



# PHARMACEUTICAL LAW & INDUSTRY



## REPORT

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### **Wyeth v. Levine: Limits on the Scope of FDA Preemption And Implications for Drug and Medical Device Manufacturers**

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#### **I. Preemption Defense Provides Little Shelter for Prescription Drug Makers**

**O**n March 4, 2009, the United States Supreme Court, in the case of *Wyeth v. Levine*, rejected what many industry observers had predicted would curb product liability litigation involving prescription pharmaceuticals: judicial endorsement of the argument that the U.S. Food and Drug Administration's (the "FDA") approval of a drug's label provided a complete defense to state-law tort claims premised on the inadequacy of the label.<sup>1</sup> Deprived of this shield against mounting litigation expenses, pharmaceutical compa-

<sup>1</sup> *Wyeth v. Levine*, No. 06-1249, — S. Ct. —, 2009 WL 529172 (Mar. 4, 2009) (7 PLIR 249, 3/6/09).

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nies instead now face both a new regime within the FDA and the continued threat of unpredictable litigation exposure to a myriad of state product liability law schemes.

#### **II. Wyeth v. Levine: Turning Back the Clock on FDA Assertion of Federal Preemption**

At its core, *Wyeth v. Levine* was a medical malpractice case. Vermont resident Diana Levine was a patient at a local clinic where she was treated for migraine headaches with two drugs: Demerol for her headache and Phenergan for her nausea. Phenergan is Wyeth's brand name for the antihistamine promethazine hydrochloride. Phenergan is marketed in an injectable form that is delivered directly into a patient's vein, the "IV-push method," or via an "I-V drip" protocol in which the drug is mixed with a saline solution in a hanging intravenous bag. The label for Phenergan contained a warning against intra-arterial use due to the likelihood of severe arteriospasm and the possibility of resultant gangrene.

In April 2000, Levine visited the clinic and received an intramuscular injection of Demerol and Phenergan. She returned to the clinic later that day for a second injection after the initial injection failed to relieve her symptoms. The physician assistant used the IV-push method for the second injection, and the needle penetrated an artery. Levine subsequently developed gangrene resulting in the amputation of her right hand and forearm. Since Levine was a musician, she sustained significant damages in the form of lost income. Her case became a national cause célèbre after Levine settled her claims against the clinic and medical personnel and successfully pursued an action for damages

against the manufacturer, Wyeth.<sup>2</sup> The gravamen of Levine's claims was that the Phenergan label in use at the time of her injury, failed to adequately warn of the higher risk of adverse effect associated with the IV-push method. She also claimed that Phenergan was not "reasonably safe" to use as prescribed because the risk of gangrene and amputation exceeded the claimed therapeutic benefits.

At the trial court level, Wyeth lost a summary judgment motion premised on the argument that federal law preempted Levine's failure-to-warn claims. Wyeth initially argued that there was both field preemption and conflict preemption which together provided a complete defense since (a) the warnings on the Phenergan label had been provided by the FDA when it approved Wyeth's New Drug Application ("NDA") for Phenergan in 1955 and (b) subsequent changes have been made to the original label. The trial court rejected both preemption contentions. The trial court also did not find that there was any evidence of a substantial regulatory record documenting an attempt by either Wyeth or the FDA to engage each other on the issue of whether a stronger warning against intra-arterial injection was necessary. A more complete examination of the regulatory record during the trial uncovered no stronger evidence that the issue of the adequacy of the warning regarding intra-arterial injection had been rigorously explored by Wyeth or the FDA.

In what is likely to be a harbinger of how future courts address this evidence, the Vermont trial court instructed the jury that it could consider Wyeth's evidence of compliance with FDA regulation but that mere compliance did not establish that the warnings were adequate. Equally problematic for Wyeth's position was an FDA regulation which permits a drug manufacturer to change a product label to add or strengthen a label without prior approval, commonly referred to as the "Changes Being Effected" or "CBE" regulations.<sup>3</sup>

After the jury reached a verdict in Levine's favor and found that Wyeth was negligent for failing to provide an adequate warning, Wyeth moved for judgment as a matter of law again on preemption. In denying the motion, the trial court again concluded that there was no conflict between the FDA regulations and Levine's state-law claims because Wyeth could have strengthened the warnings consistent with FDA regulations and it failed to do so.<sup>4</sup>

Unsurprisingly, what appears to be a basis for the Supreme Court's holding is the belief that preservation of consumers' state rights of actions is a necessary complement to a federal regulatory scheme which does

not itself provide any remedies for consumers harmed by unsafe pharmaceutical products. The Court notes in its opinion that it granted Wyeth's petition for *certiorari* not just because of the preemption issues but also because the FDA had recently—and apparently in a marked departure from its historical position—announced that agency approval should preempt state tort law.<sup>5</sup> The Court then set forth an analytical framework which left no mystery as to how the majority would find on the issue of whether Levine's state tort claims were preempted: in the absence of evidence demonstrating congressional intent to preempt traditional areas of state authority, there must be a presumption against preemption.

A review of the legislative history of the 1906 Pure Food and Drug Act, which was replaced by the 1938 Food, Drug and Cosmetic Act ("FDCA") and its subsequent amendments, led the Court to two critical conclusions. First, there was evidence that Congress intended to preserve state law claims going so far as to add a savings clause in a round of 1962 Amendments that expressly provided that a provision of state law could only be invalidated if there was a direct and positive conflict with the FDA. The 1962 Amendments also switched the burden of establishing that a drug was safe and effective to the manufacturers and away from the FDA which historically needed to establish that a drug was harmful before it could be removed from the market.

A second and arguably more persuasive fact was that in 1976 Congress amended the FDCA to add an express preemption provision for medical devices but made no parallel provision for prescription drugs. Equally significant to the Court as this legislative activity preceding Levine's lawsuit, was the fact that in 2007 Congress again revisited the FDCA and granted the FDA statutory authority to require a manufacturer to revise its label based on safety information available *after the drug's approval*. Congress did not however enact a proposed provision in the Senate's version of the bill which would have required prior FDA approval for all changes to drug labels.<sup>6</sup> From the Court's perspective, the conclusion was inevitable: not only could prescription drug manufacturers make a change to their label without prior FDA approval, they also had an obligation to keep their labels up-to-date.

The Court then dispatched Wyeth's attempt to use preemption as a complete defense. Wyeth's strongest and primary argument was premised on its contention that it was "impossible" for it to comply with federal labeling regulations and state law duties derived from state law claims. Wyeth took the position that the CBE regulation was not availing with respect to the Phenergan label because it permits a manufacturer to revise the label based on "newly acquired information" and

<sup>2</sup> See, e.g., Adam Liptak, *Drug Label, Maimed Patient And Crucial Test for Justices*, N.Y. Times at A1 (Sept. 19, 2008); David G. Savage, *Drug makers seek shield from suits*, L.A. Times at 16 (Sept. 7, 2008); Miriam Hill, *When can a drug consumer sue? The principle of 'preemption' could strengthen FDA*, Philadelphia Inquirer at C1 (Nov. 2, 2008).

<sup>3</sup> FDA regulations provide that a manufacturer can change a label to add or strengthen a contraindication, warning, precaution, or adverse reaction to add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the product without FDA approval and upon the filing of a supplemental application. See 21 C.F.R. § 314.70(C)(6)(iii)(A)-(C).

<sup>4</sup> *Levine v. American Home Products, Inc.*, 2004 WL 5456809 (Vt. Super. July 30, 2004) (trial court order denying Wyeth's motion for judgment as a matter of law).

<sup>5</sup> In 2006, the FDA published a notice of final rulemaking which sets forth new regulations governing the content and format of prescription information. 71 Fed. Reg. 3922 (Jan. 24, 2006) (4 PLIR 69, 1/20/06). Included in the notice was the broad statement that the agency believed that its approval of a drug label preempted conflicting or contrary state law. "FDA believes that under existing preemption principles, FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law." *Id.* at 3934.

<sup>6</sup> See Food and Drug Administration Revitalization Act, S. 1082, 110th Congress, § 208 at 107-04 (2007) as passed (proposing new § 506D).

the plaintiff failed to point to any newly-discovered evidence of the risks of IV-push administration. The Court, however, pointed to the FDA's own explanation of the proposed scope of this provision which noted that "newly acquired information" referred to both new data as well as new analyses of previously submitted data. Thus, since evidence in the case established that Wyeth first received notice of a case in which a Phenergan injection led to gangrene and an amputation in 1967, as additional adverse events were reported over time, the company could have added a stronger warning against IV-push administration.

Wyeth also was not successful in persuading the Court that if it had unilaterally added a warning, it would have violated federal law governing unauthorized distribution and misbranding. As a practical matter, the Court did not believe that the FDA would bring an enforcement action against Wyeth for strengthening a warning. As a legal matter, it did not believe that a stronger warning would have rendered Phenergan a "new drug" as that term is defined in the regulations or a "misbranded drug" since the misbranding regulations are focused on labels that fail to provide adequate warnings. In short, in light of Wyeth's ability to adopt (at least on a temporary basis) a label with a stronger warning and in the absence of "clear evidence" that the FDA would not have approved a supplemental application to revise the label, there was no basis for concluding that it was "impossible" for Wyeth to comply with both federal and state labeling requirements.

Wyeth also failed to persuade the Court that, as a matter of policy, requiring it to comply with state law duties would obstruct and undermine the purposes and objective of the federal drug labeling regulation scheme. The Court found no merit to this argument which it concluded rested on a misapprehension of both Congress's intent and the FDA's power to announce the preemption of state law. First, the Court found that the evidence in the record established that while the FDCA was enacted to protect consumers from unsafe or ineffective drugs, it did not provide any remedies to those harmed by the products. Instead, the lack of an express preemption provision and the availability of relief for consumers via state rights of actions strongly suggested the lack of any intent to preempt state tort remedies. As additional support, the Court cited to its own preemption jurisprudence which held that the case for finding federal preemption is weakened when there is evidence that Congress is aware of state law in a field of interest yet decides to tolerate the tension between federal regulation and state law.

In light of this evidence of a strong presumption against FDCA preemption of state tort law, it is not surprising that the Court declined to give any deference to the FDA's assertion in the preamble to the Final Rule that regulatory approval of a label preempted state tort liability. To merit deference, the FDA was required to show that prior to announcing its explanation of the impact of state law on its federal scheme, it must be the result of thorough analysis, be consistent and be persuasive. The FDA failed on all three accounts: the Final Rule and preamble were finalized without offering the states or other interested parties an attempt to comment on the proposal; it was at odds with the record evidence of Congress's purposes; and it reversed without explanation its historically anti-preemption stance. The Court was struck by the fact that the preamble omitted

any discussion of how state law had interfered with FDA regulation in the nearly 100 years since the FDCA was enacted. To the contrary, the Court cited to numerous reports which concluded that the FDA had limited resources to monitor the thousands of drugs on the market and this supported the conclusion that (1) state tort suits were a necessary safety net for consumers and (2) state law could and had existed peaceably with federal regulation and that the regulators themselves had condoned this arrangement.

### III. Reconciling *Levine* and *Riegel*: Moving Forward in the Face of Uncertainty

As the Court noted in *Wyeth v. Levine*, the FDCA does provide for express preemption of state law claims involving medical devices that have been subjected to premarket approval (PMA) by the FDA. In *Riegel v. Medtronic Inc.*, in an 8-1 decision, the Court barred a suit claiming a New York man suffered permanent injury when a Medtronic heart catheter burst during an angioplasty procedure.<sup>7</sup> The Court ruled that federal medical device law preempts state tort claims against manufacturers whose products are approved through the FDA's PMA process.

Under the FDCA, federal law bars the imposition of any state "requirements" that are "different from" or "in addition to" requirements established by the FDA. The Court previously held that this express preemption provision does not bar state law claims against makers of devices that have gone through FDA's 510(k) process, also known as "pre-market notification," because that process does not create device-specific federal requirements that trigger preemption. In an earlier case, *Medtronic Inc. v. Lohr*, the Court left unanswered the question of whether the PMA process—which is more rigorous than the 510(k) process—creates the kind of device-specific federal requirements that are needed to trigger preemption.<sup>8</sup>

In the *Riegel* case, petitioner Donna Riegel argued that claims arising out of injuries caused by the bursting of a balloon catheter during angioplasty should be allowed to go forward, even though the catheter used in surgery received PMA approval. The Court, however, rejected that argument and held that the express preemption language governing medical devices barred such litigation. The decision aligns with the majority of cases in which courts have considered the issue of "whether approval via the PMA process" bars state claims. Thus, going forward, at least in the short term, manufacturers are confronted with two problematic legal frameworks for analyzing product liability litigation risk.

With respect to prescription drug manufacturers, *Wyeth v. Levine* does not completely foreclose the availability of a complete preemption defense. The Court, however, has offered little guidance about what constitutes a regulatory record which would support a finding of preemption beyond the obvious case of a manufacturer who has been ordered not to strengthen or add a particular warning. Guidance may come from the lower courts in a handful of cases that were stayed pending a decision in the *Wyeth v. Levine* case. These cases in-

<sup>7</sup> 128 S. Ct. 999 (2008).

<sup>8</sup> 518 U.S. 470 (1996).

clude two Third Circuit Court of Appeals cases in which prescription drug manufacturers successfully prevailed on a preemption defense and which the Court has now remanded back to the Court of Appeals for further review.<sup>9</sup>

The picture is even cloudier for medical device manufacturers. As anticipated, post-*Riegel*, medical device manufacturers scored numerous legal victories. For example, in *In re Medtronic, Inc. Sprint Fidelis Leads Products Liability Litigation*, a district court dismissed all twenty-one counts in an MDL master complaint including claims alleging consumer fraud and a number of derivative claims (e.g., loss of consortium).<sup>10</sup> However, plaintiffs have already won a motion to file a proposed revised and amended complaint to plead a claim for damages based on what they claim are newly received FDA documents and a revised allegation—consistent with *Wyeth v. Levine*—that Medtronic failed to amend a warning on the product without FDA approval.<sup>11</sup>

In the wake of *Levine* and *Riegel*, the United States Congress has taken initial steps to restore consumers'

<sup>9</sup> See *Colacicco v. Apotex, Inc.*, No. 08-437, — S. Ct. —, 2009 WL 578682 (Mar. 9, 2009) (vacating judgment and remanding to the United States Court of Appeals for the Third Circuit for further consideration in light of *Wyeth v. Levine*); *Pa. Employees Benefit Trust Fund v. Zeneca, Inc.*, No. 07-822, — S. Ct. —, 2009 WL 578681 (Mar. 9, 2009) (same) (7 PLIR 280, 3/13/09).

<sup>10</sup> 592 F. Supp. 2d 1147 (D. Minn. 2009), *mot. for reconsideration denied*, No. 08-1905 (RHK/JSM), 2009 WL 294353 (Feb 5, 2009).

<sup>11</sup> *In re Medtronic, Inc. Sprint Fidelis Leads Prods. Liability*, 2009 WL 624085 (D. Minn. 2009).

rights to pursue state law claims against the manufacturers of medical devices. On March 5, 2009, House Energy and Commerce Health Subcommittee Chairman Frank Pallone, Jr. (D-N.J.) and House Energy and Commerce Chairman Henry Waxman (D-Calif.) introduced the Medical Device Safety Act of 2009 (H.R. 1346) (“MDSA”). If passed, the MDSA would authorize state product liability lawsuits for medical devices, effectively overturning the U.S. Supreme Court’s 2008 decision in *Riegel v. Medtronic*. Introduction of this legislation came just one day after the Supreme Court’s ruling in *Wyeth v. Levine*.

The MDSA was referred to the House Energy and Commerce Committee and has seventy-three co-sponsors. Also on March 5, 2009, Senate Health, Education, Labor and Pensions Chairman Edward Kennedy (D-Mass.) introduced companion legislation in the Senate (S. 540). The Senate bill has eighteen co-sponsors and has been referred to the Senate Health, Education, Labor and Pensions Committee. Supporters of the new legislation include editorial writers in the *New England Journal of Medicine* and the leadership of the American Bar Association, which have both adopted the position that state product liability suits are necessary to hold manufacturers accountable and to ensure safe medical devices.<sup>12</sup>

<sup>12</sup> Gregory Curfman, M.D., Stephen Morrisey, M.D., and Jeffrey M. Drazen M.D., *The Medical Device Safety Act of 2009*, *New Eng. J. Med.* (2009), <http://content.nejm.org/cgi/content/full/NEJMe0902377> (last visited Mar. 24, 2009); Letter from H. Thomas Wells, Jr., President of the American Bar Association, to Sen. Frank Pallone, Jr., Chairman, Subcommittee on Health, Committee on Energy and Commerce (Dec. 29, 2008).