IN THE UNITED STATES DISTRICT COURT

FOR THE EASTERN DISTRICT OF CALIFORNIA

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BEFORE THE HONORABLE FRANK C. DAMRELL, JR., JUDGE

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TERRY O'NEIL,

Plaintiff,

vs. No. CV-06-01063 FCD

SMITHKLINE BEECHAM CORP, et al,

Defendants.

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REPORTER'S MOTIONS TRANSCRIPT

FRIDAY, JANUARY 18, 2007

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Reported by: MICHELLE L. BABBITT, CSR #6357

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FRIDAY, JANUARY 21, 2008; 10:00 A.M.

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THE CLERK: Calling civil case 06-01063, O'Neal versus SmithKline.

It's on for a motion for summary judgment, Your Honor.

MR. GOLDMAN: Good morning, Your Honor.

Ron Goldman for plaintiff and opposing parties.

MR. ESFANDIARI: Good morning, Your Honor.

Bijan Esfandiari on behalf of the plaintiff.

MR. GOLDMAN: I'll be arguing the presumption; Mr. Esfandiari will be arguing the other motions.

MR. BROWN: Good morning, Your Honor.

Mark Brown for the defendant, GlaxoSmithKline.

MS. COHN: Halli Cohen for defendant.

THE COURT: Counsel, let me take up some preliminary matters. There is plaintiff's motion to strike the proffered evidence regarding Prozac and the amicus briefs. I think the objection of relevancy has not been persuasive. I think that would be helpful to the Court. I think it has some relevancy. It's not compelling, but could be helpful.

If the FDA has considered SSRI data in the aggregate in the past and courts have overruled this type of objection,

to the extent it can be of help to the Court, I'm going to allow the Prozac evidence, and I'll permit the consideration of the amicus briefs. Again, I don't think they're entirely persuasive, but they can be helpful to the Court and the Court has considered such amicus briefs in the past, and so I'll overrule those objections and deny the motion to strike.

I'll sign the defendant's order on the ceiling. I think there's -- I've reviewed the documents. It seems to me that there's a fairly limited number of documents that would appear that could well be the type of documents that would be subject to ceiling, and there's certain propriety in doing so.

Most of the documents have been unsealed. I'll sign the defendant's order. I want to get down to the issues of this case.

MR. ESFANDIARI: Could we be heard on those issues?

THE COURT: I've made my ruling.

MR. ESFANDIARI: Thank you, Your Honor.

THE COURT: I'm much more interested in the substance of the issue itself. I'm not sure this is -- I'm trying to find out and I want to understand, prior to February '97, what is the reasonable evidence of an association between Paxil and the increased suicidality of pediatric patients?

I'm not suggesting this will be comprehensive, but I want to get a better understanding then I have been able to

glean from the briefing.

MR. GOLDMAN: The evidence that was there from '89 and '91, and, in fact, it's very interesting, if I may get it, is a submission that was brought this morning. The evidence was contained in the clinical trial studies that was in the possession of GlaxoSmithKline.

That evidence showed significantly significant associations between suicidality and the ingestion of the drug.

What happened --

THE COURT: Were they conducted by the defendant or by some third party?

MR. GOLDMAN: No, on behalf of GSK.

What happened when they gave the submissions into the FDA, there was inappropriately counted some suicide activity in what's called the run-in period.

In a clinical trial, there is a period of time, usually about two weeks, when all of the patients, subjects of the trial, are given a placebo to wash out whatever may be in their system from other drugs.

The randomization takes place at the end of that run-in or wash-out period. The terms are used interchangeably. The trial actually starts from that time period.

During the run-in period, there is a certain

selection-out process that takes place as well; for instance, if someone during the run-in period responds favorably to the placebo, they take them out of the trial. If someone responds with suicidality, they're not supposed to count it, because we don't know whether that is from a drug that's being washed out or whatever else it might be.

But what happened is that GlaxoSmithKline counted suicidality events in the run-in period and added them into the randomized data. That skewed the data. That information was not obvious in its submission. In the first submission, it was noted by an asterisks, and the later submission, it wasn't even noted that way. There was data in their hands.

We have submitted the declarations of Doctors Grimson and Glenmullen where they handled all of that history showing that, in fact, there was in the early times as much as a -- depends on the studies that they're looking at, but at least somewhere close to three to eight times greater risk of using Paxil than there was using of using a placebo, risk of suicidality.

THE COURT: I want to be clear about this. The clinical studies, on their face, you could derive some association from the initial clinical studies?

MR. GOLDMAN: That's correct. However, the way the data was presented to the FDA, those associations were hidden. They were not obvious.

THE COURT: Gets into the Buckman case. What about this whole motion of fraud on the FDA?

MR. GOLDMAN: That's not our theory.

THE COURT: What's your theory?

MR. GOLDMAN: Our theory is there was a failure to warn physicians about risks that were known or reasonably scientifically knowable to GSK at or before the suicide of our decedent, Benjamin Bratt.

We're not depending upon fraud on the FDA, and I'm not suggesting right at this stage that it's necessary to understand whether or not the use of the run-ins was fraudulent, advertent, inadvertent. It doesn't matter.

What matters is that it was knowable or reasonably scientifically knowable back at that time and throughout the history of the proceedings; that it took from '92 through 2006 and -- 2004, actually, for it to emerge as a doctrine of the FDA. And, actually, it emerged earlier than that when GSK recognized what was going on. So the data was there.

What's interesting, and the reason I wanted to highlight something that was in the submission that was brought up by counsel today, if you look at page four of their timeline, you see where it says May 2, 2002, February 26, 2006 --

THE COURT: Is that what I just received this morning?

MR. GOLDMAN: I just got it this morning too, Your

Honor. I only had a fast chance to take a quick spring through this.

THE COURT: I suspect it's not the first time you've seen this.

MR. GOLDMAN: I'm not talking about the --

THE COURT: What have I got?

MR. BROWN: Your Honor, what we did was to try to sort of distill down the chronology in an easy-to-read format.

THE COURT: That's a different document?

MR. BROWN: The chronology, correct; that begins with the timeline.

THE COURT: I'm not going to fish it out now. Tell me what it says.

MR. GOLDMAN: Let me read to you what GSK's timeline says from May 2, 2002 to February 6, 2003:

> "GSK submits to FDA additional analyses of results from review of data originally submitted to FDA on May 10th, '91, regarding the original Paxil NDA."

That begins the unraveling of what happened.

The data was there. The data was there from '91, '89 and forward that showed this reasonable -- this association between Paxil and ingestion and suicidality.

THE COURT: What constitutes "reasonable evidence"? This constitutes reasonable evidence?

MR. GOLDMAN: Scientifically reasonable evidence is evidence that emerges from the clinical trials and the analysis of the data and the statistical analysis of the data.

That's why Dr. Grimson, the person who is the expert in the statistics, and Glenmullen, the expert in psychiatry and has been studying this for quite some time, they have been able to put together, based upon the data that then existed and in the hands of GSK, the information that shows those risks were there in the data back at that time.

Now, the fact that the FDA didn't appreciate that risk at that time, if, in fact, they didn't, is not the issue before this Court.

The issue is: What is the duty of the manufacturer to warn?

The regulations put that duty not on the FDA. They put the duty on the manufacturer to warn. Once that's appreciated, we don't get into the issue of Buckman. We don't get into the issue of fraud on the FDA. We get into the issue of, as famously once said: "What did they know and when did they know it?"

It's pretty clear from the data they knew well before Benjamin Bratt.

THE COURT: If the FDA concludes that the data you just described was not sufficient for qualified experts to

reasonably conclude that a hazard was associated with this drug, what do I do with that? I'm assuming counsel is going to respond. They submitted the information and the FDA says: That's not enough. Scientifically, it doesn't cut the mustard.

What do I do with that?

MR. GOLDMAN: The short answer to that is: It doesn't matter what the FDA did. It matters what information GSK had and their duty under the regulations and the law to warn the physicians out there prescribing the drug.

THE COURT: Let's talk about the implications of what I just said in terms of preemption.

MR. GOLDMAN: Right. What I'm trying to get at here is that when the FDA evaluates data, they're evaluating the data submitted by the manufacturer. The FDA doesn't do clinical trials, does no independent research, has no subpoena power, no ability to get behind the numbers or the data that's submitted to them.

In the course of the litigation, we have pulled out from them through the discovery process a great deal of information.

THE COURT: So I can understand what is going on, when the data is submitted, does that include any documentation about the opinions of the experts within the defendant's organization?

Do they say: This is insufficient? Or does the raw data go to the FDA and they decide it's sufficient?

How does it work?

Does GSK tell FDA: Here's the data. You do with it what you will? Or: Here's the data, what do you think of it?

MR. BROWN: Typically, once the data is compiled and analyzed, there are conclusions drawn when --

THE COURT: By you?

MR. BROWN: When conclusions are capable of being drawn, they are expressed. But the point here is that the FDA independently evaluates the data, the information that's been submitted.

With respect to the early clinical trials, the record in this case is absolutely clear that the FDA, when it evaluated the data related to the suicide attempts and the suicides that occurred during the run-in phase of the trial that the plaintiff's counsel points to, the safety reviewer for FDA, Dr. Martin Bracker, specifically understood and evaluated and recognized when those events occurred.

In fact, in the safety review that we attached as Exhibit 3 to the Arning declaration on page 23 and 24, there is an overt recognition on June 19th of '91 about those events.

So we do think there's a Buckman problem raised, as

the Court recognized, by the allegations that they made that the company did not provide all of the information that it was required to under the FDA statute and the regulations.

THE COURT: I understand what you're saying. Just so I understand the process, you submitted data and you also interpreted that data independent of the FDA?

MR. BROWN: Right.

THE COURT: What was your interpretation? What did you conclude?

MR. BROWN: That there was no increased risk of suicide in the clinical trials.

THE COURT: And the FDA concurred in that?

MR. BROWN: Yes. That's reflected in page 24 of Dr. Bracker's report of '91.

THE COURT: Could experts differ on this issue? I understand Glenmullen and the others in the plaintiff's court found that that was sufficient. Is this a battle of experts? I'm just talking about the data, it's interpretation. Obviously there's a different opinion here; right?

MR. GOLDMAN: That's correct. I think this is not the format in which the fact-finding process takes place. We have submitted expert opinion that says that data was there. It was there before and -- at and before '91, and a proper analysis of that data did show or reasonably should have shown to GSK that there was an association attached to these

risks.

THE COURT: We haven't exhausted the discussion on this particular set of facts with respect to the initial filing.

Is there anything more you want to add or can we go to any other basis that you find? Your conclusion is that there was reasonable evidence?

MR. GOLDMAN: Of course. We know that as we stand here today. Everybody agrees that there is --

THE COURT: Pre '97?

MR. GOLDMAN: What I'm trying to say is the data that underpins the current understanding of suicidality was all there. It was there previously; that it took this labyrinth process to get here is exactly what the regulations try to avoid, that when the risk is known, they're supposed to act quickly and put that risk on the table.

THE COURT: Are you saying there were other studies that were conducted that forms the bases of the current conclusions? You're saying that was sufficient in '91, whatever it was, to reach the conclusions they made in 2006?

MR. GOLDMAN: There were other studies, but '97 and behind, there wasn't much. Importantly, when they started looking at the worldwide data, that confirmed what their data actually showed early on.

THE COURT: Are you saying the signal was strong

enough at the time for a scientific conclusion?

MR. GOLDMAN: Yes. It was eight times --

THE COURT: Pre '97?

MR. GOLDMAN: Pre '97. That's what our expert evidence is before this Court.

THE COURT: What about the 329 study? How did that originate?

MR. BROWN: If I may, Your Honor.

In connection with the original conclusion of Paxil for the indication of depression in adult patients, the agency in its approval letter specifically requested that the company conduct studies on the use of the drug in pediatric patients.

It was, in fact, expressed directly in the original approval letter.

THE COURT: Why was that?

MR. BROWN: Because the agency is always interested in the use of a product in a population other than what it's been approved in, because there's a recognition that drugs, although they're often approved to only originate for adult use will be used off label in pediatric patients.

THE COURT: Did that cautionary attitude, was that the result of what we're talking about now, these associations?

MR. BROWN: Absolutely not.

THE COURT: There were associations, right, of some

type between suicide ideation and the use of the drug?

MR. BROWN: First of all, in the clinical trials that supported the original NDA file that led to the original approval, none of those patients were pediatric patients.

THE COURT: Why is that important? Help me on that. As a practical matter, if I see there was an association of suicide ideation with anybody and enough of it, the last person I want to see using it is a child. That may not be scientific, but I'm just talking as a grandfather and human being.

Why is it that you have to parse this -- I'm understanding in prescribing you would have to.

What's the importance of that?

MR. BROWN: Before I address that, if I may, it's important that there's a clear understanding of the factual record.

With respect to the original clinical trials, there was no signal of an increased risk of suicide or suicidality in any of the clinical trials that were performed.

So there was, in fact, no signal. Again, the studies were conducted in adult patients. Obviously with severely depressed people, there are going to be suicides as a result of the underlying disease condition.

And so one of the challenges that's occurred in the last 20 years is to determine the extent to which suicides

that occur in depressed patients occur as a result of depression because of the compounding factors or because there's an increased risk.

What we know to this day, FDA has reviewed and evaluated all the data and has determined there is no increased risk of suicidality or suicide in adult patients. We know that. That is the current state of the regulatory analysis.

With respect to this case and why it's important to evaluate and consider what occurred back in '90 and '91, the plaintiffs are arguing that you should extrapolate the adult clinical data to the pediatric patients.

That's simply not permissible, and, in fact, it's contrary and counterintuitive to exactly the way in which the FDA reviewed and evaluated the clinical trial data when it did a comprehensive analysis over 18 months during the 2003, 2004 period with respect to pediatric patients.

It looked at that patient population very differently and it followed that analysis with a comprehensive analysis of the data collected in over 372 trials involving a hundred thousand adult patients.

So from a regulatory standpoint, it's typical for FDA to review and evaluate the safety risk in different patient populations.

And I think that's the explanation.

THE COURT: Do you want to respond to that?

MR. GOLDMAN: Yes. This is part of the crux of the problem. When that data was correctly analyzed in '91 and '89 data, if you take out -- incidentally, every scientist that has been deposed in this case and in every one of those cases has admitted that counting the runs-in is improper and shouldn't be done.

It was finally admitted by GSK that shouldn't be done. Even the CEO -- Dr. Gardena admitted that shouldn't have been done. When you take those run-ins out, you get between a three and nine times greater risk of suicidality.

It was an interesting --

THE COURT: In the adult population?

MR. GOLDMAN: Yes. Let me get to what really was done. If you take a number and say: Okay. We have 544 patients in the study on Paxil, and you have X number that showed signs of suicidality, if you take run-ins and add it to the X, which were patients that were in the study, you get a number in your numerator which is not accounted for in the denominator.

They never added those that were in the run-in period to that denominator, so the figures get all whacky, quite frankly. They are not accurate. They are, in fact, wrong.

When you correctly analyze the data, and Dr. Grimson explains this far better than I can, when you correctly

analyze the data, that data did show there was between a three and nine times greater risk approximately in adults.

That was pretty clear that there was a strong association between the ingestion of Paxil and suicidality. This gets into the whole problem with the pediatric issue in this way.

Most states, including California, honor the Learned Intermediary Doctrine. Most states -- in fact, it's nationally correct to say that when a drug is put out on the market and it is approved, that a physician is not bound by the statements of the FDA, which says this is approved for adult use only or it has not been studied in pediatric use.

The physicians are permitted to exercise their independent scientific judgment on a case-by-case, patient-by-patient basis to determine whether or not in their opinion this particular child should be given this particular drug.

Given that, it is ever so much more important that the physicians be given the complete and correct information so that they can make those judgments.

THE COURT: What would be the complete information?

MR. GOLDMAN: Complete information in this case is that the studies that showed -- first of all, they shouldn't have counted the run-ins at all, but those studies should have been published. The warnings should have been out

there.

THE COURT: Does the FDA decide what gets published and what doesn't get published?

MR. GOLDMAN: No.

THE COURT: What gets published? Everything?

MR. GOLDMAN: No.

THE COURT: I understand some studies are published and some aren't.

MR. GOLDMAN: There's an interesting article that came out in the New England Journal of Medicine yesterday which shows that the studies that are published are almost all the studies that show a bias in favor of the drug. The studies that don't show it, don't make it to publication.

THE COURT: Who's fault is that?

MR. GOLDMAN: That's a long story.

THE COURT: Are you suggesting GSK has an obligation to publish all of its clinical studies?

MR. GOLDMAN: They do now. Congress said they have to. They've got to put them all up there.

THE COURT: Let's get back to what you were saying. The physician did not have access to the studies that we're referring to now, including the runs-in and such at the very outset?

MR. GOLDMAN: Two primary sources or three by which most doctors get their information:

One is the label, which they usually go to the Physicians Desk Reference, PDR, which --

THE COURT: FDA label as such?

MR. GOLDMAN: Yes. That's one source.

The other is loosely referred to "Dear Doctors letters" or "Dear Healthcare Professional letters" which are sent by the company. They don't go through FDA roots to get there. They're just sent by the company.

The third primary area is from publications such as the New England Journal of Medicine, Lancet and so forth. Those are the primary sources of physician information. We know our doctors are pretty busy these days, but they're either looking at labels or the publications that they see.

If they get a "Dear Doctor letter," that becomes even more important because that's directed and directed on a particular drug that they may be using or contemplating to use.

Those are the sources. If there are no warnings in those sources, if Dr. X is contemplating giving a 13-year old a drug not studied for pediatric use and he sees a warning: "This may cause suicidality in some patients, adult patients," he's got to reevaluate whether or not in this younger person whether or not there's a risk that is unacceptable and take many factors into consideration.

THE COURT: I assume there was no "Dear Doctor

letters" in the first couple of years?

MR. BROWN: That's correct.

THE COURT: What about the arguments counsel is making with respect to an added burden you have aside from the warning issued by the FDA that you have a more proactive responsibility if you find that their clinical studies appear and there's some association as there appears in this case.

What are your legal obligations under those circumstances, as you see them?

MR. BROWN: The legal obligations, if there are adverse events associated with the use of the drug, the company is required under FDA rules to submit those adverse event reports directly to FDA.

There is both a requirement in the investigation on new drug regulation as well as in the new drug application regulations that imposes as duty on the company annually to report all clinical trial experience associated with the use of the drug, even studies that are not conducted by the company, so to the extent the company is aware of that information.

The very important point here with respect to all of the other methods of communication outside of the FDA approved labelling that is central to the preemption issue and before the Court is this:

If there's no reasonable evidence of an association

that prohibits the warning to be included in the prescribing information, the official form of the labelling, then there is no opportunity, and, in fact, it's prohibited from that -- that same prohibited warning is also prohibited of being precluded in written material, developed, disseminated or produced by on or behalf of the company. It's the same set of rules.

THE COURT: As a practical matter, your obligation to the consumer is discharged when you turn over whatever information you have by way of clinical studies or conclusions of the FDA, that shuts the door on any liability, in your mind, because of preemption?

MR. BROWN: That's correct, provided there is no reasonable evidence of an association.

THE COURT: Let me ask you this. Suppose GSK says: Our people are really concerned. They think there is reasonable evidence, but FDA, for whatever reason, is not doing anything about it.

What is your obligations as a company to the consumer under the given law we're dealing with here? I understand the preemption issue here, which may apply.

Do you feel you have any obligation to disclose to a doctor that you have misgivings, nothing's happened and you want to let them know?

MR. BROWN: If there's new information, absolutely.

The regulation speaks to that. In fact, it says --

THE COURT: Is it for you to disclose to the FDA or go straight to the physician and tell him?

MR. BROWN: There is an obligation to inform physicians through precisely the same regulation. It says: As soon as there is reasonable evidence of an association, that duty attaches.

THE COURT: To do what?

MR. BROWN: To revise the labelling or to announce the warning. It happens all the time.

THE COURT: You send a "Dear Doctor letter" out, for example?

MR. BROWN: Correct. That may be the most expeditious method of informing the public and physicians before you can develop the concise or precise labelling language that you want to communicate. Those warnings happen all the time.

Again, the important thing to remember and what the FDA said in fact two days ago when it published a proposed rule describing its long-standing interpretation of the relationship between changes being effected, label changes, and the reasonable evidence of an association standard is that must be based on new evidence.

So if there is new evidence that comes --

THE COURT: I gotcha. If the warning contradicts the label, in other words, the argument here, this is a ceiling.

This is all you need to do. And you say: Oh, no, that's really not true. Despite conflict preemption, we think there's reasonable evidence that needs to come out and doctors need to be informed.

How do you square that with your theory of conflict preemption and the fact this is a misleading label? You ignore that, I guess, if the exigencies are such that you need to warn doctors or patients?

MR. BROWN: Not at all. The new warning would be based on new information and new evidence.

THE COURT: I'm talking about pre-label change. Maybe this doesn't happen. Everything happens, I guess. Bottom line: You've been looking at these studies. This is not new. Your doctors and scientists are saying: There is really some problem here. We really are concerned.

I think this stuff evolves. Hundreds of thousands of studies, some are favorable; some are unfavorable, and you conclude, not based on something new -- new in the sense you suddenly become aware. The scientists say: This is a problem. Our label isn't getting it done.

What do you?

Notify the doctor? Or simply say: Let the FDA worry about it?

MR. BROWN: Typically, what happens is a company in that context will present that information to the FDA and

say: We've done this analysis.

THE COURT: They disagree with you. What do you do then?

MR. BROWN: They make will rules.

THE COURT: You have an obligation to patients, don't you?

MR. BROWN: You have an obligation to patients, but the obligations are based --

THE COURT: Liability only stops -- the door is shut -- once you get into the FDA, your obligations are over with; is what you're telling me?

MR. BROWN: Not precisely. What I'm saying is if FDA says that you're prohibited from doing something, you are prohibited under federal law from doing exactly that.

THE COURT: I understand that. I'm not suggesting you're willfully ignoring your patients. What you're telling me is the system is such, that even though you may disagree with the FDA's conclusions, you're stuck, as it were.

FDA -- whatever they say is what you live by and you have no contravening obligation because the system doesn't permit it. Am I wrong?

MR. BROWN: There are appeal mechanisms and there are opportunities to challenge FDA's decision-making with respect to the scientific questions pursuant to APA type appeals.

THE COURT: Right. Here you've got a case and these

preemption cases -- I'll be very candid. I don't know where I'm going on this. You can feel free to argue all you want. I'm interested in your answers, clearly, in this case.

You have the plaintiff saying: Look. We've got all these -- even the folks at GSK. I'm not suggesting that's the case. FDA gets to dragging its feet, won't get it done; therefore, my client is stuck and people are in danger and lives are threatened. Their lives are in danger, but nothing can happen unless the FDA says: Now he's put a black box out and you'll now say there's been a real problem.

The evidence has been accumulating over the years. I'm not saying that's the facts, but that is what the plaintiff has been telling me, and this started from day one. And because of the FDA, nothing happened. And you folks are saying: There's nothing we can do about it. That's what you're telling me, I think.

MR. BROWN: A couple of points I'd like to make. First of all, the record does not reflect that hypothetical scenario.

Secondly, what they are focusing on and talking about are all things that the FDA reviewed and considered. None of this is new. All of this is reviewed and evaluated, and if you look at what FDA said in 2003 and 2004 -- I think this is very instructive in terms of the Court's question as it relates to the allegations that are being made by the

plaintiffs about things that occurred years ago.

In October 2003, the FDA said, after doing this analysis of pediatric data involving eight different manufactured drugs, which GSK didn't have access to, it says, quote:

> "The data do not clearly establish an association between the use of antidepressants and increased suicidal thoughts or actions by pediatric patients."

In January 2004 the briefing memo that was sent to the FDA Expert Advisory Committee before the February meeting, again, talking about the FDA's analysis. It says -- this is in the Logrin memo -- quote:

> "While there are signals of increased risks of events suggestive of suicidality for several of these drugs, the signals for the most part are coming from a single trial within each of those programs. An important additional point; however, is that we are not yet confident what the identified events represent."

There are continuing statements later on in 2004.

All of that means that FDA determined at that time that there was no reasonable evidence of an association, which is the federal standard forewarning that applies in

this case.

THE COURT: Let me ask the plaintiff. What is this defendant supposed to do? They're being told by the government there's no clearly established association between the use of this antidepressant and suicidality in pediatric patients. They're being told that.

Let's assume everything is on the up and up. We're not talking about fraud. They got the information you're talking about. They just aren't satisfied there's enough information to establish reasonable evidence.

What is the company supposed to do under those circumstances?

MR. GOLDMAN: Warn, because the regulations require it. It goes beyond just what the FDA says is the common law duty and the regulatory duty to the physician through that route to the patient, and they have a duty to warn. There is no power in the FDA to issue by ipse dixit fiat an order of misbranding and thereby cause anything to happen.

What happens, the regulatory scheme is such that it's not left to the FDA to make that final judgment. To the contrary, if they feel, which in this case they did and did voluntarily do a 314.70 supplement where they disclosed the risk finally -- and I think that was in 2006. When they finally did it, they used that route.

Notwithstanding their protestations about the

historym. There was no new data, but interpretation of the data that existed well before. What happens if the FDA says: You know what, we don't think even though you, the manufacturer, do think there is an association, we don't want you to put out a warning. You have to warn. The reason is because the statutory duty is larger. The misbranding is not to warn.

What occurs if there is that disagreement, the FDA then has to go to the Department of Justice and say to the --

THE COURT: How often does that happen?

MR. GOLDMAN: I don't think there's ever been -- I know there's never been a case of over warning where they have gone to DOJ and said: They have to take that warning out. That's just never happened.

Guess who gets to decide in the end result? A judge or a jury. That's where it goes. It goes there through that process. It is not a decision or an order from the FDA.

MR. BROWN: If I may?

THE COURT: You may.

MR. BROWN: It's a good question as to whether the Federal Government has ever instituted a civil or criminal enforcement action for over warning. I've thought about that question as well. What I would say to that in response is this:

If the Court looks at the correspondence that the FDA

sent to Wyeth relating to Effexor, which is part of the record, after Wyeth made a label change for Effexor in August of 2003 through this CBE regulation, I think that that demonstrates that where the FDA has a concern, it notifies the company that you need to remove the objectionable language or face withdrawal of approval of the application.

There are -- in our case with respect to GSK and Paxil, I would point the Court to the Arning declaration that describes in great detail the exchange between the company and FDA related to label changes that were proposed and implemented in 2006 related to young adults, where earlier, during the period May through August of 2007, that interaction points out very specifically that FDA specifically told the company to remove the language that it had included.

Now, one of the reasons we cannot point to a lot of cases where the FDA has brought actions against over warning is, in part, because the dialogue that occurs administratively in connection with a NDA is proprietary trade secret and confidential and never sees the light of day.

The second reason is most companies value their relationship with the FDA to the point where when they're looking down the gun barrel, they're not really interested in having the Federal Government actually shoot and fire.

So what they do is conform their conduct. If the Court examines the extent to which conflict preemption principles are reflected in the Geier opinion, it essentially says that you don't have to get to that point to find conflict preemption. You don't have to have an actual violation.

There are cases where companies that refuse to include FDA required warnings and did not do so were the subject of enforcement actions; in fact, I had one in the Northern District of California about 17 years ago that was a $4 million product seizure of collagen that did not include -- where the collagen corporation did not include a warning that FDA had required.

So I think there's an explanation for that. I think that's important to understand.

The other thing that I think is important to understand is this: From a statutory standpoint, every time an application is submitted by FDA, it's required to include proposed labelling and warnings. When FDA reviews that, they are statutorily required under 21 USC 355(D) -- it's one of the slides in the material that I handed up -- statutorily required to disapprove the application if the labelling is false or misleading.

So Paxil was approved on 13 separate occasions during the period December '92 through January of 2004. In every

one of those cases, the agency determined that the warning that the plaintiffs advocate in this case should not be included in the labelling.

I think it's also important to understand that while the FDA was reviewing and analyzing the pediatric data that was originally submitted by GSK in May of 2003, which then sparked the FDA to request the data to be submitted and evaluated by all of the other antidepressant manufacturers, that during that period from May of 2003 until FDA approved a revised warning to pediatric patients in January 2005, there were three FDA approvals of Paxil labelling: August of 2003, October 2003, and January of 2004, without the very warning that is the basis of all of the plaintiff's claims in this case.

There is a clear and direct conflict. Again, those approvals represent findings under Pennsylvania Employees that that labelling was neither false nor misleading under federal law; otherwise, FDA would not have been statutorily authorized to approve the product or the labelling.

MR. GOLDMAN: If I may, a couple of points, I would like to respond to. The business of the FDA ordering or telling GSK to remove language they had been using for the past year from the label -- and I respectfully submit that's not really what happened. It's more nuance than that.

What happened, and I think it's Defense Exhibit 44,

which says: Wait a minute. We're talking about class labelling here for this section label. You want to talk about a different aspect of it, submit a separate application. That's all it says. It doesn't say: We respect it. It says: Submit a separate supplement.

So that's way different than a rejection that they had been using that label without FDA objection for a year which disclosed the warning and the risk.

Let's talk about the 13 times that counsel speaks of. Those 13 times weren't a review for suicidality. Those were reviews to determine whether the FDA should sanction the drug for use in other conditions, such as compulsive -- Excessive Compulsive Disorder, what have you.

There's no evidence they said: Let's look again at this data over here. I think that's not really fair to say that the FDA had looked at it these 13 times. They were looking at other indications.

As a person, human, grandfather as we are, there are patients here whose lives are at stake. They have data. They have that data in their hands that's known or reasonably knowable. These are lives that are potentially at stake. That duty runs from them. They can't hide behind, as was characterized, the Byzantine or labyrinth processes of the FDA for getting time to sell their drug without putting that warning out there.

These are real repercussions to real people, Your Honor. I think that to suggest that they can now come in and say that what the FDA has always recognized, these regulations as minimum standards up until the current administration, since I got out of law school in '62, these were minimum standards.

Suddenly in 2000 they became the ceiling and the floor, or at least more recently that's what they're talking about. This is a sea change that they're trying to put on us. They don't have the authority to make that kind of a sea change and arrogate unto themselves.

THE COURT: "They" being the GSK?

MR. GOLDMAN: No. The FDA. That's why it's very important if you choose to be in the health care business as a drug manufacturer, you cannot walk away from that obligation, that duty, which is both statutory, regulatory and common law to let the physicians know what the truth or what's out there or what the associations are because we have to trust the physicians. That's the law. That's what we have built as our system of healthcare delivery, and they need the information.

THE COURT: So I owe no deference to the FDA, based upon the fact they've changed their position?

MR. GOLDMAN: Inconsistency is one reason why I think deference is not appropriate in this case. There's a

wonderful analysis of the McNellis case, which I'm sure Your Honor has read. If you allow this to be put forth in the manner that is now being suggested by GSK, you wind up where really you are violating the very regulation and rules that are established in the system.

Because if we say that there is preemption, we have thereby nullified the duty to warn as soon as you know when you get the information because they're saying all we have to do is hand it over to the FDA and let it go --

THE COURT: Give me your analysis of Geier and Medronics. What do I do with those cases on the issue of deference?

MR. GOLDMAN: First of all, when you're talking about Geier, you're talking about an analysis that is specific to a preemption statute. You have a totally different scheme that the Supreme Court was looking at. They were looking at a scheme, where, first of all, an agency that had the power to test, the power to evaluate, they did their own homework and they built a system to gradually phase in an aspect of the product.

All the Supreme Court really said in looking at 360(K), which is a totally different statute and regulatory scheme: Look, they have gone into this with such specificity and such independent evaluation and study that this statute that they were construing would be construed to permit

preemption.

That's not the case here. There's no similar statute.

To the contrary, what we have here is as recently as an executive order that came down fairly recently. I have the number here, but it's slipping my mind. That came down with the amendments recently -- when was that?

THE COURT: When you come up with that, give it to me.

MR. GOLDMAN: I can. The point I'm making is that every time Congress has spoken, they have said something that smacks of anti preemption.

When the statutes here are considered and when the regulations which require, raise the duty of issuing of the warning, as soon as they have the information, if you preempt it, you nullify that statutory scheme.

The mission of the FDA is to protect the public health. That is a contrary interpretation to protection of the public health, and, therefore, entitled to no deference.

THE COURT: Before I get response from counsel, as I understand it, you're telling the Court that there was sufficient information out there for the clinical study initially to provide a reasonable basis?

You're not relying on 329 or any subsequent studies as such, except by analogy, but the predicate that you're relying upon here are those studies, those run-ins at the outset and your experts' opinions with respect to their

conclusions regarding the reasonable evidence that those studies disclose; is that it?

MR. GOLDMAN: Let me address 329 for a moment, because 329 did have information that was the kid study, pediatric study -- I think it's Exhibit 26 -- which shows that information came out to them about suicidality showing the signal of association between suicidality and pediatric use. They had to break the double-blind study because some of these kids were getting so bad.

That information was in the hands of GSK prior to the death, suicide of Benjamin Bratt.

THE COURT: Explain that to me.

MR. BROWN: I think that mischaracterizes the evidence in the record, Your Honor. The study itself was not completed until after October of '97 which is when the blind was broken. That's correct. Under rules of statistical analyses, there is a penalty associated with breaking a blind in a study. So the evidence was not available to the company, as a result of, quite frankly, the way in which the study was run.

The important point though about Study 329, so the Court isn't unnecessarily distracted by that particular study that I want to cite to, is that although FDA characterized that study years later as indicating that there may be a signal in the study, it has never found that that study

represented an increased risk of suicide or suicidal behavior or thinking.

So regardless of what occurred with respect to that study, it does not constitute reasonable evidence of an association requiring a stronger warning.

So I think the key point here from a factual standpoint -- and this case is different from a lot of other preemption cases around the country because the extensive regulatory history and the facts in this case demonstrate that there was no reasonable evidence of an association.

FDA said there was no reasonable evidence of an association, and had the company included the warning that the plaintiffs advocate, it would have violated federal law.

The Kallas brief was a pediatric case involving Zoloft. In that case, the brief that was filed in that case which is part of the record here, was also part of the record in the Tucker case, the Colacicco case and at least one other case.

The FDA said -- the Department of Justice on behalf of the FDA said as of October, November, 2002, there was no reasonable evidence of an association with respect to accessorized generally and suicide or suicidality.

That's, I think, why this case is different from a lot of others. I do believe that the Court -- although the Court raised the question of deference in the context of an

argument that the plaintiffs are making that the FDA has been inconsistent with respect to the preemptive effect of its regulations, I think if the Court looks in great detail at the December 2000 proposed rule that then ultimately was finalized in January 2006, what the FDA said in December of 2000 is not inconsistent with the position it took in January 2006, because the proposed changes in the rule related to the addition of a highlighted section, "minimum graphic requirements."

It had nothing to do with changing the standard for warnings or the content of warnings, and there is no inconsistency. But even in -- FDA has never said its warning statement or warning standards are minimum requirements.

If you actually look at the context in which those statements are made -- they're made in '98 in the context of medication guides to be handed out by pharmacists who are typically regulated by the states, and it did not relate at all to the standard forewarning or the central issue in this case.

So we think deference, even if the Court believes there is inconsistency, and some have, that shouldn't control whether there's a conflict or no conflict in this case.

In fact, what I would point the Court to is that last night or yesterday there was an opinion that came out of the

Western District of Oklahoma, Dobbs versus Wyeth, that has a pretty good analysis --

THE COURT: Last name?

MR. BROWN: Dobbs versus Wyeth relating to Effexor. Also like Paxil, Zoloft, Prozac, also an SSRI where the Court found that state court claims were preempted in that case. It's an adult case not a pediatric case, but the analysis is very helpful. If I could read just into the record --

THE COURT: This is the judge?

MR. BROWN: I looked at that. I'm not sure I'm pronouncing his name correctly. Judge Degiusti. Here is what he found:

> "The record establishes that the type of express warning which plaintiff's claim defendant should have included in it's Effexor label had been considered and rejected by FDA as not supported by credible evidence at the time Mr. Dobbs used Effexor."
>
> "Where the FDA has evaluated scientific evidence regarding an alleged risk associated with the drug, has considered whether that evidence warrants a label warning and has expressly rejected the need for such warning as not supported by

> credible evidence, the state law determination that such a warning is required creates a conflict for the manufacturer as between federal and state law and imposes inconsistent federal and state obligations."

It's the precise fact scenario here. There is a completely inconsistent approach in that FDA said that GSK could not have added the warnings that the plaintiffs asked for.

With respect to the plaintiff's argument that in 2007 FDA did not reject a stronger warning with respect to adult patients, again, the record points to a different conclusion. This is Exhibit 40 to the Arning declaration and this is the letter from FDA to GSK dated May 1st, 2007, right on the first page. It says:

> "We have completed our review of your supplemental applications and they are approvable. Before these applications may be approved, you will need to make revisions to your labeling as outlined below so as to ensure standardized labelling pertaining to adult suicidality with all the drugs to treat major depressive disorder. You need to make

those changes."

That's a clear directive and rejection of any other warning, and the record and the dialogue between the company and the agency make that point very clearly.

Again, back to deference just briefly. If the Court believes that there has been inconsistency, we do believe under deference principles and Auer, that substance deference is warranted because the FDA's interpretation of the preemptive effect of its regulation is not plainly contrary or inconsistent with the regulations themself.

We think our deference is, in fact, appropriate if the Court believes there was an inconsistency.

THE COURT: Counsel?

MR. GOLDMAN: Dobbs. I think there are several interesting things, aside from the fact it's a Prozac case and the science may or may not be the same with Paxil. I think the way the Court phrased the issue is important.

THE COURT: The Court in Dobbs?

MR. GOLDMAN: The Court in Dobbs. We can cite cases, the vast majority of which have said there's no preemption. There is a new case that says there is preemption. The force of the reasoning of those two lines of cases, the Court is going to make the decision as to where the force of the reasoning is best.

But I think it's important because the Court in Dobbs

lays out the issue I think quite clearly where it says defendants argue that even if it had sufficient scientific evidence or information on which to base the addiction of such warning on this label prior to Mr. Dobbs 2002 suicide, it could not lawfully do so at the time because the FDA had expressly rejected the propriety of including a suicidality warning on labels -- it's Effexor and similar antidepressant drugs.

The way this is being argued, it doesn't matter that you have the scientific information. It doesn't matter that the regulations require the warning. It doesn't matter that doctors will be disarmed in making their prescribing information.

If the FDA says: Don't put it in, which they did not do in this case, but even if they had, it wouldn't matter. It's contrary to the regulations, but it brings into sharp relief what the contest is here: The duty under the regulations or does it stop, as the Court has asked on several occasions, just because the FDA has said no, without any enforcement action being taken?

The company has the right -- no, the duty when it has scientific information to say: I'm sorry, FDA. You're telling me not to warn doctors when I have information that cries out for a warning. I must do so because that's my moral, ethical and legal duty under the law and under the

facts.

So there are lines of cases and the Court is certainly going to analyze and look at them. If you look at Motus and McNellis --

THE COURT: I'm familiar with them.

MR. GOLDMAN: And the Court has to choose which voice it wants to bring to this discussion, a voice that says it stops and doctors are disarmed or the voice that says, no, the duty is there, the duty must be honored. And even if it has to say to the government: Let's go. Let's go to the Department of Justice and inquire what would the Department of Justice say when it interviews the manufacturer and they say here's our science: We've been warning for a year on this stuff.

It's likely the Department of Justice will say: Your science be damned. The FDA said, no, and seek to enforce it. I think that's the practical reality what we're facing and that's why there haven't been such actions.

When we look at in the light of how the issue is cast, it brings to life the vast stakes that are before this Court in trying to make a determination as to what the scope of that duty is. If the Court appreciates the scope of the duty as I've tried to explain it and perhaps not very well, as I've tried to explain it, that duty transcends what the FDA is trying to say in its brief.

If the FDA wanted to intervene, they certainly could, but they didn't. They're piling FDA briefs on, and the FDA, they know where this courtroom is. If they want to come in and have a voice, they should have come in and we could have had a discussion with them right here as well.

Your Honor is being deprived of that kind of discussion between our position and FDA's counsel.

THE COURT: We could ask them for an amicus brief.

MR. BROWN: Yes, you may, Your Honor. Many judges have. Generally, the FDA won't participate at this stage of a proceeding unless invited to do so.

THE COURT: I've given that thought, to be honest.

MR. GOLDMAN: But they're not here. I can't talk to them. The Dobbs analysis is incorrect. I think if one looks at the Skidmore analysis on deference, that's the appropriate one.

Interesting enough, although it's quoted in the dissent, there's a reference to a case called Christianson --

THE COURT: We're getting close to the end of this very enjoyable colloquy. My reporter is on her last pins, I think.

Counsel, do you have some argument you want to make?

MR. ESFANDIARI: No. You rejected both of my arguments.

MR. GOLDMAN: Christianson versus Harris County, 529

U.S. 576. What I'm referring to is at 587, which Justice Stephens referred to in his dissent in Geier. In Christianson -- that's a 2006 case, pretty recent. Here, however, we confront an interpretation contained in an opinion letter. I think a brief is not much different than that, nor is a preamble.

Here's what he says:

> "Not one arrived after, for example, a formal adjudication or notice and comment rule making. Interpretations such as those in opinion letters like interpretations contained in policy statements, agency manuals and enforcement guidelines, all of which lack the force of law do not warrant Chevron-style deference."

It goes on that:

> "Enforcement guidelines are not entitled to the same deference as norms that derive from the exercise of the secretary delegated law-making powers."

Then, of course, they cite back to Skidmore.

Do what I'm saying id what is before the Court in terms of the deference issue, there is little that commends itself for deference, but certainly no higher than Skidmore. For whatever persuasive power the Court thinks it's worth,

that's all it's worth.

THE COURT: You can conclude.

MR. BROWN: A couple of final points I'd like to point out:

The only way that the plaintiffs can escape the grasp of conflict preemption is to argue the FDA was wrong. That really does nothing more than highlight the conflict.

If they argue, as they have, that GSK defrauded the FDA by withholding reportable evidence that would have caused the FDA to find reasonable evidence of an association, then Buckman preempts the claims as well.

I think it's important to understand, as we've heard today, that the only evidence that the plaintiffs point to prior to February '97 that support their claim that there was reasonable evidence of an association is the data that was submitted in '89 to the FDA in the original NBA.

We know FDA reviewed and evaluated the data originally. They reviewed and evaluated the data when the additional analyses were submitted in 2002.

We know through the various approvals that FDA determined what the precise labelling and warnings ought to be, and in so doing, rejected any other warning and found no reasonable evidence of an association.

We respectfully request, Your Honor, that based on the facts in this case that there is a direct and a positive

conflict and that conflict preemption principles should attach.

Thank you.

MR. GOLDMAN: I wish I had more words.

THE COURT: You've been very eloquent, counsel.

Matter stands submitted.

MR. GOLDMAN: Thank you.

MR. BROWN: Thank you.

(Whereupon, proceedings concluded at 11:30 a.m.)

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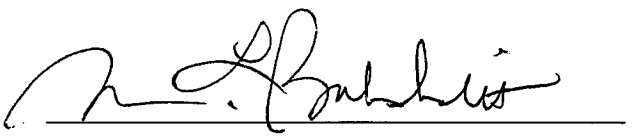
I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.



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