

May 28, 2019

Supreme Court Clarifies That Judges, Not Juries, Must Determine Whether FDA Actions Preempt State Failure-to-Warn Claims Against Drug Manufacturers

On May 20, 2019, the U.S. Supreme Court ruled in *Merck Sharpe & Dohme Corp. v. Albrecht* that, in analyzing whether a state law failure-to-warn claim against a drug manufacturer is preempted by federal law, the question of FDA “disapproval” of a proposed warning is for a judge, not a jury, to decide. In a 2009 case, *Wyeth v. Levine*, the Court stated that federal preemption would be established if a drug manufacturer could demonstrate by “clear evidence” that it would be “impossible” to provide the warning the plaintiff claims to be necessary to avoid state tort liability without violating federal (FDA) requirements. Justice Breyer’s majority opinion in *Albrecht*, joined by five other justices, held that this standard is met when a judge determines that “the drug manufacturer fully informed FDA of the justifications for the warning required by state law and . . . the FDA, in turn, informed the drug manufacturer that the FDA would not approve a change to the drug’s label to include that warning.” Justice Thomas wrote a separate concurring opinion, and Justice Alito, joined by Justices Roberts and Kavanaugh, wrote an opinion concurring in the judgment.

While drug manufacturers will likely welcome the majority opinion’s conclusion that judges are better equipped than juries to opine on complicated FDA regulatory questions, the Court’s explanation of how the “clear evidence” standard can be met suggests that manufacturers will not often be able to satisfy it. Thus, preemption of state law failure to warn claims against drug manufacturers is likely to remain an infrequent exception to the general rule of no preemption.

Legal and Factual Background

In *Wyeth v. Levine*, the Court held that FDA’s approval of a warning in a drug’s labeling did not bar state law tort claims alleging that the labeling was inadequate. The Court noted that although FDA approves a new drug’s labeling, the manufacturer retains primary responsibility for ensuring its adequacy. Because the manufacturer could have strengthened or added warnings to its FDA-approved drug labeling under FDA’s “Changes Being Effected” (CBE) regulation prior to receiving FDA approval of a labeling change, the Court determined it was possible for the manufacturer to satisfy both state tort law and federal labeling requirements. Therefore, the Court ruled, the manufacturer was not entitled to impossibility preemption. At the same time, the Court acknowledged that a state law failure-to-warn claim would be preempted if there were “clear evidence” that FDA would not have approved the warning that state law requires.

Albrecht involved claims by hundreds of plaintiffs who used Merck’s osteoporosis drug Fosamax and alleged that Merck failed to adequately warn them of the heightened risk of atypical femoral fractures caused by the drug. The factual record demonstrated, however, that Merck had provided FDA with information about these types of fractures and had unsuccessfully sought FDA approval to add a warning about them in the drug’s labeling.

Specifically, in 2008, Merck submitted a Prior Approval Supplement (PAS) proposing to add discussion of “low-energy femoral shaft fractures” to the Warnings and Precautions and Adverse Reactions sections of the labeling, with multiple references to “stress fractures.” In a 2009 Complete Response Letter (CRL), FDA agreed that the change to the Adverse Reactions section was warranted (with minor modifications), but rejected the proposed changes to the Warnings and Precautions section. The CRL stated, among other things, that discussing “the risk factors for stress fractures” was “not adequately supported by the available literature and post-marketing adverse event reporting.” Merck then proceeded to update the Adverse Reactions section of the labeling via a CBE supplement, but not the Warnings and Precautions section, consistent with FDA’s CRL. In litigation, Merck argued that FDA’s rejection of the proposed Warnings and Precautions language meant that the agency would have rejected an attempt to add a warning relating to atypical femoral fractures via the CBE process (prior to October 2010, when FDA eventually concluded that a warning was appropriate).

Thus, Merck argued, it would have had to violate federal law to provide the warning that plaintiffs argued was required to avoid liability under state law. The district court agreed and held that the plaintiffs' failure-to-warn claims were preempted.

The Third Circuit reversed on appeal. The court construed the "clear evidence" standard from *Levine* to impose a heightened burden of proof for preemption that demands a manufacturer present "clear and convincing" evidence that it was "highly probable" that FDA would not have approved a change to the drug's labeling. The court also held that whether this burden is met presents a question of fact that ought to be decided by a jury, not a judge. Seizing on ambiguity in the language of FDA's CRL to Merck, the plaintiffs argued that the agency did not conclude that *any* new warning about atypical femoral fractures was unsupported by the evidence, but only that Merck's *particular* proposal, which used the broader term "stress fractures" rather than "atypical femoral fractures," was not appropriate. While the Third Circuit did not completely discount the argument that FDA could have proposed alternative language had it concluded that a new warning was warranted, the court nevertheless held that plaintiffs had provided sufficient evidence for a reasonable juror to conclude that FDA would have approved a properly worded warning relating to atypical femoral fractures.

The Supreme Court's Decision

The Supreme Court vacated and remanded the Third Circuit's decision for further proceedings, finding that the Third Circuit incorrectly treated preemption as a question of fact for a jury, rather than a question of law for a judge. Although the Court declined to decide the merits of Merck's preemption defense on the facts presented, the majority opinion's discussion of the type of evidence that may constitute "clear evidence" of impossibility provides guidance to lower courts assessing such preemption arguments. Specifically, Justice Breyer's majority opinion sets forth several key principles:

- "Clear evidence" that federal law prohibited a manufacturer from adding a warning to a drug's labeling requires the manufacturer to show that (i) it fully informed FDA of the justifications for the warning, and (ii) FDA, in turn, notified the manufacturer that it would not approve a labeling change to include that warning.
- A manufacturer will "not ordinarily" be able to meet the clear evidence requirement because the CBE regulation permits a firm to make labeling changes, without prior approval, to add or strengthen warnings to reflect newly acquired information.
- The only agency actions that may constitute clear evidence are those taken "pursuant to the FDA's congressionally delegated authority." FDA may communicate its disapproval of a warning in one of three ways: (i) notice and comment rulemaking setting forth specific labeling standards, (ii) rejection of a warning via issuance of a CRL in response to a new drug application or supplement, or (iii) "other agency action carrying the force of law," such as an exercise of FDA's statutory authority to order safety-related labeling changes under 21 U.S.C. § 355(o)(4)(A).
- In this context, the existence of "clear evidence" that FDA would have refused to approve a warning is not an evidentiary question for a jury. The relevant question is instead "whether the relevant federal and state laws irreconcilably conflict." Because judges are normally familiar with administrative law and are generally better equipped than juries to evaluate agency determinations, preemption is a question of law for a judge to decide. Related factual questions are "subsumed" within the legal analysis.

In a separate concurring opinion, Justice Thomas stated that he would reject Merck's preemption argument because "neither agency musings nor hypothetical future rejections" qualify as "Laws" capable of preemption. In contrast to the majority's view that a CRL could have preemptive effect because federal law authorizes FDA to communicate its disapproval of a warning through such a letter, Justice Thomas reasoned that a CRL is technically not a final agency action and therefore cannot have preemptive effect.

Justice Alito, in a separate opinion concurring in the judgment, which was joined by Justices Roberts and Kavanaugh, agreed with the majority that preemption is a question of law for a judge to decide. But Justice Alito sharply criticized the majority opinion's potentially "misleading" discussion of the law and the facts. Among other things, Justice Alito noted that the majority failed to discuss the implications for preemption of FDA's statutory authority to order safety-related labeling changes under 21 U.S.C. § 355(o)(4)(A), which was enacted in 2007. Justice Alito "assume[s]" that the Third Circuit will consider this issue on remand.

Takeaways for Drug Manufacturers

The ramifications of *Albrecht* are likely to be limited only to branded drug manufacturers, not generic drug manufacturers. In 2011, in *PLIVA v. Mensing*, the Court held that because a generic drug is required to bear the same labeling as its brand name counterpart and because generic drug manufacturers cannot add or strengthen warnings via the CBE process, state failure to warn claims are preempted on the basis of impossibility. Nothing about *Albrecht* changes this analysis.

For branded drug manufacturers, *Albrecht* represents an incremental expansion of the Court's preemption jurisprudence. Although Justice Breyer's majority opinion clarifies and builds upon the prior holding of *Levine*, it nevertheless leaves unanswered questions for lower courts to grapple with in the future. For example, as alluded to by Justice Alito's opinion concurring in the judgment, the significance of FDA's statutory authority to order safety-related labeling changes may be highly relevant to the preemption analysis in certain cases. Under 21 U.S.C. § 355(o)(4)(A), if FDA becomes aware of new information that it determines should be included in the labeling of a drug, FDA "shall" notify the drug manufacturer and initiate a labeling change. In circumstances where FDA learns of information regarding a new risk—whether from the manufacturer, a citizen petition by a third party, or FDA's own analysis—and declines to require a labeling change, the "logical conclusion" according to Justice Alito is that FDA determined that a change was unwarranted. Yet Justice Alito does not address how one would determine when FDA stopped evaluating a potential safety risk and conclusively declined to require a labeling change, suggesting that these would be highly fact-dependent decisions. Justice Breyer's majority opinion does not squarely address whether this type of implicit disapproval could constitute an agency action with the force of law sufficient to have preemptive effect.

Going forward, branded drug manufacturers engaging with FDA regarding new safety information and potential labeling changes should be mindful that informal agency feedback and correspondence (e.g., meeting minutes or emails reflecting an FDA employee's view that a particular warning may not be warranted) are unlikely to be sufficient to have preemptive effect. Where a manufacturer and FDA disagree on a proposed warning, forcing FDA either to approve the warning or reject it via issuance of a CRL may often be the prudent course of action.

If you have any questions about this decision, please contact any member of Ropes & Gray's [FDA regulatory](#) practice or your usual Ropes & Gray advisor.