WARNING: FEDERAL PREEMPTION MAY BE GETTING WORSE

By Dustin B. Herman

The Supreme Court's preemption jurisprudence is already bad enough, but things might get a lot worse. As it currently stands, generally speaking, lawsuits involving generic drugs are preempted, but suits involving brand-name drugs are not. The Supreme Court is currently (at the time of this writing) deciding whether to accept cert on the Fosamax litigation. If the Court accepts cert, it will be revisiting its landmark decision in *Wyeth v. Levine*, 555 U.S. 555 (2009) – which held suits against brand-name drug manufacturers were generally *not* preempted.

Even if the Court denies cert in this case (there is no circuit court split yet), it will certainly be revisiting *Wyeth* in the not-so-distant future. This is something to pay attention to because the Supreme Court could significantly increase the breadth of its "impossibility" conflict preemption as it pertains to brand-name drugs when it has the opportunity to revisit *Wyeth*.

Wyeth v. Levine (2009)

The Court in *Wyeth* held that because brand-name drug companies can unilaterally change their labels *without obtaining prior FDA approval*, which they can do through the "changes being effected" ("CBE") process,[1] it is possible (i.e., not impossible) for those companies to comply with state laws requiring stronger warnings without violating federal law. Of course, a drug company would still need to obtain FDA approval after making a CBE change, but "absent clear evidence that the FDA would not have approved a change to [the drug's] label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements." *Wyeth*, 555 U.S. at 571. Thus, absent this "clear evidence" exception, state law failure-to-warn claims against brand-name drug manufacturers are not preempted by federal law.

PLIVA, Inc. v. Mensing (2011)

On the other hand, warning labels for *generic* drugs must mirror the corresponding brand-name drug label, and, under the current FDA regulations, a generic drug manufacturer cannot independently change its warning label; it must obtain prior FDA approval to do so.[2] Under this legal framework, the Court in *PLIVA, Inc. v. Mensing*, 564

[1] See 21 C.F.R. §314.70(c)(6)(iii)(A).

[2] Furthermore, generic drug manufacturers cannot send out "Dear Doctor" letters with additional warnings because such letters are considered part of the label. "Brochures, booklets, mailing pieces, detailing pieces [etc., etc.,] . . . for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer, or distributor are hereby determined to be labeling as defined in section 201(m) of the act." 21 C.F.R. §202.1(l)(2). In

U.S. 604 (2011) held that because generic drug manufacturers "have an ongoing federal duty of 'sameness'" with respect to the corresponding brand-name labels, it was impossible for a generic drug manufacturer to comply with both a state tort law duty to have a stronger warning label and its federal duty to have the exact same label as the corresponding brand-name drug (that is, state law required what federal law prohibited). *Mensing*, 564 U.S. at 615-18. Thus, state law failure-to-warn claims (and design-defect claims that turn on the adequacy of the warning[3]) brought against generic drug manufacturers are preempted by federal law.

In her dissenting opinion in *Mensing,* Justice Sotomayor said, wait a minute, the generic drug company didn't even fulfill its federal obligation to reach out to the FDA and propose a label change when it became aware of safety problems with its warning label, so it wasn't necessarily "impossible" to comply with both federal law and state law, it's just that the company didn't even try. *Mensing*, 564 U.S. at 636-37. "Accordingly, as in *Wyeth,* I would require the Manufacturers to show that the FDA would not have approved a proposed label change." *Id*. at 637 (arguing that there should be no preemption unless the manufacturers met the "clear evidence" exception set forth in *Wyeth*).

Justice Thomas, writing for the majority, countered by focusing on what state law required: "Although requesting FDA assistance would have satisfied the Manufacturer's federal duty, it would not have satisfied their state tort-law duty to provide adequate labeling. State law demanded a safer label; it did not instruct the Manufacturers to communicate with the FDA about the possibility of a safer label." *Mensing*, 564 U.S. at 619. "The question for 'impossibility' is whether the private party could independently do under federal law what state law requires of it." *Id.* at 620.

Reading *Wyeth* and *Mensing* together, the bottom line is that if a drug company can unilaterally – that is, independently – change a warning label *without obtaining prior* FDA approval (even if subsequent approval is required), failure-to-warn claims are *not* preempted; but if prior FDA approval is necessary, then such claims are preempted. *Wyeth's* exception to this rule applies in cases where there is "clear evidence" that the FDA would have rejected the warning that plaintiffs claim was required by state law. But the Court gave no further instruction on what it meant by "clear evidence" or who gets to decide what counts as clear evidence (judge or jury). The Fosamax case brings these issues to a head.

In re Fosamax

Fosamax is a brand-name drug used to treat osteoporosis and is in the class of drugs known as bisphosphonates. "Between 1995 and 2010, scores of case studies, reports,

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essence, generic drug manufacturers are prohibited from giving any warnings to doctors or to the public that have not already been given by the brand-name manufacturer.

[3] See *Mutual Pharma., Inc., v. Bartlett*, 133 S.Ct. 2466 (2013).

and articles were published documenting possible connections between long-term bisphosphonate use and atypical femoral fractures." *In re Fosamax (Alendronate Sodium) Products Liab. Litigation*, 852 F.3d 268, 275 (3d Cir. 2017).

In 2008, Merck, the manufacturer of Fosamax, attempted to update its Fosamax label to warn about atypical femur fractures. Importantly, even though it could have, Merck chose not unilaterally change the label through the CBE process. Instead, it chose to seek prior FDA approval of the proposed change. The proposed change, however, often referred to atypical femur fractures as "stress fractures." In May 2009, the FDA rejected the labeling change, stating "'stress fractures' may not be clearly related to the atypical subtrochanteric [femur] fractures that have been reported in the literature." *In re Fosamax*, 852 F.3d at 277 (quoting the FDA's May 2009 Complete Response Letter).[4] Merck chose not to propose a new label without the reference to stress fractures.

In October 2010, after receiving a report from an independent expert task force, the FDA required Merck to include a warning about atypical femur fractures on its Fosamax label. Merck again requested that the warning include references to "stress fractures," but the FDA, again, rejected such proposed language because, "the term 'stress fracture' represents a minor fracture and this would contradict the seriousness of the atypical femoral fractures associated with bisphosphonate use." *In re Fosamax*, at 279 (quoting FDA's response letter to Merck).

Judge Pisano, the judge presiding over the Fosamax MDL, found that the FDA rejection of the proposed label change in May 2009, "constitutes clear evidence that the FDA would not have approved a stronger warning prior to Mrs. Glynn's fracture." *In re Fosamax (Alendronate Sodium) Products Liab. Litigation*, 951 F.Supp.2d 695, 705 (D.N.J. 2013), *vacated*, 852 F.3d 268 (3d Cir. 2017). Accordingly, Judge Pisano held Mrs. Glynn's claims were preempted under the exception in *Wyeth*, and later held all the Fosamax suits that involved femur fractures occurring prior to September 14, 2010 (the date the independent expert task force report was released) were also preempted.

3rd Circuit Holds "Clear Evidence" is a Jury Question

The 3rd Circuit reversed, holding that when the Court said "clear evidence" in *Wyeth,* it was referring to the evidentiary standard of "clear and convincing" evidence, and that the question of whether there was "clear evidence" that the FDA would have rejected a proposed label change that did not include the references to stress fractures – was a question for the jury.

> The basic question that *Wyeth* poses to a factfinder—in a counterfactual setting, what do you think the FDA would have done?—requires an

[4] The proposed label change also included a change to the adverse events section related to atypical femur fractures, which the FDA approved.

> evaluative inference about human behavior based on correspondence, agency statements, contemporaneous medical literature, the requirements of the CBE regulation, and whatever intuitions the factfinder may have about administrative inertia and agency decision-making processes. This assessment is certainly complex, but it does not require any special legal competence or training.
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> We therefore conclude that the question of whether the FDA would have approved a plaintiff's proposed warning is a question of fact for the jury. A state-law failure-to-warn claim will only be preempted if a jury concludes it is highly probable that the FDA would not have approved a label change.

In re Fosamax, 852 F.3d 268, 293 (3d Cir. 2017).

Despite there being no circuit court split, Merck has appealed this case to the Supreme Court and asked the Court to weigh in on whether the "clear evidence" exception under *Wyeth* is a question for the judge or jury. Tangled up with that question is whether the rejection of the proposed warning label in 2009 provides clear evidence that the FDA would have rejected a label that did not include references to stress fractures. Merck had a strong incentive to downplay the risks of atypical femur fractures, and referring to them as stress fractures was a good way to do it. Indeed, the FDA said such a comparison would "contradict the seriousness of the atypical femoral fractures associated with bisphosphonate use." *In re Fosamax*, 852 F.3d at 279 (quoting FDA's response letter to Merck). Nevertheless, Merck argues that the FDA's May 2009 letter represented the FDA's conclusion that *any* additional warning regarding atypical femur fractures was unwarranted.

Buckman Co. v. Plaintiffs' Legal Comm. (2001)

Another underlying issue is whether Merck, in fact, provided the FDA all of the relevant data regarding the relationship between atypical femur fractures and Fosamax use. If Merck withheld evidence in its possession from the FDA, then surely claims against Merck could not be preempted, right? Not so fast. Merck argues, as many defendants have in the past, that *Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341 (2001) bars a plaintiff from making any arguments that are premised upon the defendant violating the FDA's reporting requirements. *Buckman* was a case in which the manufacturer had gone bankrupt and the plaintiffs went after a consulting company that had helped the manufacturer get the product past the FDA. Thus, the only conduct at issue was the communications with the FDA. *Buckman* held that claims based "solely" on fraud on the FDA were preempted. *Buckman*, 531 U.S. at 352–53.[5]

[5] "[I]t is clear that the [*Medtronicv. Lohr*] claims arose from the manufacturer's alleged failure to use reasonable care in the production of the product, not solely from the violation of FDCA requirements. In the present case, however, the fraud claims exist solely by virtue of the FDCA disclosure requirements." *Buckman*, 531 U.S. at 352–53.

But the Court in *Buckman* never held that evidence of a manufacturing defendant misleading the FDA or withholding information from the FDA is somehow completely off limits. Nevertheless, courts constantly cite the "policy underlying" *Buckman* for the proposition that a plaintiff is barred from making any argument that the defendant withheld relevant information from the FDA; some courts have even limited discovery related to such allegations. See *In re Incretin-Based Therapies Products Liab. Litigation*, 142 F.Supp.3d 1108, 1131 (S.D.Cal. 2015), *vacated*, 721 Fed.Appx. 580 (9th Cir. 2017) (holding that the district court erred in limiting discovery based on *Buckman*).

Is the FDA a Hockey Goalie?

In short, plaintiffs argue that the FDA rejected Merck's proposed label in May 2009 because it included misleading language regarding stress fractures, and that the FDA would have approved a warning without a reference to stress fractures – just as it did in October 2010 (or, at a minimum, there is not "clear evidence" the FDA would have rejected such a warning). Thus, the plaintiffs' claims are not preempted, and Merck can be taken to trial for its failure-to-warn about the dangers of its drug.

Merck argues, no, in May 2009 the FDA was rejecting *any* additional warnings about atypical femur fractures, and it wasn't until October 2010 that the FDA was ready to allow such a warning. That is, in May 2009, the FDA was wrong, and it didn't get it right until October 2010 – and, under *Buckman*, it doesn't matter whether any relevant information was withheld from the FDA during that timeframe.

Merck's position comes down to this: A drug company is entitled to immunity under the doctrine of federal preemption whenever the FDA is wrong – or is lagging behind – or doesn't have all the information – or has been intentionally misled. In essence, Merck (and the rest of the pharmaceutical industry) wants to turn the FDA into a hockey goalie, such that just getting a drug past the FDA – by any means necessary – will immunize a pharmaceutical company from liability.

In revisiting *Wyeth*, the Court may address one or all of these issues, but the Court is unlikely to leave the 3rd Circuit's opinion intact. Stay tuned folks; there may be big changes ahead.