Litigation

Oral Argument in *Wyeth v. Levine* Marks Change in Drug Litigation Preemption Debate

*By Eric Lasker**

On November 3, 2008, the Supreme Court heard oral argument in *Wyeth v. Levine*[1] to decide the extent to which FDA approval of drug marketing and labeling should preempt personal injury lawsuits brought against prescription drug manufacturers. As of the drafting of this article, the Court has yet to hand down its ruling, and the outcome of the dispute between the two litigating parties is far from clear. What is clear, however, is that there has been a fundamental shift in the nature of the preemption debate. While prescription drug product liability plaintiffs historically have argued that FDA regulatory oversight imposes only "minimum standards" that state common law can exceed without any preemptive conflict, in the *Levine* argument plaintiff's counsel conceded that state tort law claims would be preempted by some types of FDA regulatory action. In so conceding, counsel effectively abandoned the "minimum standards" shibboleth, opening the door to case-by-case determinations of preemption focused on the nature of FDA's drug-specific regulatory decisions.

If accepted by the Court, plaintiff's concession in *Levine* means that preemption arguments will become a permanent fixture in prescription drug product liability litigation. The unanswered question is where the *Levine* Court will draw the line between FDA actions that preempt state tort law and FDA actions that do not. This article first reviews the plaintiffs' preemption concession in the *Levine* oral argument and then discusses the elements of FDA regulatory action—what did FDA know and what did it do with that knowledge—that may be determinative in future preemption disputes in prescription drug litigation.

I. Plaintiff's Abandonment of the Minimum Standards Preemption Argument

Plaintiffs have long argued in prescription drug product liability litigation that there can be no conflict between FDA regulation of prescription drugs and state tort law because FDA sets only minimum standards of safety in the labeling and marketing of prescription drugs. Under this view, FDA approval establishes only the "floor" upon which state tort law could build without conflicting with federal law. This position prevailed in the Vermont Supreme Court in the *Levine* case, which soundly rejected Wyeth's argument that the failure-to-warn personal injury claim brought by Ms. Levine conflicted with FDA approval of the drug label:

> [A] system under which federal regulations merely set minimum standards with which manufacturers must comply is fully consistent with Congress' primary goal in enacting the FDCA, which is to protect consumers from dangerous products, as well as Congress' stated intent that the FDCA must not weaken the existing laws, but on the contrary it must strengthen and extend that law's protection of the consumer.[2]

The Vermont Supreme Court opinion rejected the possibility of preemption by viewing state tort law as a complementary supplement to federal safety objectives. "[S]tate law serves as an appropriate source of supplementary safety regulation for drugs by encouraging or requiring manufacturers to disseminate risk information beyond that required by FDA under the act."[3]

In contrast, pharmaceutical manufacturers and FDA have argued that FDA approval involves a balance between providing sufficient warnings to inform physicians of drug risks and avoiding unwarranted warnings that could discourage medically beneficial drug treatment. In the preamble to its January 2006 Final Rule on prescription drug labeling, FDA explained that it viewed its regulation of prescription drugs as imposing both a floor and a ceiling on drug warning labels.[4] FDA explained:

> Given the comprehensiveness of FDA regulation of drug safety, effectiveness, and labeling under the act, additional requirements for the disclosure of risk information are not necessarily more protective of patients. Indeed, they can erode and disrupt the careful and truthful representation of benefits and risks that prescribers need to make appropriate judgments about drug use. Exaggeration of risk could discourage appropriate use of a beneficial drug.[5]

When viewed from this perspective, state tort law claims conflict with FDA prescription drug regulation when they impose liability based on a lay jury's judgment as to necessary warning language that differs from the balance struck by FDA.

In the proceedings first in the Vermont Supreme Court and then in their United States Supreme Court briefing in *Levine*, the plaintiff appeared to hold strongly to the "minimum standards" position. In the *Levine* oral argument, however, the plaintiff took a dramatically different course, acknowledging that there could be a preemptive conflict between FDA drug approval and state tort law in some circumstances. That concession was made first in response to a question by Justice Alito that focused specifically on the facts in the *Levine* case, where Wyeth had been held liable for failing to contraindicate IV-push administration of the drug phenergan despite FDA's approval of a label that allowed for such use:

> 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 that drug; and then, as some of the other arguments have referenced, the very day after 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?

* *Eric Lasker is a partner in the Washington, D.C. law firm Spriggs & Hollingsworth, where he specializes in pharmaceutical, toxic torts and environmental litigation defense. Mr. Lasker represented two groups of amicus curiae in* Wyeth v. Levine.

Plaintiff's Counsel: *That would 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.[6]

Justice Alito's question was obviously designed to present the starkest conflict between an FDA regulatory decision and a state common law duty, and the question could not have come as a surprise to the plaintiff's counsel. Under the plaintiffs' traditional formulation of the preemption argument, the answer to this (and any similar) question is straightforward: because FDA is deciding only upon the "minimum standard" in drug labeling, FDA's decision cannot conflict with a state common law duty imposing a higher standard, and state common law accordingly is not preempted. Ms. Levine's counsel's decision instead to concede preemption in this hardest-case fact scenario must have been a premeditated calculation to strike a more moderate legal position before the Court, perhaps in tacit response to the Court's rejection of the minimum standards argument in its medical device preemption opinion last term in *Riegel v. Medtronic, Inc*.[7]

Having abandoned the minimum standards, bright-line position, however, the plaintiff's counsel appeared not to have clearly thought out where to redraw the preemption line. This problem became readily apparent when Justices Scalia and Souter began pressing the plaintiff's counsel on the implications of his concession. By conceding that a labeling decision by a fully informed FDA is preemptive at least on the day after that decision was made, the plaintiff's counsel tied the preemption question not to the nature of FDA regulatory determinations generally (*i.e.*, Can FDA regulatory determinations ever conflict with state tort law liability?) but to the nature of the specific FDA regulatory determination at issue (i.e., Did FDA's regulatory determination conflict with state tort law liability in this instance?). While the plaintiff's counsel may have hoped to limit the magnitude of his concession by conceding preemption only on the "very day after" FDA made its regulatory decision, he had no analytical support for a temporal preemption requirement. Instead, he was quickly placed in the position of arguing that the viability of a state tort law claim depended upon a showing that there was at the time of the alleged injurious prescription additional information about the drug risks as to which FDA was unaware when it made its labeling decision:

Justice Souter: … 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 FDA was told, then there is not pre-emption. Is that a fair statement of your position?

Plaintiff's Counsel: That's fair …[8]

The plaintiff's counsel appeared at this point to recognize the implications of his concession (as did many of his plaintiff counsel brethren in the gallery who, from the author's vantage point, could be heard whispering strident objections to his answers). But his efforts to modify his argument led him to even more tenuous ground. The plaintiff's counsel fell back on another traditional plaintiff preemption argument that a drug is "misbranded" under the federal labeling regulations if a drug manufacturer fails to revise a drug label "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug."[9] Plaintiffs traditionally have relied upon this regulation to argue that a drug manufacturer is obligated to add safety warnings to a drug label independent of any FDA regulatory determination and can be held liable under state tort law for failing to do so. But having acknowledged that an informed FDA regulatory determination approving the existing label would preempt state tort law liability, plaintiff's counsel was unable to explain how the purported separate federal regulatory obligation to include appropriate safety warnings on a label would change the preemption analysis. This led to the following, somewhat bizarre, exchange in which plaintiff's counsel argued that a drug could be misbranded under federal law but immune from civil liability for inadequate warning under state tort law:

Justice Souter: [I]f 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 preemption.

Plaintiff's Counsel: I – I think there is preemption, but that doesn't mean …

… Let me try to untangle it this way. The fact that there is pre-emption and you cannot bring a State law failure-to-warn claim doesn't mean that the drug isn't misbranded …

Justice Souter: In other words, I think you are saying if there—if there would be pre-emption it may be misbranded, but there cannot be any recovery in a State tort suit.

Plaintiff's Counsel: That's correct.[10]

For long-time followers of preemption jurisprudence, the plaintiff's concession in the *Levine* argument that FDA regulatory approval preempts at least some state tort law claims harkens back to a similar concession made by plaintiffs in *Cipollone v. Liggett Group, Inc.*, in an oral argument in January 1992 shortly after Justice Thomas replaced Justice Marshall on the Court. *Cipollone* addressed the question whether the Federal Cigarette Labeling and Advertising Act (the "1965 Act") and/or the Public Health Cigarette Smoking Act (the "1969 Act") preempted state tort law claims against cigarette manufacturers. At the time, the question whether state tort law imposed "requirements" that could give rise to preemption was at least somewhat in doubt.[11] Instead of trying to hold the line against any preemption of state tort law, however, the plaintiff's counsel acknowledged in oral argument that the 1969 Act did protect cigarette manufacturers from tort claims based on the argument that they should have provided warnings stronger than those required in the Surgeon General's warning.[12] What followed was a sharply divided but seminally important opinion in which the Supreme Court for the first time held that federal law preempted certain types of state tort law personal injury claims.[13]

With the plaintiff likewise having conceded the broader preemption argument in *Levine*, the stage appears set for the *Levine* Court as well to issue a major ruling limiting the scope of a burgeoning area of state tort law litigation.[14] As

with *Cipollone*, however, the Court is unlikely to issue a broad preemption ruling that would preclude prescription drug state tort law claims in all cases. Although Wyeth did not make the type of broad concession that defined plaintiff's argument, Wyeth focused its appeal in *Levine* on the strong factual record of FDA's informed control over the phenergan label, and thus provided the Court with many avenues for a narrow preemption ruling. The key question discussed below, then, is down which avenue the Court—and as a result prescription drug preemption in general—is likely to proceed.

II. Drawing the Line on Prescription Drug Preemption

Predicting the Supreme Court's ruling from questioning at oral argument is a perilous task at best, but if we are to assume that the Court will accept plaintiff's concession and find that an informed FDA regulatory determination is preemptive, the Court will still be faced with three major questions: (1) What is an "informed" FDA for purposes of preemption? (2) What types of FDA regulatory action are preemptive? and (3) Which side bears the burden of proof in answering questions 1 and 2? Each of these questions is addressed in turn.

A. What is an Informed FDA for Purposes of Preemption?

FDA regulations impose significant pre-approval and post-marketing disclosure requirements on drug manufacturers,[15] and these requirements are designed to insure that FDA has all of the safety information needed to ensure the proper labeling and marketing of prescription drugs. Preemption opponents contend, however, that FDA is understaffed and unable to meaningfully process the information that it receives. Moreover, the very comprehensiveness of FDA's disclosure requirements provides fertile grounds for plaintiff arguments that pharmaceutical manufacturers have not provided FDA with required safety information that would have led FDA to a different labeling determination. If FDA is not informed of the drug's risks, the argument continues, then a state tort law requirement imposed with knowledge of those risks cannot be contrary to any FDA determination and cannot be preempted.

During the *Levine* argument, the United States appearing as amici curiae in support of Wyeth, agreed that preemption should not apply where a pharmaceutical manufacturer failed to provide the FDA with new information that FDA believes would negate the provisions on the label.[16] But as Ms. Levine's counsel subsequently noted, "the dispute is… what constitutes new information."[17] Plaintiffs will argue for a broad definition of "new information" that would encompass virtually any piece of scientific data that relates to a given risk, including the accumulation of additional anecdotal reports of injury (even if the rate of such reports as a percentage of prescriptions has not changed from prior history) or new analysis of prior submitted data. Under this broad definition, any preemption defense would be short lived indeed, ending as early as the first new case report to be received after FDA approval of a drug label.

In its *Levine* argument, the United States provided the Court with a more sensible definition of new information, citing to the recently enacted changes being effected ("CBE") regulation in which FDA clarified its long-standing understanding of the type of new safety information that would authorize a pharmaceutical manufacturer to add warnings to a drug label prior to—but still subject to—FDA approval.[18] As now clearly defined in 21 C.F.R. § 314.3(b), "newly acquired information" means:

> [D]ata, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

This definition identifies the type of new information that FDA considers sufficient for a presumptive change in a drug label and, accordingly, provides a meaningful standard for a court in deciding questions of preemption. If new safety information is not of the type that FDA views sufficient to allow a CBE labeling change, then FDA's lack of knowledge of the information cannot form the basis for a state tort law requirement that a pharmaceutical manufacturer add warnings to a drug label without conflicting with FDA's regulatory authority.

B. What Types of FDA Regulatory Action are Preemptive?

Having defined the type of safety information FDA must have to make an informed decision, the next question that courts will face is what types of FDA regulatory action are preemptive. In a case-by-case analysis, preemption will arise where state tort law would impose a requirement on a pharmaceutical manufacturer that is different from the requirement imposed by FDA based upon the same information. But what actions must FDA have taken to establish that the requirements imposed in the approval of the drug label reflect FDA's considered judgment of the safety information before it?

The easiest case is when there is concrete evidence that FDA had specifically considered and rejected increased warnings based upon the same safety information identified by plaintiffs in state tort litigation. Indeed, it was plaintiff efforts to pursue state law claims in this factual scenario in the early 2000s with respect to SSRI antidepressants and nicotine replacement therapies that caused FDA to assert preemption arguments through amicus filings and that has resulted in the most significant implied preemption appellate rulings in drug litigation to date.[19]

Although there was evidence of an express FDA rejection of stronger warning language in *Levine*, the questioning at the oral argument focused on a more common fact pattern in which a specific FDA regulatory decision can only be inferred. In *Levine*, the plaintiff argued that the phenergan label should have included a contraindication against IV-push administration, but Wyeth demonstrated that the FDA-approved label both warned of the danger of IV administration of the drug and, in four separate provisions, included instructions to doctors that were specific to IV-push administration.[20] In this fact pattern, the drug label itself (both warning of risks and instructing on use) demonstrates an informed and balanced decision by FDA with respect to the warning at issue that should preempt state tort law claims.

Moving further along the spectrum brings us to the most difficult cases in which FDA approves a drug label but then takes no action whatsoever over an extended period of time as additional safety information is received. While arguments for preemption can be made in these cases as well, this fact pattern likely will continue to pose the greatest challenge to pharmaceutical companies pursuing preemption defenses.

C. Which Side Bears the Burden of Proof?

At the close of his argument, Ms. Levine's counsel sought to impose a new hurdle to pharmaceutical manufacturers asserting preemption: that the manufacturer should bear the burden of proving that there was no new safety information of which FDA was unaware that could have resulted in a different FDA labeling determination.[21] This argument provoked an apparent split between Justices Kennedy and Breyer, with Justice Kennedy suggesting that requiring a pharmaceutical manufacturer to prove that it had fully informed FDA of safety risks ran afoul of many states' rebuttable presumption of regulatory compliance, and Justice Breyer suggesting that a drug company should at least bear a burden of producing evidence showing that it had disclosed to FDA the safety information at issue.[22]

Given the potentially central importance of Justice Breyer and/or Justice Kennedy in forming a majority opinion, the issue of how the burden of proof is allocated may play a key part in the *Levine* ruling. The importance of this issue is demonstrated by Ms. Levine's ultimate argument in her counsel's oral presentation to the Court. Faced with the specific language in the phenergan label relating to IV-push administration, Ms. Levine's counsel argued that FDA "was never put to the test of deciding comparative risks and benefits of IV push versus IV drip."[23] This assertion was not, however, based upon any affirmative evidence. (When questioned by Justice Souter, counsel pointed only to the lack of any FDA correspondence mentioning such an analysis.[24]) Rather, Ms. Levine's counsel relied on pure ipse dixit reasoning, arguing that "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."[25]

Ms. Levine's argument that FDA can be presumed to have ignored safety information in its files flies in the face of FDA's statutory charge to insure the safety and efficacy of prescription drugs and the extensive federal regulatory regime in which pharmaceutical manufacturers are required to provide safety information both prior to initial drug approval and post marketing. While pharmaceutical manufacturers would be well advised to be proactive in dealings with FDA to insure a proper documentary record of FDA's consideration of safety risks, the argument that pharmaceutical companies can ignore federal labeling requirements (so as to comply with varying state tort law requirements) based upon assumed FDA disregard for properly submitted safety information is fanciful at best. The burden of proving such FDA disregard so as to allow for state tort law claims should lie with the plaintiff as part of his ordinary burden of proof.

CONCLUSION

With the concessions made by plaintiff's counsel in the *Levine* oral argument, it appears likely that the Supreme Court will recognize the viability of an implied preemption defense in prescription drug product liability litigation. But the scope of that preemption defense remains uncertain. With important questions to be decided as to what FDA must know and what FDA must do for preemption to apply, and uncertainty as to who will bear the burden of proof, the Supreme Court in *Levine* should provide much needed guidance to the parties in future prescription drug product liability cases.

Endnotes

1 128 S. Ct. 1118 (2008) (No. 06-1249), *granting petition for certiorari from*, *Levine v. Wyeth*, 944 A.2d 179 (Vt. 2006).

2 Levine v. Wyeth, 944 A.2d 179, 190 (Vt. 2006) (internal citations and quotation marks deleted), *cert. granted*, 128 S. Ct. 1118 (2008) (No. 06-1249).

3 *Id.* at 192 (quotation marks omitted).

4 *See* Final Rule, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006).

5 *Id.* at 3935. *See also* Brooks v. Howmedica, 273 F.3d 785, 796 (8th Cir. 2001) ("There are... a number of sound reasons why the FDA may prefer to limit warnings on product labels. Warnings about dangers with less basis in science or fewer hazards could take attention away from those that present confirmed, higher risks."); Dowhal v. SmithKline Beecham Consumer Healthcare, 88 P.3d 1, 13 (Cal. 2004) ("Against the benefits that may be gained by a warning must be balanced the dangers of overwarning and of less meaningful warnings crowding out necessary warnings, the problems of remote risks, and the seriousness of the possible harm to the consumer.").

6 Wyeth v. Levine, Transcript of Oral Argument at 33-34, 2008 WL 4771230 (U.S. Nov. 3, 2008) (emphasis added).

7 128 S. Ct. 999, 1008 (2008) ("State tort law that requires a manufacturer's catheters to be safer, but hence less effective, than the model the FDA has approved disrupts the federal scheme.")

8 *Levine*, 2008 WL 4771230 at 38.

9 21 C.F.R. § 201.80.

10 *Levine*, 2008 WL 4771230 at 39-40.

11 Eight years earlier, a majority of the Court had suggested that there could be a preemptive conflict between state tort claims and federal requirements but had held in the case before it that an injured worker was not preempted from bringing a punitive damages claim against the owner of a nuclear energy plant regulated by the Nuclear Regulatory Commission. *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238 (1984).

12 *See* Cipollone v. Liggett Group. Inc., No. 90-1038, 1992 WL 687857, **18-19 (U.S. Jan. 13, 1992). In an earlier oral argument prior to Justice Thomas's appointment to the Court, plaintiffs had argued more strongly against preemption in any circumstances. *See Cipollone v. Liggett Group, Inc.*, No. 90-1038, 1991 WL 636252 (U.S. Oct. 8, 1991).

13 Cipollone v. Liggett Group. Inc., 505 U.S. 504 (1992).

14 State tort law claims against pharmaceutical manufacturers have increased dramatically in recent years, as evidenced by the twenty federal multidistrict litigations challenging the adequacy of FDA-approved drug labeling pending in federal court; all but one of which began in 2000 or later. See Jud. Panel on Multidistrict Litig., Distribution of Pending MDL Dockets (May 13, 2008), *available at* http://www.jpml.uscourts.gov.

15 *See* 21 C.F.R. §§ 314.50, 314.80, 314.81,

16 *Levine*, 2008 WL 4771230 at 16.

17 *Id.* at 33.

18 *Id.* at 19-20; *see also* Final Rule, Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49603-01 (Aug. 22, 2008).

19 *See* Colacicco v. Apotex, Inc., 521 F.3d 253, 272 (3d Cir. 2008) (state tort law claims against SSRI manufacturer preempted because "FDA has publicly rejected the need for a warning that plaintiffs argue state law requires"); *Dowhal*, 88 P.3d at 11(Cal. 2004) (holding preempted a nicotine replacement therapy warning requirement under California Proposition 65 that was specifically rejected by FDA).

20 *See Levine*, 2008 WL 4771230 at 5-6.

21 *Id.* at 47.

22 *Id.* at 48-51.

23 *Id.* at 42.

24 *Id.* at 43.

25 *Id.* at 42.