's all you can do.

8 A. -- yes, recognizing that the basis for
9 the specific numbers that had been included in
10 here were from the very first preliminary
11 analysis of our clinical trial.

12 Q. I'm not sure what you meant when you
13 said that the basis for the specific numbers had
14 been included in here were from the very first
15 preliminary analysis of our clinical trial data.
16 Can you explain that?

17 A. Yes. Thank you.

18 The numb -- the numbers contained
19 in here were brought forward for review by the
20 GPLC, and we clearly suggested and thought that
21 a -- a labeling change was appropriate. The --
22 the basis for this, as I said, is someplace
23 between 50 and 100 studies.

24 I brought forward to, I believe,
25 Dr. Breier, Dr. Toleffson and other individuals

1 the results of the very first successful run of
2 that -- of that data. And so that was the basis
3 for what went in here.

4 Q. Okay.

5 A. It's -- it's very much like the first
6 time that you run a long column of numbers on an
7 adding machine and get a result.

8 Q. Is schizophrenia a risk factor for
9 diabetes?

10 A. The data appears to be that there is an
11 increased risk in the patient population with
12 schizophrenia so that it would constitute a risk
13 factor.

14 Q. So, it's Dr. Beasley's opinion that
15 schizophrenia is a risk factor for diabetes?

16 A. That's my understanding of the
17 literature and, therefore, that is my opinion.

18 Q. Dr. Beasley, let me just ask you a
19 question or two about some of the exhibits that
20 you've been asked about during your deposition.

21 First of all, if we could look at
22 the Plaintiff's Exhibit 229. If you will
23 recall -- and I want to look at page 4 of that.
24 If you recall that, this is the one that contains
25 the statement no routine blood monitoring

1 required.

2 Do you see that?

3 A. Yes, I do.

4 Q. Dr. Beasley, as a physician with respect
5 to the prescription of antipsychotic medications,
6 does that have some particular meaning to you?

7 A. Yes, it does.

8 Q. Can you tell us what that is?

9 A. This would be in the area of
10 antipsychotic prescribing, a statement that we
11 would -- that one would not need to routinely
12 monitor white blood cell counts, which is the
13 case with one antipsychotic that's available on
14 the market.

15 Q. And is the monitoring of white blood
16 cell count, does that have anything to do with
17 blood glucose, or hyperglycemia or type 2
18 diabetes?

19 A. No, it does not.

20 Q. Dr. Beasley, do you recall questions put
21 to you -- I think it was with respect to one of
22 the particular e-mails that made a reference to
23 two full-time people hired at Lilly to work on
24 the Zyprexa and hyperglycemia issue?

25 A. Well, there were two full-time people

1 assigned. And these were -- these were people
2 that were principally assigned in this area.

3 Q. I just want to ask you about those
4 people. Who were those people, particularly?

5 A. That would be Dr. Cavazzoni and
6 Dr. Missy Sowell.

7 Q. And those two individuals were assigned
8 full-time to do work on the hyperglycemia issue
9 with respect to Zyprexa?

10 Dr. Beasley, the question I want to
11 put to you is: Who is Dr. Sowell that you made
12 reference to?

13 A. Dr. -- Dr. Missy Sowell. She was an
14 endocrinologist, diabetes and metabolism
15 specialty physician holding both an M.D. and
16 Ph.D.

17 Q. Now, Dr. Beasley, in reference to the
18 two people you've testified about who were
19 assigned to work full time on the hyperglycemia
20 issue, were there additional resources other than
21 those two people put to work on the hyperglycemia
22 issue at Lilly?

23 A. There would have been statistical
24 resources and system analyst resources.

25 Q. You were also asked questions about the

1 meeting in Atlanta with the endocrinology outside
2 consultants; do you recall that?

3 A. That's correct.

4 Q. And there was mention in that one e-mail
5 with respect to the fact that those individuals
6 had advised Lilly to look at continuous-type
7 analysis of the Zyprexa data.

8 Do you recall that?

9 A. That's correct.

10 Q. Did Lilly take that advice?

11 A. To my understanding, yes. There were a
12 number of activities undertaken during the fall
13 and into the winter with medical supervision by,
14 again, Dr. Cavazzoni, involvement of internal
15 statistical resources. I believe Dr. Sowell was
16 probably involved to some extent. And then there
17 were two separate outside consultants that were
18 involved in analyses, Dr. David Allison, actually
19 earlier in the year, and then later Dr. John
20 Buse.

21 Q. And to the best of your knowledge,
22 Dr. Beasley, has Lilly continued with the project
23 of the continuous-type analysis of the Zyprexa
24 data with respect to blood glucose?

25 A. I'm not familiar with the specifics of

1 subsequent analysis, but Lilly has certainly
2 continued a number of projects and analyses in
3 this area. It continues to be, obviously, an
4 important area that is continuing to be studied
5 and evaluated.

6 Q. Now, you were asked some questions about
7 what is marked as Plaintiff's Exhibit 1349, and,
8 in particular, about page 6 of that exhibit. I
9 want to put that in front of you. That's the
10 exhibit that shows the number of patients at that
11 time in the Zyprexa clinical trials and the
12 duration of exposure with respect to those
13 patients.

14 Do you recall those questions?

15 A. Yes, I do.

16 Q. And let me just ask: This is the
17 exhibit that shows the number of Zyprexa patients
18 that got, for example, more than one dose of the
19 drug, exposure to the drug more than a month,
20 then those who had exposure to the drug more than
21 six months, and those who had exposure more than
22 a year.

23 Do you recall questions about that?

24 A. That's correct.

25 Q. Now, Dr. Beasley, was safety data

1 gathered from all of the patients in each of
 2 those groups?
 3 A. Safety data was -- was obtained for all
 4 individuals who were exposed to the -- to the
 5 drug.
 6 Q. Are there recognized international
 7 standards, Dr. Beasley, with respect to the
 8 duration of exposure in drug studies like the
 9 clinical trials performed on Zyprexa?
 10 A. There are. There are what are referred
 11 to as the CIOMS guidelines that are generally
 12 used and recognized by most regulatory agencies.
 13 And these -- these are the guidelines that sort
 14 of dictate or indicate how many patients should
 15 be treated for how long before a new drug
 16 application can be submitted.
 17 Q. Now, with respect to Zyprexa -- and,
 18 again, referring specifically to the
 19 international guidelines for the duration of
 20 exposure for patients in the clinical trials,
 21 what can you tell us about how the Zyprexa
 22 clinical trials matched up with those guidelines?
 23 A. Well, the guidelines suggest a number of
 24 patients that should be treated for one or more
 25 doses, and that is 1500, and for one or more

1 doses with olanzapine or Zyprexa it was 3,139.
 2 The guidelines actually recommend a
 3 range for six months or greater -- and this is
 4 300 to 600. And the number with olanzapine was
 5 876, and the guidelines for one year is 100. And
 6 the number of Zyprexa, olanzapine patients was
 7 301.
 8 Q. Now, I want to ask you about the --
 9 what's marked as Plaintiff's Exhibit 1605, and
 10 particularly, page 11 of that exhibit.
 11 If you'll recall, that's the
 12 exhibit that refers to study HGAJ and
 13 particularly the nonfasting glucose levels at any
 14 time.
 15 Do you recall those questions?
 16 A. That's correct.
 17 Q. Now, you were specifically asked with
 18 respect to the Zyprexa patients about the
 19 percentage of patients who had a high glucose
 20 reading at any time during that study.
 21 Do you remember that?
 22 A. Yes, I do.
 23 Q. And that percent is what?
 24 A. That is 2.6 percent.
 25 Q. Now, there's another value there for

1 Zyprexa patients; is that correct?
 2 A. Yes, there is.
 3 Q. Now, what was not asked of you, and I
 4 want to ask of you, is -- is there a value for
 5 the Zyprexa patients in that study for moving
 6 from normal or high glucose to a low glucose
 7 level?
 8 A. Yes, there is.
 9 Q. All right. With respect to the 7.7
 10 percent for Zyprexa patients, can you tell us,
 11 what does that signify?
 12 A. Well, that signifies the number of
 13 individuals who at some time during up to six
 14 weeks of treatment with values being measured
 15 weekly had what was defined as a hypoglycemic
 16 value, an abnormally low value of glucose.
 17 Q. Now, can you make a comparison between
 18 the number of Zyprexa patients that went to low
 19 glucose as compared to the percentage that went
 20 to high glucose?
 21 A. It was 2.6 percent that went to high and
 22 7.7 percent that went to low. That's the percent
 23 for low, or the lows are probably about 2.8 times
 24 as many patients as went to high.
 25 Q. All right. And with that many -- with

1 that percentage of Zyprexa patients going to a
 2 low glucose level, what does that tell us, if
 3 anything, about the significance of that, quote,
 4 at any time glucose measurement?
 5 A. Well, that would suggest that it's --
 6 it's very difficult to interpret these data as
 7 particularly meaningful. As I was suggesting,
 8 this is one analysis that we would take into
 9 consideration with the analysis of end point
 10 data, similar data at end point, and then mean
 11 change data, which would actually be mean change
 12 to high, mean change to low, and mean change to
 13 end point. So, we really consider five basic
 14 analyses in terms of coming to any final
 15 interpretation or conclusion.
 16 Q. And overall, when all of the data is
 17 considered from that particular study, what did
 18 the data show with respect to glucose levels?
 19 A. My recollection is that the
 20 interpretation was that there was no difference
 21 from haloperidol.
 22 Q. Now, there had been questions during
 23 your depositions about clinical studies and
 24 controlled clinical trials on potential new
 25 drugs.

1 Do you recall questions like that?
 2 A. That's correct.
 3 Q. Did you have any experience in your
 4 residency program and training with respect to
 5 clinical trials of potential new drugs for
 6 psychiatric illnesses?
 7 A. I was actually asked to take on a
 8 part-time job outside my residency by university
 9 faculty who were conducting clinical research on
 10 new drugs as a co-investigator.
 11 Q. Let me ask you the same question I asked
 12 about medical school. Did you have any
 13 particular national honor or recognition during
 14 your psychiatric residency program?
 15 A. I was -- during my senior year I was
 16 named a Laughlin Fellow.
 17 Q. What does that mean?
 18 A. Which was a fellowship to attend and
 19 participate in the activities of the American
 20 College of Psychiatrists, which is an honorary
 21 psychiatric society, I think for approximately 12
 22 to 15 recipients throughout the United States and
 23 Canada.
 24 Q. Now, I think you told us you started
 25 your job at Lilly after you completed your

1 residency in psychiatry?
 2 A. That's correct.
 3 Q. And what year was that?
 4 A. That would have been 1987. It was
 5 7/7/87.
 6 Q. So you've been at Lilly now how long?
 7 A. A little over 19 years.
 8 Q. Now, during those 19 years, I'd like to
 9 ask you to tell us about the -- the nature of
 10 your work. And, first, with respect to the study
 11 and research on new drugs to treat -- treat
 12 psychiatric illnesses.
 13 What has been your job with respect
 14 to that?
 15 A. Well, that has been the core if -- or
 16 certainly a large component of my -- my job.
 17 Through my first 17 years or so here, I think I
 18 probably supervised, wrote, directed the analysis
 19 of probably something around 20 clinical trials
 20 in that -- in that time period with -- with
 21 several drugs we talked about yesterday.
 22 Q. Now, would you tell us, what has been
 23 your job, if any part of it, at Lilly for the
 24 last 19 years concerning the evaluation and
 25 analysis of observed adverse events in patients

1 taking a drug?
 2 A. Well, that's -- that's an integral part
 3 of running and analyzing any clinical trial.
 4 That has been very much sort of my focus and,
 5 frankly, the thing that -- that the company at
 6 this point views me as relatively expert in,
 7 which is why I'm in the consulting position I'm
 8 in.
 9 Q. Tell us, were there specialists at Lilly
 10 in endocrinology and, in particular, in diabetes,
 11 who participated in the review and evaluation of
 12 this issue about hyperglycemia and diabetes as it
 13 concerns Zyprexa?
 14 A. Yes. There were at several levels.
 15 Q. All right. First, have there been
 16 specialists in endocrinology and diabetes at
 17 Lilly who were principally focused in their
 18 careers on these questions?
 19 A. Yes. There have been a -- a series
 20 of -- of endocrinologists and diabetologists that
 21 were actually assigned to work on the Lilly team.
 22 So although not psychiatrists or neuroscientists,
 23 their principal assignment was to the team, the
 24 product team.
 25 Q. And other than the specialists in

1 endocrinology and diabetes who were assigned to
 2 work principally on the team, have there been
 3 other individuals with those specialties who have
 4 been involved in studying the hyperglycemia issue
 5 as it concerns Zyprexa?
 6 A. Yes, there certainly have been
 7 individuals. And we discussed one yesterday
 8 on -- I think it was on one of the e-mails. A
 9 number of the -- of the endocrinologists and
 10 specifically the diabetologists have had the
 11 opportunity to review data and give advice and
 12 suggestions about continued experimentation in
 13 the work.
 14 THE COURT: Are we at a good spot
 15 to take a break?
 16 MR. LEHNER: This would be a fine
 17 spot, Your Honor.
 18 THE COURT: Ladies and gentlemen of
 19 the jury, we'll take a 15-minute break.
 20 We'll be in recess.
 21 (Jury out.)
 22 (Break.)
 23 (Jury in.)
 24 THE COURT: Please be seated.
 25 We resume with Dr. Beasley's

1 deposition?

2 MR. LEHNER: Thank you, Your Honor.

3 THE COURT: And the record should
4 reflect that all members of the jury are present.

5 Q. Now, the questions that I want to ask
6 you right now have to do with performing clinical
7 trials with proposed new drugs, okay?

8 A. Yes.

9 Q. First, let's start with an uncontrolled
10 trial. Can you explain, and if it's helpful,
11 make a diagram, of what -- what you actually do
12 in performing an uncontrolled trial with a new
13 drug?

14 A. I can.

15 Q. And tell us what you're doing.

16 A. First off, I'm writing the title
17 Uncontrolled. And this is the type of trial
18 that's done early in development that we talked
19 about yesterday where --

20 Q. All right.

21 A. -- there is only a group of individuals
22 that are treated with the drug. There are no
23 other treatments in this trial.

24 Q. All right. Now, tell us what you
25 actually do in an uncontrolled trial with the

1 drug.

2 A. Let me illustrate some -- some
3 individuals in this trial. We have ten people in
4 this trial.

5 Q. And the circles represent what?

6 A. The circles represent the people. So,
7 this group of ten people in this uncontrolled --

8 Q. You've got nine of them there. You
9 better put one more.

10 A. Got to put the one more -- are treated
11 for some period of time with the proposed drug.
12 There is -- there is nobody else being treated
13 with anything but the drug in this particular
14 trial.

15 Q. All right. Then, what do you do?

16 A. Well, you observe these individuals.

17 Q. You observe them.

18 A. You do physical examinations, you do
19 blood studies, you collect your history of
20 medical problems, you collect the minor symptoms
21 that they might be having, such as headaches,
22 prior to being treated with drug. And then you
23 repeat these examinations periodically during the
24 course of trial.

25 Q. All right. Now --

1 A. You observe things.

2 Q. All right. Now, give us an example of
3 what kind of observations are made in an
4 uncontrolled trial.

5 A. Well, if we're talking about something
6 like an adverse event, we could say flu-like
7 symptoms, and a number of these individuals might
8 have flu-like symptoms. Let's say there's seven
9 of them. So we have seven, ten, flu-like.

10 Q. Now, Dr. Beasley, if, in your example
11 the seven out of the ten patients in the
12 uncontrolled drug trial were observed to have
13 flu-like symptoms, what conclusions could you
14 draw, if any, whether the drug caused the
15 flu-like symptoms?

16 A. Well, in this particular trial, you
17 wouldn't draw any conclusions about causation or
18 causality. You would simply draw the conclusion
19 that there were a lot of flu-like symptoms
20 experienced in these individuals during this
21 trial.

22 Q. Could you, in fact, make any conclusion
23 with respect to the question: Does the drug
24 cause flu-like symptoms?

25 A. No. That would not be considered

1 scientifically appropriate.

2 Q. Why not?

3 A. Because there are many things that could
4 cause flu-like symptoms, since this is a -- very
5 common occurrence. It could be the flu virus; it
6 could be common cold viruses; it could be
7 environmental exposures; it could be contaminated
8 sushi that someone ate the evening before or, if
9 it were served on an inpatient unit to all these
10 individuals, lots of different potential causes.

11 Q. Now, if you would, could you tell us
12 about a controlled trial and illustrate that on
13 your diagram?

14 A. Well, that would be the -- the next step
15 in terms of types of studies, and here we would
16 have --

17 Q. What does the second box you're drawing
18 represent?

19 A. This is going to be a comparison
20 treatment, a comparison group with placebo.

21 Q. As you're writing the word "placebo"
22 there, you'll have to tell us what that means.

23 A. This would be a -- an inactive
24 substance. It could be cornstarch. It could be
25 lactose. It is a -- it is a capsule or a pill

1 that looks identical to that given to patients
2 who are receiving the drug, but it is an inactive
3 or inert substance. It has no chemical action in
4 the body.

5 Q. All right. And who is in the placebo
6 group?

7 A. Well, generally, these would be done
8 with similar-sized groups. So, obviously, in
9 clinical trials the numbers are actually larger.
10 But in this illustrating example, we're having
11 ten drug-treated patients, ten placebo-treated
12 patients. I'll just draw that to make it clear
13 that that's all that one, and that was just the
14 uncontrolled.

15 Q. All right. Now, are -- if you want a
16 controlled clinical trial, you've described two
17 groups and you initially described the
18 observation of adverse events. Would that also
19 be observed in the placebo group?

20 A. You would do everything identically to
21 the individuals in the drug group and the placebo
22 group.

23 Q. And provide an example for us regarding
24 the observation of adverse events in the placebo
25 group.

1 A. Well, if you had a similar number --
2 suppose we had seven of ten, okay.

3 Q. Now, what does that represent?

4 A. This represents seven of the ten placebo
5 patients also experiencing flu-like symptoms.

6 Q. Now, if you, in fact, had a controlled
7 clinical trial with the observations of adverse
8 events that you have portrayed in your diagram,
9 what, if anything, would you be able to conclude
10 about whether the drug caused the flu-like
11 symptoms?

12 A. Well, here's where we use the -- the
13 mathematics of statistics to compare the -- the
14 percentage, in this case it would be the
15 percentages of patients. And given the very
16 similar number, we would conclude that there is
17 not a significant difference here. And the way
18 that we would interpret that is that it would be
19 unlikely -- because there is similarity, it would
20 be unlikely that the drug caused the flu-like
21 symptoms. We would conclude that other things
22 unknown to us, but, again, with a lot of
23 possibilities, would have caused the flu-like
24 symptoms.

25 Q. Are you familiar with the term called

1 blinded as it refers to controlled clinical
2 trials?

3 A. Yes, I am.

4 Q. Could you tell us what that means?

5 A. That means that neither the -- the
6 doctors who are giving the drug or -- and/or
7 evaluating the patients, performing the
8 examinations, nor the patients know which patient
9 is receiving drug and which patient is receiving
10 placebo.

11 Q. And why is that important, if it is?

12 A. The reason that that is important is to
13 prevent the -- the -- either the reporters, the
14 doctors, or the reporters, the patients, from
15 believing that they might have something -- some
16 effect because they know what they're receiving
17 and reporting consistent with their belief. It's
18 done to do what we would call prevent bias in
19 reporting.

20 Q. All right. Now, Dr. Beasley, if you
21 would, could you draw a vertical line down your
22 diagram there so we can let me ask you questions
23 about a related but different topic?

24 And now I want to ask you: Are you
25 familiar -- and we've already heard some

1 questions today about something called a
2 spontaneous report of an adverse event.

3 Are you familiar with that?

4 A. Yes, I am.

5 Q. Can you tell us what that is and
6 illustrate that for us, please?

7 A. That would be a report that would be
8 received by the company from a wide variety of
9 sources about a patient treated with the drug.
10 When I say wide variety of sources, it could be
11 from a physician treating the patient, a
12 pharmacist who had heard about the patient, the
13 patient, him or herself, a relative of the
14 patient. Many different individuals that would
15 call us and report that a patient had experienced
16 a particular event, a spontaneous adverse event.

17 Q. All right. Now --

18 A. Which -- such as flu-like symptoms.

19 Q. Now, so, in your diagram when you put an
20 X on the circle under the spontaneous column,
21 what is that intended to represent?

22 A. That's intended to represent that the
23 patient has had something that -- whoever the
24 reporter was considered adverse in this case.

25 So, in this case flu-like.

1 Q. Now, with a spontaneous report of an
2 individual taking a drug who reports experiencing
3 flu-like symptoms, what can -- what conclusions
4 can you draw, if any, about whether the drug is
5 somehow related to the flu-like symptoms?
6 A. Well, this does two things: One, what
7 it does is alerts us to the fact that similar to
8 this uncontrolled trial, we have an individual
9 who was taking the drug who at the same time what
10 we call a temporal association was having
11 flu-like symptoms. Past that, we would draw no
12 conclusions based on this -- on this report.
13 Q. And why -- why could you not draw any
14 conclusions about whether the drug caused the
15 flu-like symptoms in the spontaneous report?
16 A. It's because we really don't have a -- a
17 control group with which to make comparisons.
18 And this is particularly the case when you've got
19 something that would be relatively common in the
20 population that could be occurring due to a great
21 many possible causes, or what we call etiologies.
22 Q. Now, tell us, Dr. Beasley, suppose the
23 company received several or many spontaneous
24 reports of -- following your example -- patients
25 who took a drug and experienced flu-like

1 symptoms. And tell us what you're representing
2 there.
3 A. This would be additional reports,
4 spontaneous adverse event reports.
5 Q. All right, now, tell us what
6 conclusions, if any, can be drawn from the
7 receipt of numerous spontaneous reports from
8 these patients who took a drug and then
9 experienced flu-like symptoms.
10 A. Particularly with a common event, like
11 flu-like symptoms, we would not be able to draw,
12 again, any sort of -- of causal conclusion or
13 association. It would certainly alert us to the
14 fact that these things, again, had been reported
15 in temporal association and would alert us to the
16 need to further investigate this -- what had been
17 observed as a temporal link in clinical trials,
18 in prospective studies, in a number of potential
19 ways.
20 Q. Dr. Beasley, the diagram regarding the
21 controlled clinical trial and spontaneous events,
22 we've not put an exhibit sticker on that.
23 Has that been marked as Beasley
24 Exhibit 5?
25 A. It's been marked 5. I don't see a

1 "Beasley" on it.
2 Q. Let's add that. Has it now been marked
3 as Beasley Exhibit 5?
4 A. Yes, it has been.
5 Q. Let me hand you what we've marked as
6 Beasley Exhibit 6 and ask if you can identify
7 that.
8 A. Well, this is a Zyprexa label. Let
9 me --
10 Q. Can you look at the date on the last
11 page and orient yourself?
12 A. Let me look on the back. This is
13 marked -- this is dated 10/02/96. So I believe
14 this would be the original label.
15 Q. Dr. Beasley, to whom is the product
16 labeling or package insert directed?
17 A. This would be to the individuals who
18 would be prescribing the medication.
19 Q. And who is it, Dr. Beasley, that decides
20 what information is included in the Zyprexa
21 labeling or package insert.
22 A. The FDA.
23 Q. Now, there have been questions during
24 your deposition about weight gain as an adverse
25 event observed in patients taking Zyprexa.

1 Do you recall that?
2 A. Yes.
3 Q. Let me ask you to turn over to page 2 of
4 Beasley Exhibit 6, and I want to ask you,
5 generally, were prescribing physicians provided
6 information on weight gain observed with Zyprexa
7 in the original product labeling or package
8 insert?
9 A. Yes, they were.
10 Q. First, I want to direct you to Table 1
11 on the second page. Can you tell us what was --
12 what information was provided about weight gain
13 as an observed adverse event with Zyprexa?
14 A. Well, again, this was both observed and
15 the information provided here was in reference to
16 what was both observed and then reported as an
17 adverse event by the clinicians conducting the
18 studies.
19 And it was reported that weight
20 gain occurred, was reported in 6 percent of the
21 olanzapine-treated patients and 1 percent of the
22 placebo-treated patients. These data were the
23 aggregation or the combination of all the
24 placebo-controlled data on the medication.
25 Q. Now, let me ask you to turn over to

1 the -- essentially, the next table over on the
2 next page. Do you see that one, called common
3 treatment, emergent adverse events?

4 A. Yes.

5 Q. And would you tell us, please, what's
6 reported about weight gain in that table?

7 A. Well, this is the table of -- that
8 represents what were called common or the most
9 common treatment adverse events that were
10 reported at 5 percent or greater. And this
11 reports the same numbers, weight gain 6 percent,
12 and placebo 1 percent.

13 Q. Now, if I could direct your attention to
14 the bottom of that page. And if you could tell
15 us: Is there additional information about weight
16 gain provided to the prescribing physician in the
17 original package insert for Zyprexa?

18 A. Yes, there is.

19 Q. Tell us what that is, please.

20 A. In addition to restating the information
21 regarding weight gain reported as an adverse
22 event, this is a summary of information regarding
23 what was observed when patients were weighed on
24 scales to actually determine their weight.

25 And the first set of information

1 that is contained describes the olanzapine
2 patients compared to placebo patients during the
3 acute or short-term or six-week trials. And then
4 it -- excuse me -- it goes on to describe the
5 experience of all patients treated in the
6 longer-term extensions of all studies. And it
7 reports that the olanzapine-treated patients gain
8 an average of 2.8 kilograms compared to an
9 average of 0.4 kilogram loss in the placebo
10 patients. And that when we look at the 7 percent
11 or greater gain in body weight, that that was 29
12 percent of olanzapine-treated patients compared
13 to 3 percent of placebo-treated patients. And,
14 again, this is in the acute phase of the study.

15 Q. All right.

16 A. It goes on to describe the data to --
17 regarding long-term and, again, here's where all
18 patients were used with a -- what we call a
19 median or sort of a central point between the
20 fewest number of days and the longest number of
21 days of treatment being 238 days. And this
22 reports that 56 percent of patients gained 7
23 percent or greater of body weight and that the
24 average weight gain during this period was 5.4
25 kilograms. The additional information is

1 provided that the greatest amount of weight gain
2 was seen in patients who, based on what we call
3 body mass index or BMI, with patients with the
4 lowest value for that at baseline.

5 Q. Now, there's also been some question
6 during your deposition about the adverse events
7 of hyperglycemia and diabetes and diabetic
8 acidosis.

9 Do you recall that?

10 A. Yes, I do.

11 Q. Is there information about those adverse
12 events observed in patients taking Zyprexa
13 included in the original package insert?

14 A. They're listed in the other adverse
15 events observed during the premarketing
16 evaluation of olanzapine.

17 Q. And could you particularly let me
18 reference you to under that column, the column of
19 Endocrine System?

20 A. Yes.

21 Q. And can you tell us what is provided to
22 a prescribing physician regarding the information
23 about diabetes there?

24 A. That diabetes mellitus was observed
25 infrequently and that diabetic acidosis was

1 observed rarely.

2 Q. Now, could I refer you to the Metabolic
3 and Nutritional Disorder section and ask you the
4 same question: What information was provided in
5 that section regarding hyperglycemia observed in
6 patients taking Zyprexa?

7 A. In this section, hyperglycemia was
8 indicated to be an event that was observed with
9 an infrequent frequency.

10 Q. Now, Dr. Beasley, because these events
11 of hyperglycemia and diabetes and diabetic
12 acidosis are included in the package insert for
13 Zyprexa, does that mean Zyprexa causes them?

14 A. No. What that means is that they were
15 observed during the conduct of trials in patients
16 who were included in the clinical trials.

17 Q. Dr. Beasley, why was information about
18 weight gain and hyperglycemia and diabetes
19 included in the original package insert for
20 Zyprexa?

21 A. That, along with the other information
22 that's provided here, is so that physicians take
23 the entirety of the information, judge, make the
24 risk/benefit analysis for use in their patients
25 and be aware of what had been observed.

1 Q. Now, we've had some testimony from you
2 with respect to spontaneous reports of adverse
3 events.

4 Do you recall that?

5 A. Yes, I do.

6 Q. And did Lilly receive spontaneous
7 reports of adverse events from patients taking
8 Zyprexa after Zyprexa was approved and went on
9 the market?

10 A. Yes.

11 Q. Tell us, what did and does Lilly do, if
12 anything, to monitor its receipt of reports of
13 adverse events?

14 A. Well, this would be the -- the primary
15 function of the pharmacovigilance and
16 pharmacoepidemiology department, or now global
17 product safety. And the first component is,
18 actually, taking and receiving the reports. So,
19 these are generally called in to us and entered
20 into computer systems by individuals.

21 The next thing that is done with
22 this group of individuals would follow up on
23 these reports to attempt -- I really should
24 emphasize attempt -- to obtain additional
25 clinical information that might have been missing

1 from the -- the initial report when it
2 was presented to the company.

3 Q. What do the people at Lilly actually do
4 to try to follow up spontaneous reports of
5 adverse events?

6 A. They can make telephone calls. They can
7 send letters. This is the -- this is the
8 collection process for the individual cases.

9 The next step in the -- in the
10 process is for these to be reviewed as -- as
11 groups of reports. And here there are physicians
12 and what we call surveillance scientists that
13 would be involved, along with
14 pharmacoepidemiologists. And there would be a
15 number of types of reports that would be -- that
16 would be prepared.

17 There are periodic reports to the
18 Food & Drug Administration, periodic reports to
19 other regulatory agencies that -- that summarize
20 these -- these data. There is the potential for
21 what we would call ad hoc requests, meaning that
22 an agency would send a specific request outside
23 the -- the routine periodic reports for
24 information. And then the group could also
25 provide periodic internal review.

1 Q. Let me ask you about that, specifically.

2 And after Zyprexa went on the
3 market and Lilly received reports of
4 hyperglycemia, in particular, was there any
5 particular internal review that Lilly performed
6 with respect to those events?

7 A. Well, there was a -- there was a
8 sequence of them. We had weekly or biweekly
9 meetings. Actually, the pharmacovigilance
10 function, the product team, the U.S. affiliate,
11 to discuss all adverse events that were being
12 observed.

13 My first recollection of a -- of a
14 specific review of the topic of hyperglycemia
15 was, I think, sometime early in 1997.

16 Q. All right. And what was done at Lilly?

17 A. I think there was something on the order
18 of 10 to 15 cases, some with rather high
19 glucoses. We felt that we should obtain the
20 consultation from an
21 endocrinologist/diabetologist so these cases were
22 summarized and presented to one of our internal
23 diabetologists who then provided us with a -- a
24 verbal report.

25 Q. And what was the report with respect to

1 the review of the spontaneous reports of
2 hypoglycemia at that time?

3 A. His belief was that the cases were
4 sufficiently confounded to make it impossible to
5 conclude that there was a causal association in
6 these -- in these cases he reviewed.

7 Q. You've used the word "confounded."

8 Would you explain for us what that
9 means?

10 A. That would mean that there were
11 alternative -- multiple alternative risk factors
12 or frank causes, in his opinion, or that the
13 cases really did not show sufficient change to
14 constitute an event that would not be expected as
15 just fluctuation in the normal course of a
16 patient with diabetes.

17 Q. After that internal review of the
18 spontaneous reports of hyperglycemia, do you
19 recall, Dr. Beasley, whether Lilly received any
20 inquiry from a Dr. Wirshing with respect to that
21 topic?

22 A. I believe that we received a -- a
23 request for information from, at the time,
24 Dr. Donna Ames and her -- subsequently, her
25 husband, Dr. Wirshing. Our understanding was

1 that they were intending to potentially publish a
2 case series, and they were requesting information
3 from us on what had been observed in our clinical
4 trials.

5 Q. All right. What specifically did Drs.
6 Ames and Wirshing ask of Lilly, and how did Lilly
7 respond?

8 A. Well, they asked what data we had
9 pertinent to the -- to the topic.

10 Q. And did Lilly provide them with
11 anything?

12 A. My recollection is that we provided them
13 with a -- both a summary of the data from our
14 integrated summary of safety analysis, and I
15 believe that may have also included some summary
16 of -- of the post-marketing data, but I'm less
17 certain about that.

18 Q. All right. Let me hand you what I've
19 marked as Beasley Exhibit 7 and ask you if you
20 could recognize that and tell us what that is?

21 A. I need to --

22 Q. Surely. Take a look at it.

23 A. Review of Glucose Changes in Patients
24 Treated With Olanzapine, and it says for Donna --
25 Donna Ames Wirshing. So, this was probably the

1 report that was provided. There's an internal
2 date of September, 1997.

3 It's a -- it's a fairly lengthy
4 document. It appears to be, again, based on our
5 integrated summary of -- of safety, some of the
6 analysis that we talked about. And let me see if
7 there are -- just integrated database.

8 We also appear to provide them with
9 a reference -- a reference list. So this would
10 be information from both the -- the
11 haloperidol-controlled clinical trials and the
12 placebo-controlled clinical trials and a --
13 copies of a literature search on the topic.

14 Q. And, to your knowledge, Dr. Beasley, did
15 Drs. Ames and Wirshing eventually publish?

16 A. This was an article I think we discussed
17 yesterday in which they reported on a series of
18 cases that they had observed.

19 Q. Dr. Beasley, at the time Lilly pulled
20 together the information contained in what we've
21 marked as Beasley Exhibit 7, what were the
22 conclusions that were permitted by the data that
23 Lilly had with respect to whether Zyprexa was
24 causally related to hyperglycemia?

25 A. Well, given the data that we had at the

1 time of our submissions which are reflected here,
2 we did not see an association.

3 And what we indicate that, given
4 the exposure we -- it was considered that the
5 number of events reported was actually quite
6 small, and that post-marketing spontaneous
7 adverse event reports of alterations in blood
8 glucose are consistent with the safety profile
9 observed in the clinical trials.

10 Q. Now, Dr. Beasley, you, I think,
11 previously gave testimony that you were involved
12 directly and primarily regarding Zyprexa through
13 the early part or some early part of 2001; is
14 that -- am I correct in that?

15 A. 2000 -- I had very direct involvement
16 through early 2001. I had more focused
17 involvement in that period from 1997 through
18 2001.

19 Q. And toward the end of your direct
20 involvement with Zyprexa, were you involved in
21 any review, overall review of the Zyprexa data?

22 A. Yes. I think this is something that we
23 have discussed, that there was a large review
24 undertaken primarily initiated out of both
25 pharmacovigilance and myself representing the

1 team that I have referred to as the Beasley/Kwong
2 analysis, I believe.

3 The work actually extended over a
4 significant period of time with a lot of
5 individuals involved in actual completion of that
6 work that was ultimately submitted to the Food &
7 Drug Administration.

8 Q. All right. Let me hand you what's been
9 marked as Beasley Exhibit No. 10, which is a
10 rather large document that I'll put in front of
11 you.

12 Can you look at that and tell us
13 what that is, please?

14 A. The cover letter says: Response to FDA
15 request. Enclosed is our response to your May,
16 2000 letter requesting information about
17 olanzapine. This -- this review had been, again,
18 internally initiated and not in response to a
19 request from -- from FDA, but toward the end of
20 its preparation, such a request arrived. So,
21 this document was provided to them.

22 Q. All right. Now, can you tell us,
23 Dr. Beasley, what was involved and what kinds of
24 data were included in the overall review that
25 resulted in the document submitted to the FDA

1 we've marked as Beasley Exhibit 10?
 2 A. There were a number of different aspects
 3 of data included. The ones that I'm most
 4 familiar with are the analysis of the clinical
 5 trial data, but also the spontaneous adverse
 6 event data. I believe this also includes a -- a
 7 review of the literature, both clinical and
 8 preclinical. And given that it was submitted to
 9 the FDA, I believe it would have included
 10 regulatory correspondence regarding hyperglycemia
 11 and diabetes as well.

12 Q. And, Dr. Beasley, based upon the review
 13 that you participated in and submitted to the FDA
 14 that we've marked as Beasley Exhibit 10, can you
 15 tell us the date of that submission?

16 A. This would have been -- let's see -- the
 17 cover letter, but also let me see if I can --
 18 would have been July of 2000.

19 Q. Now, based upon the review that was
 20 submitted to FDA in July of 2000, Dr. Beasley,
 21 were any conclusions possible with respect to the
 22 question whether Zyprexa is causally related to
 23 hyperglycemia and diabetes?

24 A. Taking the data in -- in total, all the
 25 extensive material, we believe that the data did

1 not support an association between the drug and
 2 hyperglycemia/diabetes.

3 Q. All right. Thank you, Dr. Beasley.
 4 Now, in addition to Lilly's review
 5 of the spontaneous reported data and Lilly's
 6 review and analysis of the controlled clinical
 7 trials with Zyprexa, were there other different
 8 types of studies that looked at the specific
 9 question whether Zyprexa was exerting some direct
 10 effect to cause hyperglycemia?

11 A. There were a large number of studies and
 12 activities going on both clinically and
 13 preclinically under this group that Dr. Breier
 14 had organized. I'm most familiar with two
 15 studies that were conducted in humans referred to
 16 as clamp studies.

17 Q. All right. First, tell us -- you said
 18 there were two studies referred to as clamp
 19 studies?

20 A. That's correct.

21 Q. All right. Tell us, first, what was it
 22 that the two clamp studies were directed at
 23 looking at?

24 A. Okay. Type 2 diabetes is thought to be
 25 caused by two types of what we call

1 pathophysiology together, or abnormalities in the
 2 body is what pathophysiology means. One is
 3 the -- the failure of what we call the insulin
 4 receptor. And this is a -- a molecule on cells
 5 in the body that insulin, which is a hormone,
 6 interacts with to allow glucose to move into the
 7 cells. So you've got to have this receptor
 8 working right in order for glucose to move into
 9 the cells so that you lower blood glucose levels
 10 and the cells are able to use glucose as energy.

11 Q. Are you familiar with the term,
 12 Dr. Beasley, insulin sensitivity?

13 A. Yes.

14 Q. Tell me what that means.

15 A. That would be a measure of how well
 16 these insulin receptors work.

17 Q. All right.

18 A. The other thing that is thought to be
 19 necessary for the development of type 2 diabetes,
 20 clinical type 2 diabetes, would be the failure of
 21 the pancreas, which is an organ that sits in
 22 the -- in the abdominal cavity, close to the
 23 stomach, to put out sufficient amounts of
 24 insulin.

25 The pancreas is signaled to release

1 insulin when glucose is high in the blood. It
 2 releases this insulin, goes to insulin receptors,
 3 and this allows glucose to be transported into
 4 cells. So, the thinking is to be frankly or
 5 actual clinical type 2 diabetes, you have to have
 6 failure of the insulin receptor, decreased
 7 insulin sensitivity, and a decrease in the
 8 pancreas' ability to make enough insulin to
 9 compensate for poor insulin sensitivity.

10 Q. All right. Let me ask you, first,
 11 about -- actually the second thing you mentioned.
 12 That is the failure of the pancreas to actually
 13 produce insulin or to produce enough insulin.
 14 Was there one of the clamp studies directed at
 15 that question?

16 A. Yes, there was. And, again, why did we
 17 take on these studies? The thinking behind this
 18 was that it was important to us to do a study
 19 that would look at whether or not olanzapine was
 20 causing the effects in the body that would lead
 21 to type 2 diabetes. So, that was the purpose
 22 in -- in doing the studies.

23 Q. Now, first, I want to ask you to
 24 describe the clamp study that was directed at the
 25 question whether Zyprexa exerted some adverse

1 effect that would cause the pancreas not to
 2 produce insulin or not to produce enough insulin?
 3 A. Uh-huh.
 4 Q. First, tell us what was that study
 5 called and how did you perform it?
 6 A. That's a hyperglycemic clamp study.
 7 Q. And please tell us in layperson's
 8 language how that's done.
 9 A. First of all, you have your parallel
 10 treatment groups as we've talked about this
 11 morning. You have -- in this case it was
 12 placebo, another antipsychotic, and olanzapine.
 13 And before patients receive -- or, actually,
 14 these are what we call normal volunteers. These
 15 were healthy -- healthy subjects. They were
 16 tested. And the way they were tested was by this
 17 thing that's called a hyperglycemic clamp.
 18 They have an intravenous line
 19 inserted into their arm. They are then given
 20 glucose, actually large --
 21 Q. Glucose is what?
 22 A. Sugar. Large amounts of glucose, blood
 23 sugar, into this line into their body. And then
 24 the pancreas has the opportunity to react to
 25 this. And what is measured is the amount of

1 insulin that the body produces in response to
 2 this -- this extra glucose. Then the patients,
 3 are -- or the subjects are treated.
 4 Q. When you say "treated," what do you
 5 mean?
 6 A. They receive double-blind either
 7 placebo, olanzapine or this other medication. In
 8 this case, they received it for two weeks, and
 9 then they were retested. I think it's probably
 10 worth stating that -- that this -- this type of
 11 sophisticated study was -- I did not design this
 12 study.
 13 Q. Who did design it?
 14 A. This would have been designed by our
 15 endocrinology colleagues.
 16 Q. All right, Dr. Beasley, before we
 17 changed the tape I was asking you about the
 18 hyperglycemic clamp study. Now, let me just ask:
 19 Were the results of the study performed by Lilly
 20 looking at whether Zyprexa exerted an adverse
 21 effect on the pancreas to produce insulin -- were
 22 the results of that study published?
 23 A. They were published in a peer-reviewed
 24 journal.
 25 Q. Let me hand you what's been marked as

1 Beasley Exhibit 11.
 2 A. Actually, it's not -- you need to add
 3 the Beasley.
 4 Q. Let me write the Beasley on it. Sorry.
 5 Let me hand you what's been marked
 6 as Beasley Deposition 11. And can you tell us
 7 what that is, please?
 8 A. This would be the academic publication
 9 regarding the results of the -- the study we've
 10 just discussed.
 11 Q. Now, Dr. Beasley, tell us, what did the
 12 results show of the study done by Lilly to see
 13 whether Zyprexa exerted an adverse influence on
 14 the pancreas such that the pancreas produced a
 15 little or insufficient insulin?
 16 A. The results are summarized in the -- in
 17 the last paragraph of the abstract. We found no
 18 evidence that treatment of healthy volunteers
 19 with olanzapine or the other drug -- left that
 20 one out, decreased the insulin secretory response
 21 to a prolonged hyperglycemic challenge. The
 22 results of this study do not support the
 23 hypothesis that olanzapine or the other drug
 24 directly impair pancreatic beta cell function.
 25 Q. All right. Dr. Beasley, let me ask you,

1 this hyperglycemic clamp study methodology, is
 2 that a recognized methodology to look at the
 3 question whether the pancreas is affected to
 4 produce insufficient or no insulin?
 5 A. That's my understanding from my
 6 endocrine colleagues.
 7 Q. Now, Dr. Beasley, turning to the second
 8 prong of these clamp studies, did Lilly perform a
 9 study looking at the question of whether Zyprexa
 10 produced insulin insensitivity?
 11 A. Yes, that was what was referred to as
 12 the euglycemic clamp study.
 13 Q. Just a moment. Do we have some more
 14 exhibit stickers, by any chance? If not, I'll
 15 just --
 16 All right, the euglycemic clamp
 17 study, now, can you tell us, again, in
 18 layperson's language, what was the euglycemic
 19 clamp study looking at?
 20 A. Well, this looks at insulin receptor
 21 sensitivity. And here in contrast to the last
 22 study, you first give a lot of insulin, and you
 23 also give some glucose. And you determine,
 24 essentially, how much glucose you can give at a
 25 fixed amount of insulin and how well the body

1 uses that amount of glucose.

2 Q. Let me hand you what we've marked as
3 Beasley Exhibit 12 and ask, first, were the
4 results of the euglycemic clamp study performed
5 by Lilly published?

6 A. Yes, they were.

7 Q. All right. Now, let me ask you to look
8 at Beasley Exhibit 12.

9 Can you tell us what that is?

10 A. This would be the academic publication
11 of the -- of the study that we've just discussed.

12 Q. Can you tell us, Dr. Beasley, what were
13 the results of the euglycemic clamp study
14 performed by Lilly to look at the question
15 whether Zyprexa affected insulin sensitivity?

16 A. That's probably, again, best summarized
17 in the abstract, in the last part of the
18 abstract. In summary, this study did not
19 demonstrate significant changes in insulin
20 sensitivity in healthy subjects after three weeks
21 of treatment with olanzapine or a --

22 Q. Now, Dr. Beasley, given the results of
23 the two clamp studies performed by Lilly, based
24 upon the results of those studies, what
25 conclusions, if any, did Lilly draw regarding

1 whether Zyprexa demonstrated a causal and a
2 mechanistic effect on producing type 2 diabetes?

3 A. Well, these studies certainly did not
4 support the hypothesis that olanzapine was
5 causing either type of pathophysiology that would
6 cause diabetes. It was not causing the things
7 that would cause diabetes in these two studies.

8 Q. Dr. Beasley, do you know the general
9 recommendations from the American Diabetes
10 Association with respect to screening blood
11 glucose for type 2 diabetes?

12 A. I -- I believe that I do.

13 Q. All right. Can you tell us what those
14 are?

15 A. I think it's a recommendation of a
16 fasting blood glucose every three years at age 45
17 and older. And I believe there is some
18 discussion about if an individual is obese and
19 has other risk factors, conducting these
20 investigations or blood tests at an earlier age.

21 Q. And those recommendations by the
22 American Diabetes Association for screening blood
23 glucose for type 2 diabetes, to whom do they
24 apply?

25 A. Well, all Americans. I mean, they --

1 that's a universal healthcare recommendation by
2 this -- by this organization.

3 Q. So, I mean, do they apply whether the
4 person is suffering from schizophrenia?

5 A. Yes.

6 Q. Or do they apply in people who are not
7 suffering from schizophrenia?

8 A. To my understanding, yes. They don't
9 draw any -- any distinction. The only -- the
10 only distinctions are the -- the age cutoff, and
11 then earlier if risk factors are present.

12 Q. And would those general recommendations
13 regarding screening for type 2 diabetes by
14 looking at blood glucose, would that apply to
15 people who were taking antipsychotic medication
16 like Zyprexa?

17 A. They would apply to -- as we've said, to
18 anyone. I mean, again, irrespective of their --
19 of their health status with the exception of
20 this -- of this age cutoff.

21 Q. And let me just ask: Would the general
22 recommendations of the American Diabetes
23 Association to have a screening for type 2
24 diabetes by looking at blood glucose also apply
25 to people who were not taking antipsychotic

1 medication like Zyprexa?

2 A. Yes.

3 Q. Let me hand you what's marked as Exhibit
4 13, Dr. Beasley.

5 Can you tell us what that is?

6 A. Do you want to --

7 Q. I beg your pardon. I keep forgetting to
8 write "Beasley" on there.

9 Let me hand you what's marked as
10 Beasley Deposition Exhibit 13. Can you make
11 reference to the date on the last page, and then
12 tell us what that is?

13 A. Well, it's a -- it's a Zyprexa package
14 insert, and I'll need to check the date.

15 I see a copyright 2006 date here.
16 Literature revised as of March 20, 2006. So,
17 this was the package insert that was approved as
18 of that date.

19 Q. All right. Could you turn to page 8 of
20 that document, please?

21 A. Yes.

22 Q. And, in particular, I want to ask you
23 about certain language contained in the warning
24 section related to hyperglycemia and diabetes
25 mellitus.

1 Do you see that?
 2 A. Yes, I do.
 3 Q. All right. Now, could you read the
 4 first three sentences of that for us, please?
 5 A. Yes. Hyperglycemia, in some cases
 6 extreme and associated with ketoacidosis or
 7 hyperosmolar coma or death, has been reported in
 8 patients treated with atypical antipsychotics,
 9 including olanzapine. Assessment of the
 10 relationship between atypical antipsychotic use
 11 and glucose abnormalities is complicated by the
 12 possibility of an increased background risk of
 13 diabetes mellitus in patients with schizophrenia
 14 and the increasing incidence of diabetes mellitus
 15 in the general population.
 16 Given these confounds, the
 17 relationship between atypical antipsychotic use
 18 and hyperglycemia-related adverse events is not
 19 completely understood.
 20 Q. Let me first ask you, Dr. Beasley, the
 21 reference there to an increased background risk
 22 of diabetes mellitus in patients with
 23 schizophrenia. Can you explain for us in
 24 layperson's language what that means?
 25 A. I believe it means what we were

1 discussing yesterday, that there is the belief,
 2 understanding, and data to support that a higher
 3 percentage of individuals with schizophrenia and
 4 without schizophrenia, everything else being
 5 equal, would have diabetes.
 6 Q. And then making reference to the
 7 increasing incidence of diabetes mellitus in the
 8 general population. Can you explain in
 9 layperson's language what that means?
 10 A. I understand that to mean that there is
 11 a continuing increase in the number of new cases
 12 of diabetes being observed every year. So that
 13 it's becoming more frequent in the population.
 14 Q. All right. And in the second sentence,
 15 is it those two things that are referred to as
 16 confounders?
 17 A. Those two things would be confounders,
 18 given these confounders.
 19 Q. Now, can you tell us just in layperson's
 20 language, what does "confounder" mean?
 21 A. That means things that are present that
 22 make sort of understanding or interpretation
 23 difficult or impossible.
 24 Q. And by the way, you told Mr. See
 25 something on direct examination that one of the

1 things we like to do in studies is to blind them
 2 so in order to prevent -- what's the word?
 3 A. Bias.
 4 Q. Bias.
 5 A. On reporting by the investigator or the
 6 patient.
 7 Q. And how does blinding prevent bias?
 8 A. That prevents the -- both the -- both
 9 the investigator and the patient from knowing the
 10 medication they're on and because of knowing the
 11 medication they're on, making assumptions or
 12 coming to beliefs about what they're experiencing
 13 and then reporting it.
 14 Q. Right. If you blind the study, if the
 15 individual does not know, the doctor doesn't
 16 know, such as a researcher, right?
 17 A. Correct.
 18 Q. And the patient doesn't know which
 19 medication they're taking, you're more likely to
 20 get an objective as opposed to a subjective
 21 biased analysis, correct?
 22 A. That's correct. That is the intent of
 23 blinding.
 24 MR. LEHNER: That concludes that
 25 portion, Your Honor. I think there's a couple

1 minutes that the Plaintiffs have.
 2 MR. ALLEN: You're passing the
 3 witness?
 4 MR. LEHNER: Yes. We'll have you
 5 play your section.
 6 MR. ALLEN: Your Honor, the State
 7 of Alaska has two minutes and 16 seconds in
 8 cross.
 9 THE COURT: Why don't you do that
 10 and we'll keep on moving.
 11 CROSS-EXAMINATION
 12 Q. (BY MR. ALLEN) When you testified to me
 13 earlier today and yesterday, was your testimony
 14 truthful and accurate?
 15 A. Yes, it was.
 16 Q. And when you wrote your e-mails
 17 concerning the clinical trials to the people
 18 throughout Eli Lilly, were your e-mails truthful
 19 and accurate?
 20 A. To the best of my knowledge, those data
 21 were correct at the time I wrote them.
 22 Q. And by the way, you also made it clear
 23 today and I don't think you discussed it with
 24 your lawyer. If I'm not mistaken, you said by
 25 1999, in Europe, that hyperglycemia and diabetes

1 was in the equivalent of the warning section?
 2 A. Yes, it was.
 3 Q. So, by 1999 the patients and doctors
 4 over in Europe were being warned about
 5 hyperglycemia and diabetes?
 6 A. There was a warning slash precautions in
 7 that label written in Europe.
 8 Q. And where is the warning in the United
 9 States package insert like Europe's in 1999 on
 10 hyperglycemia and diabetes?
 11 A. There is not one.
 12 Q. Where is that black-box warning on
 13 Zyprexa in 2002 like Japan had concerning
 14 hyperglycemia, diabetes, diabetic ketoacidosis?
 15 A. There is not one.
 16 Q. Is there any particular reason why Eli
 17 Lilly and the doctors in the United States should
 18 be treated differently than the doctors in Japan
 19 and Europe?
 20 A. From our perspective and my perspective
 21 we were, in fact, labeling the molecule
 22 appropriately. There are clearly differences in
 23 the labeling. Different countries evaluate
 24 materials differently and have different
 25 interests in their package insert.

1 Q. Lilly's interest is the same throughout
 2 the world, isn't it?
 3 A. Yes.
 4 Q. You want to give the doctors in the
 5 United States the same information in the same
 6 manner you give doctors over in France, don't
 7 you?
 8 A. Absolutely.
 9 Q. You want to give doctors in Japan the
 10 same information you give doctors in the United
 11 States and vice versa, don't you?
 12 A. Yes.
 13 MR. ALLEN: Your Honor, that
 14 concludes our offer.
 15 MR. LEHNER: We'll take down the
 16 screen and I'll offer some exhibits.
 17 THE COURT: Sure.
 18 MR. LEHNER: Your Honor, at this
 19 time on behalf of Eli Lilly I'd like to introduce
 20 into evidence what's been marked as EL2169. It
 21 was referred to as Beasley No. 7 in his
 22 deposition. That's a review of glucose changes
 23 in patients treated with olanzapine September,
 24 1997 for Donna Ames Wirshing, customer response
 25 team.

1 Exhibit 2175 --
 2 THE COURT: Let's take them one at
 3 a time and see if there's --
 4 MR. SUGGS: No objection to 2169,
 5 Your Honor.
 6 THE COURT: EL2169 is admitted.
 7 MR. LEHNER: The next exhibit would
 8 be -- is marked as EL2175. It was referred to in
 9 Dr. Beasley's deposition as No. 11, and that is
 10 the article published in the Journal of Clinical
 11 Endocrinology and Metabolism, entitled
 12 Hyperglycemia Clamp Assessment of Insulin
 13 Secretory Responses in Normal Subjects Treated
 14 with Olanzapine, Risperidone and Placebo, by
 15 Sowell, et al.
 16 MR. SUGGS: Your Honor, we object
 17 to that in light of the Court's rulings on
 18 published medical articles.
 19 MR. LEHNER: Your Honor, I think
 20 what we've been doing is in conjunction with
 21 previous articles publishing these to the
 22 jury and consistent with the Alaska Rule on
 23 medical articles.
 24 THE COURT: Counsel, please
 25 approach.

1 (Bench discussion.)
 2 MR. LEHNER: We had these marked
 3 for identification --
 4 THE COURT: Previous articles that
 5 the State was introduced were introduced for
 6 notice purposes. Why isn't this introduced --
 7 MR. LEHNER: Notice of what? These
 8 are really beyond notice.
 9 THE COURT: They aren't necessarily
 10 notice.
 11 MR. LEHNER: These are Lilly's
 12 studies, too. It's work that Lilly has done. I
 13 think it's more than notice.
 14 MR. SUGGS: They're not notice of a
 15 potential problem.
 16 MR. LEHNER: They're not notice.
 17 This is work that they did -- this is Lilly.
 18 MR. SUGGS: You're offering them
 19 for the truth of the matter asserted?
 20 MR. LEHNER: Sure. It's a
 21 published medical article. You can contest the
 22 truth of the matter asserted within them, if you
 23 want to. This is Lilly's work.
 24 MR. SUGGS: I thought the Court's
 25 prior ruling was that with respect to --

1 THE COURT: The normal rule for
2 published treatises is you talk about them, you
3 can recognize them, you can do that, but you
4 don't admit them unless there's some other
5 reason.
6 MR. LEHNER: That would be true. I
7 agree for articles that are not written by the
8 company that are not based upon the company's own
9 work. They are being admitted as this is Lilly's
10 work. This is Lilly's efforts to produce. You
11 can contest whether they're true or not.
12 THE COURT: Why isn't it a business
13 record?
14 MR. SUGGS: I don't -- I don't
15 think the company, Eli Lilly's in the business of
16 writing published medical articles.
17 THE COURT: Well, they do have to
18 do research on their drugs.
19 MR. SUGGS: The reason for the rule
20 is because -- the rules recognize documents like
21 this and published medical articles should not be
22 given more weight. They carry with them sort of
23 a mantle and that's why you can talk about them,
24 but they don't go to the jury.
25 MR. LEHNER: That would certainly

1 be true for articles done by third parties, but
2 this is based on Lilly research, and as
3 Dr. Beasley testified, a large component -- and
4 as others have testified previously -- a large
5 component of what these companies do --
6 MR. SUGGS: I don't see anything in
7 the rule that draws the conclusion of what goes
8 to the jury or not --
9 THE COURT: I'm going to admit the
10 articles, to the extent that information Lilly
11 had or didn't have is an essential element of
12 this case and both articles that were otherwise
13 doing that -- it goes to -- it -- there's both a
14 business record component of it, but it -- I
15 would also find there's a reliability to the
16 extent that Lilly had this article and knew about
17 it, that's -- that's a relevant issue as well to
18 the defense, and --
19 MR. SUGGS: I understand your
20 ruling, Your Honor. If that is the case, would
21 the Court be open to our on rebuttal offering the
22 later clamp studies as notice?
23 MR. LEHNER: They may already be
24 in.
25 MR. SUGGS: We had them marked as

1 identification --
2 THE COURT: I don't know if there's
3 a relevance question about time with those, but
4 you certainly can come in --
5 MR. SUGGS: Our cause of action
6 precedes a day -- one of the studies was 2007. I
7 believe there was another one that was 2006.
8 THE COURT: We can look at it with
9 respect to the time of the label.
10 I'll admit 2175.
11 (End of bench discussion.)
12 THE COURT: 2175 is admitted, and
13 objections are preserved.
14 MR. SUGGS: Same ruling with 2176.
15 THE COURT: Same ruling as to 2176,
16 that must be admitted with the objections
17 preserved.
18 MR. LEHNER: So Your Honor, I will
19 move 2175 and 2176, which is the Evaluation of
20 Insulin Sensitivity in Healthy Volunteers Treated
21 with Olanzapine, Risperidone and Placebo,
22 published in The Journal of Clinical
23 Endocrinology and Metabolism.
24 THE COURT: I think I just admitted
25 2175 and 2176 with objections preserved, and

1 those documents may be published.
2 MR. LEHNER: Thank you very much.
3 THE COURT: Who is your next
4 witness, Mr. Lehner?
5 MR. KANTRA: Your Honor, Eli Lilly
6 and Company would call Dr. Robert Baker to the
7 stand.
8 THE COURT: Mr. Kantra, you'll be
9 examining Dr. Baker?
10 MR. KANTRA: I will be.
11 THE COURT: Dr. Baker, if you'll
12 please remain standing and we'll get you sworn.
13 (Dr. Robert Baker sworn.)
14 THE CLERK: For the record, sir,
15 please state your full name, spelling your first
16 and last name.
17 THE WITNESS: It is Robert Baker,
18 R-o-b-e-r-t, B-a-k-e-r.
19 THE CLERK: Thank you, sir.
20 THE COURT: Please be seated.
21 Mr. Kantra.
22 DIRECT EXAMINATION
23 Q. (BY MR. KANTRA) Good morning, Dr.
24 Baker.
25 A. Hi.

1 Q. Where do you work?
 2 A. I work at Eli Lilly and Company in
 3 Indianapolis.
 4 Q. How long have you been working there?
 5 A. For eight years.
 6 Q. What type of work do you do?
 7 A. I'm a physician and I'm currently
 8 supervising the other physicians who oversee the
 9 safety of Lilly's products.
 10 Q. Is that all of Lilly's products?
 11 A. Yes, all of our products, all
 12 therapeutic areas.
 13 Q. Does that include Zyprexa as well?
 14 A. It does.
 15 Q. How many safety physicians do you
 16 supervise?
 17 A. About 25.
 18 Q. During the time that you've been working
 19 at Lilly, was there a time where your
 20 responsibilities focused primarily on Zyprexa?
 21 A. Yes, that's what I did when I started at
 22 the company.
 23 Q. And can you describe the nature of your
 24 work on Zyprexa when you first joined the
 25 company?

1 A. Yes. I was responsible for working on
 2 Zyprexa's use in bipolar mania and particularly
 3 in helping to understand and communicate about
 4 that with physicians in the United States.
 5 Q. And when you say communicating with
 6 physicians, can you say a little bit more about
 7 the nature of your job responsibility as it
 8 involved talking with physicians outside the
 9 company?
 10 A. Yes. I was employed in the U.S. medical
 11 part of Lilly, and our job there was coming in as
 12 people who had practiced as physicians in the
 13 U.S. to understand about practice and the sort of
 14 questions and needs that doctors had, and couple
 15 that with expertise that we got from the company
 16 about our drugs, in order to be able to answer
 17 directly sometimes questions for them and also
 18 work with our marketing department and other
 19 groups who were preparing information to
 20 communicate with doctors.
 21 Q. And as part of your responsibilities at
 22 Lilly when you joined, were you responsible for
 23 understanding and having a general overall
 24 appreciation for how Zyprexa was developed as a
 25 drug before FDA approved it in 1996?

1 A. Yes.
 2 Q. I understand that you were promoted to
 3 medical director of the neuroscience group in
 4 2005; is that correct?
 5 A. Yes, that's right.
 6 Q. And in that capacity, did you still have
 7 responsibility for Zyprexa?
 8 A. Yes. That, along with the other
 9 neuroscience psychiatry products that Lilly had
 10 in the U.S.
 11 Q. And then when did you take your current
 12 position in the safety group at Lilly?
 13 A. I was promoted into this job toward the
 14 end of 2006.
 15 Q. And in your work on behalf of Eli Lilly
 16 and Company, did part of your -- do part of your
 17 responsibilities include reading and
 18 understanding the literature as it relates to
 19 Zyprexa and diabetes?
 20 A. Yes.
 21 Q. And is part of the reason for your
 22 understanding the need for your understanding in
 23 that regard so that you can communicate with
 24 physicians outside the company with respect to
 25 Lilly's understanding of those studies and

1 articles?
 2 A. That's part of it, yes.
 3 Q. So, before we talk more about your work
 4 specifically on Zyprexa, I want to help the jury
 5 understand what you did before you came to Lilly.
 6 And so tell us where you graduated
 7 from medical school.
 8 A. Northwestern University in Chicago.
 9 Q. And you had a year of general medicine
 10 internship after that; is that right?
 11 A. Yes, at the University of Pittsburgh.
 12 Q. And that was followed by a residency in
 13 psychiatry?
 14 A. Yes.
 15 Q. And where did you do that residency in
 16 psychiatry?
 17 A. That was also at the University of
 18 Pittsburgh.
 19 Q. Do you have a specialty that you have
 20 developed and been board certified in?
 21 A. Yes. That's psychiatry.
 22 Q. And why did you want to become a
 23 psychiatrist?
 24 A. Well, I -- I was planning to be a
 25 psychiatrist when I came to medical school. My

1 father was a psychiatrist.

2 And as I grew up, he'd take me
3 sometimes along with him to the hospital or to
4 the office, and I'd see at church or other places
5 people would talk to him about how he helped them
6 or the family members. So I think that that's
7 what made me interested in it. And then once I
8 got to medical school, I wavered a little bit.
9 But once I started seeing patients with mental
10 illness, that's what I thought my calling was.

11 Q. When you finished your training, your
12 residency in psychiatry, where did you go to
13 work?

14 A. My first job out of training was for the
15 Commonwealth of Pennsylvania. I worked at the
16 State hospital for Pennsylvania for the first
17 three years after I graduated.

18 Q. Can you describe for the jury the type
19 of patients you treated at the State hospital in
20 Pennsylvania?

21 A. Sure. In Pennsylvania, the State
22 hospital would be for people who are very sick or
23 who weren't getting better in other settings.
24 So, when I was working there, people wouldn't
25 even come into our hospital unless they'd been in

1 some other hospital for a few weeks and weren't
2 getting better. So they tended to be people who
3 were quite ill, and probably the majority of them
4 were probably people with schizophrenia, but
5 other disorders as well.

6 Q. Did those other disorders include
7 bipolar disorder?

8 A. Yes.

9 Q. While you working at this State hospital
10 in Pennsylvania, did you have an opportunity to
11 participate in clinical trials of antipsychotic
12 medications?

13 A. Yes.

14 Q. And did those clinical trials involve
15 patients with schizophrenia?

16 A. Yes.

17 Q. Did the drugs that you were evaluating
18 in those clinical trials include all of the
19 approved atypical antipsychotics at the time you
20 joined Lilly?

21 A. Yes, all of those, plus another one,
22 Sertindole, that had never been approved in the
23 United States.

24 Q. And that would have included, then, I
25 assume from your answer that you did work on

1 clinical trials involving Zyprexa?

2 A. Yes.

3 Q. And that would have been one of the
4 trials that actually supported the approval by
5 FDA?

6 A. Yes.

7 Q. In your work on clinical trials, did you
8 participate in clinical trials that occurred
9 during different phases of development?

10 A. Yes.

11 Q. So you participated in phase 2 and phase
12 3 clinical trials; is that right?

13 A. Phase 3 and phase 4.

14 Q. After you finished working or while you
15 were working at the State hospital in
16 Pennsylvania, did you also do work at an
17 institution called the Western Psychiatric
18 Institute?

19 A. Yes. Western Psychiatric Institute was
20 the hospital or the setting of the University of
21 Pittsburgh Psychiatry Department. So after my
22 first three years working in the State hospital,
23 I moved into a faculty job at the University of
24 Pittsburgh, although in that role continued to
25 work for the next six or seven years still doing

1 some work at the same State hospital.

2 Q. And did you work -- did you develop a
3 schizophrenia research program during the time
4 you were affiliated with the State hospital?

5 A. That's right. The work I was doing at
6 the State hospital was at a research unit that
7 was jointly sponsored by the State of

8 Pennsylvania and by the University of Pittsburgh,
9 and I directed that.

10 Q. After you finished your work both at the
11 State hospital and WPI, you moved on then to the
12 University of Mississippi; is that right?

13 A. Yes.

14 Q. And can you tell the jury what you did
15 while you were at the University of Mississippi
16 Medical School?

17 A. I was there for three years and I would
18 supervise the university's inpatient psychiatry
19 facilities and also their psychopharmacology
20 research that was ongoing.

21 Q. And you were at the University of
22 Mississippi until when?

23 A. Until -- until 1999.

24 Q. So when you joined Lilly, you had been a
25 practicing psychiatrist for about 12 years; is

1 that right?

2 A. Yes. I finished my training in '86, so
3 13 years.

4 Q. In addition to the responsibilities
5 you've already described with respect to Zyprexa
6 and then your safety work at Lilly, have you also
7 been involved in committee work at Lilly that has
8 watched over the movement of new products that
9 are in development from the preclinical phase,
10 before they go into humans into the clinical
11 trial phase?

12 A. Yes.

13 Q. Okay. And are you generally familiar,
14 then, with the process by which a drug moves from
15 discovery to preclinical to clinical trials?

16 A. Yes.

17 Q. Okay.
18 And can you tell the jury, then,
19 just briefly, what it is that happens after a
20 drug is identified for testing? What is the
21 first kind of testing that happens with respect
22 to a new compound?

23 A. Sure. After a potential drug, a drug
24 that we're hoping could be useful for patients is
25 synthesized, all the first testing takes place in

1 a laboratory setting, more or less test tubes
2 using models that look like they may be
3 predictive of a therapeutic benefit, models that
4 look like they might screen for side effects.
5 All of that testing takes place first.

6 Q. Then does it move into animals after
7 that?

8 A. Right. Actually most of them don't pass
9 that first stage of testing but those that look
10 like they have enough benefit and enough safety
11 to be promising as drugs for people, would next
12 be tested in animals, usually starts with mice or
13 rats. And if it's successfully passing through
14 that, then we move to other animal species.

15 Q. And what is the general period of time
16 over which these kinds of preclinical studies
17 take place?

18 A. Well, it varies quite a bit. I'd say
19 the minimum is several years. The average is
20 probably three or four years.

21 Q. And what -- how does testing actually
22 then begin in humans after this preclinical phase
23 is finished? What does a company need to do at
24 that point?

25 A. Well, a couple of things. Firstly,

1 before we test the medicine in humans, we
2 would -- we would make contact and talk with the
3 regulatory groups that are overseeing the use.
4 So, if we wanted to test it in the United States
5 or if we were planning for its use eventually in
6 the United States, we file an application. It's
7 called an IND, which is investigational new drug
8 application. That goes into the FDA and we tell
9 them what we've known from testing so far, what
10 our plans are with it. And if they don't object
11 to it, then we move to the first human dose of
12 the medicine.

13 That's an important -- very
14 important time because we really need -- we've
15 done all the screening through animals that's
16 focused mostly on the safety. But before we put
17 it into patients or before it goes into many
18 people, we start testing the safety. That's
19 typically in normal volunteers and the first
20 human dose would be a very low dose, it would be
21 a single dose.

22 You watch what happens and if that
23 goes well, you build up to higher doses and you
24 give it over a longer period of time,
25 scrutinizing very much in particular what safety

1 findings, what laboratory findings might be
2 caused by the medicine.

3 Q. When you say laboratory findings, would
4 that include things like measurements of blood
5 sugar levels?

6 A. Sure.

7 Q. This process that you described with
8 healthy individuals participating in clinical
9 trials of the drug, is that known as the first
10 phase of clinical trials?

11 A. Yes.

12 Q. And are there two other phases that then
13 follow after that?

14 A. Right.

15 Q. Can you tell the jury -- before a drug
16 is approved for market. Can you tell the jury
17 what those two phases consist of?

18 A. So after this first phase, if it looks
19 like people are tolerating it, if our screening
20 and that is again promising that it's going to be
21 safe enough, then we go to what is called Phase
22 2. Phase 2 is where for sure you'd start testing
23 it in patients who have the illness that you're
24 thinking the drug may be effective for.

25 So in that phase what you're

1 testing for is can you get a signal that the
2 medicine is going to work. Are you confirming
3 your hypothesis or the idea that it's going to
4 work? You're looking, can people tolerate it?
5 How safe is it for them? Is it safe enough to go
6 into wider-scale testing? And you're trying to
7 get some sense of what's the right dose that
8 you're going to use in your more definitive
9 trials.

10 And assuming all that works -- many
11 medicines don't make it through these stages, but
12 assuming that they do, then the next phase is
13 Phase 3. That's where you do the big clinical
14 trials in order to test the questions that the
15 FDA is going to want to look at for the medicine
16 coming onto the market. Is there enough evidence
17 that the drug works? Is there enough evidence
18 that it's safe in order for them to consider
19 approving it for use.

20 Q. How many patients would typically be in
21 one of these large Phase 3 clinical trials?

22 A. Well, that varies, but in Phase 2 you
23 would might be starting with hundreds of patients
24 whereas Phase 3 you're more likely to have 1,000
25 or more.

1 Q. After the company finishes its studying
2 of various patients with the illness that's the
3 subject of the trials and it wants to get
4 approval from FDA, what does it do to obtain that
5 approval?

6 A. It's a submission. We refer to it as
7 submission but it's called NDA, new drug
8 application. The company has to pull together
9 all the information it has from all these phases
10 of the trial as well as the company's conclusions
11 from that information, and the company's proposal
12 for what the drug label might look like, and
13 sends that information into the FDA, which then
14 starts reviewing it and considering the approval.

15 Q. Can you give the jury a sense of when
16 you say the information is submitted as part of
17 the NDA, what's the volume of information that's
18 given to the FDA?

19 A. It's a lot. When this was in paper
20 copies, it's boxes and boxes, and they'd send a
21 tractor-trailer to carry it from Lilly to the
22 company.

23 Q. What is your understanding once an NDA
24 goes into the FDA of how FDA goes about reviewing
25 the new drug application?

1 A. My experience has been that the FDA has
2 scientists that more or less parallel what we
3 would have at the pharmaceutical company. So
4 they will have people that are experts in the
5 drug's chemical formulation and things like how
6 it would be manufactured and how stable the pill
7 is. They have experts in toxicology, the animal
8 results.

9 They'd have physicians who are
10 expert in safety. Physicians who are expert in
11 the therapeutic area that -- the type of illness
12 that you're proposing it for. They have
13 statisticians who are very good at the analysis
14 and the whole team works together and they give
15 recommendations to the -- to the director who has
16 overall responsibility for deciding about
17 approval and labeling.

18 MR. KANTRA: Can we bring up TG021?
19 And for the jury's benefit, can we --

20 MR. SUGGS: Your Honor, I'm going
21 to object to this. I sent an e-mail -- can we
22 approach the bench, please?

23 THE COURT: Sure.
24 (Bench discussion.)

25 MR. SUGGS: I sent an e-mail to Mr.

1 Lehner last night telling him I was going to
2 object to this. This man is a fact witness. The
3 last date shown on here is 1996. He didn't start
4 working with the company until 1999. He's got no
5 personal knowledge of any of these things.

6 MR. KANTRA: As you heard through
7 his testimony, he's been part of a committee at
8 Lilly which oversees the drug development process
9 and as will become evident in his testimony later
10 as part of his responsibilities he went back and
11 understood the filings and the development over
12 time, and he's prepared to testify about that.

13 THE COURT: Subject to you tying up
14 that he went back and reviewed the filings over
15 time and that he would then be familiarized
16 himself with this document, I'll allow the
17 testimony.

18 MR. KANTRA: Thank you, Your Honor.
19 (End of bench discussion.)

20 Q. (BY MR. KANTRA) Dr. Baker, just one
21 question before we go and look at this particular
22 slide.

23 In your role, when you joined Lilly
24 and in your time at Lilly, have you been privy to
25 and do you understand the milestones that we've

1 just described generally as they pertain
 2 specifically to olanzapine?
 3 A. Yes.
 4 Q. Okay.
 5 MR. KANTRA: With that, I would
 6 bring up TG021.
 7 Q. (BY MR. KANTRA) And if we go all the
 8 way to the left-hand side of that screen, can
 9 you -- can you tell the jury when olanzapine was
 10 first synthesized --
 11 THE COURT: Again, you've used -- I
 12 just want to be clear, you used TG021 --
 13 MR. KANTRA: Sorry, Your Honor.
 14 That's just an internal reference for our
 15 purposes. It's a slide that Dr. Baker helped to
 16 prepare.
 17 THE COURT: So this isn't going to
 18 be offered as an exhibit?
 19 MR. KANTRA: No.
 20 A. Your question was when olanzapine was
 21 first synthesized. More than 25 years ago, 1982.
 22 Q. (BY MR. KANTRA) If we follow the
 23 timeline, the phase, what period of time were
 24 those animal studies and other preclinical
 25 studies conducted?

1 A. About four years.
 2 Q. And then when would Lilly have sought
 3 permission from FDA to begin testing in humans in
 4 clinical trials?
 5 A. 1986.
 6 Q. Over what period of time did Lilly
 7 conduct clinical trials of Zyprexa before seeking
 8 approval from FDA?
 9 A. Nine years.
 10 Q. And in how many thousands of patients
 11 did Lilly conduct these trials on before
 12 submitting it to FDA?
 13 A. It was a little over 3,000 people.
 14 Q. And at what point did Lilly make this
 15 new drug application, this NDA submission that
 16 you've described?
 17 A. Well, as you see above 1995 on the
 18 slide, it was September of 1995.
 19 Q. And that submission to FDA in September
 20 of 1995 would have included the clinical trial
 21 data including things like blood sugar levels
 22 from patients who participated in those trials?
 23 A. Sure. Just like I mentioned in general,
 24 all that information was sent in.
 25 Q. And how long did FDA review the new drug

1 application before approving it?
 2 A. They spent about a year reviewing it.
 3 Q. And then approval came in September of
 4 1996?
 5 A. Right.
 6 MR. KANTRA: Can we bring up
 7 AK8905?
 8 MR. SUGGS: A copy for me, Counsel?
 9 MR. KANTRA: That's your exhibit.
 10 We can get it if you want.
 11 MR. SUGGS: I still need a copy of
 12 it.
 13 MR. KANTRA: That's perfectly fine.
 14 Nick, we're going to focus down on
 15 that bottom part of the screen there.
 16 Q. (BY MR. KANTRA) Dr. Baker, if you take
 17 a look at this e-mail here, first thing you
 18 notice that the date on this is August 31st of
 19 2000; is that right?
 20 A. Yes.
 21 Q. At about the time that you began to
 22 focus on diabetes-related issues and Zyprexa?
 23 A. Exactly.
 24 Q. And you are one of the people -- in
 25 fact, I think you're the first person to whom

1 this e-mail is addressed; is that right?
 2 A. Yes.
 3 Q. Let's look down at the bottom of this
 4 e-mail where it presents what's called a proposed
 5 plan. And, in particular, if you'd look at the
 6 second line of that, it talks about what I refer
 7 to as glucose issues.
 8 You see that?
 9 A. I do.
 10 Q. And, in particular, it says Baker No. 1
 11 after that, right?
 12 A. Yes.
 13 Q. Okay. Does that mean that you were the
 14 only physician at Lilly who was examining issues
 15 relating to diabetes and Zyprexa?
 16 A. No, not at all.
 17 Q. So, who else at Lilly from a physician
 18 perspective would have been examining that issue
 19 as of 2000?
 20 A. Well, firstly, these folks in these
 21 e-mails were the other psychiatrists. There were
 22 four of us working for Lilly in the U.S. doing
 23 the job that I had mentioned earlier.
 24 Understanding about our product, communicating
 25 with physicians in the U.S. All of us had the

1 job of understanding the side effects, the
2 adverse event profile, the safety profile of the
3 drug, generally.

4 But then I became the one that was
5 most focused on getting all the details and
6 helping to educate and talk about that with my
7 colleagues in the U.S. There would have been
8 other physicians playing that same role working
9 for Lilly in the other countries where the
10 medicine was on the market in order to help
11 answer questions for their doctors.

12 And the way that I did my role
13 principally was talking to all the many
14 physicians and scientists in the company who were
15 working on the safety of Zyprexa. So, in the
16 core group, what we called the product team,
17 there were psychiatrists. There was an
18 endocrinologist, safety physicians who were
19 focused on the safety of Zyprexa. There was a
20 pharmacovigilance department that would look at
21 adverse events, things that we heard from doctors
22 or patients and record those for Zyprexa. There
23 were other endocrinologists, a number of
24 endocrinologists in the company that were helping
25 look at this particular question related to

1 glucose.

2 And then in addition to that, there
3 were all the scientists and physicians who had
4 worked on the development that we had talked
5 about previously up to that point.

6 Q. When you talk about the psychiatrists on
7 the product team that you would have been
8 interacting with, would that have included Dr.
9 Cavazzoni and Beasley?

10 A. Yes.

11 Q. Before your work --

12 MR. KANTRA: Go ahead and take that
13 down.

14 Q. (BY MR. KANTRA) Before you focused your
15 efforts on the diabetes issues, had Lilly
16 evaluated the issue of weight and diabetes before
17 August of 2000?

18 A. Yes.

19 Q. And can you tell the jury some of the
20 kinds of things that would have included that
21 kind of information that would have been
22 submitted to FDA?

23 A. I'm sorry. Could you clarify the
24 question?

25 Q. Sure. Before August of 2000, were there

1 submissions that Lilly would have made to the FDA
2 that would have focused on glucose and weight
3 gain?

4 A. Yes. Sure. That would have been part
5 of -- information on that would have been part of
6 the initial submission that came before the
7 approval and other submissions that had been made
8 after that, but there was also a submission that
9 was focused just on this topic of glucose that
10 had taken place in July of 2000. In fact, it
11 was -- reading through that was one of the first
12 things that I did when I took on my
13 responsibilities in August.

14 Q. In addition to the NDA application and
15 this reading of this special submission that
16 you've just described, would there have been
17 information in individual study reports about
18 clinical trials that the company was conducting
19 that would have been submitted to FDA?

20 A. Yes. As we finish each of our clinical
21 patient research trials, we submit that
22 information, a study report to the FDA. So that
23 would have come with each trial over time.

24 Q. And as part of those individual study
25 clinical reports would there have been

1 information about blood sugar levels in those as
2 well?

3 A. There's a review of all the safety and
4 laboratory findings, so that would include the
5 blood sugar results, yes.

6 Q. During this trial, we've heard reference
7 to the fact that the FDA was engaged in -- in
8 ongoing analysis beginning in 2000 of weight gain
9 and hyperglycemia as it related to atypical
10 antipsychotics like Zyprexa.

11 Are you familiar with that?

12 A. Yes.

13 Q. Okay. When did Lilly first become aware
14 of FDA's interest in this area?

15 A. FDA had communicated that to us in May
16 of 2000.

17 MR. KANTRA: Can we bring up what's
18 been marked as EL2581?

19 Q. (BY MR. KANTRA) I want to direct your
20 attention to the top of this letter and ask you
21 what the date is there in the upper right-hand
22 corner?

23 A. May 1st, 2000.

24 Q. Do you recognize this letter?

25 A. Yes.

1 Q. And it's the letter in which FDA
2 requests that the manufacturers of atypical
3 antipsychotics provide comprehensive information
4 on hyperglycemia to the FDA; is that right?

5 A. Yes.

6 MR. KANTRA: Nick, if we could go
7 down to look at the paragraph that begins with
8 "to assist."

9 Q. (BY MR. KANTRA) And that sentence there
10 says: To assist us in fully evaluating the
11 possibility that atypical antipsychotics may
12 produce disturbances in glucose metabolism, we
13 are requesting that the sponsors of these agents
14 provide us with more extensive safety
15 information.

16 How did Lilly understand this
17 request from FDA in terms of what they were
18 seeking?

19 MR. SUGGS: Objection, Your Honor.
20 Lack of foundation as to what Lilly understood.

21 THE COURT: Can you repeat the
22 question again?

23 MR. KANTRA: Yes, I said: In
24 response to this request from FDA, what was
25 Lilly's understanding of the request that was

1 being made of the company.

2 THE COURT: I'll overrule the
3 objection.

4 MR. KANTRA: Thank you.

5 THE WITNESS: We understood that
6 they were asking us to help them to assist them
7 as they were evaluating this question about
8 hyperglycemia and diabetes and to assist them
9 through providing information about it.

10 Q. (BY MR. KANTRA) And was this request
11 directed only at Lilly?

12 A. My understanding is that it went to all
13 the manufacturers of atypical antipsychotics, so
14 that would have included the manufacturers of
15 Clozaril and -- clozapine, risperidone,
16 quetiapine, as well as olanzapine.

17 Q. Did Lilly ultimately respond --

18 MR. KANTRA: Go ahead and take that
19 down.

20 Q. (BY MR. KANTRA) Did Lilly ultimately
21 respond to this request from FDA?

22 A. Yes. We provided a number of
23 submissions in response to this request.

24 Q. When did it first respond to FDA's
25 request?

1 A. The first was the July, 2000 submission
2 that I mentioned a couple of minutes ago.

3 MR. KANTRA: Can we bring up
4 EL2043?

5 THE WITNESS: Sorry.

6 MR. KANTRA: May I approach?

7 THE COURT: You may. And
8 Mr. Kantra, feel free to move around the
9 courtroom as you need to.

10 Q. (BY MR. KANTRA) Dr. Baker, I put this
11 before you. Ask you to take a look at the first
12 volume in particular. Tell me whether you
13 recognize this.

14 THE COURT: Before we get into
15 this, is this a good spot for a break?

16 MR. KANTRA: That would be great.

17 THE COURT: Ladies and gentlemen of
18 the jury, we'll take our second break of the day,
19 and we'll try to keep it to 15 minutes.

20 (Jury out.)

21 THE COURT: We'll be off record.

22 (Break.)

23 (Jury in.)

24 THE COURT: Please be seated.

25 We're back on the record and all

1 members of the jury are present.

2 Mr. Kantra.

3 MR. KANTRA: Thank you.

4 Q. (BY MR. KANTRA) Dr. Baker, I think we
5 had left off, I had shown you what has previously
6 been marked as EL2043?

7 A. Yes.

8 Q. And do you recognize that document?

9 A. Yes.

10 Q. And is that Lilly's July, 2000 response
11 to FDA's request in May for information on
12 Zyprexa and hyperglycemia?

13 A. It is.

14 MR. KANTRA: If you could bring
15 up --

16 Q. (BY MR. KANTRA) Actually before we do
17 that, let me ask you, Dr. Baker: Did you help
18 prepare slides that would help the jury
19 understand the submissions that Lilly made in
20 response to the May, 2000 letter?

21 A. Yes.

22 MR. KANTRA: Okay. Can we bring up
23 TG104? 5?

24 Q. (BY MR. KANTRA) And if we look up on
25 this slide here, does this reflect a summary of

1 the information that was included in the response
2 to the May, 2000 letter?

3 A. It does.

4 Q. Okay. And if we begin up at the top
5 with respect to the literature that was sent in
6 to FDA, about how many pieces of -- how many
7 articles were sent to the FDA?

8 A. It was over 100. Lilly had reviewed the
9 literature going back -- well, going back for
10 decades looking for information about glucose
11 abnormalities during treatment with antipsychotic
12 medicines or associated with schizophrenia.

13 Q. And I see in the second bullet point up
14 there, it refers to historical animal study data
15 and clinical studies?

16 A. Yes. We've reviewed for the FDA the
17 information that had come during the course of
18 the drug's development that we had talked about
19 earlier through the animal studies, Phase 1, 2,
20 and 3, as well as studies that had been completed
21 after the drug had been approved.

22 Q. And that next to last bullet point up
23 there refers to a new analysis of clinical trial
24 data; is that right?

25 A. Yes.

1 studies, but comes in because a doctor
2 communicates to us, say, through a sales rep or a
3 pharmacist or a patient if they called our 800
4 number and said, hey, I'm having this discomfort.

5 We take that information and it's
6 called a spontaneous adverse report, and we have
7 to clarify the information and that's all
8 reported -- we analyze it ourselves, but we
9 report it also to the FDA.

10 Q. Did this submission also include copies
11 of submissions that had been made to regulatory
12 authorities outside the United States?

13 A. It summarized those.

14 Q. Would that have included information
15 regarding a change to the European label
16 regarding diabetes in 1999?

17 A. Yes.

18 Q. You mentioned -- turning back to that
19 new analysis of clinical trial data, can you tell
20 us what the two primary conclusions were from
21 that analysis?

22 A. Yes. Two -- two important conclusions.
23 One was that in looking at -- again, this was an
24 analysis that was looking for the proportion of
25 patients that developed hyperglycemia or

1 Q. And, roughly, there was a number at the
2 end of that bullet point. What does that
3 represent?

4 A. 6,374 people were in this analysis. So
5 this made it a very important analysis. This was
6 the biggest data set that was existing at that
7 time looking at antipsychotic medicine, and this
8 was a review that was done pulling all that
9 together to look specifically at the blood
10 glucose measures that had been drawn during the
11 study in order to answer the question of how many
12 people were having elevations from the beginning
13 of the study to sometime in the course of the
14 study that would suggest -- that might suggest
15 that they were having hyperglycemia or diabetes.

16 Q. And then the last bullet point up there
17 refers to a review of spontaneous adverse event
18 reports after 4 million patient exposures.

19 Can you remind the jury what
20 spontaneous adverse event reports are?

21 A. Yes. That's an important part of what
22 we do in the safety division that I'm in, which
23 is that spontaneous report is different than a
24 report that happens in a clinical trial. This is
25 information that we get that is not from our

1 diabetes, presumed hyperglycemia or diabetes
2 based on blood sugar changes in the course of
3 their treatment. And we looked at olanzapine
4 versus the other comparisons that were in this
5 database. Placebo, risperidone, haloperidol.

6 What we found is that there was no
7 difference in the rate of crossing those
8 thresholds between olanzapine and the other
9 treatments. That was one finding.

10 But the other important finding is
11 that then they looked back taking all those
12 patients who had crossed the thresholds and
13 looked at the question of, hey, we know in the
14 general population that there's some things that
15 would make you more at risk of hyperglycemia,
16 like older age or if you're obese when you come
17 in, and we looked for did those sorts of risk
18 factors hold up to indicate who's likely to have
19 those blood sugar increases in the course of
20 treatment. And indeed, not surprisingly, that's
21 what we found.

22 Q. Did Lilly reach any conclusions as to
23 whether labeling changes were made based on this
24 July, 2000 submission?

25 A. Yes. Lilly looked at that question and

1 stated to the FDA that they felt that no labeling
 2 change was needed to what was already in the
 3 label at that time.
 4 Q. And moving on to the -- the second
 5 submission that Lilly made in regards to FDA's
 6 response, I want to direct your attention to May
 7 of 2001 and ask you if that was the date or the
 8 month in which Lilly made another submission to
 9 FDA.
 10 A. Sorry, could you repeat that?
 11 Q. Sure. The second submission that Lilly
 12 made in response to the FDA's request was in May
 13 of 2001; is that right?
 14 A. Yes.
 15 MR. KANTRA: Can we bring up
 16 EL2127?
 17 Q. (BY MR. KANTRA) Are you familiar with
 18 this submission, Dr. Baker?
 19 A. Yes.
 20 MR. KANTRA: And can we bring up,
 21 Nick, TG1071?
 22 Q. (BY MR. KANTRA) And, Dr. Baker, using
 23 these slides that you've helped to prepare, can
 24 you describe for the jury the information that
 25 was contained in this submission to FDA?

1 A. Yes. This included new information that
 2 we had since the submission the year before. And
 3 so on this slide what's mentioned is it included
 4 the first two epidemiology studies that Lilly had
 5 done looking at this question about diabetes
 6 occurring in people taking antipsychotic
 7 medication.
 8 Q. And let's take -- let's take the studies
 9 one at a time.
 10 With respect to the first study,
 11 the GPRD study, what were the findings with
 12 respect to whether or not the risk of diabetes
 13 was increased over the general population?
 14 A. This study was done in the United
 15 Kingdom, and it confirmed that people on
 16 antipsychotic medicine had occurrence of more
 17 diabetes during their treatment than people that
 18 weren't on antipsychotic medicine. This is
 19 comparing the antipsychotics to people that
 20 weren't taking antipsychotics.
 21 Q. Was that a surprising finding to you?
 22 A. No. This, again, confirms something
 23 that we had seen pretty strongly in the
 24 literature review that was sent to the FDA the
 25 year before, which is that people with

1 schizophrenia, for whatever reasons, are having
 2 higher rates of diabetes, significantly higher
 3 than people who didn't have schizophrenia.
 4 Q. And was there a comparison that looked
 5 at the question of whether there was more
 6 diabetes observed in patients who were treated
 7 with atypical antipsychotics than the
 8 first-generation agents?
 9 A. That's right. In this case it looks
 10 significantly more common on atypical
 11 antipsychotics than on the older typical, or
 12 first-generation, as you've called them.
 13 Q. Was there enough information in that
 14 study to be able to make an assessment of the
 15 risk with respect to Zyprexa?
 16 A. No. At that time Zyprexa was relatively
 17 newly available in the U.K. So about 75 percent
 18 of those patients were on risperidone and not
 19 olanzapine. There wasn't enough of a judgment to
 20 make a comparison of how it stacked up to other
 21 treatments.
 22 Q. Let's look to the other study that Lilly
 23 submitted in May, and that's the AdvancePCS
 24 study. That study found that there was an
 25 increased risk as compared to the general

1 population?
 2 A. Yeah, that's been consistent and it was
 3 consistent again here.
 4 Q. And with respect to atypicals against
 5 the first-generation agents, this study found in
 6 contrast to the first study that there was no
 7 significant difference, is that right?
 8 A. That's right.
 9 Q. What about the comparison that looked at
 10 Zyprexa in this study against another atypical
 11 antipsychotic, risperidone?
 12 A. Yes. This one was much bigger study
 13 than the U.K. study. This is a U.S. study, and
 14 the two atypical antipsychotics that were mostly
 15 in this one were olanzapine and risperidone. So
 16 we could make that comparison and we found that
 17 the rates of diabetes as measured in this study
 18 were no different between those two drugs.
 19 Q. And were these published?
 20 A. Yes.
 21 MR. KANTRA: Could we have EL2013
 22 and EL3385?
 23 Q. (BY MR. KANTRA) Let's look first at
 24 EL2013.
 25 Are you familiar with that article?

1 A. Yes.

2 Q. Okay. And does that represent the GPRD
3 analysis that -- that Lilly did that you've just
4 described?

5 A. That's right.

6 MR. KANTRA: Okay. And can we
7 bring up -- yeah, bring up EL3385. Can we pull
8 that up just a little bit?

9 Q. (BY MR. KANTRA) And does that show the
10 AdvancePCS study that Lilly conducted and that
11 you've described as well?

12 A. Yes.

13 Q. And these articles appeared and were
14 published in peer-reviewed journals; is that
15 correct?

16 A. Yes.

17 MR. KANTRA: Nick, if we could go
18 back a minute, or not go back, but can we go to
19 TG1072?

20 Q. (BY MR. KANTRA) And in addition to
21 these two epidemiology studies that you've just
22 described, did Lilly also take a look -- another
23 look at the clinical trial data regarding
24 hyperglycemia and diabetes and Zyprexa?

25 A. Yes. That's what's referred here as the

1 Allison clinical trial analysis. Dr. David
2 Allison, who was somebody outside of Lilly
3 working with us on -- on this question, helped
4 Lilly in this analysis.

5 Q. And the study looked at glucose
6 elevations in two different ways in this study;
7 is that right?

8 A. That's right.

9 Q. And those two different ways -- can you
10 describe the two different ways that the company
11 did that?

12 A. Yes. I had mentioned in the last
13 analysis, the submission of the year before, that
14 what Lilly had looked at was comparing blood
15 glucoses when the patient started treatment to
16 what happened in the course of treatment to do --
17 we called a categorical analysis, to see what
18 percentage of patients go above a certain level.
19 This one repeated an analysis of that and looked
20 at more different categories. Looked at it more
21 ways.

22 Q. Can I stop you there.

23 When you say categories, categories
24 that would be indicative of hyperglycemia or
25 diabetes?

1 A. Exactly.

2 Q. Okay. What was the other way they
3 looked at it?

4 A. The other way we looked at it was
5 looking at all patients. What's the average
6 change that they had from before they start on
7 the treatment to when they finish treatment. So
8 then you subtract the glucose at the end from
9 what it is at the beginning, that's what you do
10 for each individual, and you average it so it
11 looks across everybody.

12 Q. Does this second analysis, the average
13 change analysis that you just described, tell you
14 whether patients developed diabetes or not?

15 A. No, that just tells you the average
16 change across the whole population. It can't
17 tell you for what percentage of people was that
18 an abnormal change or one significant for disease
19 versus what percentage is not an important
20 change.

21 Q. Let's start with that second analysis
22 that you've just described and look at the
23 average changes.

24 What did that show?

25 A. Well, it showed that in olanzapine there

1 did tend to be increase from the time people
2 started treatment to the time they finished
3 treatment on average. It tended to go up some.
4 Also, what we were doing that is comparing that
5 to what we found on other treatment groups, to
6 placebo, to haloperidol, to risperidone, to
7 clozapine.

8 In one case there wasn't a
9 difference between those, that was risperidone,
10 the other atypical antipsychotic. The change
11 from beginning to end was not different on
12 average between olanzapine and risperidone. But
13 compared to placebo or compared to haloperidol,
14 there was a greater increase in the average
15 glucose in patients on olanzapine compared to
16 those other treatments. And compared to
17 clozapine, there was significantly less increase
18 than had been seen with clozapine.

19 Q. Why don't we turn then to the other
20 analysis that you described that looked at
21 potential cases of hyperglycemia or diabetes and
22 can you tell us what were the findings in that
23 analysis or that part of the analysis.

24 A. Yeah. Here's again one that looks at
25 the rate of whether individual patients having an

1 increase varies from one treatment to another.
 2 This confirmed the previous analysis that there
 3 was no difference at any of the comparisons at
 4 any of the thresholds.

5 Q. Did Dr. Allison prepare a manuscript
 6 reporting the results of this study?

7 A. Yes.

8 MR. KANTRA: And if we can go back
 9 to EL2127, I believe -- yeah. And can you go to
 10 the last document there, which is going to be Tab
 11 3?

12 Q. (BY MR. KANTRA) And Dr. Allison
 13 prepared a manuscript that was ultimately
 14 submitted for publication; is that right?

15 A. Yes. It was submitted.

16 MR. KANTRA: And go one more in,
 17 Nick, if you could. And can you blow up the
 18 title and the authors?

19 Q. (BY MR. KANTRA) Does that represent the
 20 manuscript that was prepared by Dr. Allison?

21 A. Yes.

22 Q. Why don't we turn to the third
 23 submission that Lilly made, and that was in
 24 October of 2002; is that right?

25 A. Yes.

1 Q. Okay.

2 MR. KANTRA: Can we bring up
 3 EL2032?

4 THE COURT: Did you say 2302?

5 MR. KANTRA: Sorry. 2032.

6 THE COURT: 2032.

7 Q. (BY MR. KANTRA) Do you recognize this
 8 submission?

9 A. I do.

10 Q. And was this actually the third
 11 submission that Lilly made to FDA?

12 A. Yes. This was the third.

13 Q. And what was -- what was the new
 14 information that Lilly was sharing with FDA in
 15 this particular submission?

16 A. There were a number of things. I
 17 prepared -- helped prepare a slide on that.

18 MR. KANTRA: Why don't we bring up
 19 TG1073.

20 Q. (BY MR. KANTRA) Up at the top there's a
 21 reference to literature studies; is that right?

22 A. Yes.

23 Q. And what did the company's survey of the
 24 literature show?

25 A. We reviewed and provided the things that

1 were new since our 2000 submission, and among
 2 those were a number of published
 3 pharmacoepidemiology studies. They were
 4 consistent on some points, but some variation
 5 from one to another in terms of whether they find
 6 differences from one treatment to another. That
 7 was inconsistent.

8 Q. And then there was -- there was a study
 9 which is identified on the slide as a TED
 10 clinical trial analysis.

11 What does TED stand for?

12 A. TED is an acronym, treatment-emergent
 13 diabetes, TED.

14 Q. And what did this study evaluate?

15 A. This, I think, was one of the most
 16 useful analyses that was done on Lilly's clinical
 17 trial, at least useful from the standpoint of
 18 helping clinicians. Because this one, again,
 19 looked at some of the questions that we had
 20 looked at in the past such as comparisons of
 21 apparent diabetes occurring during treatment on
 22 one drug versus another.

23 But this went beyond that to really
 24 emphasize who is most likely to get that diabetes
 25 happening in the course of treatment to help

1 doctors with giving them some notion among all
 2 these patients you have with schizophrenia, who
 3 are the ones that would be most at risk.

4 Q. This was an analysis that was in
 5 approximately 5,000 patients; is that right?

6 A. Right. Again, this was really the
 7 largest data set that was available at that time.

8 Q. And more than 20 clinical trials?

9 A. Yes.

10 Q. And what did this study tell us, then,
 11 in terms of what risk factors were most
 12 significantly associated with the development of
 13 treatment-emergent diabetes?

14 A. Well, this one confirmed what we had
 15 seen before, that which treatment was chosen was
 16 not a predictor. It wasn't a risk factor for the
 17 likelihood of having diabetes in the course of
 18 treatment. This one --

19 Q. When you say treatment, that would be
 20 whether a patient was assigned to Zyprexa or
 21 another drug?

22 A. That's right.

23 Q. Okay.

24 A. Or Zyprexa versus placebo as well.

25 Q. Okay.

1 A. But this one also, as I mentioned,
2 looked at risk factors and among those, the most
3 powerful was the blood glucose measurement before
4 the person gets the medicine. In fact, what this
5 found is that people who had borderline, somewhat
6 elevation of their glucose when they started, not
7 at a diabetes level, but elevated had more than
8 ten times as much likelihood, more than ten times
9 of getting diabetes during their treatment than
10 if their blood glucose had been normal before
11 they went onto the treatment.

12 Q. And was there any other factor that was
13 also among the most significant risk factors for
14 predicting diabetes?

15 A. Well, yes, we looked -- we looked beyond
16 that -- that was a known risk factor. We looked
17 the things that the ADA or general knowledge on
18 diabetes would have told you are risk factors,
19 like if a person is older or has hypertension or
20 if they're obese. And if you look at those,
21 they, again, hold up on this analysis.

22 And if a person has two or more of
23 those risk factors versus somebody that has one
24 or less, if you have two or more versus one or
25 less, you're more than five times as likely to

1 get diabetes in the course of treatment. So this
2 was important information for doctors.

3 Q. And was there an analysis of the extent
4 to which weight gain was a risk factor for
5 diabetes?

6 A. That's right. And it also found that if
7 you had weight gain in the course of treatment,
8 that that was a risk factor for being more likely
9 to have diabetes in the course of treatment than
10 you didn't have weight gain. A much, much weaker
11 risk factor than the others we described, but it
12 was a significant -- it was a significant risk
13 factor.

14 Q. In addition to sharing this information
15 with the FDA in October of 2002, was the
16 information from this TED study that you've just
17 described published in the peer-reviewed
18 literature?

19 A. It was.

20 MR. KANTRA: Can we bring up
21 EL3801?

22 Q. (BY MR. KANTRA) Dr. Baker, do you
23 recognize this article?

24 A. Yes. This is the TED study,
25 treatment-emergent diabetes.

1 Q. And this is titled A Retrospective
2 Analysis of Risk Factors in Patients with
3 Treatment-emergent Diabetes During Clinical
4 Trials of Antipsychotic Medications and that's
5 published in the British Journal of Psychiatry?

6 A. Yes.

7 Q. And that was in 2004 when that was
8 published?

9 A. I'm thinking it's 2005.

10 Q. Okay.

11 MR. KANTRA: Let's look at TG1074
12 if we can for a minute.

13 Q. (BY MR. KANTRA) We heard Dr. Inzucchi
14 testify earlier about some mechanistic clamp
15 studies that found no direct effects on either
16 the pancreas or on insulin resistance, and I
17 wanted to ask you if you're familiar with those
18 studies.

19 A. Yes.

20 Q. And were those studies disclosed to FDA
21 in October of 2002?

22 A. Yes. Lilly had conducted two of them,
23 and the results were in this 2002 submission.

24 Q. And those were also published in a
25 peer-reviewed literature as well?

1 A. Right.

2 Q. The next --

3 MR. KANTRA: We're okay with that
4 now, Nick, you can take that down.

5 Q. (BY MR. KANTRA) The next submission,
6 the fourth submission that Lilly made to FDA
7 regarding whether or not there were -- the
8 important information with regard to Zyprexa and
9 diabetes was in March, 2003; is that right?

10 A. Yes.

11 MR. KANTRA: Can we bring up
12 TG1075 -- actually before -- before we do that,
13 can we bring up EL2033?

14 Q. (BY MR. KANTRA) And does this -- let me
15 give you this analysis as well.

16 Do you recognize this submission?

17 A. I do.

18 Q. And this is the submission that went
19 into FDA in March of 2003?

20 A. Yes.

21 Q. This was --

22 MR. KANTRA: If we can bring up
23 TG1075.

24 Q. (BY MR. KANTRA) And this reflected
25 Lilly's analysis of spontaneous adverse event

1 reports after more than 9 million patient
2 exposures; is that right?

3 A. Right.

4 Q. And it looked at spontaneous adverse
5 event reports, and what did it conclude?

6 A. It reviewed -- Lilly reviewed these and
7 found that there was no conclusion that could be
8 drawn from these data regarding causation of
9 diabetes.

10 Q. From these spontaneous adverse event
11 reports?

12 A. From these, yes, sir.

13 Q. Let me go to a submission that Lilly
14 made three months later in June of 2003. That
15 would be the fifth submission that was made in
16 this instance.

17 MR. KANTRA: And can we bring up
18 EL2036?

19 Q. (BY MR. KANTRA) And do you recognize
20 this submission?

21 A. Yes.

22 Q. Okay. This is the June submission to
23 FDA and further response to its request in 2000?

24 A. That's right.

25 MR. KANTRA: Let's bring up TG1076.

1 Q. (BY MR. KANTRA) And this information
2 included, again, more new clinical trial analyses
3 that Lilly had conducted.

4 Can you describe these analyses for
5 the jury?

6 A. Yes. Since the previous submission
7 Lilly had completed two new analyses. The first
8 one on the list is -- it's like the previous
9 treatment-emergent diabetes submission, but
10 whereas that one was looking at clinical trials
11 for patients with schizophrenia, this was taking
12 the same analyses in patient who had bipolar
13 disorder.

14 Q. And what did it find in terms of whether
15 or not the same risk factors were most predictive
16 of developing diabetes?

17 A. This one was very consistent with the
18 other one. It did not find that whether they
19 were on olanzapine or the alternative treatment,
20 placebo or other treatments for mania, it did not
21 find any difference in likelihood of developing
22 diabetes based on that. But, again, this held up
23 that the nonrisk factors that they may have at
24 baseline such as obesity, such as advanced age,
25 were risk factors.

1 And again, by far the most powerful
2 predictor was the blood sugar before they started
3 treatment. If that was high, that was an
4 important risk.

5 Q. There's a second study that's described
6 up there as the PED study.

7 What did that represent?

8 A. Yes, PED is preexisting diabetes. So
9 this was looking at patients who had already
10 diabetes when they started treatment. We
11 wouldn't have looked at those in the other
12 studies of treatment-emergent diabetes. So this
13 trial went back to those patients and looked at
14 what happened to them when they got medicine.

15 Q. And looked at the question of whether
16 their diabetes got worse over time? Is that
17 right?

18 A. Exactly.

19 Q. And what did they find -- what did Lilly
20 find in regard to this study?

21 A. Well, a couple things. One, as you'd
22 expect in diabetes, that it's different from
23 patient to patient. Some people are worsening;
24 some are getting better in the course of
25 treatment. But on average across all the

1 treatments, there's a little bit of worsening
2 over time.

3 And then the other thing it found
4 was, again, the comparison, is this different if
5 you're on olanzapine than other treatments. In
6 this case it was haloperidol was the one that we
7 had the most patients to compare to and found no
8 significant difference in that worsening.

9 Q. There's a third clinical trial report
10 that was included in this analysis as well, which
11 is described by the study code HGHJ. And that
12 compared Zyprexa against ziprasidone, right?

13 A. Right.

14 Q. Ziprasidone is Geodon?

15 A. Right.

16 Q. That was one of the newer atypical
17 antipsychotics?

18 A. Right. This was a brand-new study.
19 This was a six-month-long study of treatment in
20 schizophrenia and it compared olanzapine to the
21 newest drug, ziprasidone, which appeared to have
22 less weight gain effect than olanzapine or for
23 that matter the others that were available at the
24 time.

25 Q. And what did this study find with

1 respect to changes in blood sugar levels?
 2 A. It found no difference in terms of
 3 average blood sugar from beginning to the end of
 4 the study. No difference between olanzapine and
 5 ziprasidone. And it also, again, looked at the
 6 question not of the average, but individual
 7 patients. Are there more on olanzapine than
 8 ziprasidone that got diabetes or hyperglycemia in
 9 the course of treatment? Well, first time with
 10 ziprasidone, but, again, the finding was no
 11 difference.
 12 Q. And was that despite a significant
 13 difference in weight gain?
 14 A. Yes. There was considerably more weight
 15 gain on average with olanzapine than there was
 16 with ziprasidone.
 17 Q. Was there also as well in this
 18 particular submission additional literature that
 19 the company had become aware of with respect to
 20 Zyprexa and hyperglycemia?
 21 A. I believe this one reviewed the
 22 literature again.
 23 Q. Finally, let's talk about the most
 24 recent special submission that focused just on
 25 glucose that went into the FDA.

1 MR. KANTRA: And if we can take a
 2 look at EL2041.
 3 Q. (BY MR. KANTRA) Dr. Baker, do you
 4 recognize this as the submission that went into
 5 FDA in February of 2006?
 6 A. Yes.
 7 Q. And in this particular analysis, was
 8 there a look at both the clinical trial data and
 9 the spontaneous adverse event data?
 10 A. Yes.
 11 Q. And what was found with respect to
 12 whether or not the findings in this analysis were
 13 consistent with the earlier analyses in regard to
 14 the risk of diabetes whether it was higher on
 15 Zyprexa or not?
 16 A. This one was looking at the adverse
 17 events related to diabetes or hyperglycemia and
 18 it found looking at the adverse events in
 19 clinical trials were consistent with what we'd
 20 seen in clinical trials previously. It looked at
 21 the spontaneous reports and the conclusion that
 22 had been called in to Lilly the conclusion with
 23 those was, again, consistent with what we had
 24 seen in our earlier reviews.
 25 Q. Now, we'd been talking about special

1 glucose submissions that focused exclusively just
 2 on the issue of whether or not there were
 3 differences in regards to changes in blood sugar
 4 elevations or differences in regards to diabetes
 5 and hyperglycemia. Would these have been the
 6 only documents that would have been submitted to
 7 FDA that looked at blood sugar levels,
 8 hyperglycemia, and diabetes?
 9 A. No. These were the only submissions
 10 that -- during that time period that focused just
 11 on that question, but there were many other
 12 submissions in which that question would have
 13 been addressed as part of the submission.
 14 Q. And can you identify the types of other
 15 ways in which information on blood sugar
 16 elevations would have been provided to FDA?
 17 A. Yes. For all of our products there's --
 18 there are periodic reports of new safety
 19 information. That's what our safety group will
 20 do on a regular basis.
 21 Q. You supervised the people who actually
 22 prepare those reports?
 23 A. I supervise the physicians, yes.
 24 Q. Okay.
 25 A. In addition to that, and I think I

1 mentioned this before, as we do new clinical
 2 studies, when those are reported -- completed and
 3 the analysis is completed, those are submitted as
 4 a study report to the FDA.
 5 Q. And what about when -- when Lilly
 6 actually requests a new indication, it was
 7 approved originally for schizophrenia, but each
 8 time the company submits for a new indication, is
 9 there information relating to glucose for that?
 10 A. That's right. Each of those submissions
 11 is somewhat similar to the first initial new drug
 12 application submission in that we submit all of
 13 the clinical data and other information that is
 14 supporting the new indication, the new treatment
 15 group that we're requesting in that.
 16 And so they would include the
 17 safety information from those studies, it would
 18 include an overall summary of safety findings
 19 with the drug, and it would include, again, for
 20 the FDA to review the Zyprexa label and proposed
 21 changes to the -- to the label in each of those
 22 submissions.
 23 Q. And when you say that they would be
 24 reviewing the labeling, that would include any
 25 review of the safety information in the labeling;

1 is that right?
 2 A. Yes, sir, of course.
 3 Q. Dr. Baker, are you familiar with the
 4 labeling and package inserts for Zyprexa,
 5 generally?
 6 A. Yes.
 7 Q. And are you familiar, in particular,
 8 with the package insert for Zyprexa from 1996
 9 when the drug was originally approved?
 10 A. Yes.
 11 Q. Okay.
 12 MR. KANTRA: Can we bring up 2954A?
 13 If you go down to the bottom of
 14 that first page, Nick.
 15 Q. (BY MR. KANTRA) See the date down
 16 there? 1996?
 17 THE COURT: That's EL2954A?
 18 MR. KANTRA: Yes.
 19 Q. (BY MR. KANTRA) Is that the 1996 label
 20 for Zyprexa?
 21 A. Yes.
 22 Q. And moving from the 1996 to April of
 23 2000, are you familiar with the labeling for
 24 Zyprexa as it existed in April of 2000?
 25 A. Yes.

1 Q. Okay.
 2 MR. KANTRA: Can we look at 2937A?
 3 And can we go to the last page of that document?
 4 And if we could look at the part that says
 5 literature revised.
 6 Q. (BY MR. KANTRA) And is this the package
 7 insert that represents the literature as -- the
 8 package insert as it stood in April of 2000?
 9 A. Right.
 10 MR. KANTRA: Take that down.
 11 Q. (BY MR. KANTRA) I want to ask you if
 12 you're also familiar with the labeling for
 13 Zyprexa as it stood in October of 2000.
 14 A. Yes.
 15 MR. KANTRA: And can we bring up
 16 EL2585? And, again, can we go to the last page
 17 of that document? You see the literature revised
 18 section there, Nick?
 19 Q. (BY MR. KANTRA) And does this represent
 20 the October, 2000 package insert for Zyprexa?
 21 A. Yes.
 22 Q. Are you familiar with the labeling for
 23 Zyprexa as it stood in September of 2003?
 24 A. Yes.
 25 MR. KANTRA: And can we bring up

1 EL2953? And if we can go to the last page again.
 2 2953 -- sorry, I misspoke on that.
 3 Q. (BY MR. KANTRA) Does that represent the
 4 literature as it stood on that date in September
 5 of 2003?
 6 A. Yes.
 7 Q. Are you familiar with the package insert
 8 for Zyprexa as it stood in January of 2004?
 9 A. Yes.
 10 MR. KANTRA: Can we bring up 2945A?
 11 Q. (BY MR. KANTRA) And if we can go to the
 12 last page, again, for that.
 13 It shows a date of January 14th,
 14 2004. Is that the January, 2004 package insert
 15 for Zyprexa?
 16 A. Yes.
 17 THE COURT: Again, that's an EL
 18 document?
 19 MR. KANTRA: Sorry. EL2945A.
 20 Q. (BY MR. KANTRA) And finally, are you
 21 familiar with the labeling for Zyprexa as it
 22 existed in October of 2007?
 23 A. Yes.
 24 MR. KANTRA: Can we bring up
 25 EL2958? Again, if we can go to the last page of

1 that at the bottom.
 2 Q. (BY MR. KANTRA) You see where it says
 3 Literature Revised?
 4 A. I do.
 5 Q. And does that show the labeling as it
 6 existed as of October of 2007?
 7 A. Yes.
 8 Q. All right. I want to take you back for
 9 a minute to the October, 2002 submission that we
 10 talked about a moment ago.
 11 And, in particular, I want to ask
 12 you if you were aware of a teleconference that
 13 took place between FDA and Lilly regarding the
 14 substance of that particular submission?
 15 A. Yes.
 16 Q. Is it Lilly's standard practice for its
 17 regulatory group to document interactions with
 18 FDA regarding Zyprexa?
 19 A. Yes, Zyprexa or any of our products that
 20 we'd document.
 21 MR. KANTRA: Can we have EL2037?
 22 Q. (BY MR. KANTRA) You see this is marked
 23 as a note to file?
 24 A. Right.
 25 Q. And is it a note to file that would

1 capture Lilly's understanding of the interaction
2 with FDA?

3 A. That's the point, yes.

4 Q. And does the title of this, the subject
5 of the communication reflect October 17, 2002,
6 FDA meeting and briefing document?

7 A. Yes.

8 Q. Okay. And if we go to -- let me just
9 ask you: What was your understanding of the
10 communication that took place between FDA and
11 Lilly regarding the information that was
12 submitted to FDA in October of 2002?

13 MR. SUGGS: Your Honor, can we
14 approach, please?

15 THE COURT: You may.
16 (Bench discussion.)

17 MR. SUGGS: This witness wasn't
18 part of this meeting. I mean, he's not copied on
19 this thing. They're just using this to talk
20 about these documents. He doesn't have personal
21 knowledge if he's talking as a fact witness.

22 THE COURT: A curious objection
23 coming from the Plaintiff.

24 Do you want to set a little bit of
25 a foundation?

1 could get back to us on the methodology of the VA
2 study and the expected timing of the data being
3 sent to the division from the VA.

4 Can you tell us a little bit more
5 about what that VA study was?

6 A. Yes. This was an epidemiology study
7 that was, again, looking at the risk of diabetes
8 in patients with schizophrenia, and looking in
9 particular at the question of whether rates would
10 be different between antipsychotic agents, and it
11 was conducted in the Veterans Administration
12 system in the United States.

13 All the VA hospitals and clinics
14 looking for patients with schizophrenia and
15 exploring this question.

16 Q. And does -- does this refresh that the
17 FDA was actually involved in helping to design
18 that study?

19 A. Lilly's understanding was that, yes,
20 they were in contact with -- close discussion
21 with the investigators about this study
22 throughout.

23 Q. Do you recall when the results from that
24 study were first presented to the public?

25 A. It was around the end of summer of that

1 MR. KANTRA: This is going in as a
2 business record is the foundation that I'm
3 setting up for this.

4 THE COURT: Okay. I'll allow this.
5 You could cross-examine.

6 (End of bench discussion.)

7 Q. (BY MR. KANTRA) Let's take a look at
8 the third paragraph on this, Nick.

9 And in particular, you see the
10 first sentence there that says that Dr. Katz
11 noted that the division was not in a position at
12 this time to draw conclusions regarding glucose
13 dysregulation?

14 A. Yes.

15 Q. And is that consistent with your
16 understanding of the communication that was made
17 between Lilly and FDA as of October of 2002?

18 A. Yes, as of this point.

19 Q. And if we go on further in that
20 paragraph, to the next sentence it says that he
21 stated they expected to have results from the VA
22 study fairly soon, that they actually expected
23 the results in the summertime. Then it goes on
24 to say that Dr. Katz told us that Dr. Judy
25 Racoosin was leading this effort and the division

1 year, 2003.

2 Q. And do you recall what the results of
3 that study showed?

4 A. Yes. They found similar diabetes risk
5 between risperidone, olanzapine and quetiapine.

6 MR. KANTRA: Can we go then, to
7 take a look at EL2016, and can we blow up the
8 title there for a minute?

9 Q. (BY MR. KANTRA) This is an article
10 entitled Diabetes Risk Associated with the Use of
11 Olanzapine, Quetiapine and Risperidone in
12 Veterans Health Administration Patients with
13 Schizophrenia published in the American Journal
14 of Epidemiology.

15 Are you familiar with this article?

16 A. Yes.

17 Q. And is this the article that includes
18 the results that were first presented in August
19 of 2003?

20 A. That's right.

21 Q. Okay.

22 MR. KANTRA: And if we can go,
23 Nick, and look at table 4. And, in particular,
24 if we can look at the last line of that table?

25 Q. (BY MR. KANTRA) Did this study include

1 information about the rates of diabetes across
2 the atypical antipsychotic medications?
3 A. Yes. What you see on the bottom line
4 here are the rates of diabetes. These rates,
5 these numbers are per hundred patient years. So,
6 in other words, if there's a doctor that's
7 treating 100 patients with schizophrenia, which
8 many of us would have in a typical practice, this
9 is saying that you're -- that they should expect
10 to see that four of those are going to be
11 developing new diabetes in the course of a year
12 on average.

13 And what you see going across,
14 they're comparing the different treatment arms,
15 looking for what's the relative rates, are they
16 different on one of these atypical antipsychotics
17 versus another? So, the first one on the list is
18 olanzapine. 4 point --

19 MR. KANTRA: Just a second. Nick,
20 can you go back up, just so we can see the top of
21 the chart to see how the drugs -- thanks.

22 A. Okay. So I probably don't need to read
23 it for you, then. You can see olanzapine, 4.1
24 per hundred; risperidone, 3.9 per hundred;
25 quetiapine, 4.3 per hundred; clozapine, 4.9 per

1 hundred; and haloperidol, the typical
2 antipsychotic, 3 per hundred.

3 MR. KANTRA: And if we can go to
4 internal page 3 of this document. And, in
5 particular, if we can go to the results section,
6 look at the second paragraph. And, in particular
7 the second and third sentences of that.

8 Q. (BY MR. KANTRA) And what were the
9 conclusions of the authors with respect to
10 whether or not there were significant differences
11 among the atypical antipsychotics with respect to
12 the risk of diabetes?

13 A. So, what you just looked at were the
14 rates of diabetes, and then they did statistical
15 analyses on those to try to control for other
16 risk factors and looked at the risk of which
17 atypical you're on. And what they said -- what
18 they concluded is that the differences in risk,
19 differences in risk between olanzapine,
20 risperidone and quetiapine are negligible.

21 Q. And this was the study in which FDA was
22 involved in the design; is that right?

23 A. Yes, it was a very important study and
24 it was with one that the FDA had told us they
25 were quite interested in.

1 Q. And the labeling change that FDA
2 requested in September of 2003 was approximately
3 a month after that?

4 A. That's right.

5 MR. KANTRA: You can take that
6 down.

7 Q. (BY MR. KANTRA) I want to direct your
8 attention to another issue that's been discussed
9 in this trial, and that is with respect to a
10 Japanese labeling change that took place with
11 respect to Zyprexa in 2002.

12 And I'll ask you if you're familiar
13 with that labeling change?

14 A. Yes.

15 Q. And was it that labeling change that
16 included a contraindication for the use of
17 Zyprexa in patients who had diabetes?

18 A. In Japan, right.

19 Q. Okay. And what is a contraindication?

20 A. Contraindication means the label is
21 saying, don't use this drug in this situation.
22 So in that case, in patients with diabetes.

23 Q. Did Lilly advise FDA about the fact that
24 the Japanese had made a change to their label to
25 add this contraindication?

1 A. Yes.

2 Q. And within what time frame did it do so?

3 A. I remember it was prompt. I don't know
4 exactly how many days it was.

5 Q. Do you recall when the labeling change
6 for the Japanese took place? In what month of
7 2002?

8 A. I believe it was in April.

9 Q. Okay. As you mentioned before, it would
10 be Lilly's standard practice to document any
11 interactions with FDA, the regulatory group would
12 do that; is that correct?

13 A. That's been my experience, yes.

14 Q. Okay.

15 MR. KANTRA: Can we bring up
16 EL2044? And, again, can we look at the subject
17 of the communication which is -- I think that's
18 going to be at the top of the document.

19 Q. (BY MR. KANTRA) And the subject of the
20 communication shows it as being a communication
21 regarding labeling change in Japan; is that
22 right?

23 A. Yes.

24 Q. Okay.

25 MR. KANTRA: And if we go down,

1 then, Nick, to the beginning of the section, the
 2 first sentence of the discussion details.
 3 Q. (BY MR. KANTRA) And it states there that
 4 on Friday, April 12th, 2002, Drs. Breier and
 5 Brophy -- let's pause on that for a second.
 6 Dr. Breier, who is he in April of
 7 2002?
 8 A. He was the leader of the Zyprexa product
 9 team, the global Zyprexa team.
 10 Q. And Dr. Brophy who is a part of the
 11 regulatory group there; is that right?
 12 A. Dr. Brophy is the director of the
 13 neuroscience regulatory group at Lilly.
 14 Q. So they contacted Dr. Laughren to inform
 15 the division of neuropharmacological drug
 16 products that the olanzapine label in Japan was
 17 being revised to include information regarding
 18 hyperglycemia and diabetes and the warnings and
 19 the contraindications sections?
 20 A. Right.
 21 Q. Is that consistent with your
 22 understanding of the information that was
 23 conveyed to FDA on that date?
 24 A. Yes.
 25 Q. Are you aware that Lilly submitted two

1 special reports regarding the Japanese label
 2 change to FDA?
 3 A. We did.
 4 Q. And did those submissions provide FDA
 5 with information on the specific adverse events
 6 on which the Japanese regulatory authority relied
 7 to change the label?
 8 A. Yes.
 9 Q. Okay. Did you personally review those
 10 adverse events?
 11 A. Yes.
 12 Q. Okay.
 13 MR. KANTRA: Can we bring up
 14 EL2645?
 15 Q. (BY MR. KANTRA) And do you recognize
 16 this as the submission that went into FDA with
 17 respect to the individual cases that supported
 18 the labeling change in Japan?
 19 A. Yes.
 20 Q. Okay. And by the way, how many cases
 21 supported that labeling change in Japan, if you
 22 recall?
 23 A. There were nine -- nine people.
 24 Q. Was there a second document as well that
 25 provided additional information from Lilly to the

1 FDA about this Japanese labeling change?
 2 A. That's right.
 3 Q. Okay.
 4 MR. KANTRA: Can we bring up
 5 EL2629?
 6 Q. (BY MR. KANTRA) And this is a document
 7 that's entitled Analysis of Japanese Data on
 8 Hyperglycemic and Diabetic Spontaneous Serious
 9 Adverse Events Associated With the Use of
 10 zyprexa. And the date on this document, as with
 11 the last one, is April of 2002; is that right?
 12 A. That's right.
 13 MR. KANTRA: And if we can go to
 14 internal page 6 of this document. And, in
 15 particular, if we can look at the first paragraph
 16 of section 3.
 17 Q. (BY MR. KANTRA) And this reflects that
 18 there were a total of 13 cases that were reviewed
 19 of the nine that ultimately submitted that
 20 supported that change, and with respect to these
 21 cases, what did the review of these cases show in
 22 regards to these patients?
 23 A. Well, it's summarized on the screen, but
 24 these were from Japan, the sort of spontaneous
 25 adverse events that we talked about earlier,

1 things that were communicated to Lilly. And what
 2 it showed was that for most of these patients --
 3 it was not clear. It was not clear what was
 4 leading to problems for them in some cases and in
 5 other cases it was pretty clear that there
 6 were -- there were compounds, there were other
 7 issues involved. So, for example, two of these
 8 unfortunately were fatalities. Looking at those
 9 two myself, to me it was very clear that there
 10 were other things leading to their death, not
 11 olanzapine. But overall, we looked at these and
 12 our conclusion on these cases was that there
 13 could be no definite conclusion about -- about
 14 what it would mean for olanzapine.
 15 Q. In some of those cases as reflected up
 16 there showed that a couple of patients weren't
 17 even taking Zyprexa at the time of the event,
 18 correct?
 19 A. That's correct. Out of these
 20 patients -- out of these 13, two of them were not
 21 even on the medicine. They were on it sometime
 22 in the past.
 23 Q. It also suggests up there that four of
 24 these patients had a known diagnosis of diabetes
 25 before they started taking Zyprexa?

1 A. That's right. There were at least four
2 that had diabetes because it had been documented
3 before they were even on Zyprexa.

4 Q. And another five of them that were
5 suggestive of undiagnosed preexisting diabetes,
6 right?

7 A. That's right. There were patients with
8 things like fasting blood sugars that would have
9 put them even in the diabetes range even if the
10 doctor had not made an official diagnosis of
11 diabetes before they went on to olanzapine.

12 Q. Did Lilly disagree with this labeling
13 change in Japan?

14 A. Yes.

15 Q. Why?

16 A. Because we thought the con -- the
17 conclusion was wrong.

18 Q. Based on the data that was available?

19 A. We'd looked at these cases and did not
20 feel that these cases merited a change especially
21 as you look at these patients in light of
22 everything that we knew from cases we were
23 getting, all these reviews that we had been
24 doing, all the clinical trial data. We were
25 confident, we are confident that -- that it

1 wasn't the right -- the right choice,
2 scientifically, medically speaking.

3 Q. Did you believe -- did Lilly believe
4 that a contraindication with respect to patients
5 who had diabetes could be potentially harmful to
6 patients?

7 A. Yes, we were very concerned about that.

8 Q. Why?

9 A. Well, because we know that Zyprexa -- is
10 a medicine for some individuals is -- is the best
11 choice for treating their mental illness, and we
12 knew that this would mean -- this would mean that
13 patients who had diabetes, it was taking away the
14 choice from the doctor about weighing risks
15 against that potential benefit for patients that
16 may need it or maybe even patients that were
17 already on it for whom it was working. That
18 wasn't a good thing.

19 MR. KANTRA: Judge, I can either
20 move into a new topic or we can take a break
21 here. Either way is fine.

22 THE COURT: I take it that you've
23 got quite some time left with this witness. Why
24 don't you keep going until 1:30 and then we'll
25 break.

1 Q. (BY MR. KANTRA) Why don't we talk, then,
2 about the September 2003 label change and ask
3 you, first, whether you recall that in September
4 of 2003 FDA, in fact, asked Lilly to change its
5 label to add a warning with respect to diabetes?

6 A. That's right.

7 MR. KANTRA: Can we bring up
8 EL2135?

9 Q. (BY MR. KANTRA) Dr. Baker, do you
10 recognize this as the letter that requested that
11 Lilly change its labeling with respect to
12 diabetes?

13 A. Yes.

14 Q. And this letter wasn't sent only to
15 Lilly, was it?

16 A. No. My understanding was that the
17 manufacturers of all the atypical antipsychotic
18 drugs had the same request.

19 Q. And, in fact, that second paragraph of
20 that letter says just that, doesn't it?

21 A. Oh, yes. It says it refers to all
22 atypical antipsychotics.

23 Q. If we look --

24 MR. KANTRA: Nick, if we go down a
25 little bit further to the actual text of the

1 warning itself. And if we can go in particular
2 to the sentence that begins with "assessment of
3 the relationship."

4 Q. (BY MR. KANTRA) Dr. Baker, this class
5 labeling from FDA acknowledges that there is the
6 possibility of an increased risk of diabetes in
7 patients with schizophrenia, right?

8 A. Yes.

9 Q. And after three years of evaluating
10 data, FDA didn't state in this warning that there
11 was a causal relationship between Zyprexa and
12 diabetes, did it?

13 A. To the contrary, it said that it's not
14 completely understood what the relationship was
15 between treatments and the development of these
16 events.

17 Q. And the FDA didn't rank the atypical
18 antipsychotics with respect to the risk of
19 diabetes, did it?

20 A. That's right. Again, to the contrary.
21 It said that the data available at this time were
22 not sufficient for such a ranking.

23 Q. And in contrast to Japan, this labeling
24 didn't tell physicians in the U.S. that Zyprexa
25 shouldn't be used in patients with diabetes,

1 right?

2 A. Right.

3 Q. Now, the labeling also --

4 MR. KANTRA: If we can drop down,
5 Nick, to the next paragraph.

6 Q. (BY MR. KANTRA) The labeling also
7 included information about monitoring for
8 patients, right?

9 A. Yes.

10 Q. Okay. And what kind of information did
11 this labeling provide with respect to monitoring?

12 A. Excuse me. It said that any patients
13 started on atypical antipsychotics should be
14 monitored for symptoms of diabetes. All patients
15 should be assessed for the risk factors for
16 diabetes because of the -- the likelihood of
17 developing diabetes during treatment.

18 Q. And with respect to patients who have
19 diabetes, was there information on that as well?

20 A. Right. It said that patients who do
21 have diabetes need to be monitored, have their
22 sugars monitored in course of their treatment
23 with the treatment with atypical antipsychotics.

24 Q. Were these positions of monitoring
25 consistent with routine good clinical practice?

1 A. Yes. All of these things would have
2 been part of routine good medical care, even
3 before the labeling.

4 Q. How did the information that was
5 included in this new warning that was put in the
6 label as of October of 2003 compare to
7 information that the company had been sharing
8 with physicians outside the label before
9 September of '03?

10 A. I think these changes echoed much of
11 what Lilly had been sharing in other ways with
12 physicians before this time.

13 Q. How did Lilly respond to FDA's request
14 to change the label?

15 A. We agreed. We accepted the request.

16 Q. And why did Lilly accept this change?

17 A. FDA had asked for it and we made the
18 change.

19 Q. Okay. What involvement did you have, in
20 particular, with respect to the September, 2003
21 labeling change?

22 A. I was part of the team at Lilly -- at
23 Lilly that discussed it and made the decision to
24 accept the change, and then I particularly played
25 a role as part of the U.S. medical group in

1 communicating this as soon as it changed to
2 physicians using Zyprexa.

3 Q. And what were the ways in which Lilly
4 went about letting physicians know that there had
5 been a change in the labeling as of 2003 about
6 this diabetes warning?

7 A. Many different ways.

8 Q. Okay. And can you tell the jury some of
9 those ways that Lilly communicated that
10 information?

11 A. Sure. We changed the label so all the
12 package inserts that they would get with the
13 medicines or on our web site, the label was
14 changed. We issued a press release so that it
15 would be picked up in the news or in physicians'
16 newsletters about this.

17 We -- I took part myself actually
18 in right away training or sales representatives
19 and instructed them to let all the doctors that
20 they're calling on know about it to let them know
21 the very next time that they spoke to any of the
22 doctors that they're talking to. We made slides
23 and provided it to people that were speaking,
24 physicians speaking on Lilly's behalf so that
25 they could discuss it with physicians as well.

1 We prepared a medical letter for
2 doctors describing this and the background behind
3 it. We made it available through the electronic
4 formats that doctors would use like the
5 Hippocrates, some people use it as a electronic
6 database for adverse events. And Lilly mailed
7 letters to doctors in the United States
8 describing this label change.

9 Q. And are you familiar with the letter
10 that was actually sent to physicians?

11 A. Yes.

12 Q. And when was that letter sent?

13 A. It was sent very shortly after this
14 change, within a couple weeks.

15 MR. KANTRA: Can we bring
16 up EL2972?

17 Can you blow that up just a little
18 bit, Nick?

19 Q. (BY MR. KANTRA) You see the date on this
20 letter?

21 A. October 6th, 2003.

22 Q. Do you recognize this as the letter that
23 was sent to physicians in regards to the change
24 in labeling?

25 A. Yes.

1 Q. What is the information that's conveyed
2 to physicians in regards to this particular
3 letter?

4 A. It conveys in the cover sheet that the
5 FDA had asked for this, and it included in this a
6 copy of the press release describing the change.

7 Q. And -- as well it includes the package
8 insert that includes the new warning?

9 A. As with any of these, it included our
10 label, sent a copy of the new label.

11 Q. Had FDA requested of this letter --
12 actually, if we go down just to the bottom of
13 that letter, can we see the signature there? You
14 see the reference to Dr. Tohen?

15 A. Yes.

16 Q. That was set out by the leader of the
17 Zyprexa product team?

18 A. At this time, yes, Dr. Tohen had taken
19 over from Dr. Breier as the leader of the team.

20 Q. Had FDA requested that Lilly send out
21 this letter as of October of '03?

22 A. No, Lilly sent this because we wanted
23 physicians to know right away about the change.

24 Q. Did Lilly ultimately send out another
25 letter at the request of FDA?

1 this, and it may be that sometime next week I may
2 have to give you a day off while I do things with
3 the lawyers to get it ready for closing arguments
4 and jury instructions. I'll keep you posted when
5 that goes on.

6 Once again, I'd remind you, please
7 don't discuss this case with anyone or let anyone
8 discuss it with you. Please try to keep an open
9 mind until you've heard all of the evidence in
10 this case, and please do not read any or listen
11 to any media or anything on the Internet that
12 might have something to do with the subject
13 matter of this case.

14 Have a nice weekend, and I'll see
15 you all on Monday at the usual time.

16 (Jury out.)

17 THE COURT: Please be seated.

18 We're outside of the presence of
19 the jury. Just a couple of things before we end.

20 You'll be getting me stuff, I take
21 it, by the end of the afternoon so I can do work
22 this weekend. I looked at my calendar and it
23 appears highly unlikely that I can take an
24 afternoon to deal with jury instructions. That
25 kind of leaves me two choices. Either we'll

1 A. That's right.

2 Q. And was the substance of that Dear
3 Doctor letter different from the letter that
4 Dr. Tohen sent?

5 A. No.

6 Q. You were involved, Dr. Baker, with the
7 most recent label change regarding hyperglycemia
8 in 2007?

9 A. I was.

10 Q. Okay.

11 MR. KANTRA: Actually, as I'm
12 looking at this, we're looking at another -- a
13 different label change.

14 THE COURT: This looks like a good
15 breaking point.

16 Ladies and gentlemen of the jury,
17 we've reached the end of our trial day. Some of
18 you have asked if we're -- as I understand it, if
19 we're sort of still on schedule to have this case
20 go to you towards the end of next week, and I
21 think we are, at least for now. It's going to
22 depend on a bunch of things, but that's what I'm
23 hearing. So I'm just letting you know that.

24 When exactly, it's probably going
25 to be towards the end of next week that we do

1 start at 4:15 one evening and do jury
2 instructions then and go late, or we'll take a
3 morning. Which of those two I will do will
4 depend on what I need to do to get this case to
5 the jury before the end of next week.

6 If it looks like we're going to
7 need Thursday for evidence and those things,
8 we're probably going to be working late Wednesday
9 night or Thursday night. If it looks like the
10 evidence actually closes towards Wednesday, I'm
11 more inclined to use the day on Thursday, so then
12 do what we need to do on Friday. We'll play that
13 by ear for now and see where we're going.

14 The other thing -- and I don't
15 really need -- the presiding judge was meeting
16 with the paralegals association, I think, and
17 suggested that it might be interesting for the
18 paralegals association to get a demonstration of
19 the technology that's being used in this
20 courtroom, something that I continue to be
21 impressed with. If we do that, what it might end
22 up meaning is that I'll see if I can find some
23 other judge's courtroom to do my afternoon
24 hearings, and let you set up something during the
25 day but I'll talk to the presiding judge.

1 Assuming that we can set that up, is that okay
2 with the people that might have to do the
3 demonstrations and do the work?

4 MS. GUSSACK: Yes, Your Honor.

5 THE COURT: I appreciate that and
6 I'll talk to the presiding judge and let her know
7 that and we'll see what we can work out.

8 MR. ALLEN: Judge, I'll put on the
9 seminar for technology.

10 MR. LEHNER: I'll supply the yellow
11 pads.

12 THE COURT: I'm surprised that some
13 of the attorneys haven't been invited to the
14 various trial lawyers or defense lawyers
15 seminars, but I'll let the lawyers take care of
16 themselves.

17 Anything else we need to talk
18 about?

19 MS. GUSSACK: No, Your Honor.

20 MR. ALLEN: Margarita.

21 THE COURT: I think I gave you
22 my -- we'll be off record now.

23 THE CLERK: Please rise. Superior
24 Court now stands in recess. Off record.

25 (Trial adjourned at 1:33 p.m.)

1 REPORTER'S CERTIFICATE

2
3 I, SANDRA M. MIEROP, Certified Realtime
4 Reporter and Notary Public in and for the State of
5 Alaska do hereby certify:

6 That the proceedings were taken before me at
7 the time and place herein set forth; that the
8 proceedings were reported stenographically by me
9 and later transcribed under my direction by computer
10 transcription; that the foregoing is a true record
11 of the proceedings taken at that time; and that I am
12 not a party to, nor do I have any interest in, the
13 outcome of the action herein contained.

14 IN WITNESS WHEREOF, I have hereunto subscribed
15 my hand and affixed my seal this 21st day of March,
16 2008.

17
18
19
20 _____
SANDRA M. MIEROP, CRR, CCP
Notary Public for Alaska
My commission expires: 9/18/11

21
22
23
24
25