Hickey v. Hospira, Inc.
102 F.4th 748 (5th Cir. 2024)

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WHY IT MADE THE LIST

Hickey v. Hospira makes the list of "top food and drug cases" in 2024 because the Fifth Circuit recognized that implied preemption applies with equal force to drugs entering the market under the Section 505(b)(2) process as would apply to those coming to market under the more onerous New Drug Application process of Section 505(b)(1).

It is also important as a strong circuit court decision in the library of preemption cases relating to failure to warn cases brought against prescription drugs and the oft-used arguments in failure to warn cases relating to the "Changes-Being-Effected" (or "CBE") method for labeling changes. The CBE arguments are often presented as a way to claim that implied preemption would not have prevented the sought after label change being litigated in a failure to warn context. The *Hickey* case arose from the long running Taxotere MDL and in it, the Fifth Circuit reviewed a denial of summary judgment and outlines the basis for why preemption would prevent liability for failure to warn. Although it ultimately remanded the case for the district court to review one item, the case itself lays out a straightforward analysis as to why preemption would apply where there was no basis to make label changes outside of FDA's specific approval.

DISCUSSION

Factual Background

This case arose from an MDL relating to the use of a version of drug to treat breast cancer. The branded version, called Taxotere, was manufactured by Sanofi US Service Inc. and Sanofi-Aventis U.S. LLC ("Sanofi") and the generic form is referred to as docetaxel. The defendants in this case were Hospira, Inc. and Hospira Worldwide, LLC ("Hospira") and Accord Healthcare, Inc. ("Accord") who received approval (as outlined more specifically below) from FDA upon expiration of Sanofi's patent in 2011.[1] The labeling included identical warnings about alopecia (hair loss) as an adverse reaction and instructed doctors to explain that it was one of the drug's most common side effects. The label did not say whether the loss could be permanent.

However, in March 2015, a patient advocacy group raised the issue with FDA and after the data was reviewed, Sanofi was instructed to update its label to indicate cases

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[1] Hickey v. Hospira, Inc., 102 F.4th 748, 751–52 (5th Cir. 2024).

of permanent hair loss had been reported. FDA did not conclude there was a causal connection. Accord updated its label in 2016 and Hospira did the same in 2017.[2]

Nonetheless, Plaintiffs in this case were alleging that the drug was causing permanent, not just temporary hair loss—alopecia (a condition referred to as permanent chemotherapy-induced alopecia (PCIA)). Plaintiffs were claiming the warnings were inadequate on this point.

Background of Implied Preemption for Prescription Drugs

Regulatory Pathway to Market for Prescription Drugs and Labeling Requirements

The pathway to market for prescription drugs takes three basic routes. Each of these is summarized by the court in *Hickey*.[3] Specifically, the method for approval of a brand-new drug is contained in § 505(b)(l) of the Federal Food, Drug, and Cosmetic Act (FDCA).[4] This section requires manufacturers to file a New Drug Application (NDA), which includes, inter alia, "full reports of investigations which have been made to show whether such drug is safe for use and whether such drug is effective in use."[5] The first drug of a specific kind to be approved under § 505(b)(l) is called the Reference Listed Drug (RLD). Manufacturers who want to sell the same drug or a drug that is similar enough "may use two abbreviated pathways to obtain FDA approval with less burden and expense."[6]

One pathway is § 505(j), which permits the manufacturer of a generic drug to submit an Abbreviated New Drug Application (ANDA).[7] With limited exceptions, the generic drug must in nearly all respects be identical to the RLD. Because a § 505(j) drug is the same as the RLD, the manufacturer may rely on the safety and efficacy data submitted in the RLD's NDA.[8]

The final path—the one at issue in *Hickey*—is § 505(b)(2), "which is available for drugs that differ from the RLD in ways that are slight enough for the manufacturer to still rely on the RLD's safety and efficacy data."[9] The application must provide only that information needed to support the modification(s) of the listed drug.[10] This pathway is often referred to informally as the "paper NDA" since it relies almost entirely on the clinical data submitted by the RLD. Unlike the generic drugs, § 505(b)(2) drugs are *not required* to use the exact same labeling as the RLD.[11] It is this difference that impacts the way the preemption argument is considered and one of the keys to the decision's significance.

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2 *Id.* at 752.

3 *Id.* at 750–51.

4 *Id.*; *see* 21 U.S.C. § 355(b)(l).

5 *Id.*; *see* 21 U.S.C. § 355(b)(l)(A)(i).

6 *Hickey* at __.

7 *Id.*; *see* 21 U.S.C. § 355(j).

8 *Id.*

9 *Hickey*, 102 F.4th at 751; *see* 21 U.S.C. § 355(b)(2).

10 *See* 21 C.F.R. § 314.54(a).

11 *Id.*

As with the RLD, FDA approves the exact text that will be included in the drug's labeling.[12] Of note, a manufacturer may only change a drug label after FDA approves a supplemental application. But in some circumstances, the CBE regulation allows manufacturers to implement a labeling change before obtaining FDA approval.[13]

The CBE regulation, however, is available only to "'add or strengthen . . . warning' where there is 'newly acquired information' about the 'evidence of a causal association' between the drug and a risk of harm."[14] The regulation defines "[n]ewly acquired information" as "data, analyses, or other information not previously submitted to the Agency," including but not limited to, "data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA."[15] Again, it is this CBE tool that is the focus of decisions involving RLD or "paper NDA" preemption.

Implied Preemption for Label Claims and impact of CBE

The argument in *Hickey* was whether defendants should have made label changes under the CBE process or, as defendants argued, the purported data proposed by plaintiffs did not meet the standards of revealing "risks of a different type or greater severity or frequency." The issue of first impression of any circuit court was how to evaluate newly acquired information following approval of the 505(b)(2) product. The Fifth Circuit agreed, stating that where the risks do not meet such standard, impossibility preemption would be established.[16] The court further agreed that the district court erred by failing to enforce such requirement.[17]

The factual background is important in this type of preemption case because the focus of the court's analysis will be on when approval was granted, what the company and FDA knew at that time about the particular risk at issue, and whether a CBE could have been implemented. In *Hickey*, the Fifth Circuit took pains to go through the available pre-approval scientific literature, the post-approval scientific literature, and defendants' adverse event reports. The court concluded that these particular defendants did not have "newly acquired information showing that PCIA occurred with any greater severity or frequency than before the approval of their drugs . . . ." The court did remand due to one medical abstract that would need analysis to see if it would be sufficient to change that conclusion, but otherwise ordered that these defendants would not be liable to the particular plaintiffs relating to failure to warn claims.

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[12] *Hickey*, 102 F.4th at 751 (citing Wyeth v. Levine, 555 U.S. 555, 568, (2009)) (citing 21 U.S.C. § 355)).

[13] *See* 21 C.F.R. § 314.70(c)(6).

[14] *Hickey*, 102 F.4th at 751 ((citing Merck Sharp & Dahme Corp. v. Albrecht, 587 U.S. 299, 304–05, 139 S.Ct. 1668, 203 L.Ed.2d 822 (2019)) (ellipses in original) (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A)).

[15] *Id.* (citing 21 C.F.R. § 314.3(b)).

[16] *Hickey*, 102 F.4th at 756–57.

[17] *Id.* at 755.

IMPACT

This case is important because it recognizes and outlines the way in which a prescription drug product approved under the "paper NDA" process is treated for purposes of implied preemption and the failure to warn claims around the use of CBE. While clearly specific to the timeline and data relating to risks, the importance of this decision is the focus on what would be required for label change and the applicability of preemption where the proposed warning does not present newly acquired information under the statutory definition.