4-30-2014

In re: Fosamax Products

PRECEDENTIAL

UNITED STATES COURT OF APPEALS
FOR THE THIRD CIRCUIT

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No. 12-2250

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IN RE: FOSAMAX (ALENDRONATE SODIUM)
PRODUCTS LIABILITY LITIGATION (NO. II)

PATRICK WELCH, et. al,
Appellants

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On Appeal from the United States District Court
for the District of New Jersey
(D.C. No. 3-11-cv-3045; MDL No. 2243 and 3-08-cv-00008)
District Judge: Hon. Joel A. Pisano

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Argued
December 18, 2013

Before: JORDAN, VANASKIE and GREENBERG,
Circuit Judges

(Filed: April 30, 2014)

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OPINION OF THE COURT

JORDAN, Circuit Judge

This case involves product liability claims by individuals who allegedly suffered bone fractures because they took Fosamax® – a drug used to treat or prevent osteoporosis and Paget's Disease – or the generic equivalent of that drug, alendronate sodium. Those plaintiffs sued Merck Sharp & Dohme, Corp. ("Merck"), the manufacturer of Fosamax®, as well as several entities that manufacture the generic equivalent (the "Generic Defendants"). The United States District Court for the District of New Jersey granted judgment on the pleadings in favor of the Generic Defendants because it determined that the state-law claims against them were pre-empted by federal law. The District Court certified the finality of that order pursuant to Federal Rule of Civil Procedure 54(b), and a number of the plaintiffs have appealed. For the reasons that follow, we will affirm.

I. BACKGROUND

A. Statutory and Regulatory Background[1]

The Food, Drug, and Cosmetic Act ("FDCA"), ch. 675, 52 Stat. 1040 (codified as amended at 21 U.S.C. § 301 *et seq.*), provides the framework for federal regulation of prescription drugs in the United States. Under the FDCA, a manufacturer must seek approval from the United States Food and Drug Administration ("FDA") to market a new drug and,

[1] Be prepared for an avalanche of acronyms; for practical purposes, it is unavoidable.

in doing so, must first file a New Drug Application ("NDA") and then prove the drug's safety and efficacy and propose accurate and adequate labeling. 21 U.S.C. § 355(b)(1), (d). As the Supreme Court has recognized, "[m]eeting those requirements involves costly and lengthy clinical testing." *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2574 (2011).

Congress has amended the FDCA several times, including in 1984 by passage of the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), codified at 21 U.S.C. §§ 355, 360cc and 35 U.S.C. §§ 156, 271, 282. The Hatch-Waxman Act governs the production and sale of generic versions of previously approved brand-name drugs. In short, it allows the manufacturers of generic drugs to "gain FDA approval simply by showing equivalence to a … drug that has already been approved by the FDA." *Mensing*, 131 S. Ct. at 2574 (citing 21 U.S.C. § 355(j)(2)(A)). A manufacturer seeking approval of a generic drug will file an Abbreviated New Drug Application ("ANDA") demonstrating that the generic drug and the FDA-approved brand-name drug are bioequivalent;[2] in addition to having the same active ingredients, the brand-name drug and the generic version must share the same route of administration, dosage form, dosage strength, and

[2] The FDA defines "bioequivalence" as "the absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar circumstances in an appropriately designed study." 21 C.F.R. § 320.1(e).

labeling.[3] 21 U.S.C. § 355(j)(2)(A)(ii)-(v). The statutory aim is to "allow[] manufacturers to develop generic drugs inexpensively, without duplicating the clinical trials already performed on the equivalent brand-name drug." *Mensing*, 131 S. Ct. at 2574.

B. Factual and Procedural Background[4]

The FDA gave a green light to Merck's NDA for Fosamax® in September 1995. Teva Pharmaceuticals USA, Inc., one of the Generic Defendants, then developed alendronate sodium – a generic form of the branded drug – and obtained FDA approval on its ANDA in February 2008. The other Generic Defendants subsequently obtained approval for alendronate sodium formulations as well.[5]

Alendronate sodium is a bisphosphonate drug that, as already noted, is "used for treating bone conditions such as osteoporosis and Paget's disease." (J.A. Vol. 2 at 45.) The

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[3] This is, necessarily, a general and incomplete summary of a complicated regulatory scheme.

[4] These facts are taken from the complaint and treated as true because, "[i]n reviewing the grant of a Rule 12(c) motion, we must view the facts presented in the pleadings and the inferences to be drawn therefrom in the light most favorable to the nonmoving party." *Rosenau v. Unifund Corp.*, 539 F.3d 218, 221 (3d Cir. 2008) (quoting *Jablonski v. Pan Am. World Airways, Inc.*, 863 F.2d 289, 290-91 (3d Cir. 1988)) (internal quotation marks omitted).

[5] The parties treat all of the Generic Defendants as manufacturers of alendronate sodium, and so shall we.

drug acts "by inhibiting bone resorption [or absorption] and suppressing bone turnover."[6] (*Id.*) Consequently, it also inhibits primary mineralization,[7] which is involved in the formation of new bone. Meanwhile, secondary mineralization of existing bone continues, which increases the bone's mineral content and results in higher bone mineral density. According to the plaintiffs, higher bone mineral density "does not necessarily correspond with reduction of fracture risk"; rather, it can make bone "highly mineralized, homogenous, brittle, and more susceptible to fracture." (*Id.* at 46.) According to some studies, the effects of alendronate sodium linger after treatment ends, with one study reporting that bone turnover may be inhibited by 50% even 5 years after discontinuing treatment.

On February 28, 2011, 91 plaintiffs, who are citizens of 28 different states, filed this products liability suit in Missouri state court against both Merck and the Generic Defendants (collectively, the "Defendants") for damages

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[6] Bone turnover, or bone remodeling, is the "absorption of bone tissue and simultaneous deposition of new bone; in normal bone the two processes are in dynamic equilibrium." *Dorland's Illustrated Medical Dictionary* 1623, 1991 (32d ed. 2012). "Up to the age of 30 to 40, the two activities ([absorption] and formation) are balanced. Later in life, [absorption] exceeds new bone formation." J.E. Schmidt, *Attorney' Dictionary of Medicine*, at B-166 (Pub. No. 609 Rel. No. 46 Oct. 2012).

[7] "Mineralization" refers to "[t]he introduction of minerals into a structure, as in the normal mineralization of bones." *Stedman's Medical Dictionary* 1214 (28th ed. 2006).

related to "long bone fractures" that they suffered after taking prescribed doses of Fosamax® or alendronate sodium.[8] (*Id.* at 21-41.) The grounds they asserted for liability focused on the Defendants' alleged "concealment of risks associated with [Fosamax® and/or alendronate sodium]," "gross exaggeration of the purported fracture reduction benefits conferred by the drugs," and "overpromotion of the drugs for non-approved, or 'off-label,' indications." (*Id.* at 17.) Specifically, they brought product liability claims under theories of design defect, failure-to-warn, negligence, breach of express warranty, breach of implied warranty, fraudulent misrepresentation, and negligent misrepresentation.

With the consent of the Generic Defendants, Merck removed the action to the United States District Court for the Eastern District of Missouri. The United States Judicial Panel on Multidistrict Litigation later centralized the action with

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[8] The following entities were named as the Generic Defendants in the complaint filed in state court: Apotex Corp.; Barr Laboratories, Inc.; Barr Pharmaceuticals, Inc.; Mylan Inc. f/k/a Mylan Laboratories, Inc.; Mylan Pharmaceuticals Inc.; Sun Pharma Global, Inc. o/b/o and f/k/a Caraco Pharmaceutical Laboratories, Ltd.; Sun Pharmaceutical Industries, Inc.; Teva Pharmaceuticals USA, Inc.; Watson Laboratories, Inc.; Watson Pharmaceuticals, Inc.; and Watson Pharmaceuticals, Inc. o/b/o and f/k/a Cobalt Pharmaceuticals Co. On the District Court's docket, Cobalt Laboratories, Inc. was also listed as one of the Generic Defendants.

The corporate disclosure statements before us attempt to clarify the identities of several of the Generic Defendants, but those details are not relevant here.

several other Fosamax®-related lawsuits in a multi-district litigation ("MDL"), MDL No. 2243, in the United States District Court for the District of New Jersey.

Once the MDL was established, the Generic Defendants moved under Rule 12(c) of the Federal Rules of Civil Procedure for judgment on the pleadings, arguing that the plaintiffs' claims are pre-empted by federal law under the Supremacy Clause of the United States Constitution. The District Court granted the motion, holding that claims against the Generic Defendants relate to duties under state tort law that directly conflict with duties under federal regulations. It read the strict-liability design-defect claims as alleging that "alendronate sodium should have been designed differently to comply with state tort law." (*Id.* at 188.) The District Court's pre-emption decision anticipated reasoning given by the Supreme Court in its opinion last term in *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466 (2013). While the District Court did not have the benefit of the *Bartlett* opinion, it was guided by another recent Supreme Court case, *PLIVA, Inc. v. Mensing*, which it understood to say "that a federal duty of sameness arising out of [the] FDA's regulatory requirements preempts any conflicting tort duty arising under state law." (J.A. Vol. 2 at 188.) The District Court thus concluded that the claims against the Generic Defendants are pre-empted because, just as those defendants cannot lawfully change drug labeling for alendronate sodium, they cannot lawfully change the active ingredient design of the drug either.

In a series of orders, the Court dismissed all of the Generic Defendants from the case, leaving only Merck as a

defendant.[9] Several of the plaintiffs – 73 of the 91 (hereinafter the "Appellants") – then filed this appeal.

II. JURISDICTION

We first determine whether we have jurisdiction over this appeal before we proceed with the merits. The "parties have indicated their consent to our appellate jurisdiction, but 'it is well established that we have an independent duty to satisfy ourselves of our appellate jurisdiction regardless of the parties' positions.'" *Papotto v. Hartford Life & Accident Ins. Co.*, 731 F.3d 265, 269 (3d Cir. 2013) (quoting *Kreider Dairy Farms, Inc. v. Glickman*, 190 F.3d 113, 118 (3d Cir. 1999)). The scope of our review concerning questions of our own jurisdiction is plenary. *United States v. Pelullo*, 178 F.3d 196, 200 (3d Cir. 1999). "[I]f we determine that we do not have jurisdiction over this appeal, our 'only function

[9] The District Court initially denied the Generic Defendants' motion for judgment on the pleadings as to Watson Pharmaceuticals, Inc. and Watson Laboratories, Inc. (collectively, the "Watson Defendants") because, under Rule 12(c), the Court took as true the Plaintiffs' allegation that the Watson Defendants were not generic manufacturers. However, the Court subsequently granted the Watson Defendants' motion for reconsideration, thereby granting judgment on the pleadings to them as well. In addition, the District Court initially denied the Generic Defendants' motion for judgment on the pleadings as to plaintiffs who had filed a motion for remand and/or notice of voluntary dismissal. The Court later resolved the motion for remand and "dismisse[d] … Plaintiffs' claims against Generic Defendants as preempted." (J.A. Vol. 1 at 11.)

remaining [will be] that of announcing the fact and dismissing the case.'" *Elliott v. Archdiocese of N.Y.*, 682 F.3d 213, 219 (3d Cir. 2012) (second alteration in original) (quoting *Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 94 (1998)).

Pursuant to 28 U.S.C. § 1291, we have jurisdiction over appeals from "final decisions of the district courts of the United States." 28 U.S.C. § 1291. "Generally, an order which terminates fewer than all claims pending in an action or claims against fewer than all the parties to an action does not constitute a 'final' order for purposes of 28 U.S.C. § 1291." *Elliot*, 682 F.3d at 219. However, under Rule 54(b) of the Federal Rules of Civil Procedure, "a district court may convert an order adjudicating less than an entire action to the end that it becomes a 'final' decision over which a court of appeals may exercise jurisdiction under 28 U.S.C. § 1291." *Id.*

This appeal was originally taken from the District Court's order that, *inter alia*, dismissed all claims except those against Merck.[10] The District Court, at the time, did not enter judgment under Rule 54(b). We *sua sponte* raised the issue of jurisdiction, and the parties acknowledged in a Rule 28(j) letter that this appeal was taken from a non-final order for purposes of 28 U.S.C. § 1291. The parties have since jointly sought and obtained certification from the District Court under Rule 54(b) for "entry of a final judgment as to

[10] The District Court exercised diversity jurisdiction under 28 U.S.C. § 1332 after it "disregard[ed], for purposes of jurisdiction, the citizenship of fraudulently joined" parties. (J.A. Vol. 1 at 10.) That ruling is not challenged on appeal, and we see no reason to disturb it.

one or more, but fewer than all, claims or parties." Fed. R. Civ. P. 54(b).

Obtaining a final judgment cures the jurisdictional defect of an otherwise premature appeal. *N.J. Tpk. Auth. v. PPG Indus., Inc.*, 197 F.3d 96, 102 n.5 (3d Cir. 1999) ("We conclude that any jurisdictional defects inherent in the District Court's [earlier, non-final] order were cured by the [Rule] 54(b) certification, and that we therefore have jurisdiction to consider th[e] appeal."); *see also Cape May Greene, Inc. v. Warren*, 698 F.2d 179, 185 (3d Cir. 1983) ("[A] premature appeal taken from an order which is *not final* but which is followed by an order that *is final* may be regarded as an appeal from the final order in the absence of the showing of prejudice to the other party." (internal quotation marks omitted)). Therefore, despite the premature filing of the initial notice of appeal, we now have jurisdiction to consider the District Court's rulings in favor of the Generic Defendants.

III. DISCUSSION[11]

A. The Claims at Issue on Appeal

The Appellants challenge only the judgment entered against them on their design-defect claims, which were held to be pre-empted. Before turning to the merits, we need to determine the scope of the claims before us, as some shape-shifting has been attempted. The parties, and particularly the Appellants, have been trying to catch up with precedential developments, most importantly the Supreme Court's *Bartlett* decision. Consequently, as more fully described herein, the Appellants' arguments have changed from their opening to their reply briefs. In their reply brief, the Appellants contend that they preserved their appeal on "all aspects of their design defect claims, including … those based on negligent design theories." (Appellants' Reply Br. at 3.) They assert that their negligence-based design-defect claims are grounded on the

[11] The Appellants technically appealed the District Court's order, signed on April 2, 2012, that granted in part and denied in part the plaintiffs' motion for remand. In that order, the Court dismissed the claims against the Generic Defendants as pre-empted, "[t]o the extent" its previous judgment on the pleadings did not already reach all of the Generic Defendants. (J.A. Vol. 1 at 11.) The Appellants' arguments focus on, and demonstrate an intention to appeal, only the portion of the order relating to the judgment on the pleadings. We review *de novo* an order granting judgment on the pleadings pursuant to Rule 12(c) of the Federal Rules of Civil Procedure. *Rosenau v. Unifund Corp.*, 539 F.3d 218, 221 (3d Cir. 2008); *Werwinski v. Ford Motor Co.*, 286 F.3d 661, 665 (3d Cir. 2002).

theory that the Generic Defendants were negligent "because of their failure to properly analyze Alendronate Sodium to discover the product's defects and for negligently continuing to sell Alendronate Sodium after they were, or should have been aware, that it was defectively designed."[12] (*Id.* at 13.)

The Generic Defendants respond that the Appellants waived any arguments regarding negligence-based design-defect claims by raising them for the first time in their reply brief and that, instead, the only claims on appeal are the Appellants' strict-liability design-defect claims. We agree.

"We have consistently held that '[a]n issue is waived unless a party raises it in its opening brief, and for those purposes a passing reference to an issue … will not suffice to bring that issue before this court.'" *Ethypharm S.A. France v. Abbott Labs.*, 707 F.3d 223, 231 n.13 (3d Cir. 2013) (alterations in original) (quoting *Laborers' Int'l Union of N. Am. v. Foster Wheeler Energy Corp.*, 26 F.3d 375, 398 (3d Cir. 1994)). The Appellants contend that they did raise the issue of negligence in their opening brief, and they point to their Statement of the Issues, which says: "The only issues for this Court's determination are whether the district court erred when it granted the [G]eneric [Defendants'] motion to dismiss on the basis of federal preemption as to plaintiffs'

[12] The Appellants do not identify which count in their complaint allegedly constitutes their negligence-based design-defect claim, but Count XI, titled "NEGLIGENCE," is the only one pled against the Generic Defendants that seems to fit that description. (J.A. Vol. 2 at 74.)

design defect claims."[13] (Appellants' Opening Br. at 2.) The idea, it seems, is that the words "design defect claims" are broad enough to encompass negligence-based design-defect claims. However, the Appellants' Summary of the Argument in their opening brief states more specifically that "[t]he district court erred in dismissing appellants' *risk-utility based* design defect claims." (*Id.* at 9 (emphasis added).) Count IX, titled "STRICT LIABILITY – DEFECTIVE DESIGN," is the only design-defect claim against the Generic Defendants brought under a risk-utility based theory, specifically that the "foreseeable risks exceeded the benefits associated with [alendronate sodium's] design or formulation" and that alendronate sodium "lacked efficacy and/or posed a greater likelihood of injury than other osteoporosis treatments."[14]

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[13] The Appellants misidentify the motion for judgment on the pleadings as a motion to dismiss in that statement.

[14] Count IX alleges, in part:

> 232. When placed into the stream of commerce, ALENDRONATE SODIUM was defective in its design or formulation and was unreasonably dangerous in that its foreseeable risks exceeded the benefits associated with its design or formulation. When placed into the stream of commerce, ALENDRONATE SODIUM was defective in design or formulation in that it lacked efficacy and/or posed a greater likelihood of injury than other osteoporosis treatments on the market and was more dangerous than ordinary consumers or their physicians could reasonably foresee or anticipate.

(J.A. Vol. 2 at 69-70.) It is also the only count from the Appellants' complaint that they mention in their opening brief. Nowhere in the opening brief do they raise any arguments specific to a negligence-based design-defect claim or, for that matter, make any reference to such a claim at all.[15]

> 233. Alternatively, when placed into the stream of commerce, ALENDRONATE SODIUM was defective in design and was unreasonably dangerous in that its label failed to warn physicians and patients of the dangers associated with long-term use of bisphosphonates, including, but not limited to the risk of severely suppressed bone turnover, brittle bones and a greater susceptibility to stress fractures or long bone fractures; and the label failed to instruct physicians and patients about the limited length of time ALENDRONATE SODIUM was actually effective in preventing fractures.

(J.A. Vol. 2 at 69-71.)

[15] The shift to negligence-based arguments in the Appellants' reply brief is not surprising given that the Supreme Court's *Bartlett* decision – which, as discussed below, addressed strict-liability design-defect claims – issued during the pendency of this appeal. According to the Generic Defendants, "[t]he bottom line … is that [the Appellants] placed their bets on the First Circuit's *Bartlett* decision [that credited the theory embraced by the Appellants in their opening brief] … and they lost." (Appellees' Br. at 3.) After the Supreme Court overturned the First Circuit's *Bartlett*

Therefore, fairly read, that brief is limited to the risk-utility based strict-liability design-defect claim set forth in Count IX.[16]

The Appellants' reply brief arguments, which go beyond the scope of Count IX and are outside of anything addressed in the opening brief, must be seen as waived. We thus decline to consider whether there is any basis for distinguishing between negligence-based design-defect claims and strict-liability design-defect claims for pre-emption purposes, and we withhold comment on whether

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opinion, the Appellants did not seek to file a revised opening brief. They proposed for the original briefing to be continued with the Generic Defendants' answering brief and their reply brief.

[16] The Appellants note that their design-defect claims under a risk-utility theory are rooted in the Restatement (Third) of Torts: Product Liability, which provides:

> A prescription drug … is not reasonably safe due to defective design if the foreseeable risks of harm posed by the drug … are sufficiently great in relation to its foreseeable therapeutic benefits that reasonable health-care providers, knowing of such foreseeable risks and therapeutic benefits, would not prescribe the drug or medical device for any class of patients.

Restatement (Third) of Torts: Products Liability § 6(c) (1998).

negligence-based design-defect claims are or are not pre-empted.[17]

B. Pre-emption of the Appellants' Strict-Liability Design-Defect Claims

"[T]he States possess sovereignty concurrent with that of the Federal Government, subject only to limitations imposed by the Supremacy Clause." *Tafflin v. Levitt*, 493 U.S. 455, 458 (1990). That Clause of the Constitution provides that federal law "shall be the supreme Law of the Land[,] … any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. The idea is simply stated, but it is seldom simple to determine whether the dissonance between a federal and state law is such that it requires the former to pre-empt the latter.

Circumstances giving rise to pre-emption are typically divided into three categories: "state law must yield" (1) when a federal statute includes "an express provision for preemption"; (2) "[w]hen Congress intends federal law to 'occupy the field'" in an area of law; and (3) when a state and federal statute are in conflict.[18] *Crosby v. Nat'l Foreign*

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[17] Our lack of comment is not a tacit endorsement of the Appellants' negligence theory. We have yet to hear how the Generic Defendants' duties under negligence-based design-defect claims would be any different from their duties, discussed below, under strict-liability design-defect claims, *i.e.*, changing the labeling, changing the composition, or removing the product from the market.

[18] Field pre-emption and conflict pre-emption may be viewed as "implied" pre-emption, as opposed to "express"

Trade Council, 530 U.S. 363, 372 (2000) (citation omitted); *see also Farina v. Nokia Inc.*, 625 F.3d 97, 115 (3d Cir. 2010) (recognizing three different types of pre-emption). The last variety is the one at issue here, and it comes in two sub-varieties: impossibility pre-emption, which is when "compliance with both federal and state regulations is a physical impossibility," and obstacle pre-emption, which is when a state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Maryland v. Louisiana*, 451 U.S. 725, 747 (1981) (internal quotation marks omitted); *see also MD Mall Assocs., LLC v. CSX Transp., Inc.*, 715 F.3d 479, 495 (3d Cir. 2013). The Generic Defendants' arguments are confined to impossibility pre-emption.

In *Wyeth v. Levine*, 555 U.S. 555 (2009), the Supreme Court considered impossibility pre-emption in the context of pharmaceutical regulation and state tort law. The plaintiff in that case brought claims against the manufacturer of a brand-name drug, alleging that the manufacturer failed to adequately warn of the risks posed by a particular way of administering the drug. *Id.* at 559. The manufacturer argued that the claims were pre-empted because it was impossible for it to comply with its state-law duty to modify the drug's labeling without violating its duties under federal law. *Id.* at 568. The *Levine* Court "start[ed] with the assumption that the historic police

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pre-emption. *Roth v. Norfalco LLC*, 651 F.3d 367, 374 (3d Cir. 2011). As the Supreme Court has recognized, though, "the categories of preemption are not 'rigidly distinct.'" *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372 n.6 (2000) (quoting *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 n.5 (1990)).

powers of the States were not to be superseded … unless that was the clear and manifest purpose of Congress." *Id.* at 565 (internal quotation marks omitted) (citation omitted). The Court said that manufacturers of brand-name drugs remain responsible for updating drug labeling and, as the manufacturer had not submitted evidence that the FDA would not have approved a change to the brand-name drug's label, the manufacturer "failed to demonstrate that it was impossible for it to comply with both federal and state requirements."[19] *Id.* at 573. On the way to that conclusion, the Court "briefly review[ed] the history of federal regulation of drugs and drug labeling," *id.* at 566, and stated that, "[i]n keeping with Congress' decision not to pre-empt common-law tort suits, it appears that the FDA traditionally regarded state law as a complementary form of drug regulation," *id.* at 578.[20]

The Appellants assert that, under *Levine*'s presumption against pre-emption, we "should err on the side of not finding preemption … unless Congress has clearly spoken." (Appellants' Opening Br. at 13.) The Supreme Court's more recent opinions in *Mensing*, 131 S. Ct. 2567 (2011), and *Bartlett*, 133 S. Ct. 2466 (2013), however, hold that certain

[19] The *Levine* Court also rejected the brand-name drug manufacturer's obstacle pre-emption argument. *Levine*, 555 U.S. at 573-81.

[20] The Court concluded that impossibility pre-emption was not applicable to design-defect claims against brand-name manufacturers because federal law reflects "the [brand-name] manufacturer's ultimate responsibility for its label and provides a mechanism for adding safety information to the label prior to FDA approval." *Id.* at 571.

state-law claims against manufacturers of generic drugs conflict directly with federal law and are without effect because of impossibility pre-emption. "When such preemption is found, liability cannot attach if the manufacturer has complied with the applicable federal standard." Restatement (Third) of Torts: Products Liability § 6 cmt. b. The Appellants, recognizing the import of *Mensing* and *Bartlett*, argue that their strict-liability design-defect claims are materially distinguishable from the claims at issue in those cases.[21] To assess their arguments, then, we first consider *Mensing* and *Bartlett* in detail.

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[21] The Appellants cite several decisions for the proposition that "[e]very circuit court of appeals … has found no FDCA pre-emption of design-defect claims." (Appellants' Opening Br. at 18 (citing *Wimbush v. Wyeth*, 619 F.3d 632, 646 (6th Cir. 2010); *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 87-88 (2d Cir. 2006); *Tobin v. Astra Pharm. Prods., Inc.*, 993 F.2d 528, 537 (6th Cir. 1993); *Graham v. Wyeth Labs.*, 906 F.2d 1399, 1405 n.9 (10th Cir. 1990); *Abbot v. Am. Cyanamid Co.*, 844 F.2d 1108, 1114-15 (4th Cir. 1988); and *Hurley v. Lederle Labs. Div. of Am. Cyanamid Co.*, 863 F.2d 1173, 1177-78 (5th Cir. 1988)).) All of those cases pre-date the Supreme Court's *Mensing* and *Bartlett* decisions, however, and are distinguishable because they address pre-emption in the context of claims against manufacturers of branded, not generic, drugs. The Appellants also try to analogize this case to *Medtronic, Inc. v. Lohr*, 518 U.S. 470 (1996), in which the Supreme Court held that the FDA's "substantial equivalency" requirement for streamlined medical device approval did not pre-empt state-law design defect claims. (Appellants' Opening Br. at 26.) But the process for obtaining FDA approval of generic drugs under

1. The Mensing *Decision*

In *Mensing*, the Supreme Court consolidated appeals arising from decisions made by the United States Courts of Appeals for the Fifth and Eighth Circuits. Both plaintiffs in the two underlying cases had sued the manufacturers of metoclopramide tablets, a generic drug, alleging that long-term use of the drug caused them to develop a severe neurological disorder. *Mensing*, 131 S. Ct. at 2572-73. They brought failure-to-warn claims, one under Louisiana law and the other under Minnesota state law. Their contention was essentially that, "'despite mounting evidence that long term metoclopramide use carries a risk of [the neurological disorder] far greater than that indicated on the label,' none of the [generic drug] [m]anufacturers had changed their labels to adequately warn of that danger." *Id.* at 2573. The manufacturers countered with the argument that, as the Court put it, "federal statutes and FDA regulations required them to use the same safety and efficacy labeling as their brand-name counterparts," such that they could not simultaneously fulfill their federal obligation while updating the labels for metoclopramide under their state tort law duty. *Id.* at 2573. The Fifth and Eighth Circuits each rejected that argument and held that the plaintiffs' failure-to-warn claims were not pre-empted by federal law. *See id.*

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the Hatch-Waxman Act is materially different from the streamlined medical device approval process. As the *Mensing* Court noted, "different federal statutes and regulations may … lead to different pre-emption results." *Mensing*, 131 S. Ct. at 2582.

The Supreme Court granted *certiorari* on the question of "whether federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, … state-law [failure-to-warn] claims." *Id.* at 2572. The answer was "yes." As the Court explained, "when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes." *Id.* at 2581. The Court observed that the tort laws of Louisiana and Minnesota "require a drug manufacturer that is or should be aware of its product's danger to label that product in a way that renders it reasonably safe." *Id.* at 2573. At the same time, federal FDA regulations "require that the warning labels of a brand-name drug and its generic copy must always be the same – thus, generic drug manufacturers have an ongoing federal duty of 'sameness.'" *Id.* at 2574-75 (citing 57 Fed. Reg. 17961 (1992)). The particular issue was therefore whether "it is 'impossible for a private party to comply with both state and federal requirements.'" *Id.* at 2577 (quoting *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995)).

The Court considered three arguments – two from the plaintiffs and one from the FDA[22] – for why generic drug manufacturers could comply with state-law warning requirements and avoid liability while also satisfying the

[22] The United States filed an amicus brief setting forth the FDA's views. *See* Brief for the United States as Amicus Curiae Supporting Respondents, *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011) (Nos. 09-993, 09-1039, 09-1501), 2011 WL 741927; *Mensing*, 131 S. Ct. at 2575 n.3.

FDA's requirement that generic drugs always have the same labeling as their brand name counterparts. First, the plaintiffs argued that the FDA's "changes-being-effected" ("CBE") process allows generic drug manufacturers to update warnings on labels,[23] but the Court concluded that the CBE process only allows those manufacturers to update their labeling to match the brand-name drug's labeling. *Id.* at 2575. Second, the plaintiffs submitted that the manufacturers can send out letters to inform physicians of new warnings. *Id.* at 2576. The Court held that the manufacturers cannot do that, though, because the FDA considers such letters to be "labeling" that must be consistent with the labeling provided with the drug. *Id.* (citing 21 C.F.R. § 201.100(d)(1)). Third, the FDA argued that generic drug manufacturers can satisfy both state- and federal-law duties by proposing stronger labeling to the FDA when they believe new warnings are needed. *Id.* The Court determined, however, that even if those manufacturers have a federal duty to ask for FDA assistance to change labeling, "federal law would permit [them] to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so." *Id.* at 2578. The Court

[23] As the Supreme Court summarized, the CBE process "permits drug manufacturers to 'add or strengthen a contraindication, warning, [or] precaution,' or to 'add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product'" by filing a supplemental application with the FDA. *Mensing*, 131 S. Ct. at 2575 (alteration in original) (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A), (C)). In the CBE process, "drug manufacturers need not wait for preapproval by the FDA, which is ordinarily necessary to change a label." *Id.*

observed that one "can often imagine that a third party or the Federal Government *might* do something that makes it lawful for a private party to accomplish under federal law what state law requires of it," but "[i]f these conjectures suffice to prevent federal and state law from conflicting for Supremacy Clause purposes, it [would be] unclear when, outside of express pre-emption, the Supremacy Clause would have any force." *Id.* at 2579.

Because it was impossible for the generic drug manufacturers to "independently do under federal law what state law requires of [them]" – to change the drug label – the Supreme Court held that the state law failure-to-warn claims against the manufacturers were pre-empted. *Id.* As other circuit courts have observed, and we concur, *Mensing* holds that manufacturers cannot unilaterally change a generic drug's labeling, and therefore a state-law claim premised on such a manufacturer being obligated to revise its label is pre-empted. *See Drager v. PLIVA USA, Inc.*, 741 F.3d 470, 476 (4th Cir. 2014); *Morris v. PLIVA, Inc.*, 713 F.3d 774, 776-77 (5th Cir. 2013) (per curiam); *Bell v. Pfizer, Inc.*,716 F.3d 1087, 1095-96 (8th Cir. 2013); *Schrock v. Wyeth, Inc.*, 727 F.3d 1273, 1288 (10th Cir. 2013).

2. The Bartlett *Decision*

While the present case was pending, the Supreme Court decided *Bartlett*, which considered whether design-defect claims under New Hampshire law were pre-empted.[24] 133 S. Ct. at 2473. The Court noted that the claims were

[24] We granted the Generic Defendants' motion to stay this appeal pending the Supreme Court's decision in *Bartlett*.

strict-liability design-defect claims because New Hampshire law imposes a duty on manufacturers to ensure that their products are not "unreasonably dangerous," a duty which can be achieved in the context of pharmaceuticals in two ways – "either by changing a drug's design or by changing its labeling."[25] *Id.* at 2474. Importantly, the Court held that manufacturers do not have the option of redesigning a generic drug because, under the FDCA's requirements, "were [a manufacturer] to change the composition of its [generic drug], the altered chemical would be a new drug that would require its own NDA to be marketed in interstate commerce." *Id.* at 2475. The *Bartlett* Court thus observed that "New Hampshire law ultimately required [the defendant manufacturer] to change [the drug's] labeling." *Id.* at 2474. But under *Mensing*, "federal law prevents generic drug manufacturers from changing their labels." *Id.* at 2476. Accordingly, "federal law prohibited [the generic drug manufacturer] from taking the remedial action required to avoid liability under New Hampshire law," and the rule of impossibility pre-emption applied. *Id.*

In the course of its analysis, the Supreme Court also rejected "as incompatible with … pre-emption jurisprudence" the so-called "stop-selling" argument. *Id.* at 2477. That argument, which had been endorsed by the United States

[25] The Supreme Court contrasted "strict liability" and "absolute liability" by noting that a "'strict-liability' regime" is one "in which liability does not depend on negligence, but still signals the breach of a duty," while an "'absolute-liability' regime" is one "in which liability does not reflect the breach of any duties at all, but merely serves to spread risk." *Bartlett*, 133 S. Ct. at 2473.

Court of Appeals for the First Circuit, reasons that a manufacturer can avoid a conflict between its state- and federal-law duties by simply choosing to halt sales of the generic drug. *Id.* The Supreme Court said, however, that its "pre-emption cases presume that an actor seeking to satisfy both his federal- and state-law obligations is not required to cease acting altogether in order to avoid liability. Indeed, if the option of ceasing to act defeated a claim of impossibility, impossibility pre-emption would be all but meaningless." *Id.* (internal quotation marks omitted); *see also Strayhorn v. Wyeth Pharm., Inc.*, 737 F.3d 378, 398 (6th Cir. 2013) (noting the Supreme Court's unqualified rejection of the stop-selling theory).

3. Analysis

The Appellants attempt to distinguish *Mensing* and *Bartlett* by arguing that those decisions were limited to the pre-emption of "warnings-based" claims. (Appellants' Reply Br. at 1, 6.) They say that the claims at issue here do not necessarily require the Generic Defendants to unilaterally change the labeling for alendronate sodium, so the Generic Defendants' state-law duties do not "conflict with … any specific provisions of the FDCA" and thus do not raise impossibility pre-emption. (Appellants' Opening Br. at 16.) In support of that argument, the Appellants draw our attention to the Supreme Court's choice of language in *Bartlett*: "[S]tate-law design-defect claims *that turn on the adequacy of a drug's warnings* are pre-empted by federal law under [*Mensing*]." *Bartlett*, 133 S. Ct. at 2470 (emphasis added). Under the Appellants' reading of the case, *Bartlett* only stands for the pre-emption of strict-liability design-defect

claims against generic manufacturers when a state imposes a duty to strengthen a drug's warning.[26]

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[26] The Appellants lay particular emphasis on comment k to § 402A of the Restatement (Second) of Torts as an example of what *Bartlett* held to be pre-empted. That comment requires manufacturers of "[u]navoidably unsafe products" to provide adequate warnings in order to avoid strict liability for design defects. 2 Restatement (Second) Torts § 402A cmt. k (1965). It states:

> There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. … Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous. … The seller of such products, … with the qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.

Id. In other words, comment k is a defense to a strict-liability design-defect claim when a product that is unavoidably unsafe is accompanied by proper warnings. *See* Restatement (Third) Torts: Products Liability § 6 Reporter's Note cmt. f

That is too narrow a reading of the Supreme Court's instructions. As the United States Court of Appeals for the Fourth Circuit has held, "[t]ogether, [*Mensing* and *Bartlett*] establish that under the FDCA a generic [drug manufacturer] may not unilaterally change its labeling or change its design or formulation, and cannot be required to exit the market or accept state tort liability." *Drager*, 741 F.3d at 476. Thus, to the extent it is impossible for a generic drug manufacturer to comply with its duty under a state tort law unless it takes one of those actions, that law is pre-empted by the FDCA. *Id.*

At oral argument, the Generic Defendants emphasized that, although the claims at issue were brought under the laws of 28 different states, they could only avoid liability by taking one of the options that *Mensing* and *Bartlett* say they cannot be forced to take: (1) changing alendronate sodium's labeling, (2) changing the drug's design, or (3) ceasing sales of the drug altogether. In the end, the Appellants were forced

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(citing cases recognizing comment k to § 402A of the Restatement (Second) Torts as a defense).

However, the Supreme Court's *Bartlett* decision did not hinge on the availability of the comment k defense. The Court determined that it is not possible, under federal law, for a manufacturer to redesign a generic drug. *Bartlett*, 133 S. Ct. at 2475. Thus, a generic drug manufacturer facing liability under a risk-utility legal framework – regardless of whether a comment k defense is available – is in an impossible position: keep the drug the same and violate state law, or change the drug and violate federal law. *Id.* ("In the drug context, either increasing the 'usefulness' of a product or reducing its 'risk of danger' would require redesigning the drug … .").

to concede that point, in effect if not in words. They tried to avoid the "scope of *Mensing*'s reach" by saying that their design-defect claims are not intended to relate to any drug warnings accompanying alendronate sodium.[27] (Appellants' Opening Br. at 10.) They also state that they "do not seek a 'change' in [alendronate sodium's] design" (*id.* at 21), which is not yielding much, since the *Bartlett* decision clearly holds that such a redesign is impossible under federal law for a generic drug manufacturer. The Appellants are left with their position that their strict-liability design-defect claims impose liability "for the [Generic Defendants'] willful choice to sell a particular product" with an unreasonably dangerous design. (*Id.*) In other words, they are trying to resurrect the "stop-selling" theory, under which the Generic Defendants can only avoid state-law liability by halting their sales of alendronate sodium.[28] But *Bartlett* categorically rejected that theory, and that ends the argument.[29]

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[27] They note that plaintiffs in other cases have been "guilty of sloppy draftsmanship" for asserting design-defect claims that "allege[] that part of what makes a product defective by design is that the 'design' of the product did not include appropriate warnings." (Appellants' Opening Br. at 12.) But, they say, they have "carefully pleaded their complaint" to avoid such a reliance on the adequacy of alendronate sodium's warnings. (*Id.*)

[28] The Appellants also argue that, when the comment k defense is not available or applicable, "states applying [§] 402A generally impose *no duty* on a manufacturer to either re-design their product or strengthen their warnings" because it promotes a "risk-spreading goal." (Appellants' Reply Br. at 10 (emphasis added).) To the extent the Appellants ask us to consider an absolute-liability regime,

Admittedly, the Supreme Court was careful in both *Mensing* and *Bartlett* to consider pre-emption in the context of the specific state laws at issue in those cases. But we have not been directed to any specific state law regime by the Appellants and we need not ponder hypothetical state laws. When we pressed the Appellants at oral argument to give an example of a strict-liability design-defect claim under any relevant state regime that would not ultimately result in some combination of the same three options for the Generic Defendants – *i.e.*, changing the labeling of alendronate sodium, changing the design of the drug, or pulling the drug from the market – they were unable to identify such a claim. Nothing in the briefing offered any state-specific pre-emption analysis either. Therefore, it is unnecessary for us to embark

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that argument was waived because it was not raised in their opening brief. *See Ethypharm S.A. France v. Abbott Labs.*, 707 F.3d 223, 231 n.13 (3d Cir. 2013) (finding an issue waived "unless a party raises it in its opening brief"). Like the *Bartlett* Court, we need not address absolute liability claims, and we "save for another day the question whether a true absolute-liability state-law system could give rise to impossibility preemption." *Bartlett*, 133 S. Ct. at 2474 n.1.

[29] The Generic Defendants argue that the Appellants waived their stop-selling theory with respect to their design-defect claims for not raising it in the District Court. We do not reach that waiver issue because, even if the argument were not waived, the stop-selling rationale was expressly rejected by the *Bartlett* Court as inconsistent with impossibility pre-emption jurisprudence.

on a 28-state tour of strict-liability design-defect law.[30] *Cf. Schrock*, 727 F.3d at 1288 (finding that, as "[n]o effort [wa]s made to identify a mechanism through which [the generic drug manufacturer] could have modified or supplemented the warranties allegedly breached without running afoul of the duty of sameness identified in *Mensing* … , the [plaintiff's] claims are preempted to the extent they rest on inadequate labeling as broadly defined by the FDA.").

In sum, *Mensing* and *Bartlett* recognize that manufacturers have no control over the design or labeling of

[30] The Appellants argue in their reply brief that their design-defect claims "differ greatly from state to state and must be analyzed individually, rather than through a summary dismissal on the pleadings." (Appellants' Reply Br. at 14.) However, this contradicts the position in their opening brief that, although the "Appellants hail from 28 different states, … each [with] their own laws governing design defect claims[,] … this Court should simply consider Appellants' design defect claims as pled and in light of the *prevailing view* of preemption as to state tort law claims generally and design defect claims specifically." (Appellants' Opening Br. at 6 n.3 (emphasis added).) Moreover, the Appellants never raised any state-specific pre-emption arguments in the District Court. Rather, they only argued, in generalities, that their design-defect claims survive *Mensing*, and they rebutted the notion that some states do not "recognize defective design as a vital theory of liability." (J.A. Vol. 2 at 165.) They did not argue that a state-by-state analysis is necessary for determining whether such claims – if they are indeed recognized by all 28 states relevant to this case – are pre-empted.

generic drugs. Short of exiting the market – which *Bartlett* rejects – the Appellants have failed to identify anything the Generic Defendants can do to reconcile their conflicting duties under state and federal law.[31] Therefore, the Appellants' strict-liability design-defect claims are pre-empted.

V. CONCLUSION

For the foregoing reasons, we will affirm the District Court's judgment for the Generic Defendants.

[31] The Appellants argue that the Hatch-Waxman Act "did not give generic drugmakers a free pass in remaining ignorant of drugs' risks (or concealing those risks)." (Appellants' Opening Br. at 15.) Regardless of the appeal such policy arguments may have, they are unavailing because, as the Supreme Court stated in *Bartlett*, "sympathy for [a plaintiff] does not relieve us of the responsibility of following the law." 133 S. Ct. at 2478.