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Will High Court Provide Clarity On 'Clear Evidence'?

By **Erin Bosman, Julie Park and Samuel Cortina**
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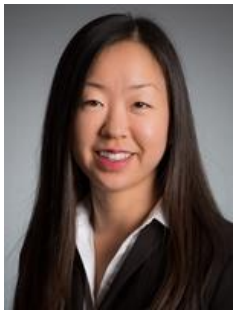

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The U.S. Supreme Court may soon revisit one of its seminal decisions defining products liability law for pharmaceutical manufacturers. That decision — Wyeth v. Levine — addressed whether a branded manufacturer could be held liable for state-law failure-to-warn claims even though federal law regulates the contents of its drug's label.

Lower courts have struggled to apply Levine's "clear evidence" standard, and the Third Circuit, in In re: Fosamax, arguably gutted it altogether. Merck & Co.'s petition for a writ of certiorari in In re: Fosamax is pending before the Supreme Court, where it awaits the views of the Solicitor General. If the Supreme Court grants certiorari, it could signal that In re: Fosamax will be overturned and lower courts (as well as branded manufacturers) will finally receive guidance on Levine's "clear evidence" standard.

Wyeth v. Levine — The "Clear Evidence" Preemption Standard

The Supreme Court's 2009 decision in Wyeth v. Levine set the stage for the current dispute over pharmaceutical preemption. In 2001, a musician named Diana Levine won a jury verdict on her state-law failure-to-warn claims against branded manufacturer Wyeth. Levine's injury occurred when she visited her local clinic to seek treatment for nausea and a migraine headache.

The physician's assistant administered Phenergan for her nausea via the IV-push method. Levine developed gangrene after the drug entered her artery, requiring the amputation of her entire forearm—a devastating result for a musician. Levine sued Wyeth, the manufacturer of Phenergan, for failure to sufficiently warn clinicians that the IV-push method was contraindicated. The Vermont jury found in favor of Levine and awarded her over seven million dollars.

Wyeth appealed, arguing that Levine's state-law failure-to-warn claim was preempted by federal law because it was impossible for Wyeth to comply with both simultaneously. Federal law, said Wyeth, generally requires any label changes to be approved by the U.S. Food and Drug Administration, whereas state law would have required Wyeth to

change the drug's label without FDA approval.

This argument missed an important caveat, according to the Supreme Court. On receipt of newly acquired evidence, a branded manufacturer may submit a Changes Being Effected (CBE) application and unilaterally strengthen a warning on its drug's label while FDA approval of the change is pending.[1] The Supreme Court reasoned that FDA regulations create a floor, but not a ceiling, as to the strength of warnings on a drug's label. A branded manufacturer can thus comply with both laws simultaneously.

However, the Supreme Court recognized an exception to this principle. The FDA would in fact create a ceiling on a label's strength of warning if the FDA rejected a CBE with a proposed stronger label. In such instances, a state-law claim should be preempted. The Supreme Court fashioned this exception in the following way:

Of course, the FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application, just as it retains such authority in reviewing all supplemental applications. But absent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements.[2]

The "clear evidence" standard was thus born. The problem with this standard is that the Supreme Court left it quite open-ended. First, the facts of Levine fall too far on one end of the spectrum to be of help in most subsequent cases; indeed, Wyeth never even "argue[d] that it attempted to give the kind of warning required by the Vermont jury."[3]

And second, the Supreme Court did not explain what "clear evidence" meant as a procedural burden, nor did it illustrate how the standard could be satisfied in circumstances other than Wyeth's. All future cases have thus been judged against this single example of a manufacturer that obviously did not meet (or try to meet) the standard.

Unsurprisingly, lower courts have struggled to apply Levine, and have even arrived at different opinions when reviewing the same regulatory history. Compare Robinson v. McNeil Consumer Healthcare[4] (finding preemption of state law claim related to children's Motrin label) with Reckis v. Johnson & Johnson[5] (rejecting preemption of state law claim related to children's Motrin label). The Third Circuit was the latest party to that struggle.

Lower Court Finds Merck Provided "Clear Evidence" that the FDA Would Have Rejected Stronger Warnings on Fosamax's Label

In In re: Fosamax, the Third Circuit overturned the district court and found state-law claims for failure-to-warn were not preempted even though the manufacturer had requested a stronger warning from the FDA but was denied.[6] Hundreds of plaintiffs alleged that Merck failed to warn that use of Fosamax may lead to thigh fractures. Those plaintiffs' cases were consolidated in a multidistrict litigation in New Jersey with a bellwether trial scheduled for April 2013.

The MDL court granted Merck's motion for summary judgment,[7] finding that the bellwether trial plaintiff's claims were preempted pursuant to Levine. It then expanded that holding to all plaintiffs in the MDL.[8]

The MDL court ordered preemption under a set of very favorable facts for the manufacturer. The FDA approved Fosamax in September 1995 for treatment of osteoporosis in postmenopausal women, and in April 1997 for prevention of osteoporosis. More than a decade later, a concerned FDA requested information from Merck regarding reports of atypical thigh fractures following use of the drug.[9] After reviewing the data, the FDA concluded that there was not "an increase ... in subtrochanteric femur fractures in women using these medications."[10]

Despite the FDA's finding of no connection between use of the drug and thigh fractures, Merck still attempted to strengthen the warning on Fosamax's label. Merck submitted a Prior Approval Supplement — a request for a label change that requires preapproval from the FDA — to add warnings about certain thigh fractures. The FDA approved some of the warnings but not others, and cautioned Merck that Fosamax would be misbranded if the FDA's directions were not followed.[11] Merck implemented only the approved changes.

Following a series of statements and reports wherein the FDA explained that it was still "considering label revisions," it finally informed Merck in October 2010 that it would begin requiring an additional warning regarding the relation between long-term bisphosphonate use and atypical fractures. Merck filed the appropriate label changes in January 2011.[12]

Upon review of those facts, the MDL court found there was "clear evidence" that the FDA would not have approved a stronger warning on the Fosamax label prior to October 2010:

However, what Merck could have or should have done is immaterial because we know what Merck did. Similarly, Wyeth v. Levine provides for preemption where there is clear evidence that the FDA would have rejected a label change, and again, we know that the FDA did reject it.[13]

The MDL court accordingly found that the plaintiffs' claims were preempted pursuant to Levine. This case, of all cases, should fulfill the "clear evidence" standard because the FDA in fact constructed a ceiling on Fosamax's label.

Third Circuit Overturns the Lower Court Even Though the FDA Rejected the Manufacturer's Proposed Label

The Third Circuit employed a different approach than the MDL court and vacated the lower court's decision based on the following reasoning:

The Wyeth "clear evidence" standard is demanding and fact-sensitive. It requires the factfinder to predict a highly probable outcome in a counterfactual world and, therefore, requires a court sitting in summary judgment to anticipate both the range of conclusions that a reasonable juror might reach and the certainty with which the juror would reach them. Here, Plaintiffs have produced sufficient evidence for a reasonable jury to conclude that the FDA would have approved a properly-worded warning about the risk of thigh fractures — or at the very least, to conclude that the odds of FDA rejection were less than highly probable.[14]

This decision lost the forest through the trees. Although the FDA had in fact rejected a proposed stronger warning on the drug's label, the Third Circuit was unpersuaded that Merck provided clear evidence regarding the outcome of a purely hypothetical situation with a label proposal that included

different words.

According to the Third Circuit, "clear evidence," although undefined by the Supreme Court, is a standard of proof synonymous with "clear and convincing evidence" (e.g., not a preponderance of the evidence standard).[15] It also describes a factual inquiry that should be left to the jury:

[The jury's] task is to predict how the FDA would have reacted in a hypothetical scenario. The jury therefore is not being asked to supply a plenary construction of the CBE regulation (or any other written instrument) in the first instance. It is instead being asked to apply the requirements of that regulation to the facts, in aid of a prediction as to the FDA's behavior.[16]

This decision forecloses the possibility that a branded manufacturer could ever prevail on a preemption defense at the summary judgment stage, because a plaintiff could always argue that the FDA would have approved a differently-worded label. This cannot be what Levine envisioned.

Petition for Certiorari and a Call for the Views of the Solicitor General

On Aug. 22, 2017, Merck filed a petition for a writ of certiorari presenting the following question: "Is a state-law failure-to-warn claim preempted when the FDA rejected the drug manufacturer's proposal to warn about the risk after being provided with the relevant scientific data; or must such a case go to a jury for conjecture as to why the FDA rejected the proposed warning?"[17]

Merck argued that the Third Circuit's decision was wrong in two major respects: First, there was no basis to transform the preponderance of the evidence standard applicable to all civil cases (absent express congressional language to the contrary) into a clear and convincing evidence standard; and second, if the evidence in this case did not satisfy the Levine standard, then none could, quashing the Levine standard altogether.

Rather than aim solely at the Third Circuit's decision, Merck also successfully fired shots at Levine as a whole. Merck posited that all lower courts have misapplied Levine because the Levine standard is "elusive" and offers "little help" to lower courts attempting to administer it.[18] Merck's tactic is atypical (e.g., most petitions highlight circuit splits and advocate for a specific interpretation already taken), and reflects the dissonance found in Levine's edict that preemption is a demanding standard but some undefined situations require it.

That approach got the Supreme Court's attention. After full briefing on the petition, the Supreme Court called for the views of the Solicitor General. The Supreme Court makes such a request — called a "CVSG" — when it is considering granting certiorari but wants a brief from the United States stating its position on the merits of the underlying decision, whether the petition is a good vehicle for review and whether the issue is sufficiently important to merit the Supreme Court's attention.

In the past decade, the Supreme Court has shaped the pharmaceutical preemption landscape through a trilogy of cases: Levine, Mensing and Bartlett. The Supreme Court found no preemption in the first case (Levine), but did find preemption in the next two cases (Mensing and Bartlett). The CVSG indicates that the Supreme Court may return to this topic soon.

If it does so, the impact of the potential decision could be broad; as Merck explained in its petition, "an unduly narrow preemption defense threatens the pharmaceutical industry and the FDA's regulatory

role."[19] The trilogy may become a tetralogy — one that not only illuminates, but also limits branded manufacturers' liability for state-law failure-to-warn claims.

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[1] 21 U.S.C. §§ 314.70(c)(6)(iii)(A), (C).

[2] Wyeth v. Levine, 555 U.S. 555, 571 (2009).

[3] Id. at 572.

[4] 615 F.3d 861, 869-70, 873 (7th Cir. 2010).

[5] 28 N.E.3d 445, 457 (Mass. 2015).

[6] In re: Fosamax (Alendronate Sodium) Prods. Liab. Litig., 852 F.3d 268, 271 (3d Cir. 2017).

[7] Wanting a more fulsome factual record, the MDL court deferred ruling on the motion for summary judgment until after trial.

[8] In re: Fosamax (Alendronate Sodium): Prods. Liab. Litig., No. 08-08 (JAP) (LHG), 2014 WL 1266994, at *2 (D.N.J. March 26, 2014).

[9] The FDA made the same request of all bisphosphonate manufacturers, the family of drugs to which Fosamax belongs.

[10] Id. at *3.

[11] In re: Fosamax, 2014 WL 1266994, at *4.

[12] Id.

[13] Id. at *9.

[14] In re: Fosamax, 852 F.3d 268, 271 (emphasis added).

[15] Id. at 285-286.

[16] Id. at 292.

[17] Brief for Petitioner in Merck Sharp & Dohme Corp. v. Albrecht (No. 17-290) 2017 WL 3701808, *1 (U.S. Aug. 22, 2017), also available at http://www.scotusblog.com/wp-content/uploads/2017/12/17-290-petition.pdf.

[18] Petition at 18.

[19] Petition at 31.