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ANALYSIS: PREEMPTION AFTER *WYETH v. LEVINE*

The Supreme Court on March 4, 2009 issued its long-awaited decision in *Wyeth* v. *Levine*, 555 US __ (Mar. 4, 2009), rejecting federal preemption of a failure to warn product liability claim involving a prescription drug.[1] By a vote of 6-3, the Court ruled that the state tort claim at issue did not conflict with the Federal Food, Drug, and Cosmetic Act (FDCA), and therefore was not preempted. Justice Breyer wrote a concurring opinion, and Justice Thomas concurred only in the result. Justice Alito, along with the Chief Justice and Justice Scalia, dissented and would have found preemption. The Court's decision rejected the US Food and Drug Administration's (FDA's) recent pronouncements on preemption and will limit lower court decisions finding preemption. Additionally, the Court affirmed that, through the many amendments to the FDCA over the years (including the 2007 FDA Amendments Act), "it has remained a central premise…that the manufacturer bears responsibility for the content of its label at all times." *Slip op.* at 14.

Although the decision leaves the door ajar for preemption claims in certain contexts, it greatly alters the strategic calculus in considering a preemption defense, as well as in regulatory dealings relating to drug labeling. It defines (and arguably expands) the scope of risk information deemed subject to the Changes Being Effected (CBE) regulation. The decision has also put pressure on Congress to reconsider preemption in the medical device context. This advisory summarizes the key points of the decision and analyzes its impact on litigation and regulatory strategy.

THE *WYETH* v. *LEVINE* DECISION

The facts of the case appear to have colored the Supreme Court's analysis. The decision involved Wyeth's injectable anti-nausea drug Phenergan®, which can be administered intravenously or through intramuscular injection. The labeling warned that, "due to the close proximity of arteries and veins in the areas most commonly used for intravenous injection, extreme care should be exercised to avoid perivascular extravasation or inadvertent intra-arterial injection." *Slip op.* at. 2, fn. 1. The labeling further indicated that "pain, severe chemical irritation, severe spasm of distal vessels, and resultant gangrene requiring amputation are likely under such circumstances."

Ms. Levine received an intravenous injection of Phenergan® in April 2000 through an IV-push, in which the drug is injected into an intravenous line already in place. The drug entered her artery, and Ms. Levine developed gangrene, necessitating amputation

1 The decision can be found at http://www.supremecourtus.gov/opinions/08pdf/06-1249.pdf.

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of her arm. Ms. Levine argued that Wyeth's labeling was inadequate because it either should not have allowed—or should more strongly have warned against—administration of the drug through an IV-push. Wyeth contended that FDA had directed it to use this particular warning and had rejected a different warning on intra-arterial injection. Those FDA decisions, Wyeth argued, preempted Ms. Levine's failure to warn claims. The Vermont courts rejected the preemption defense. The Supreme Court affirmed.

There are a number of important holdings in the Supreme Court's decision. First, the Court revived the presumption against preemption. *Slip op.* at 8. Although the majority characterized its reliance on the presumption as settled law, the Court in fact has not consistently invoked the presumption in implied preemption cases involving a conflict between state and federal law. This holding could have ramifications for the preemption defense in other contexts.

Second, the Court rejected the argument that Wyeth could not comply with both state and federal law, holding that FDA's "Changes Being Effected," or CBE regulation, allowed Wyeth to change the labeling even though the new regulation made clear it is permitted to do so only based on "newly acquired information." The Court made several key points to support this holding. First, it found that Wyeth could have analyzed adverse event reports regarding gangrene and amputations accumulating over the years, and those analyses would have constituted "newly acquired information." The substantial time—12 years—between when FDA focused on the issue and Ms. Levine's injury likely contributed to this conclusion. In this regard, the Court reasoned that "newly acquired information" for purposes of the CBE regulation includes not only new data, but also "new analyses of previously submitted data." *Slip op.* at 12.

Third, the Court rejected the argument that a unilateral change by Wyeth would have rendered the drug misbranded. In the Court's view, because the "statute contemplates that federal juries will resolve most misbranding claims, the FDA's [contrary] belief that a drug is misbranded is not conclusive." *Slip op.* at 13. The Court then voiced skepticism that FDA would bring an enforcement action where a manufacturer strengthened a label. To sustain this argument in the future, a manufacturer may need to convince the court that FDA would have found that the label demanded by the plaintiff would in fact be inadequate.

The Court's admonition that "[i]mpossibility preemption is a demanding defense," *slip op. at* 15, sums up its inhospitable approach to implied preemption. But it did not slam the door on such arguments. For example, the Court did not decide whether preemption would ensue if the evidence demonstrated that FDA would have rejected the warnings required by state law. *Slip op. at* 15. Moreover, although the decision did not describe what evidence might suffice for this showing, the Court's identification of the evidence it found lacking in *Levine* provides some strong hints:

- The evidence did not show that Wyeth "attempted to give the kind of warning required by the Vermont jury but was prohibited from doing so by the FDA." *Slip op.* at 15.
- The evidence did not show that FDA had made a specific decision to preserve the IV-push method of administration. *Slip op. at 16.*
- Wyeth did not claim to have "supplied the FDA with an evaluation or analysis concerning the specific dangers posed by the IV-push method of intravenous administration." *Slip op.* at 16.

Thus, at least where a company has provided relevant information to FDA, where the company asked for the change at issue and FDA would not permit it, or where there is no new information to be analyzed between the time FDA makes its decision and the events at issue in the case, the preemption defense should survive. How far short of that definitive level the proof can fall and still be adequate remains to be seen.

Fourth, the Court also rejected the argument that Ms. Levine's state law claim interfered with FDA's regulatory objectives. There are a number of key aspects of this holding. To begin with, the Court disagreed that FDA regulations impose both a floor and a ceiling as to drug labeling. In a robust interpretation of Congressional silence, the Court found that Congress had not intended such preemption because it had amended the

FDCA without extinguishing state pharmaceutical cases of which it "must have" been aware. *Slip op. at 18-19.*

The Court resolved the issue of how much deference to accord to FDA's assessment in the preamble to its labeling regulations in January 2006, that state tort suits obstruct the Agency's regulatory efforts. The answer was, "None." Although acknowledging that agencies are uniquely situated to determine whether state law gets in their way, *slip op.* at 20, the Court found that absent a specific regulation addressing preemption, the Agency's position merited only such weight as justified by its "thoroughness, consistency, and persuasiveness," (i.e., *Skidmore* deference). *Id.* In the Court's view, FDA had taken inconsistent positions regarding preemption, undercutting the Agency's current explanations. The Court further found that the absence of formal procedures, such as notice and comment rulemaking, undermined the reliability of FDA's assertions in the preamble. *Slip op.* at 21.

Finally, the Court distinguished *Geier* v. *American Honda,* 529 US 861 (2000), which held that the US Department of Transportation's regulations allowing manufacturers to install either airbags or passive restraints preempted state law suits premised on a duty to install airbags. In that case, the Court stated, the record demonstrated that the Agency had adopted a regulation for the specific purpose of allowing flexibility, and state law interfered with that purpose. By contrast, there was no occasion in the *Levine* case "to consider the preemptive effect of a specific agency regulation bearing the force of law." *Slip op.* at 24. Justice Breyer highlighted this point in his concurring opinion, prodding FDA to consider regulations describing when its "labeling requirements serve as a ceiling as well as a floor." *Slip op., Breyer, J. concurring* at 1. He also suggested that requirements imposed for particular labels, as opposed to requirements in regulations, might preempt state laws. *Id.*

PREEMPTION POST-*WYETH* v. *LEVINE*

The Court's apparent support for state lawsuits and its dismissive treatment of FDA's views suggest that at least some preemption arguments based on "obstacle preemption" may be challenging. However, such arguements are not necessarily fruitless. Specificity and engagement with FDA are the keys to finding openings in an otherwise broad rejection of preemption. We can think of at least six scenarios where a preemption defense should be considered.

First, where a company can show that a state law interferes with a specific FDA regulation, the defense may have some vitality. An example might be FDA's regulation regarding black box labeling. In order to avoid overuse and dilution of this most potent form of warning FDA reserves to itself the right to require a black box, and excludes that change from those a company can make through the CBE process. 21 C.F.R. § 201.80(e); 44 Fed. Reg. 37434, 37448 (June 26, 1979); 51 Fed. Reg. 43900, 43902 (Dec. 5, 1986). A state law duty to use a black box might interfere with FDA's regulatory objectives.

Second, where a company has discussed the precise adverse event at issue with FDA, including its seriousness and its prevalence, and FDA is the driving force behind the labeling language, there might be a compelling argument that FDA would not have accepted the warning required by state law. This factual situation is distinguishable from the one described by the Court in *Levine*.

Third, where the injury occurred shortly after FDA approved labeling on the adverse event at issue, and all required relevant information was provided to FDA, there might be a compelling case that requiring a different label would conflict with FDA requirements. Moreover, the defendant in such a case could reconcile its preemption argument with the Supreme Court's interpretation of the phrase "newly acquired information" in the CBE regulation.

Fourth, the Court noted that the verdict neither "mandate[d] a particular replacement warning," nor "require[d] contraindicating IV-push administration." *Slip op.* at 8. Rather, the trial court proceedings simply established that the warning was "insufficient" and "that Levine's injury would not have occurred if Phenergan's label had included an adequate warning about the risks of the IV-push method of administration." *Slip op.* at 7. The opinion thus suggests that forcing the plaintiff to greater specificity with regard to

alternative labeling could pay dividends with regard to the preemption defense.

Fifth, the Court did not address theories of liability other than failure to warn, so preemption may have some viability in design defect cases, where the state lawsuit attacks the core of FDA's responsibility—to ensure that all drugs on the market are safe and effective, and that safe and effective drugs make it to market.

Sixth, *Buckman Co.* v. *Plaintiffs' Legal Committee*, 531 US 341 (2001) remains good law, providing arguments for preemption of causes of action premised on fraud on the FDA. Indeed, last year, the New Jersey Superior Court, Appellate Division, relied on *Buckman* to find preempted a state statutory provision permitting punitive damages to be awarded against pharmaceutical companies where a jury finds that the company defrauded FDA. *McDarby* v. *Merck & Co.,* 401 N.J. Super 10 (App. Div. 2008), *certif. denied on this ground, granted on other grounds*.

These factors should be assessed in determining whether to file or withdraw motions for preemption in existing cases.

Going forward, in order to maximize the ability to present a preemption defense in future litigations, companies will need to reconsider various approaches to ensuring a strong record of FDA evaluation—and preferably definitive acceptance or rejection—of labeling for potential new risk information regarding their products. Recent regulatory developments have changed the dynamic for FDA labeling decisions, and may result in scenarios that make preemption possible post-*Wyeth* v. *Levine*. For example, FDA has amended its regulation on CBE labeling supplements expressly to require that such supplements reflect newly acquired information and rest on sufficient evidence of a causal association. As noted, although the Court in *Levine* found that the revised CBE regulation did not constrain Wyeth's ability to add risk information with respect to Phenergan and IV-push, in other cases the rule may remain helpful in limiting the argument that a company could have added information to the drug label without prior FDA concurrence. Also, the 2007 FDA Amendments Act provided FDA with significantly greater power to impose labeling changes and Risk Evaluation and Mitigation Strategies (REMS) for both newly approved and marketed drugs. Such comprehensive, drug-specific risk mitigation frameworks present important new liability risks, but they could also bolster a preemption argument where a plaintiff suggests that a company could have proactively tampered with such a complex strategy merely by adding new warnings.

In sum, although *Levine* is a setback for the industry in the area of preemption, it does not extinguish the defense. The decision counsels that pharmaceutical companies be selective in determining when to file preemption motions. Companies also should assess how the *Levine* decision affects their dealings with FDA.

We hope that you have found this client advisory useful. If you have additional questions, please contact your Arnold & Porter attorney or:

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