



## The Supreme Court's Wyeth Blunder

By John E. Calfee

*On March 4, 2009, the Supreme Court ruled in Wyeth v. Levine that Wyeth, a pharmaceutical company, is liable for injuries suffered when its drug Phenergan was given to a patient according to a method that, if done incorrectly, as it was in this case, could be very dangerous. Even though the label warned against the dangers of this method, and even though the Food and Drug Administration (FDA) had not required any further limits on this method for Phenergan, the Court opened the door for jurors to retroactively determine what should and should not be included on drug labels. The Wyeth decision will hurt new drug development and limit physicians' willingness to use certain drugs.*

*Wyeth v. Levine* is a lawsuit by a woman grievously harmed by Phenergan, a drug approved for marketing in the 1950s that is an essential treatment for severe nausea caused by migraine headaches. The plaintiff, Diana Levine, was administered the drug via the "push" form of intravenous infusion through a plastic tube. After receiving the drug, she lost an arm to gangrene, a widely feared side effect of Phenergan when it is mistakenly forced into an artery instead of a vein.

Levine sued the physician's assistant who cared for her, the supervising physician at the clinic, and the clinic where she received Phenergan. After settling with them for \$700,000, she sued Wyeth, the manufacturer of Phenergan. Her lawyers alleged that the FDA-approved Phenergan label insufficiently warned about the dangers of administering Phenergan via intravenous push and that Wyeth should have acted on its own and added a stronger warning. Wyeth argued that the lawsuit was preempted by FDA regulation and that, if successful, the lawsuit would impede the FDA's ability to balance reasonably risks and benefits in its regulatory decisions. Wyeth's position in the case was supported by FDA lawyers (although in the years prior to the

George W. Bush administration, FDA lawyers had sometimes assumed that liability lawsuits were a useful adjunct to regulation).

The case was originally brought before courts in Vermont. The Vermont courts disagreed with Wyeth on preemption, and the case was appealed by Wyeth from the Vermont Supreme Court to the U.S. Supreme Court. In the Supreme Court decision on March 4, six of the nine justices sided with Levine (although one of the six, Justice Clarence Thomas, relied on a constitutional argument about federalism rather than the merits of the case itself). The dissent was written by Justice Samuel Alito, joined by Justice Antonin Scalia and Chief Justice John Roberts. Readers of the majority and dissenting opinions will be struck by the massive disagreement among the justices on basic facts. For example, the majority claimed that the FDA had paid only "passing" attention to the risks of the push method, whereas Justice Alito reproduced numerous examples of warning language from the FDA-approved Phenergan label that to a physician would make no sense except when balancing the risks and benefits of push.

The practical essence of the decision consists of two elements. First, juries will be free to conclude purely on their own (after listening to

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expert evidence, of course) that an additional warning would have prevented the injury at issue. The significance of this position can only be appreciated after reviewing the case itself and the fact that (according to Justice Alito's opinion) the physician's assistant violated six explicit warning elements already on the label—including ones that directly addressed the dangers of causing gangrene through faulty use of the push method.

The second element arises from a crucial twist in FDA regulation. The FDA prohibits manufacturers from altering drug labels without FDA approval. The exception is the "changes being effected" (CBE) process in which a manufacturer adds a warning based upon new information and simultaneously applies for FDA approval of the labeling change. As it happens, the essential information about Phenergan, gangrene, and the push method was at least a decade old. The CBE process was analyzed extensively in the lower court decisions and in briefs to the Court, and a 2008 *Federal Register* notice by the FDA made clear that a new analysis of old information would also suffice for adding a new warning. The majority opinion seems to break new ground, however, by finding that manufacturers have an obligation to use the CBE process to add warnings based on old information even if the manufacturer merely should have performed a new analysis of the old data. Hence, manufacturers should sometimes add warnings without FDA preapproval even if there is neither new information about risks and benefits nor relevant results from a new analysis of old information.

These two principles leave manufacturers in a very difficult position. Are there any limits at all on what warnings juries may decide should have been on a label? Very few, considering how much was already on the Phenergan label. One can suppose that if the FDA explicitly rejected a specific warning, a state court can turn around and conclude that the label was inadequate and thus that the manufacturer is liable for failing to provide information it had been ordered by the FDA not to provide. The majority opinion is unclear on this point, so a resolution may have to await the results of another case, possibly *Colacicco v. Apotex*, which involves allegations that an antidepressant manufacturer should have added a suicide warning that the FDA had declined to require, despite being petitioned to do so by outside parties.

In addition, the *Wyeth v. Levine* decision seems to gut the CBE process. No matter how long after a safety issue looks to have been considered and settled, a jury may find that a label was deficient because a manufacturer should have revisited the issue, reached a conclusion

different from that reached before in the medical and regulatory community, and therefore added a warning before obtaining FDA label approval.

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What is the likely fallout from *Wyeth v. Levine*? After all, FDA preemption was never established law, and the majority opinion points out that at least one former FDA commissioner (David Kessler, who served from 1990 to 1997) claims that tort liability suits played a useful role in regulating drug safety. Perhaps the scale of drug safety litigation in this new environment will be no greater than it was in the late 1980s and early 1990s, after a litigation crisis had caused Congress to remove childhood vaccines from the liability system altogether, and when juries seemed inclined not to burden ordinary drugs with extraordinary damages verdicts. Isolated instances of mammoth litigation seemed to focus mainly on drugs that had been pulled from the market, such as the fen-phen diet drug combination (although the actual harms from that drug were minute compared to the \$15–20 billion lost in litigation by, yes, Wyeth, then known as American Home Products). But today's environment is very different. Resentment over prices and costs—which are inevitable in an industry with towering R&D costs and low manufacturing costs—has coincided with a steady drumbeat of safety alarms and vitriolic attacks against both the industry and the FDA.

In this environment, manufacturers can be expected to take careful account of the parameters established by *Wyeth v. Levine*. They are likely to pester the FDA with even more requests to augment safety warnings, reinforcing an existing tendency toward overwarning rather than underwarning. This is likely to discourage the use of valuable drugs.

Notwithstanding increased manufacturer caution, however, considerably more litigation could ensue. With so little apparent restraint on jury decisions about what manufacturers should have done, and with massive punitive damages to be gained from juries far more sympathetic to plaintiffs than to defendants, the scale and success of litigation are likely to mount. A worrisome scenario is

something resembling what has sometimes happened in securities litigation. Just as unexpected stock losses can trigger mass securities litigation, unfortunate effects from an otherwise useful or essential drug could launch numerous individual lawsuits asking for huge damages, followed by class action lawsuits with mammoth costs to all.

All this is likely to feed back into R&D. The prospect of increased litigation raises R&D costs and reduces take-up for new drugs. This is likely to have its greatest force in connection with innovative drugs that offer hope for conditions that are exceptionally difficult to treat but necessarily involve some risks. For example, the advent of monoclonal antibodies that target the immune system has revolutionized care in several areas, such as rheumatoid arthritis, but they can cause dangerous (if rare) side effects. One can only wonder how often future juries will conclude that an additional, unspecified warning would have prevented a specific victim from taking the drug that happened to do more harm than good for that particular patient. More fundamentally, manufacturers will know that the FDA's own assessment of the balance of risks and benefits (already unduly weighted toward safety) may be struck down by a jury culled from citizens routinely subjected to public expressions of hostility toward the pharmaceutical industry and the FDA.

Two other issues also merit attention. One is the possibility that Congress will revisit FDA preemption for medical devices. In *Riegel v. Medtronic*, the Supreme Court decided that FDA regulation preempts state tort liability lawsuits for devices because the 1976 law creating FDA device regulation explicitly provided for preemption (although not explicitly for liability suits but rather for things like product standards). It now seems clear that Congress can easily undo FDA preemption for devices simply by making clear that preemption does not include tort liability. Legislation to do that was introduced

in the last Congress but faced a veto from former president Bush. It may well succeed this year.

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Finally, we need to consider the impact of *Wyeth v. Levine* on physicians. In *Wyeth v. Levine*, it was hard to see how a stronger warning about the push method of administration for Phenergan could have been constructed without rising to the level of a contraindication—that is, a statement that a drug should simply not be administered at all in certain ways or situations. Although physicians are free to defy labeled contraindications, they seldom do so, and they would probably face a very high risk of a malpractice suit if something went wrong after proceeding in the face of a contraindication. One implication of *Wyeth v. Levine* seems to be to increase the power of a single jury in a single state to add a contraindication to a drug label, even when (as in this case) the FDA decided after extensive expert consultation to leave the decision to physicians working in difficult situations amid numerous factors impinging upon drug risks and benefits. Because manufacturers seem likely to implement jury-induced label warnings in all states, not just the one in which the triggering lawsuit was brought, the probable effect is a nationwide contraindication imposed by local juries. The net effect on patient welfare is unlikely to be positive.