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BLOG

Fifth Circuit Clarifies Impossibility Preemption Defense for Drug Manufacturers Facing State Law Failure-to-Warn Claims

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As part of the wider multidistrict litigation over the breast cancer drug docetaxel (branded Taxotere), on May 24, 2024, the Fifth Circuit ruled that Food and Drug Administration (FDA) labeling requirements preempt certain state law failure-to-warn theories. *Hickey v. Hospira*, 102 F.4th 748 (5th Cir. 2024).

Before selling drugs in the United States, brand drug manufacturers must obtain FDA approval, which typically requires significant cost and testing. The first drug of a specific kind is called the Reference List Drug, and, thereafter, manufacturers who want to prepare a similar, generic version may use an abbreviated pathway to obtain FDA approval with less burden and expense. *Id.* at 751. One path, at issue in *Hickey*, is available under 21 U.S.C. § 355(b)(2) (a/k/a/ § 505(b)(2)), which allows generic drug manufacturers to rely on the Reference List Drug's safety and efficacy data for a new product if it differs only slightly from the Reference List Drug. *Id.* Drugs that receive abbreviated FDA approval do not need to use the exact label language as the Reference List Drug, though the FDA must still approve the label text. *Id.* Generally, drug labels may be changed only after a manufacturer files and the FDA approves a supplemental application; however, one regulation—known as the changes-being-effected (CBE) regulation—allows manufacturers to update their label at the same time they file their supplemental application for a label change. Specifically, the CBE regulation permits a manufacturer "to add or strengthen a . . . warning where there is 'newly acquired information' about the 'evidence of a casual association' between the drug and a risk of harm." 21 C.F.R. § 314.70(c)(6)(iii)(A)); *Hickey*, 102 F.4th at 751 (citations omitted) (cleaned up). "Newly acquired information" is information that "reveal[s] risks of a different type or greater severity or frequency than previously included in submissions to FDA." *See* 21 C.F.R. § 314.3(b).

In *Hickey*, a set of plaintiffs sued generic docetaxel manufacturers, Accord and Hospira, alleging that they violated state law by failing to warn that their drugs could cause permanent chemotherapy-induced alopecia (PCIA). *Id.* at 752. The manufacturers had previously sought and received approval under § 505(b)(2) to sell docetaxel, relying on the FDA's findings of safety and effectiveness from the Reference List Drug. *Id.* The drug labels warned about alopecia as a side effect but did not state that the hair loss could be permanent. *Id.* In 2015, after concerns were raised about whether docetaxel caused PCIA, the FDA instructed the Reference List Drug manufacturer to update its label to state that cases of permanent alopecia had been reported (although without an affirmative statement regarding causation). *Id.* Accord and Hospira made similar changes via the CBE regulation. *Id.* The FDA subsequently approved the updates, noting that the "simple statement that permanent cases have been reported is all that can reliably be said given the tremendous limitations of the data." *Id.*

At the district court, Accord and Hospira moved for summary judgment on the basis of "impossibility" preemption, arguing that it would have been impossible to comply with their alleged state law duties (i.e., warning about a causal relationship) because they did not have "newly acquired information" as required to unilaterally update their labels via the CBE regulation. *Id.* at 753. The district court rejected this position, concluding that the generic manufacturers could have pointed to any of the data supporting a potential causal relationship between docetaxel and PCIA—and thus supporting a labeling change via the CBE regulation. *Id.* at 755–56.

The Fifth Circuit disagreed. To meet the requirements of "newly acquired information" under the CBE regulation, the court clarified, the data must at least "reveal risks of a different type or greater severity or frequency" than the risks described in the pre-approval scientific literature available to the defendant-manufacturers. *Id.* at 756. The district court erred in failing to recognize and enforce this principle in the context of its preemption analysis. *See id.* The Fifth Circuit then completed the analysis on the record before it, walking through the pre-approval and post-approval scientific literature to see if anything revealed met the definition of "newly acquired information." *Id.* at 757–59. It ultimately found that none of the post-approval scientific literature revealed a significantly greater risk of PCIA than the pre-approval scientific literature (and thus constituted "newly acquired information"), with the potential exception of one study, which specific issue was remanded to the district court for further review. *Id* at 758. Among other points of emphasis, the court noted that it was not enough that post-approval literature revealed instances of docetaxel-induced PCIA—it must reveal "risks of a different type or greater severity or frequency," and the literature already indicated a 6–7% incidence rate of PCIA among docetaxel patients before FDA approval. *Id.* at 759. As a result, the manufacturers did not have newly acquired information showing PCIA occurred with greater severity or frequency than before, and they were not liable to plaintiffs for failing to update their labels via a CBE regulation that was legally unavailable to them. *Id.*

The Fifth Circuit's decision in *Hickey* provides helpful guidance on the contours of impossibility preemption and specifically on what is considered "newly acquired information" under the CBE regulation, arming drug manufacturers with another defense when fighting state law failure-to-warn claims.

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