Newly Acquired Information Can Be Key In Drug Label Cases

By **Daniel Pariser, Anna Thompson and Kaitlyn Schaeffer** (October 31, 2024)

Daniel Pariser

Anna Thompson

Kaitlyn Schaeffer

The question of whether federal law preempts state law claims is often a central issue in product liability cases involving pharmaceutical products.

In the latest chapter in the preemption saga in In re: Fosamax (Alendronate Sodium) Products Liability Litigation, on remand from the U.S. Supreme Court, the U.S. Court of Appeals for the Third Circuit found in September that the defendant had failed to surmount its burden to show by "clear evidence" that the U.S. Food and Drug Administration would have rejected the defendant's proposed changes to the Fosamax label.[1]

Whether rightly or wrongly decided, the case illustrates the challenges and uncertainties faced in meeting the "clear evidence" test for conflict preemption that the Supreme Court first established in Wyeth v. Levine[2] and refined in Merck Sharp & Dohme Corporation v. Albrecht.[3]

But this article does not dwell on the latest Fosamax decision. Rather, we focus on the sometimes-overlooked threshold inquiry that precedes application of the clear evidence test: not whether the FDA would have rejected a label change, but whether newly acquired information would have allowed the defendant to submit a proposed labeling change in the first place.

That initial question — whether newly acquired evidence has been identified — remains a robust, alternative basis for federal preemption in pharmaceutical cases. And, as discussed below, both precedent and sound policy support employing a very different set of proof burdens for addressing the existence of newly acquired information than the clear evidence hurdle.

A Brief Preemption Primer

A series of U.S. Supreme Court cases — Wyeth v. Levine in 2009, PLIVA v. Mensing in 2011, Mutual Pharmaceutical Company v. Bartlett in 2013, and Merck Sharp & Dohme Corp. v. Albrecht in 2019[4] — establish the broad framework for deciding whether a state law claim involving pharmaceuticals is impliedly preempted as conflicting with federal law.

Under that framework, the key question is whether the defendant-manufacturer could have unilaterally made a label change without the FDA's prior approval. If prior approval of the agency is needed for the change, then the claim is preempted.

For brand-name pharmaceutical products, the answer to that question turns on whether the manufacturer could have taken advantage of an FDA regulation creating the "Changes Being Effected" labeling pathway, often shorthanded to CBE — a special type of labeling change that allows manufacturers to unilaterally update drug labels under limited circumstances.[5]

To make a CBE change, a manufacturer must have newly acquired information about the drug's safety.[6] Specifically, the regulation defines "newly acquired information" as "data, analyses, or other information not previously submitted to the Agency ... [that] reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA."[7]

Even under the CBE regulation, the FDA retains the discretion to later reject the proposed labeling change.[8] Changes to the label through the CBE process, moreover, must meet the same level of evidence that would apply if submitted through the conventional prior approval pathway.[9]

This means that for safety-related changes to the warnings section of the label, changes must be based on "reasonable evidence of a causal association" between the drug and the new "clinically significant risk."[10]

Wyeth and Albrecht addressed one route for conflict preemption: showing by clear evidence that the FDA would have rejected a CBE change — for instance, because the agency previously rejected the same change submitted through the prior approval pathway.[11] But that step is only reached if there is newly acquired information meeting the regulatory standard for use of the CBE process in the first place.

Refocusing the Preemption Analysis on the Existence of Newly Acquired Information

With this backdrop, we discuss below three key propositions that should govern how courts adjudicate whether newly acquired information exists to support a CBE change, and accordingly, whether pharmaceutical failure-to-warn claims are preempted.

There should be no doubt that this is a question for the court, and not the jury, to decide. Albrecht establishes as much for the clear evidence step of the inquiry, given the intricate regulatory issues involved, and all of the same reasons strongly suggest that courts should make the threshold newly acquired information decision.[12]

First, the preemption inquiry should not be collapsed into a single step, thereby importing the clear evidence burden into the different question of whether newly acquired evidence exists. For instance, in Hickey v. Hospira, the plaintiffs made that exact argument, asserting that the only relevant question for preemption was whether the FDA would have rejected the labeling change at issue if provided all relevant information.[13]

The U.S. Court of Appeals for the Fifth Circuit rejected the argument, concluding in May of this year that the "availability of the CBE regulation is a threshold issue."[14] In reaching that decision, the Fifth Circuit joined the First, Second, Fourth and Seventh Circuits, which have all held — or at least strongly suggested — that there are two separate steps in the preemption inquiry.[15]

No circuit has held to the contrary. While the Supreme Court has yet to directly address the issue, none of its preemption cases suggests it would disagree with this unanimous view of the courts of appeal.

As the Hickey court explained, the Supreme Court in Wyeth reached the clear evidence test "only after concluding that the CBE regulation was available" to the manufacturer.[16] Likewise, in Albrecht, the Supreme Court reached the clear evidence test only "after the manufacturer asserting preemption conceded" that the CBE regulation was available.[17]

Second, plaintiffs should bear the initial burden of identifying the newly acquired evidence, not the defendant. The courts that have considered this issue largely have endorsed this approach, utilizing a two-step, burden-shifting framework.

Under this framework, the plaintiff must first identify the newly acquired information that he or she believes would have triggered the defendant's obligation to update the label under the CBE regulation. Only if a plaintiff identifies such newly acquired information does the burden shift to the defendant to show that the evidence does not satisfy the regulatory requirements for label changes.[18]

This burden-shifting regime makes good sense. After all, the plaintiff is the master of his or her claim, and is in the best position to identify whatever warning is allegedly needed to render a drug label adequate, and what data or information supported an earlier change.

In contrast, if the burden to identify newly acquired information is placed on defendants, they would have to guess as to what information plaintiffs might rely on to assert a change was warranted — or else preemptively refute any study, data or analysis that could possibly serve as a basis for a labeling change under the CBE regulation. As the U.S. District Court for the Western District of Missouri aptly observed in its 2020 decision in Ridings v. Maurice, it is "not the usual practice to ask a party to prove a negative."[19]

Third, courts should require plaintiffs to identify the newly acquired information through expert testimony. On their merits, failure-to-warn claims involving pharmaceuticals raise complex scientific, medical and regulatory issues that require expert evidence. Preemption should be no different.

Judges, just like juries, should not be forced to find facts, as Albrecht requires, concerning complex scientific and regulatory matters on a bare record without help from an expert. This point has gone largely untested to date. But at least one court has agreed.

In In re: Incretin-Based Therapies Product Liability Litigation, the U.S. District Court for the Southern District of California concluded in 2021 that the animal study the plaintiffs identified as newly acquired information did not constitute newly acquired information, because the "[p]laintiffs [did] not explain how this data constitutes reasonable evidence of a causal association. There [was] no expert opinion that these observations provide reasonable evidence of a causal link."[20]

Burdens of proof can make all of the difference in the outcome of any dispute, and preemption is no exception. Parties litigating federal preemption issues should be particularly attentive to how they frame their arguments — and importantly, what burden of proof properly applies to those arguments — in this complex and ever-evolving area of law.

Daniel S. Pariser is a partner, Anna K. Thompson is counsel and Kaitlyn Schaeffer is a senior associate at Arnold & Porter Kaye Scholer LLP.

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affiliates. This article is for general information purposes and is not intended to be and should not be taken as legal advice.

[1] In re: Fosamax (Alendronate Sodium) Prod. Liab. Litig., --- F.4th ---, 2024 WL 4247311, at *26 (3d Cir. Sept. 20, 2024).

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

[3] Merck Sharp & Dohme Corp. v. Albrecht, 587 U.S. 299 (2019).

[4] Wyeth, 555 U.S. 555; PLIVA Inc. v. Mensing, 564 U.S. 604 (2011); Mutual Pharm. Co. v. Bartlett, 570 U.S. 472 (2013); Albrecht, 587 U.S. 299.

[5] 21 C.F.R. § 314.70(c).

[6] 21 C.F.R. § 314.70(c)(6)(iii).

[7] 21 C.F.R. § 314.3.

[8] 21 C.F.R. § 314.70(c)(7).

[9] 21 C.F.R. §§ 314.70(b)(2)(v)(C), 314.70(c)(6)(iii).

[10] 21 C.F.R. §§ 201.57(c)(6)(i), 314.70(c)(6)(iii).

[11] Albrecht, 587 U.S. at 302-03 (citing Wyeth, 555 U.S. at 571).

[12] Id. at 316-18.

[13] Hickey v. Hospira, 102 F.4th 748, 753-54 (5th Cir. 2024); see also, e.g., Estep v. Boehringer Ingelheim Pharms. Inc., 2020 WL 5815927, at *4 (Conn. Super. Ct. Aug. 25, 2020); Javens v. GE Healthcare Inc., 2020 WL 2783581, at *5 (D. Del. May 29, 2020).

[14] Hickey, 102 F.4th at 754.

[15] Id. at 754 & n.4 (citing In re: Celexa & Lexapro Mktg. & Sales Pracs. Litig., 779 F.3d 34, 41 (1st Cir. 2015); Gibbons v. Bristol-Myers Squibb Co., 919 F.3d 699, 708 (2d Cir. 2019); Knight v. Boehringer Ingelheim Pharms. Inc., 984 F.3d 329, 338-41 (4th Cir. 2021); Dolin v. GlaxoSmithKline LLC, 901 F.3d 803, 815 (7th Cir. 2018)).

[16] Id. at 754.

[17] Id.

[18] See, e.g., Gibbons, 919 F.3d at 708; Lyons v. Boehringer Ingelheim Pharms. Inc., 491 F. Supp. 3d 1350, 1363 (N.D. Ga. 2020); Estep, 2020 WL 5815927, at *4; McGee v. Novartis Pharms. Corp., 2022 WL 17454521, at *2 (D. Colo. Dec. 6, 2022); McGrath v. Bayer HealthCare Pharms. Inc., 393 F. Supp. 3d 161, 167 (E.D.N.Y. 2019); Neto v. Bristol-Myers Squibb, 2023 WL 3689533, at *6-7 (D. Conn. May 26, 2023).

[19] Ridings v. Maurice, 444 F. Supp. 3d 973, 980 (W.D. Mo. 2020); Silverstein v. Boehringer Ingelheim Pharms. Inc., 2020 WL 6110909, at *12 (S.D. Fla. Oct. 7, 2020) ("Plaintiffs should bear the initial burden of identifying the specific information that they

assert [defendant] acquired after the FDA approved Pradaxa and should have used it to modify the Pradaxa label. Once Plaintiff points to this specific information, [defendant] bears the burden of proving that it does not meet the definition of 'newly acquired information' under the CBE regulation. This allocation of burden avoids making [defendant] prove a negative — that it acquired no new information after Pradaxa was approved that would have justified a CBE modification.").

[20] In re: Incretin-Based Therapies Product Liability Litigation, 524 F. Supp. 3d 1007, 1026 (S.D. Cal. 2021).