IN THE SUPREME COURT OF THE UNITED STATES

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WYETH, :

Petitioner :

v. : No. 06-1249

DIANA LEVINE. :

- x

Washington, D.C.

Monday, November 3, 2008

The above-entitled matter came on for oral argument before the Supreme Court of the United States at 10:06 a.m.

APPEARANCES:

SETH P. WAXMAN, ESQ., Washington, D.C.; on behalf of the Petitioner.

EDWIN S. KNEEDLER, ESQ., Deputy Solicitor General, Department of Justice, Washington, D.C.; on behalf of the United States, as amicus curiae, supporting the Petitioner.

DAVID C. FREDERICK, ESQ., Washington, D.C.; on behalf of the Respondent.

C O N T E N T S

P R O C E E D I N G S

(10:06 a.m.)

CHIEF JUSTICE ROBERTS: We'll hear argument first this morning in Case 06-1249, Wyeth v. Levine.

Mr. Waxman.

ORAL ARGUMENT OF SETH P. WAXMAN

ON BEHALF OF THE PETITIONER

MR. WAXMAN: Mr. Chief Justice, and may it please the Court:

This case concerns conflict pre-emption under the Supremacy Clause, and the conflict presented here is stark. Repeatedly over the years, the FDA approved Phenergan injection as safe and effective under all the conditions and methods of use described in the labeling, including what is referred to as "IV push" injection. Yet a State jury, evaluating the same risk that the FDA had considered, determined that the precise labeling that FDA had required Wyeth to use in fact rendered Phenergan "unreasonably dangerous." That --

JUSTICE KENNEDY: Just at the outset, I'll just make one comment. You argue that it's impossible for Wyeth to comply with the State law and at the same time the Federal label. As a textual matter, as a logical matter, I just -- I don't understand that. I think I could design a label that's completely

consistent and that meets the requirements that the Respondents wish to urge.

Now, if you want to say that any alteration of the label violates Federal law, that's something else. But as a textual matter, as a logical matter, as a semantic matter, I don't agree with it.

MR. WAXMAN: Well, let me make sure, because I do think we do agree, and I want to make sure that I'm understood, Justice Kennedy. I think what you've articulated is the test which is, is it possible for a regulated party to comply at the same time with both Federal law and State law? In other words, could they use, as they were required by Federal law to do, to use the precise label that in approving the application in 1998 the FDA required Wyeth to use, and also use the label that the Vermont jury determined should be used, and that was stated in the complaint and in the opening and the closing a statement that you may not, should not use IV administration or IV push, in other words that you should contra -- the label should contra-indicate something --

JUSTICE GINSBURG: Mr. Waxman --

MR. WAXMAN: -- that --

JUSTICE GINSBURG: It didn't say -- it didn't say IV across the board. It said IV push is the

claim, and that was -- as I understand this, the FDA was aware of the IV use and a certain risk. But did it ever, ever discreetly consider IV push versus IV administered the usual way by a drip bag?

MR. WAXMAN: Yes it did, Justice Ginsburg, and I want to cite you to the portions of the record that demonstrate that it did. But before I do so, I just want to underscore a point that I think is clear from both our brief and the Solicitor General's brief, which is that isn't the test of preemption in any event. The question is what did the labeling say and upon what information was the labeling decision made.

But as to your particular question, there are -- first of all, there was testimony in the record from multiple parties, including experts from both sides, that the FDA was aware of all of the forms of administration and the risk, including IV push. Their experts simply disagreed with the judgment that the labeling requires. But most saliently, the labeling in this case, which is reproduced, in sort of microscopic size unfortunately, on the last two pages of the petitioner appendix and the last two pages of the joint appendix, have four separate reference that, as we explained in footnote 11 of our reply brief, only apply to IV push.

There is a reference to the use of the Tubex system. That is a direct IV push system. There is a reference to rigid plungers and small-bore needles. Again nothing to do with drip. There is a reference to a maximum rate of administration. Drip is gravity. The testimony in the case was that an instruction that a particular rate of administration not be exceeded only referred to IV push. And finally, there are cautions on the label about how the ordinary aspiration of blood to see if its bright or dark, which is only done in the context of a needle that is being used to push something into a vein, is not reliable in the context of this case because Phenergan discolors arterial blood immediately.

So the labeling plainly comprehended and warned about the specific risks of IV push administration, and that's not all. There is an advisory -- an advisory committee in 1976 was asked to look at precisely the risk of arterial exposure to Phenergan injection or any other irritant drug that is administered intravenously and it made specific recommendations, including recommendations that go directly to IV push.

JUSTICE ALITO: How could the -- how could the FDA concluded that IV push was safe and effective when on the benefit side of this you don't have a

life-saving drug, you have a drug that relieves nausea, and on the risk side you have the risk of gangrene?

MR. WAXMAN: I mean, there was testimony -- Justice Alito, I can go over the testimony, but there is -- there was testimony in this very case about those very circumstances in which direct IV injection is indicated. And there is also test -- there is also evidence in the FDA record, including if you look at the 1987 correspondence that the FDA sent to Wyeth in the context of talking about what warnings had to be provided. The FDA provided Wyeth 20 citations to 20 medical journals that addressed this problem, and in footnote 13 of our reply brief we've cited the ones that specifically address the circumstances in which IV push administration is an important tool. The point here is, I think, that --

JUSTICE GINSBURG: But that doesn't answer the question of was it -- the risk of gangrene and amputation is there. No matter what benefit there was, how could the benefit outweigh that substantial risk?

MR. WAXMAN: Justice Ginsburg, this is labeling that is directed at medical professionals. It is labeling that is directed at physicians, who have to be able to determine what method, what pharmaceutical and what method of administration to use, given the

constellation of risks and benefits that a particular patient --

JUSTICE KENNEDY: The FDA was never concerned with risks versus benefit?

MR. WAXMAN: The FDA -- well, the FDA certainly is. And the issue, Justice Kennedy, here is the FDA has to decide what information to provide to clinicians so that they can make judgments about what to use. And it -- what it did here is it provided ample, lavish warnings about the risk of intra-arterial injection and exposure of an irritant drug like Phenergan to arterial blood. It provided in the labeling to the physicians a cascading hierarchy of methods of administration. It said intramuscular injection is the preferred method. It then said with respect to intravenous injection that it is, as with any irritant drug, it is usually preferable to inject it into an IV infusion set that is known to be running properly, in other words where a line has already been established into the vein and the IV push occurs into the line that's already established.

All that information was available to physicians and the FDA has to understand and does understand that in labeling to allow medical professionals to make their judgments, taking options

away from physicians is not always better. It may not -- it may not even often be better. What the FDA has to decide in terms of telling physicians what's on the table and what's off the table and in terms of what's on the table what the relevant risks are is, is this ever -- would this ever be medically warranted? The testimony in this case and in the administrative record was yes, there are circumstances --

CHIEF JUSTICE ROBERTS: I'd like you to address the distinction between the medical device area and the drug area because in the medical device area, of course, you have an express pre-emption clause, while here in contrast you don't.

MR. WAXMAN: Yes. I mean, I think, Mr. Chief Justice, you've identified the respect in which this is difference than the medical device area. But for the salient purposes, I think the Riegel case directly points the Court to the nature of the determination that the FDA makes with respect to class 3 drugs. It goes through the same preclearance process. As we pointed out in our brief and as I think Justice Scalia's opinion in Riegel points out, the balancing time-intensive, data- intensive inquiry for medical devices was patterned after what is done for drugs, and it reflects a balancing of risks and benefits of the

particular drug in light of the conditions and methods of administration prescribed in the labeling.

CHIEF JUSTICE ROBERTS: If that's true you would have expected the Federal Drug Act to have a similar express pre-emption provision. And one reason perhaps that it didn't is that when the Drug Act was passed you had an established background of State actions; when the Medical Device Act was passed you didn't.

MR. WAXMAN: Well, let me address both the established background of State actions and then the pre-emption clause difference, if I may. The Respondent and her amici have identified 97 cases going back 150 years in which tort actions have been brought with respect to pharmaceuticals. Very few of those cases -- and they are recent -- are implicated by the rule that the Vermont Supreme Court applied in this case, which is where a fully informed FDA, informed of all the information that Wyeth had, approved a labeling standard, but a court looking at the same evidence can reach a different conclusion about what is on the label. The most -- those cases I believe all post-date Cipollone. Many of them postdate Geier. And by my count, there are fewer than 20 such cases out of all of the cases that have been decided and those issues --

that issue had never come up and never could have come up when Congress enacted the 1938 Act, because it was only the 1938 Act that established a drug-specific, preclearance regime, and really in 1962, in which the FDA was required not just to evaluate safety in terms of licensing the distribution of the drug, but to balance safety against effectiveness.

And so the -- the constellation of common law cases -- I mean, let me just say we are -- we are not seeking here a rule of field preemption. We are not seeking to preclude tort remedies for conduct that violates Federal law.

What we are saying here is -- and this goes, I think, finally to your point about the express pre-emption clause -- the presence of expressed pre-emption clauses or the absence, the presence of a savings clause or the absence, does not and cannot affect the operation of conflict pre-emption under the Federal Constitution.

Now, members of this Court are concerned about applying a broad, vague, or free-wheeling analysis of implied conflict pre-emption, but this case is heartland. A jury was asked to look at the same information and conclude that the precise language that the FDA just didn't allow, the FDA required Wyeth to

use, rendered that drug unreasonably unsafe.

JUSTICE SOUTER: Well, it required it because that is what the FDA had approved as a label. But as -- excuse me -- as I understand it, the -- the company, Wyeth, could have gone back to the FDA at any time and said, either based on experience or just our rethinking of the data that we have, we think the label ought to be changed to say "Don't use IV push." Wyeth could have done that at any time, and it simply didn't do it.

And the -- the reason I raise this is because it could have done it at any time, where, going back to Justice Kennedy's first question, where is the conflict?

MR. WAXMAN: The liability in this case was not predicated on the fact that Wyeth didn't go to the -- remember, the FDA had approved this label two years before Miss Levine was injured. In approving the label, it rejected stronger proposed language that Wyeth had presented. There was nothing that was -- Wyeth was --

JUSTICE SOUTER: But as I understand it, Wyeth's argument is not this argument. Wyeth is not saying the reason there is a conflict here is that we tried to give the kind of warning that the Vermont jury, in effect, says we should have given and the FDA didn't

allow us to do it, so that, in fact, there is a conflict between a specific rejection by the FDA of the Vermont rule and the rule that the Vermont jury applied.

MR. WAXMAN: Right.

JUSTICE SOUTER: As I understand it, Wyeth's argument is: Whatever is on the label, in fact, is the standard of conflict. It doesn't matter whether we tried or could have tried or didn't try. You simply look at the label and you look at what the Vermont jury did; and if there is a -- if there is a difference between them, there is a conflict. Am I right about your argument?

MR. WAXMAN: Yes, you are right. We -- we have both an impossibility form of conflict because, in the absence of any new information or new analyses of old information, we could not make the change in advance of getting approval. And we also have an -- an objects-and-purposes form of conflict pre-emption because the Vermont jury decided on the same information that the labeling that the FDA had approved and required was unreasonably unsafe.

And we cannot have a world in which the very day after an intensive process -- the FDA says you may distribute this drug, but you must use this specific language -- either, A, manufacturers can just run in and

change the label and ask for permission down the road; or, B, that a State jury -- let's take the easier case -- a State legislature or 50 State legislatures can decide: Because you could have gone back and asked, we can impose an obligation on you that you must have done so or must have changed the labeling. That just is inconsistent with --

JUSTICE SOUTER: Well, is it -- is it strict liability or negligence? In other words, are they saying you must have done so, or are they saying because you could have done so and didn't you did not conform to the standard of care?

MR. WAXMAN: Either a negligence theory or a strict-liability theory would be pre-empted.

May I reserve the balance of my time.

CHIEF JUSTICE ROBERTS: Thank you, counsel.

Mr. Kneedler.

ORAL ARGUMENT OF EDWIN S. KNEEDLER

ON BEHALF OF THE UNITED STATES,

AS AMICUS CURIAE,

SUPPORTING THE PETITIONER

MR. KNEEDLER: Mr. Chief Justice, and may it please the Court:

The State law duties on which Respondent's tort claims are based are pre-empted because they

conflict with the FDA's determination that Phenergan injection is safe and effective under the conditions of use recommended or suggested in the labeling.

JUSTICE GINSBURG: Mr. Kneedler, at the outset, would you clarify something that is central, I think, to this case? Some of the briefs tell us that this represents a change of policy on the part of the FDA, that in fact the FDA once approved and said torts were -- tort suits were a helpful adjunct to the FDA's own efforts to protect consumers. They helped because they prodded manufacturers to -- to disclose risks that were either unknown or under- evaluated. Was that once the FDA's policy; and, if so, when did it change?

MR. KNEEDLER: The -- the FDA, to my knowledge, has never taken the position that -- that, as a general matter, a manufacturer may change a label without -- without the existence of new information that justifies a revision. The Respondents and the amici relied primarily on some snippets of rule-making proceedings and things like that in which FDA has referred to the existence of tort remedies. But we are not arguing for the proposition that tort remedies are -- are pre-empted as a general matter.

JUSTICE SCALIA: But when -- when would there be a tort remedy? What -- what situation would

you envision?

MR. KNEEDLER: As Mr. Waxman mentioned, if -- if the State standard was the same as the Federal standard, there wouldn't be any conflict. And, for example, if -- and not to mention the fact if there was adulteration of -- of the product or if the -- if the product in the box was not the same --

JUSTICE SCALIA: What if they found out about new information which would, if properly considered, alter what the labeling ought to be? Would there be a tort remedy for the failure to bring that new information to the attention of --

MR. KNEEDLER: Well, the position we are arguing for here would not cover that situation, but -- but there could be a further situation of pre-emption, if I could just explain why. I think --

JUSTICE SCALIA: You mean if you failed to provide the FDA the new information that you think negates the provisions on the -- on the label, you still couldn't be sued?

MR. KNEEDLER: No. If you -- if you failed to provide it altogether, there would not be a -- a pre-emption defense if there were -- if your failure-to-warn claim was based on the new information that you didn't furnish.

I was -- I was going to identify the situation where -- and this has come up in the anti-depressant drug situation, for example, where there is evolving information. There has been a rule- making petition, in fact several over the years, to the FDA to change the labeling to warn against -- to warn about the possibility of suicidal ideation. And FDA has rejected that even though it's -- it's new information arising after the drug was approved. If the information is brought to the FDA's attention and FDA rejects the proposed change, then you would you have conflict pre-emption again. But if the information was never brought to the FDA's attention in the first place, then -- then there would -- it would be not inconsistent with Federal law to have a tort suit based on that. If it's -- if it's been proposed and rejected, then you're back with a conflict.

JUSTICE SCALIA: What if -- what if you brought it to the FDA's attention and the FDA just hasn't acted on it? You would be authorized to change the label on your own.

MR. KNEEDLER: You would be authorized, but if FDA then rejects -- rejects the labeling --

JUSTICE SCALIA: I understand, but in the interim, you could -- could you be subject to a State

tort suit for not changing the label when -- when you had the power to do so?

MR. KNEEDLER: I -- if -- if FDA has taken no action at all, then I think you -- you could be. I this it's very likely that FDA would have acted by the -- by the time that -- I mean, I suppose there could be a window in there before it was approved.

JUSTICE GINSBURG: But why is that -- why is that likely, considering the huge number of drugs? I mean, one figure said that there are 11,000 drugs that have this approval. Is the FDA really monitoring every one of those to see if there is some new information that should change the label?

MR. KNEEDLER: If I could make two points about that: The first is, as I said, we are not arguing that there is pre-emption in a situation where there is new information that is not brought to FDA's attention.

But the second point is that in the 2007 amendments to the Act, Congress recognized the difficulties with this and gave FDA important new enforcement tools and resources to go after the problem of things that arise after a drug is improved -- approved, that has given FDA the authority to direct a change in the label, which it did not have before.

It has given the FDA the authority to order

new clinical studies, and it has ordered FDA to set up a data system where it will get electronic notification of -- of adverse events.

I -- I should point out in the -- in the one year since these amendments were passed, FDA has, I -- I think, in 21 instances ordered clinical trials. In four instances it has ordered a revision of labeling. It has hired 430 new employees in the Center for Drug Evaluation and Research to address the post-marketing situation.

JUSTICE BREYER: Why isn't -- why isn't the fact that some certain number of people are getting gangrene, why isn't that new information?

MR. KNEEDLER: The risk -- the way FDA -- and this is set forth in the changes being affected regulation amendment that was --

JUSTICE BREYER: That was all passed long after the events here took place, I think.

MR. KNEEDLER: But -- but --

JUSTICE BREYER: So at the time, you read the regulation, I think a person would think that he was free drug manufacturer if he learned something new to strengthen -- strengthens the contraindication, put it in.

MR. KNEEDLER: As FDA explained in 2008,

when it promulgated this regulation, it's been FDA's long-standing interpretation that only new information would justify a change.

JUSTICE BREYER: Why wouldn't that be new?

MR. KNEEDLER: New information means new information about a risk that is greater in severity or frequency. If you have --

JUSTICE BREYER: If you get a certain number of cases.

MR. KNEEDLER: There is no claim -- there is no claim here that either of those -- in the record in this case, that either of those was true.

JUSTICE BREYER: That's because nobody brought up this new information point. So if nobody brought up the new information point at the trial and if the burden is on the manufacturer to show that it's pre-empted, isn't that the manufacturer's fault, because if you simply read the regulation, you wouldn't find any of all this complicated stuff about certain kinds of new information.

MR. KNEEDLER: That's a legal question not a factual. And it was argued to the Vermont --

JUSTICE BREYER: Yes it's a legal question.

MR. KNEEDLER: It was argued to the Vermont Supreme Court, and I don't think -- I don't think that

Respondent -- Respondent has noted that it wasn't raised, but I don't think it's argued that it's waived. And I think for the Court to fully address this situation, I think it would be good to take into account FDA's -- certainly going forward that is the regulatory regime --

JUSTICE BREYER: But we are not making an advisory opinion. We are deciding this case. And this case here you say new information of a certain kind would be okay, nobody argued it. You read the reg, and it doesn't seem to make all these distinctions end of case. Since the manufacturer has the burden of going into this, which apparently it didn't do. So, now we have decided this case, and we go on to the next one.

MR. KNEEDLER: Okay. If I could make just one further --

JUSTICE BREYER: What's your response to that?

MR. KNEEDLER: If I could make one further point about that. And that is the -- this act sets up a prior approval situation. In other words, Congress wanted the FDA to look at the drug in advance, balance -- against benefits as this Court said in Rutherford, and -- Brown & Williamson, strike a balance and approve it.

It would be fundamentally inconsistent with a prior approval system to have a regime in which the very next day State law could require the manufacturer to change the very labeling that FDA has struck a balance --

JUSTICE KENNEDY: I don't understand what we're talking about here. The new information was not brought up by either side --

MR. KNEEDLER: Right.

JUSTICE KENNEDY: -- showing increased frequency or increased severity?

MR. KNEEDLER: That's correct.

JUSTICE KENNEDY: Right?

And supposedly, it was burden of the drug company to show --

MR. KNEEDLER: No. The drug company says it's pre-empted, and the only escape hatch from the preemption is new information.

JUSTICE KENNEDY: You agree with -- you agree with Mr. Waxman that the FDA specifically addressed the risks and benefits of IV push as opposed to the risks of arterial exposures?

MR. KNEEDLER: It specifically addressed in the labeling that the FDA approved, and I think that's all that needs to be looked at in -- it's just as in

Riegle, where the preemption turns on that device, in that case, and the labeling that was presented. Here the preemption turns on the labeling and the drug that was presented. And FDA regulations prohibit the change unless there is new information.

If I could make one other point about Riegle. Riegle does contain an FDA -- an expressed preemption provision. But the reason why this Court found preemption in Riegle under that provision is very instructive here, because as Mr. Waxman pointed out, the premarket approval process in the two situations are essentially the same.

And what you had on the one hand was Federal action having the force of law like under the file rate doctrine or some administrative determination having the force of law approving a license or -- or a drug, a legal prohibition against changing that without new information. And on the state side, you have a rule of law under the common law of torts imposing a different obligation. Those are squarely termed --

JUSTICE KENNEDY: You're talking about changing but you can supplement without changing the label.

MR. KNEEDLER: No -- no, you cannot. Any -- any change in the wording of -- of the label is a change

that requires FDA approval unless it is --

JUSTICE SCALIA: You can supplement only when there is new information?

MR. KNEEDLER: When there is new information and even then, it has to be in the form of a new drug -- a supplemental drug application to the agency.

CHIEF JUSTICE ROBERTS: Thank you, Mr. Kneedler.

Mr. Frederick.

ORAL ARGUMENT OF DAVID C. FREDERICK

ON BEHALF OF THE RESPONDENT

MR. FREDERICK: Thank you, Mr. Chief Justice.

I'd like to start with regulation 201.80, which is set forth in an addendum to our brief at 19-A. The second sentence of which reads: "The labeling shall be revised -- this is after an applicant, a sponsor has obtained approval of the drug label -- "it shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious risk with a drug. A causal relationship need not have been proved."

The testimony at trial established that Wyeth knew or should have known from at least the '70s that there was a significance issue concerning IV push

risks.

And, Justice Alito, in answer to your question --

JUSTICE SCALIA: Excuse me. Those -- those risks were set forth on the labeling approved by the FDA. Surely that sentence means it shall be revised to include a warning as soon, as soon as there is reasonable evidence of an association of a serious hazard that the FDA has not considered. And that is not already addressed on the labeling. I mean to read it as -- as opening up stuff that's already been considered by the FDA would -- would -- would make a -- a mush out of it.

MR. FREDERICK: FDA never considered any comparative risks of IV push versus IV drip. The evidence on this was clear. Wyeth had a --

CHIEF JUSTICE ROBERTS: What about the various portions of the label in the record that Mr. Waxman addressed and Mr. Kneedler, representing the FDA, said they specifically considered IV push risks?

MR. FREDERICK: What the evidence showed was that FDA certainly was aware that there are different forms of intravenous administration of drugs, but it never considered that the risk of IV push so greatly increased the risks of a catastrophic injury --

CHIEF JUSTICE ROBERTS: Well, they have to. When they determine that it's safe to use it under those circumstances that necessarily includes a consideration of the risk. People can say it's safe for you to walk down the sidewalk. That doesn't mean there is no risk that you get hit by lightning or something else. It just means in evaluating them together, they determine that it's worth the candle in particular cases where a physician determines that that's the indicated method.

MR. FREDERICK: Mr. Chief Justice, here there was no way FDA could have made this determination because the risks of IV push are so catastrophic compared to the benefit which the testimony at trial showed --

JUSTICE SCALIA: Well, you're just contradicting the label. The fact is they could not have approved that label unless they made that determination.

Now, if you're telling me the FDA acted irresponsible -- irresponsibly, then sue the FDA.

MR. FREDERICK: No.

JUSTICE SCALIA: But the labeling made it very clear that the preferred method of administering this medicine was -- was -- was muscular and -- and that there were serious risks involved in -- in the IV push.

Moreover, your client didn't follow the labeling or your client's physician didn't follow the labeling prescription for IV push, did he?

MR. FREDERICK: The testimony at trial showed that the doctor acted with a standard of care that was not negligent, and that was based on expert testimony.

JUSTICE SCALIA: No. No. Wait, wait. He administered a -- a level of the drug that was vastly in excess of -- of -- of what the labeling said could safely be used for IV push.

MR. FREDERICK: And the testimony at trial showed that that had no bearing on her injury, because --

JUSTICE SCALIA: Had no bearing. Are you serious?

MR. FREDERICK: Yes. It did. The testimony at trial from Dr. Green disputed that point. Both courts below rejected that notion.

But the idea that a label is set in stone for all time misunderstands the way the process works. When FDA approves a drug with a drug label, it does so on the basis of small clinical trials with very few, sometimes as few as a thousand or a couple of thousand people. And when the drug is marketed and goes to lots

and lots of people that are not healthy, that are in different conditions, new problems arise. That's why the general -- the GAO found that over 51 percent of drugs have adverse drug events not known.

JUSTICE SCALIA: You established that there were new problems? I mean, if there were new problems, then -- then they could have simply supplemented the labeling. But did you establish that there were problems that had not been considered already by the FDA?

I mean, the labeling says, you know, that this is dangerous to use -- use IV push. It made it very clear that it's dangerous.

MR. FREDERICK: That was not our burden and that was not how the testimony came in at trial. But as the amicus brief by Dr. Budhwani, et al. at pages 54 establishes had Wyeth been a reasonably prudent manufacturer over the years, it would have known that the risks of IV push so far outweigh any bearing negligible benefits, that it would have offered a stronger instruction, it would have moved to revise its label either with FDA approval or --

JUSTICE SCALIA: It proposed a more restrictive label to the FDA, didn't it? And the FDA said, no, you use this label. In other words, it's --

what you're saying was not its call. It was the call of the FDA.

MR. FREDERICK: Footnote one of the Vermont Supreme Court's opinion disputes that point, because it says the label was different. And if you compare what was submitted to FDA versus what FDA looked at, there was no reference to IV push risks creating the risk of catastrophic harm versus negligible, Justice Scalia.

CHIEF JUSTICE ROBERTS: I thought your -- I thought your theory was that this type of administration of the drug should not be allowed. The label should not say here are the risks, here are the benefits. You -- your jury theory was you cannot suggest in the labeling that physicians should have this available.

MR. FREDERICK: Well, as the jury was instructed, Mr. Chief Justice, and the evidence came in at trial, it was -- it was somewhat larger than that in the sense that a State failure to warn claim doesn't prescribe particular wording. It simply says that the existing wording is inadequate. And if the case comes to this Court --

CHIEF JUSTICE ROBERTS: Well, it simply says that if you go ahead with the label like this, you don't have to pay $10 million whenever it comes wrong. That's having the effect, as our case has established, imposing

a limitation on the label.

MR. FREDERICK: But the label itself is not set in stone, Mr. Chief Justice. Manufacturers change their labels all the time as new drug risks come in. And the regulations provide that the manufacturer is responsible not only for the label, but for monitoring post-market information.

CHIEF JUSTICE ROBERTS: So your case depends upon us determining that the risk at issue here that was presented to the jury was a new risk that the FDA did not consider?

MR. FREDERICK: No. It's not dependent on that at all, Mr. Chief Justice. It is dependent on a finding that the manufacturer had a duty of due care and it didn't live up to that.

JUSTICE SCALIA: What if it referred to new drug risks, then, in your preceding sentence, where you are saying manufacturers change it all the time as new drug risks become apparent?

MR. FREDERICK: The testimony --

JUSTICE SCALIA: What you mean is whether or not new drug risks become apparent, they have to change, right?

MR. FREDERICK: The question is what does the manufacturer know and when did this manufacturer

know it? And here, the testimony at trial showed that an antinausea drug called Vistrol -- this is at page 79 of the joint appendix -- caused amputations in two cases. Pfizer voluntarily removed IV push injection for that drug. This was information in Wyeth's files; Wyeth knew this from the 1970s; and yet it did nothing to change the Phenergan label.

CHIEF JUSTICE ROBERTS: Suppose --

JUSTICE SOUTER: With respect to the obligation in this case, may I go back to an earlier question that Justice Scalia asked you? And I -- I -- if you responded to this particular point, I didn't get it.

He said that he understood that Wyeth had in fact asked the FDA to modify the label, at least to strengthen the warning against IV push, and that request was -- was denied, so that in fact that -- that created the conflict. What is your response to -- to the factual basis for that -- for that comment?

MR. FREDERICK: Well, the FDA itself said in the Solicitor General's brief at page 25 that it was deemed to be a nonsubstantive change. These were changes that were being made --

JUSTICE SOUTER: Well, regardless of what their, their semantic label was, was there a request at

least to -- to beef up the warning against using IV push? And if so, did the -- did the FDA reject it and say no, you can't do that.

MR. FREDERICK: It was a different label and it was a different strength of warning, but it didn't have to do with the relative risks and benefits of IV push versus IV drip.

JUSTICE SOUTER: What would it --

MR. FREDERICK: That was the crucial point.

JUSTICE SOUTER: What would it have said?

MR. FREDERICK: This is set out at footnote 1 of the Vermont Supreme Court opinion, which is set out in the joint -- in the petition appendix at pages 4a to 5a, and it goes on for two pages. But essentially what the -- what the comparison was was talking about the preferability of injecting it through the tubing of an intravenous infusion set that is known to be functioning satisfactorily, which would suggest to most medical practitioners and was it the case in the trial testimony given by Dr. Green below, that that would suggest an IV drip, not IV push.

When FDA then rejected it for -- for nonsubstantive reasons, it went back to the prior verbiage which is set out at 5a, which simply says if you put this drug in an artery the concentration can be

such that it will -- it will cause harm.

But our point is that these kinds of risks come to light frequently with drugs that are on the market and the need to revise these labels is the duty of the manufacturer. Section 314. --

JUSTICE SOUTER: But you -- you also, to be clear on it, as I understand it, you do not accept the position that the FDA puts forward, that the obligation depends upon the accrual of new information.

MR. FREDERICK: Well, how you --

JUSTICE SOUTER: Any information, new or old, as I understand it, on your argument raises this obligation to -- to act.

MR. FREDERICK: I think that the dispute is -- is what constitutes new information, because we don't take issue with the notion that new information can be new analysis of prior submitted data; and what the amicus brief by Dr. Budhwani et al. Points out is that there was a lot of unpublished information about the harms of Phenergan that was known to Wyeth or should have been known to Wyeth in the '80s and '90s that would have justified a change under the CEE regulations.

JUSTICE ALITO: Well, suppose the record showed that the FDA clearly considered whether IV push should be contraindicated and concluded it should not be

and prescribed the label that now appears on the drug; and then, as some of the other arguments have referenced, the very day after the FDA made that ruling, Ms. Levine was injured. Would you still -- would she still have a claim in your view, a non-pre-empted claim?

MR. FREDERICK: That be pre-empted. And the reason it would be pre-empted is because the FDA would have considered and rejected on the basis of the same information or similar information the very duty that underlies the State claim.

JUSTICE ALITO: So your argument is -- is predicated on the existence of new information. If there was no new information, then the claim is pre-empted?

MR. FREDERICK: No, it's -- well, it is not -- I think there are two things to keep analytically clear. One is can the manufacturer come forward with a label change on the basis of -- of information that is assessing the risk or reassessing the risk, and under the -- under the regulations it's absolutely clear it can do that before FDA has approved it. It is subject to FDA disapproval.

JUSTICE SCALIA: And -- and is entitled to amend the labeling automatically.

MR. FREDERICK: That's correct.

JUSTICE SCALIA: I envision a -- a scheme under which manufacturers who are worried about jury liability of -- of the magnitude that occurred in this case saying, gee, why should we take chances? And every time there is a jury verdict on some -- on some other -- some other ground not -- not prohibited by the label, they just add that to the label; and they submit it to -- to the FDA and the -- and until -- unless and until the FDA conducts an investigation and disapproves that label, that labeling change occurs.

How many -- how many -- you mentioned a number of -- of times that -- that label alterations are -- are proposed. I mean, this is going to be a massive operation for the FDA.

MR. FREDERICK: Justice Scalia, that would promote public safety, because it puts into the hands of doctors the information that enables them to make individualized risk determinations.

JUSTICE SCALIA: It would not promote public safety if you believe that the name of this game is balancing benefits and costs.

MR. FREDERICK: And Congress said --

JUSTICE SCALIA: And if you are simply eliminating certain drugs which people who -- who have real desperate need for could -- could be benefited by,

you're not benefiting the public.

MR. FREDERICK: No, and in fact that's contrary to the policy determination Congress made. In the misbranding provision, which is Section 352(f), it calls -- that the label is misbranded unless its labeling bears adequate directions for use and such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health or against unsafe dosage or methods or duration of administration or application.

JUSTICE SCALIA: And that applies even if it's approved by the FDA?

MR. FREDERICK: Yes. It's misbranded. And in the 1979 --

JUSTICE SCALIA: You're saying FDA approval doesn't -- doesn't give you any protection at all?

MR. FREDERICK: It -- it provides you a basis for marketing your --- your product.

JUSTICE SCALIA: But -- but -- but the marketing may be a misbranding?

MR. FREDERICK: In -- the FDA itself said so in 1979 in 44 Federal Register, which we cite in our brief, that even an original label may be misbranded if the drug manufacturer subsequently learns that it was not adequate for the safe use of the drug.

JUSTICE SCALIA: Well then, gee, then all of the qualifications you were making earlier about whether it's new information or a new assessment, that's irrelevant.

MR. FREDERICK: No, it's --

JUSTICE SCALIA: You're saying whenever it's unsafe, whatever the FDA has approved, you have a lawsuit.

MR. FREDERICK: No. What I'm saying is that the information developed after the original label is approved, and it is not a floor and a ceiling --

JUSTICE SCALIA: There -- there was nothing about new information in what you just said. You said it's misbranded if it's not safe, new information or not.

MR. FREDERICK: And that's --

JUSTICE SCALIA: Is that -- is that -- is that your position?

MR. FREDERICK: Our position is that the duty is on the manufacturer to make a safe label, and if the label is --

JUSTICE SOUTER: But getting to Justice Scalia's point, as I understand your answer to an earlier question, on the day that the FDA approves the label, if there is no further information indicating

danger, then any liability that is based upon what the -- the kind of information that the FDA knew would be pre-empted. The only time -- you're saying pre-emption does not occur when there is -- forget the word "new" for a moment -- when there is further information, information in addition to what the FDA was told, whether it's 1,000 years old or discovered yesterday; and if there is liability predicated on further information beyond what the FDA was told, then there is not pre-emption.

Is that a fair statement of your position?

MR. FREDERICK: That's fair, but let me just make clear that our test would require the FDA to consider and reject the specific basis on which the State law --

JUSTICE SCALIA: If that's a fair statement then you have to retract your -- your earlier assertion that whenever it's not safe it's misbranded. I mean --

MR. FREDERICK: I'm not going to retract that, Justice Scalia.

JUSTICE SCALIA: -- which is it? Whenever it's not safe, it's misbranded, or what you just responded to Justice Souter?

MR. FREDERICK: The basis -- the basis of the FDA's approval is on the basis of limited

information, which Congress has said for public safety reasons -- we are not doing a balancing here; we are doing this for public safety --

And if the label is not adequate for public safety it is a misbranded drug.

JUSTICE SOUTER: Okay, but if -- if the so-called misbranding is determined to be misbranding, based upon information which was given to the FDA, as I understand your position, you would admit that there was pre-emption.

MR. FREDERICK: I -- I think there is pre-emption, but that does not mean --

JUSTICE SOUTER: Okay. So there --

MR. FREDERICK: Maybe there is no --

JUSTICE SOUTER: In other words, there is that one exception at least to the broad statement that you gave in answer to Justice Scalia?

MR. FREDERICK: Let me try to untangle it this way. The fact that there is pre-emption and you cannot bring as State law failure-to-warn claim doesn't mean that the drug isn't misbranded under the Federal standard the FDA --

JUSTICE SOUTER: But the -- but the misbranding is of no consequence to liability.

MR. FREDERICK: Well, if --

JUSTICE SOUTER: In other words, I think you're saying if there -- if there would be pre-emption it may be misbranded, but there cannot be any recovery in a State tort suit.

MR. FREDERICK: That's correct. The -- the point --

JUSTICE SOUTER: Okay. So misbranding under those circumstances is a purely theoretical concept.

MR. FREDERICK: In that very hypothetical, yes.

JUSTICE SOUTER: Okay.

MR. FREDERICK: But the point is that the failure is that the failure-to-warn claim tracks the misbranding provision; and if you look at the jury instructions in this case, the wording is very close to the wording of the misbranding provision in terms of the adequacy of the warning that must be provided.

JUSTICE STEVENS: Mr. Frederick --

MR. FREDERICK: All State law is doing is providing a remedy that is absent from Federal law.

JUSTICE STEVENS: Mr. Frederick, I'd like to put the misbranding point to one side and just concentrate on pre-emption. And I understood you to agree with Justice Alito that there is a hypothetical case in which there would be pre-emption, and would you

tell me what particular fact distinguishes your case from his hypothetical?

MR. FREDERICK: The fact is there was no consideration and rejection of a stronger IV push warning. There was no consideration by the FDA of IV push as a means of administration distinct from other intravenous forms that would lead to a different kind of risk-benefit balancing. So with the -- in the case where there would be pre-emption, FDA would be asked, we -- we want to put a stronger warning as against this -- FDA says: We don't think there is scientific evidence. Do not put that warning on the label.

CHIEF JUSTICE ROBERTS: So now, your friends on the other side said there was specific consideration of IV push as opposed to simply arterial exposure, and that that is laid forth in the labeling. So, as I understood your answer to be, all we have to do is simply look at the record, and if we think the FDA considered specifically IV push risks as opposed to general arterial exposure, then you lose, and if we determine that they did not, then they lose.

MR. FREDERICK: And the Vermont Supreme Court was quite emphatic about this, Mr. Chief Justice.

CHIEF JUSTICE ROBERTS: Well, I don't know if the Vermont Supreme Court was emphatic about it. I

mean, the record is either -- addresses the FDA -- I'm more interested in what the FDA was emphatic about, and they either address IV push separately or they don't.

MR. FREDERICK: And you search in the joint appendix in vain for communications between Wyeth and FDA communicating about the particular risks of IV push.

JUSTICE GINSBURG: What -- can you turn to the references that Mr. Waxman and Mr. Kneedler made? They said oh, yes, IV push was considered discretely from IV drip bags.

MR. FREDERICK: I will acknowledge that the references in some instances suggest IV push. There is no doubt that the FDA knew that IV push was a method of intravenous administration, but our point is a starker one, and that is that the FDA never was put to the test of deciding comparative risks and benefits of IV push versus IV drip. And it's that point that is crucial, because the catastrophic risks of IV push are so dramatic, no reasonable person could have made a safety determination to allow this drug with its risks when there are corresponding benefits that create exactly the same kind of treatment of care for the patient.

JUSTICE SOUTER: Well, is your argument that they couldn't have considered these comparative risks, because if they had, they would have come out

differently; because they didn't come out differently, we have to infer that they didn't consider it?

MR. FREDERICK: It's two things: One, they didn't consider it and that's clearly --

JUSTICE SOUTER: No, I --

MR. FREDERICK: Second,

JUSTICE SOUTER: Apart from your analysis that they couldn't have or they would have come out differently, how did we know that they didn't consider it?

MR. FREDERICK: There are communications that went back and forth between the company. These are set out in the joint appendix. They make no reference to IV push risks as distinct from --

JUSTICE SOUTER: And do these -- when you say "communications," do you mean starting with the original application for approval of the label?

MR. FREDERICK: The original application actually is not known. It wasn't in Wyeth's files. This drug was approved in 1955. We don't know where the original label was, Justice Souter.

JUSTICE SOUTER: So, you are saying all the correspondence that we do know about, that is extant, fails to mention comparative risk.

MR. FREDERICK: That's correct. And --

JUSTICE SCALIA: But the label doesn't. I mean, the label ask discusses the high risk from IV push and sets forth particular cautions for that -- for that specific means of administration.

MR. FREDERICK: It does not, Justice Scalia. The label says -- it's talking about intravenous administration. It does not distinguish between IV drip and IV push. And Dr. Matthew testified at trial that, based on the label, he would not have been able to make a treatment determination to distinguish between the two, and that had he had that information, he clearly would have given this drug to Diana Levine through the intravenous drip method. The label simply didn't --

JUSTICE KENNEDY: If we conclude that new information is the criterion for deciding this case, if we reject the argument that misbranding at the outset allows State law to supplement the duty, but that if there's new information, then the label has to be changed -- if it that's the line we draw, can this verdict be sustained?

MR. FREDERICK: Yes, I think it can be sustained on the basis of --

JUSTICE KENNEDY: And the Vermont court's opinion?

MR. FREDERICK: I don't think that the

Vermont Supreme Court's opinion totally, because it does go into the area that you're talking about, Justice Kennedy, but if I could refer the Court to trial record testimony, which is set out in the joint appendix and more elaborately in the trial record itself, which makes clear that Wyeth knew or should have known about these comparative risks. It should have had a basis for changing its label or proposing to FDA a different label, and that would be sufficient to satisfy the Federal standards as well as the State duty of due care. And we think the judgment on that basis could be sustained.

JUSTICE STEVENS: May I ask this: When did the duty on the part of Wyeth to have a different label arise, in your view?

MR. FREDERICK: I think it probably arose in the early '70s when a -- when there was a published -- or there was an incident --

JUSTICE STEVENS: Did it arise before or after submitting the original drug application?

MR. FREDERICK: A strong argument can be made that it would have been before the 1970s application when they were reformatting. These are old drugs. We don't have evidence from the 1950s that would have suggested that the original label determination in

1955 would have caused a difference but certainly by the 1970s when -- when Wyeth was reformatting this as an old drug to comply with new standards, it should have known and it certainly should have known by the 1990s when several amputations had occurred from IV push Phenergan, which were in Wyeth's files. The people who analyzed these records, you know, were emphatic that Wyeth knew or should have known by the 1990s. And that was clear by the testimony of experts that -- that showed the comparison between Vistrol and Phenergan and on the basis of the IV push injuries that had occurred that were nonpublished. They appeared to have been reported to FDA, but Wyeth never took the trouble to do the synthesis, to connect the dots between these very terrible tragedies that had occurred from its drug, to bring about a labeling change or a modification that would have saved lives. And that is a failure on the part of the manufacturer not to comply with its standards of due care and with the regulations which require health risk information to be the basis of modifications to the labeling.

JUSTICE STEVENS: Does that boil down to a claim that there was new information that was available between the original approval and the time of the lawsuit?

MR. FREDERICK: Well, by "original approval," do you mean 1955 or do you mean in 1998 and 2000?

JUSTICE STEVENS: Either one. But is your theory really a theory based on new information or new judgment about old information?

MR. FREDERICK: It would be on the basis, I think, of both. I think we would be able to establish that there was a justification on the basis of information before the reformatted labeling took place, and that was testimony by Dr. Green at trial on the basis of Vistrol, the other amputation that had occurred with Phenergan in 1965.

And the -- the important point here is that on the basis of new information, if you are going to conclude that there is a standard that has to be met, I would urge you to consider two things: One is that the burden of showing absence of new information is going to fall on the manufacturer because it is asserting a pre-emption defense, but the way pre-emption gets argued in the courts, it is done oftentimes before discovery is permitted. So, if there is information in the drug manufacturer's files that would be relevant to a determination of the breach of duty by the drug manufacturer, if you decide pre-emption has to be done

before discovery can be done, there would be no way to get that information.

JUSTICE KENNEDY: Well, to put the burden on the manufacturer seems to me inconsistent with what 10 States have said, that there is a rebuttable presumption and inconsistent also with the instructions the jury received in this case, that you can consider the FDA label. So, I think, to me, what you say there is not borne out by what happened in this case or by those other States' --

MR. FREDERICK: Well, let me -- let me address that question because your question goes to the regulatory compliance defense and that is not a pre-emption defense. It is a defense based on State law that the manufacturer in fact was not negligent because it complied with the applicable regulations. In that -- under that scenario, Justice Kennedy, the plaintiff is going to be able to obtain discovery and make arguments to the trial court about whether or not that compliance negated or did not negate negligence. But pre-emption is a Federal defense that would be asserted typically at the outset of the lawsuit before information is obtained. And notably, before 2000, FDA did not have subpoena power of drug manufacturers. It did not have the power to force labeling changes. It didn't even

have the power to force drug manufacturers to make post-marketing studies.

JUSTICE BREYER: The --the part I'm trying to figure out is this: Suppose it was before trial. I don't care, before or after. The plaintiff comes in with a claim. All right. Manufacturer: That's pre-empted. The claim is that you should have told the FDA and added something to your label. Manufacturer: That's preempted. Plaintiff: Well, you haven't read this reg here. The reg here which has been in existence since 1965 says that we can go and add something. I mean you can go and add something to show a contra indication, and that's the end of it.

Now, in fact, 30 years later, I guess, without the horrible things happening that Justice Scalia mentioned, or maybe they did -- I don't know. But 30 years later the FDA makes another mention of new information. I take it that's in 1982. That's the first time that happened.

Now, if I'm right about that, what happens when no one says a word about that? Of course, if the manufacturer had said something about that, then maybe the plaintiff would have said: And it was new. It was new, but the manufacturer doesn't say a word. Are you following what I'm saying?

MR. FREDERICK: I'm not totally, Justice Breyer, I confess, but let me try to address it this way.

JUSTICE BREYER: I mean, I'm wondering still what happens. I believe what happened here is that in the argument in the lower courts, in the trial court, nobody said anything about the FDA's claim that the information necessary to just go ahead and change the label had to be new. Am I right about that?

MR. FREDERICK: You are absolutely right about that.

JUSTICE BREYER: So what I'm trying to figure out -- and I don't know if "burden of proof" is the right word -- where nobody says a word about it, who wins? If they had said a word about it, you need new information, maybe the manufacturer -- the plaintiff could have shown that the manufacturer had new information.

MR. FREDERICK: I think the duty is always going to be on the manufacturer, Justice Breyer. The regulations at 314.80(b) establish that the -- that the manufacturer has the responsibility to do post-marketing analysis and post-marketing surveys to determine the continuing safety of its drugs. If the manufacturer doesn't do that, it isn't complying with

the Federal regulations which have an ongoing duty on them.

And so in the case where there is silence, I would respectfully submit the manufacturer is not complying with its regulatory duty to ensure that there is current information about all of the side- effect risks of its drugs.

Thank you.

CHIEF JUSTICE ROBERTS: Thank you, counsel. Mr. Waxman, you have three minutes remaining.

REBUTTAL ARGUMENT OF SETH P. WAXMAN

ON BEHALF OF THE PETITIONER

MR. WAXMAN: Thank you, Mr. Chief Justice.

I want to make -- I do want to go to -- make a preliminary point about all the talk about misbranding here. The statute has two criminal prohibitions. One is misbranding, which is the original 1906 reactive penalty. If the FDA subsequently finds that something is false or misleading, it CAN come after you for misbranding. But this case involves the criminal prohibition against distributing drugs for which there is not an approved, effective application. And that's what's at stake here.

Now, the notion that there was any -- any misunderstanding in the trial court about whether there

was new information or whether there was -- there were incidents that the FDA didn't know about, or it didn't evaluate the risk, is just flat wrong. The plaintiff tried this -- the plaintiff's experts said the FDA knew about this risk. Wyeth knew about this risk for decades.

That is what is so wrong. That is why he stood up and said the FDA doesn't decide this question. You decide this question. And there was never, ever a suggestion in the record in this case, nor could there have been, that Wyeth ever failed to bring every single adverse-event report to the FDA's attention, every analysis that it did to the FDA's attention.

And what the record does show is that after -- between the time of the 1955 approval of the new-drug application and the 1998 rejection of the SDNA, the Supplemental New -- SNDA, the Supplemental New Drug Application, that did have more extensive, stronger warnings in this case, Wyeth filed five -- and these are all in the joint appendix -- five supplemental, new-drug applications, each one asking for more language, more warnings, about direct IV injection. It's not called "push." It's IV injection versus drip, which is a gravity method. And, in fact, Mr. Frederick says: Well, you know, in this case there could have

been stronger warnings, and that -- and this case wasn't really about -- the jury wasn't really asked to -- it didn't really say that the label had to contra indicate something that the FDA-labeling required.

That is exactly the opposite of what the trial lawyer told the jury at opening and at closing. What he said is this was unreasonably unsafe because it didn't say: Do not use by intravenous administration.

With respect to whether or not the warning -- the last SNDA which we submitted, which was in 1987 and is reprinted in the joint appendix -- not only is it an original, but there is a typewritten version that actually has the text in the type size that one can actually read. At the summary-judgment stage that the pre-emption issue was decided -- may I finish my answer?

CHIEF JUSTICE ROBERTS: Sure.

MR. WAXMAN: Summary judgment was decided at the -- pre-emption was decided at summary judgment before trial. So there was no evidence about what was new or wasn't new. In Ms. Levine's motion for summary judgment, she uses the word "new" information about labeling change. And, with respect to the proposed 1987 language, the '88 change that we asked for, she said -- and I'm reading from page 24 of her motion for summary judgment -- "In 1988, Wyeth drafted changes to the

warning which advised that the use of a free-flowing IV would ensure adequate dilution and reduce the risk of arterial injectia. Although not strong enough, this improved the labeling instruction; if followed, would have prevented the inadvertent administration of Phenergan into an artery for the reasons described."

CHIEF JUSTICE ROBERTS: Thank you, counsel. The case is submitted.

(Whereupon, the case was submitted.)