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Disagreeing with FDA Approval Decisions: Practical Consequences of the First Circuit's Celexa Decision

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Since 2009, plaintiffs in pharmaceutical product liability suits have had a predictable and largely successful three-word response to defendants' preemption arguments: *Wyeth versus Levine.* 555 U.S. 555 (2009). The Supreme Court's 2011 and 2013 generic-drug preemption decisions forced generic-drug plaintiffs back on their heels, but plaintiffs' *Wyeth v. Levine* mantra continued forcefully in brand-name drug litigation. A recent First Circuit decision could change that.

Earlier this year, the First Circuit held that *Wyeth v. Levine*'s reach has its limits, even in brand-name drug litigation. The FDA alone has the power to approve a drug to enter the market, and the First Circuit found that state law cannot impose liability for what is essentially disagreement with the FDA's finding of safety and efficacy when it exercises its drug approval power. This article examines the consequences of the First Circuit's recognition of the FDA's exclusive power over the approval process and approval decisions.

The First Circuit's Decision

The First Circuit's decision came on appeal of the dismissal of a putative class action from multidistrict litigation involving Celexa and Lexapro marketing claims. *In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34 (1st Cir. 2015). The plaintiffs alleged that Lexapro's manufacturer violated California's consumer protection statutes; according to the plaintiffs, the drug's label was misleading and inadequate in failing to state that Lexapro's efficacy is marginal for treating major depressive disorder in adolescents. *Id.* at 37-38. The plaintiffs also criticized the FDA's approval of the drug for that indication, arguing that the drug lacked sufficient efficacy data for treatment of adolescent depression. *Id.* at 38.

The First Circuit began by recognizing that the period leading up to FDA approval is distinct from the post-approval period—a difference that played a central role in the court's preemption analysis. As the court explained, federal statutes and regulations give the FDA exclusive authority over drug approvals, and the FDA's approval process is "onerous and lengthy." *Id.* at 35 (*quoting Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2471 (2013)). The FDA must make safety and efficacy determinations as part of approval, and the agency "is required to exercise its scientific judgment to determine" that the manufacturer's data and other information satisfy federal requirements. *Id.* at 36 (*quoting* 21 C.F.R. § 314.105(c)). As part of approval, the FDA also must find that the label is not "false or misleading in any particular." 21 U.S.C. § 355(d); 21 C.F.R. § 314.125(b)(6). Federal law thus vests the FDA with both power and discretion to interpret the federal safety and efficacy standards in the context of a specific drug application.

The post-approval landscape is different. After approval, the First Circuit recognized, the federal regulatory scheme gives brand-name manufacturers power to adjust labeling as new information becomes known. The FDA's Changes Being Effected (CBE) procedure allows a manufacturer to implement a change without waiting for the FDA's approval, but it is available for label changes only if based on "newly acquired information." *In re Celexa*, 779 F.3d at 37 (*citing* 21 C.F.R. § 314.70(c)(6)(iii)). Put differently, if the change is premised on information the FDA already reviewed, the manufacturer cannot unilaterally implement that change and instead must first obtain FDA approval.

The First Circuit recognized that once a manufacturer asserts an impossibility-preemption defense, that ability to unilaterally implement a change required by state law becomes determinative. The court noted that *Wyeth* rejected preemption where the manufacturer had a "federally sanctioned ability to improve the label under the CBE regulation." *Id.* at 40 (*citing Wyeth*, 555 U.S. at 581). And the court explained that *PLIVA, Inc. v. Mensing*, which found preemption where the CBE procedure was not available, "limited *Wyeth* to situations in which the drug manufacturer can, 'of its own volition, . . . strengthen its label in compliance with its state tort duty.'" *Id*. at 41 (*citing PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2581 (2011)). The court therefore found that availability of the CBE procedure is "a necessary step in defeating [the defendant's] preemption defense." *Id.*

Explaining that the legal distinction between prior approval and CBE changes "makes some pragmatic sense," the court grounded its reasoning in the FDA's authority over the drug approval process:

> CBE changes rest on the existence of "newly acquired information." A state law duty to initiate such a change is therefore not by its nature a second guess of an FDA judgment. To the extent that the underlying policy issue is one of who decides whether and how a drug can be marketed, the line so drawn lets the FDA be the exclusive judge of safety and efficacy based on information available at the commencement of marketing, while allowing the states to reach contrary conclusions when new information not considered by the FDA develops.

Id. (citations omitted). The court found that the preemption framework thus reflects the power Congress granted the FDA: "By hinging preemption on the availability of that procedure in a particular case, *Wyeth* effectively reserves the launch of new drugs to the expertise of the FDA, but then preserves a wide scope for the states in requiring manufacturers to respond to information not considered by the FDA." *Id.*

On the facts of the case, the court determined that the CBE procedure was unavailable for the change the plaintiffs sought because the plaintiffs' claims relied on information known to the FDA at the time of approval. *Id.* at 43. Their claims were therefore preempted. *Id.*

***Practical Applications of* Celexa**

The First Circuit's recognition that drug approval decisions and judgments rest in the FDA's hands alone and are not appropriate subjects of state-law claims could implicate a number of scenarios in brand-name drug litigation. In its most straightforward application, plaintiffs may no longer be able to advance a claim that a drug should have never been approved or that its design was faulty from the outset. *Cf. Wimbush v. Wyeth*, 619 F.3d 632, 642-45 (6th Cir. 2010) (pre-*Celexa*, allowing a plaintiff to sue for negligence "in bringing the drug to market"). And even where plaintiffs do not explicitly frame a claim in those terms, an examination of the key evidence could reveal that their argument is, in essence, that the manufacturer should have acted differently based on the information available prior to approval. Under *Celexa*, such a claim no longer appears actionable under state law.

In addition to affirmative claims, plaintiffs in recent years have sharpened their attacks on a drug's initially approved design to fend off preemption challenges. As a result of the Supreme Court's *Mensing* decision in 2011, defendants have begun to argue—and several courts have ruled—that preemption applies even in brand-name drug litigation where the manufacturer

is not able to change its drug or labeling without prior FDA approval. *See, e.g., Thompson v. Allergan USA, Inc.*, 993 F. Supp. 2d 1007, 1014 (E.D. Mo. 2014) (change to volume of drug in package would require prior FDA approval). The plaintiffs' bar has responded by arguing that even if a change to an existing product cannot be accomplished unilaterally, the defendant should have designed or labeled the product differently from the outset, before it received FDA approval to market the drug. *See, e.g., Trahan v. Sandoz, Inc.*, No. 3:13-cv-350, 2015 WL 2365502, at *6 (M.D. Fla. Mar. 26, 2015); *Acree v. Watson Pharms., Inc.*, No. 10-c-7812, 2012 WL 5306296, at *6 (N.D. Ill. Oct. 26, 2012). Under *Celexa*, that argument should likewise be barred.

Additionally, a defendant may have additional opportunities to utilize the *Celexa* reasoning in the *post*-approval period, where a particular drug's regulatory history includes later, interim drug approvals. In *Celexa* itself the approval decision that formed the basis for the First Circuit's holding was not the drug's initial approval but rather the a subsequent approval for a new indication.

Interim approvals of a drug combined with new drugs may present the same scenario. Certain drugs are marketed both individually and in a pill combined with another drug. When the FDA approves these "combination drugs," it must conduct a comprehensive review of each component drug and its labeling even though the component drugs are already on the market individually. Such a case may therefore present the same argument as in *Celexa*: the FDA's decisions about data available during a combination-drug approval are reserved "to the expertise of the FDA" and those decisions, under *Celexa*, should not come under fire in tort suits involving the individual or combination drugs. *In re Celexa*, 779 F.3d at 41. That argument may be particularly powerful if the FDA reviewed data on the same adverse event at issue in a lawsuit before approving the combination drug.

Finally, in addition to emphasizing the effect of FDA approval, *Celexa* reinforces that *Mensing*'s preemption framework applies outside of the generic drug context. Courts have already applied *Mensing* in other types of litigation. *See, e.g., Thompson*, 993 F. Supp. 2d at 1014 (brand-name medicated eye drops); *Horseman's Benevolent & Protective Assoc.-Ohio Div., Inc.*, 666 F.3d 997 (6th Cir. 2012) (off-track gambling restrictions on horse racing). But the First Circuit is the first appellate court to apply that test explicitly to brand-name drugs, recognizing that the CBE procedure is not available for all changes to brand-name drug labels. *In re Celexa*, 779 F.3d at 41-43; *see also, e.g., Dopson-Troutt v. Novartis Pharm. Corp.*, 975 F. Supp. 2d 1209 (M.D. Fla. 2013) (changes to boxed warning require prior FDA approval). And it makes clear that courts evaluating claims implicating post-approval changes to a drug—brand or generic—or its label must determine whether the defendant could have made the change without first obtaining the FDA's approval. *In re Celexa*, 779 F.3d at 41 (plaintiffs' showing that the CBE procedure was available is "a necessary step in defeating" the drug manufacturer's preemption defense).

Celexa, in recognizing the FDA's exclusive authority over drug approvals, may prove to be a powerful tool for brand-name drug manufacturers. Its rationale can limit *Wyeth v. Levine*'s impact in certain cases and may also be persuasive in defending against plaintiffs' argument that a drug was too dangerous, or too dangerous as labeled, to have entered the market—familiar themes in pharmaceutical product liability litigation.

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