No. 12-142

In the Supreme Court of the United States

MUTUAL PHARMACEUTICAL COMPANY, INC.,
PETITIONER

v.

KAREN L. BARTLETT

ON WRIT OF CERTIORARI
TO THE UNITED STATES COURT OF APPEALS
FOR THE FIRST CIRCUIT

BRIEF FOR THE UNITED STATES
AS AMICUS CURIAE SUPPORTING PETITIONER

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QUESTION PRESENTED

Whether the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 *et seq.*, preempts a state-law product liability claim that asserts that a drug approved as safe and effective by the Food and Drug Administration is defectively designed because its active ingredient is claimed to be unreasonably dangerous for its approved uses.

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INTEREST OF THE UNITED STATES

This case concerns whether federal law preempts a state-law tort claim alleging that a generic prescription drug approved by the Food and Drug Administration (FDA) pursuant to the Federal Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. 301 *et seq.*, is unreasonably dangerous. By virtue of FDA's regulatory responsibilities, the United States has a substantial interest in the resolution of the preemption issue.

STATEMENT

1. A manufacturer must apply for and secure FDA approval to market a "new drug" in interstate commerce. 21 U.S.C. 355(a); see 21 U.S.C. 321(p) (defining "new drug"). FDA approves two categories of such applications: a new drug application (NDA) for brand-

name drugs, and an abbreviated new drug application (ANDA) for generic versions of brand-name drugs. See 21 U.S.C. 355(a), (b) and (j).

a. Before a manufacturer may submit an NDA, it generally must submit an investigational new-drug application for, and conduct, clinical trials to investigate the drug's safety and efficacy. 21 U.S.C. 355(i); 21 C.F.R. 312.20-312.21; see *Merck KGaA* v. *Integra Lifescis. I, Ltd.*, 545 U.S. 193, 196 (2005). The investigational new-drug application must include, *inter alia*, pre-clinical research regarding the drug's safety based on "pharmacological and toxicological studies of the drug involving laboratory animals or in vitro." 21 C.F.R. 312.23(a)(8). The clinical trial process is designed to elicit reliable and comprehensive scientific evidence regarding the drug's safety and efficacy.

If the clinical trials demonstrate safety and efficacy, the manufacturer may submit an NDA. The NDA must contain, *inter alia*, extensive information about the composition, manufacture, and specifications of the drug, "full reports of [the clinical] investigations," 21 U.S.C. 355(b)(1)(A), relevant non-clinical studies, and "any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source," 21 C.F.R. 314.50(d)(1)-(2) and (5)(iv). The application must also contain "the labeling proposed to be used for such drug," 21 U.S.C. 355(b)(1)(F); see 21 C.F.R. 314.50(c)(2)(i), and "a discussion of why the [drug's] benefits exceed the risks under the conditions stated in the labeling," 21 C.F.R. 314.50(d)(5)(viii); see 21 C.F.R. 314.50(c)(2)(ix).

FDA may approve the NDA only if it determines, *inter alia*, that (i) the drug is, in fact, "safe for use" under

"the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof," and (ii) "substantial evidence" shows that "the drug will have the effect it purports or is represented to have" under the conditions of use in the proposed labeling. 21 U.S.C. 355(d). Because "[n]o drug is absolutely safe" and "all drugs have side effects," FDA, *FDA's Drug Review Process: Continued* (Mar. 13, 2012), http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm289601.htm, FDA "generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use," *United States* v. *Rutherford*, 442 U.S. 544, 555 (1979), *i.e.*, the drug's "probable therapeutic benefits must outweigh its risk of harm," *FDA* v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 140 (2000).

b. After a brand-name drug's NDA has been approved and officially listed by FDA (see 21 U.S.C. 355(j)(7)), and subject to certain periods of exclusivity (see 21 U.S.C. 355(j)(5)(F)), any manufacturer may seek approval to market a generic version of the drug under the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, known as the Hatch-Waxman Amendments. Those Amendments prescribe a process for submitting an ANDA for a generic drug, 21 U.S.C. 355(j), and were designed to balance encouraging drug development with accelerating the availability of lower-cost generic alternatives to brand-name drugs. See H.R. Rep. No. 857, 98th Cong., 2d Sess. Pt. 1, at 14-15 (1984) (*House Report*).

The ANDA approval process does not require the manufacturer to provide independent evidence of a generic drug's safety or efficacy. Instead, an ANDA must generally show that the generic drug is the relevant

brand-name drug's "pharmaceutical equivalent" (*i.e.*, it has the "same" active ingredient(s), route of administration, dosage form, and strength) and "bioequivalent" (*i.e.*, it has the equivalent "rate" and "extent" of absorption), and that it is labeled for the same conditions of use previously approved for the brand-name drug. 21 U.S.C. 355(j)(2)(A)(ii)-(iv) and (8)(B); 21 C.F.R. 320.1(c); see FDA, *Approved Drug Products with Therapeutic Equivalence Evaluations* vi-vii (32d ed. 2012) (*Orange Book*) ("pharmaceutical equivalents"). The generic drug must also have the "same" labeling as its brand-name counterpart, with exceptions not relevant here. 21 U.S.C. 355(j)(2)(A)(v). Those sameness requirements reflect the fundamental premise of the ANDA process: A generic drug can be relied upon to be as safe and effective as its brand-name counterpart for its approved conditions of use. See 54 Fed. Reg. 28,884 (1989); *Orange Book* vii ("therapeutic equivalents").

c. After FDA has approved an NDA or ANDA, the manufacturer may not unilaterally make any major changes to the conditions established by FDA's approval for a drug—whether brand-name or generic—such as major "changes in the qualitative or quantitative formulation of the drug product, including active ingredients." 21 C.F.R. 314.70(b)(2)(i); see 21 C.F.R. 314.3 ("drug substance"). Changes that would create a different active ingredient require approval of an NDA prior to interstate marketing. See FDA, *Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* 3 (Dec. 2004), http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf ("Every different active ingredient

* * * should be submitted in a separate original application.") (footnote omitted).

After an NDA or ANDA is approved, the applicant must maintain records and make reports to the Secretary. 21 U.S.C. 355(k)(1). An applicant must, *inter alia*, promptly report to FDA serious adverse events associated with use of its drug in humans and periodically submit certain new information that may affect FDA's previous conclusions about the drug's safety or effectiveness. 21 C.F.R. 314.80, 314.81, 314.98. The FDCA provides that the Secretary shall withdraw approval of a drug—brand-name or generic—if, *inter alia*, she determines that scientific data show that the drug is "unsafe for use" under the conditions stated in its labeling or may not have its purported effect. 21 U.S.C. 355(e).[1] FDA has informed this Office, however, that more typically when FDA advises the manufacturer that significant new adverse information changes the risk/benefit profile of the drug in a manner that cannot adequately be addressed through labeling changes or through FDA's other authorities, the manufacturer withdraws the product from the market. Also, since 2007, the Secretary has had authority in certain circumstances to require a brand-name drug manufacturer to conduct post-approval studies or clinical trials to assess indications of serious safety risks, or to order any drug manufacturer to make labeling changes to address new safety information. 21 U.S.C. 355(*o*)(2)(B), (3) and (4) (Supp. V 2011).

The FDCA prohibits the manufacture or distribution of any drug that is misbranded. 21 U.S.C. 331(a)-(c), (g)

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[1] The Secretary may suspend approval of a drug without notice or hearing if she finds an "imminent hazard" to public health. 21 U.S.C. 355(e).

and (k). A drug is misbranded if, *inter alia*, it is "dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. 352(j). That provision applies to any "drug," whether or not it has been approved by FDA. 21 U.S.C. 321(g)(1), 352.

2. In 1978, FDA approved an NDA for a nonsteroidal anti-inflammatory drug (NSAID) with the nonproprietary name sulindac and the brand name Clinoril. Ten years later, FDA approved the first of several ANDAs for generic sulindac and, in 1991, approved petitioner's ANDA for sulindac. Pet. App. 3a, 144a-145a.

NSAIDs, including sulindac, are known in rare instances to cause a hypersensitivity reaction called Stevens-Johnson Syndrome (SJS) and a more severe manifestation of that syndrome called toxic epidermal necrolysis (TEN). Pet. App. 3a, 23a. FDA-approved labeling for Clinoril at the time of respondent's injury in 2004 expressly listed both "Stevens-Johnson syndrome" and "toxic epidermal necrolysis" as possible "Adverse Reactions." J.A. 554. The drug's FDA-approved "Warnings" section did not refer to SJS/TEN by name, but it referred back to the Adverse Reactions section in warning that rare "hypersensitivity (see ADVERSE REACTIONS)," including "severe skin reactions[,] have occurred during therapy with sulindac," and that "[f]atalities have occurred in these patients." J.A. 553; Pet. App. 109a. The labeling for generic sulindac, including petitioner's sulindac, must be the same as that of Clinoril with exceptions not relevant here. See p. 4, *supra*; *PLIVA, Inc.* v. *Mensing*, 131 S. Ct. 2567, 2577 (2011).

Subsequently, in 2005, FDA completed a "comprehensive review of the risks and benefits, including the risk of SJS and TEN, of all NSAID products." Decision Letter, FDA Docket No. 2005P-0072/CP1, at 2 (June 22, 2006), http://www.fda.gov/ohrms/dockets/dockets/05p0072/05p-0072-pav0001-vol1.pdf. That review led FDA to recommend changes to the labeling of all NSAIDs, including sulindac. J.A. 353-354, 364, 557, 580 & n.8; see FDA, *COX-2 Selective and Non-Selective NSAIDS* (Nov. 27, 2012), http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm103420.htm. FDA's updated "Labeling Template" for prescription NSAIDs modified the Warnings section to state, *inter alia*:

> NSAIDs, including [the labeled drug], can cause serious skin events such as * * * Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. * * * Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

See *ibid.* (providing link to *Labeling Template* 3). The labeling for Clinoril and the generic forms of sulindac, including petitioner's sulindac—like the labeling for all other prescription NSAIDs—was updated accordingly. See J.A. 353, 364, 555; C.A. App. 2244.

3. a. In December 2004, respondent's doctor prescribed respondent Clinoril for shoulder pain. Respondent's pharmacist dispensed petitioner's generic sulindac. Respondent soon developed an extreme case of TEN in which 60-65 percent of the surface of her body deteriorated, was burned off, or turned into an open wound. Respondent spent months in a medically induced coma,

endured 12 eye surgeries, and was tube-fed for a year. Respondent is now severely disfigured, has a number of physical disabilities, and is nearly blind. Pet. App. 3a, 22a-23a.

b. Respondent sued petitioner in New Hampshire state court, and petitioner removed the case to federal district court. Pet. App. 3a. Respondent asserted numerous state-law claims, including failure-to-warn and design-defect product-liability claims. *Ibid.* The district court dismissed respondent's failure-to-warn claim because her "prescribing doctor admitted that he had not read the box label or insert." *Id.* at 4a. By trial, only respondent's design-defect claim remained. *Id.* at 3a. As relevant here, the district court rejected petitioner's contention that the design-defect claim was preempted by the FDCA, concluding that petitioner could comply with both state and federal law, if they differed, by refraining from distributing sulindac at all (in New Hampshire). Pet. App. 164a-166a.

A "product design" is "unreasonably dangerous" and hence defective under New Hampshire tort law, regardless whether a safer design is possible, if "the magnitude of the danger outweighs the utility of the product" in light of the "usefulness and desirability of the product to the public as a whole" and "the presence and efficacy of a warning to avoid an unreasonable risk of harm." *Vautour* v. *Body Masters Sports Indus., Inc.*, 784 A.2d 1178, 1182 (N.H. 2001) (citation omitted). Under comment *k* to Section 402A of the Restatement (Second) of Torts (comment *k*), which New Hampshire courts have adopted, design-defect liability may not be imposed with respect to a product that is "unavoidably unsafe" if the product is "highly useful" and has "an adequate safety warning." Pet. App. 7a (citation omitted).

At trial, respondent presented expert evidence based on spontaneous adverse-event reports to FDA and other information that, respondent asserted, suggested that sulindac was more likely to cause SJS/TEN than other available NSAIDs and that sulindac's overall safety profile was similar to several drugs withdrawn from the market. Pet. App. 4a-5a. Respondent also introduced the labeling for petitioner's sulindac, including the labeling as revised to include an express reference to SJS/TEN in the Warning section itself. J.A. 555-556. Petitioner cross-examined respondent's witnesses but withdrew reliance on a comment *k* defense and did not present its own affirmative case. Pet. App. 5a, 7a.

The district court instructed the jury that, to prevail on her defective-design claim, respondent must prove that "[s]ulindac's design" was "unreasonably dangerous," *i.e.*, that "the danger [from its use] outweighs the utility or usefulness of the product" "to the public as a whole." J.A. 512-513. The court further explained that respondent "must prove that the product was unreasonably dangerous even with its warning" and that the jury could find "a defect in design" only if it found that "[s]ulindac was unreasonably dangerous and that a warning was not present and effective to avoid that unreasonable danger." J.A. 514. The jury was also instructed that no design defect exists if "a warning was present and effective to avoid that unreasonable danger." *Ibid.*

The district court described to the jury numerous "FDA requirements for [drug] labels," including the order in which adverse reactions should be listed in labeling, J.A. 516-518, and instructed the jury that it could consider "FDA's requirements for drug labels" when determining whether sulindac's labeling gave an

effective "warning to avoid an unreasonable risk of danger from foreseeable uses of the product." J.A. 516. The court further instructed the jury that it could consider the evidence that FDA had "approved [s]ulindac as safe and effective for its intended uses" and had "approved [s]ulindac's label," but that the jury was free to give FDA's approval "as much or as little weight as you think it deserves, in light of all of the evidence." J.A. 515.

In light of those instructions, respondent's counsel argued to the jury that petitioner's labeling for sulindac did not provide an "effective" warning to make sulindac reasonably safe, because "serious adverse reactions" "must be in the warning section of [a drug] label"; petitioner's labeling was "in violation of the law" at the time respondent was injured because it did not sufficiently indicate that sulindac could cause SJS and TEN; and the fact that "[petitioner] was forced to change its ineffective warning to add SJS and TEN * * * after [respondent] was prescribed the drug" demonstrated that petitioner's "label [wa]s ineffective" before that change. C.A. App. 1867-1868, 1870, 1898; see *id.* at 1883, 1899-1902.

Counsel further argued that sulindac was a "needless and useless drug" with the highest adjusted "reporting" rate of SJS/TEN amongst all NSAIDs. *E.g.*, C.A. App. 1863, 1871-1872, 1877, 1883-1885. Counsel asserted that FDA merely "rubber stamped" the ANDA for petitioner's sulindac, and that "no evidence [showed] that FDA has ever done a focused analysis on [s]ulindac" to justify its "be[ing] on the market." *Id.* at 1891. FDA, counsel asserted, lacks "expertise in risk/benefit assessment" and "impos[es] a significant risk to * * * the safety of the public" because it is unable to perform its "mission

to monitor drug safety for any class of drugs." *Id.* at 1892-1894.

The jury found petitioner liable on respondent's defective-design claim and awarded respondent over $21 million in damages. Pet. App. 104a.

c. The court of appeals affirmed. Pet. App. 1a-24a. As relevant here, the court held that the FDCA and FDA's regulations did not preempt respondent's design-defect claim. *Id.* at 8a-11a. The court concluded that the logic of this Court's decision in *Wyeth* v. *Levine*, 555 U.S. 555 (2009), which held that the FDCA did not preempt the failure-to-warn claims advanced there against a brand-name drug manufacturer, "applies to design defect claims as well." Pet. App. 9a. The court acknowledged that "*Wyeth*'s holding was technically limited to failure-to-warn claims," *ibid.*, and that the judgment under state law in this case was based on the jury's "second-guessing" of FDA's "risk-benefit analysis," but it determined that *Wyeth* effectively "resolved the conflict against general preemption." *Id.* at 10a.

The court of appeals recognized that *Mensing* held that failure-to-warn claims are preempted with respect to generic drugs, because FDA regulations currently make it impossible for generic-drug manufacturers to independently change their labels to comply with any state tort-law duty requiring use of a different label. Pet. App. 9a-10a. The court also acknowledged the "force" of petitioner's contention that *Mensing*'s logic applies here, where generic-drug manufacturers also "cannot alter the composition of the drug" in response to a design-defect claim. *Id.* at 10a. But the court found no preemption, because a manufacturer could simply "choose not to make the drug at all" in order to comply with both federal and state law. *Ibid.*

SUMMARY OF ARGUMENT

A. *Mensing*'s holding that the FDCA preempts state-law failure-to-warn claims against generic-drug manufacturers controls this case. Although respondent's claim is denominated a design-defect claim, the duty under New Hampshire law to design a product that is not "unreasonably dangerous" itself includes a state-law duty to provide warnings sufficient to eliminate any unreasonable danger from the product. Respondent's claim, like the claim in *Mensing*, reflects a duty to alter FDA-approved labeling deemed inadequate. As this Court held in *Mensing*, FDA regulations currently prohibit generic-drug manufacturers from making such independent labeling changes, thus preempting respondent's claim.

The court of appeals concluded that petitioner could comply simultaneously with federal and state law by halting its sale of sulindac in New Hampshire. But that reasoning cannot be squared with *Mensing*, which reflects an implicit judgment that the option of withdrawing from a market is not sufficient to defeat impossibility preemption in this context.

B. The Court need not decide whether the FDCA would preempt a "pure" design-defect claim that does not consider the adequacy of labeling. That issue is difficult and close, with several factors weighing in favor of finding no preemption. The government nevertheless concludes that the FDCA would preempt a pure design-defect claim where, as here, the claim does not require the plaintiff to prove that the manufacturer knew or should have known of new and scientifically significant evidence that rendered the drug "misbranded" under federal law.

Congress has required federal drug-safety determinations to be made by an expert federal agency with access to the pertinent safety data on the basis of sound scientific judgments, and FDA's risk-benefit analysis is rigorous. Congress has also charged FDA with ongoing drug-safety monitoring and requires FDA to withdraw its approval of a drug if it determines that the drug is not safe for the conditions of use in its approved labeling.

A State that permitted a pure design-defect claim, however, would require a jury independently to balance the health risks and benefits for an FDA-approved drug to determine if the drug is "unreasonably dangerous." Congress's purposes of ensuring that expert, science-based judgments are made by FDA, and the assurance that FDA approval provides for market participants, would be undermined by ad-hoc reconsiderations on a State-by-State and lawsuit-by-lawsuit basis.

Tort judgments second-guessing FDA's expert drug-safety determination would undermine the federal regime to the extent that they forbade or significantly restricted the marketing of an FDA-approved drug. In this case, respondent's counsel relied on the absence of evidence that FDA was aware of data concerning sulindac's relative safety risk, but, in reality, the underlying data came from FDA; FDA was aware of and considered the publication addressing reporting rates of SJS/TEN on which petitioner relied; FDA conducted a comprehensive review of the risks and benefits of all NSAIDs; and FDA did not conclude that sulindac should be removed from the market.

ARGUMENT

RESPONDENT'S DESIGN-DEFECT CLAIM IS PREEMPTED

Under the Supremacy Clause, state laws that conflict with federal law are preempted. *Crosby* v. *National Foreign Trade Council*, 530 U.S. 363, 372 (2000); *Fidelity Fed. Sav. & Loan Ass'n* v. *de la Cuesta*, 458 U.S. 141, 153 (1982) ("Federal regulations have no less preemptive effect than federal statutes."). Conflict preemption occurs "where it is impossible for a private party to comply with both state and federal law" or where state law "'stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'" *Crosby*, 530 U.S. at 372-373 (quoting *Hines* v. *Davidowitz*, 312 U.S. 52, 67 (1941)). "[T]he purpose of Congress is the ultimate touchstone in every preemption case." *Wyeth* v. *Levine*, 555 U.S. 555, 565 (2009) (quoting *Medtronic, Inc.* v. *Lohr*, 518 U.S. 470, 485 (1996)).

This Court's decisions in *Wyeth* and *PLIVA, Inc.* v. *Mensing*, 131 S. Ct. 2567 (2011), provide the framework for evaluating this case. In *Wyeth*, the Court held that a state-law failure-to-warn claim—premised on a brand-name-drug manufacturer's state-law duty to strengthen the warning on its FDA-approved labeling—was consistent with federal law and not preempted, because FDA regulations permitted the manufacturer to "add or strengthen" warnings in its labeling to "increase the safe use of the drug" without "wait[ing] for FDA approval," when there was newly acquired evidence that was not available when FDA approved the labeling. 555 U.S. at 565, 568-569 (citation omitted). Two years later, in *Mensing*, the Court reached the opposite result with respect to failure-to-warn claims against generic-drug manufacturers. Those claims were preempted, *Mensing*

held, because FDA's regulations prohibited generic-drug manufacturers from making changes to their FDA-approved labeling without prior FDA approval. 131 S. Ct. at 2574-2575, 2580-2581.[2] It was therefore impossible for the generic-drug manufacturers in *Mensing* independently to comply with a state tort-law obligation to improve their labeling. *Id.* at 2580-2581.

Respondent's design-defect claim rests on the premise that the active ingredient of a drug that FDA approved as safe and effective for its labeled conditions of use was "unreasonably dangerous" in light of its FDA-approved labeling. But like the generic-drug manufacturer in *Mensing*, petitioner could not make changes that created a different active ingredient or strengthened the warning in its generic labeling without FDA's prior approval. The state tort law on which the jury's verdict rests therefore is preempted.

A. Under *Mensing*, It Was Impossible For Petitioner To Comply With State-Law Duties Underlying Respondent's Design-Defect Claim

1. The imposition of liability under state tort law, whether based on a theory of negligence or strict liability, is ultimately "'premised on the existence of a legal duty'" imposed by the State and the defendant's violation of that "state-law obligation." *Riegel* v. *Medtronic, Inc.*, 552 U.S. 312, 324 (2008) (quoting *Cipollone* v. *Liggett Group, Inc.*, 505 U.S. 504, 522 (1992) (plurality opinion)); see *id.* at 320, 323-325 (addressing claims of strict

[2] This Office has been informed that FDA is considering a regulatory change that would allow generic manufacturers, like brand-name manufacturers, to change their labeling in appropriate circumstances. If such a regulatory change is adopted, it could eliminate preemption of failure-to-warn claims against generic-drug manufacturers.

liability and negligence). Such law, "applied by juries under a negligence or strict-liability standard," is "designed to be[] a potent method of governing conduct and controlling policy." *Id.* at 324-325 (citation omitted).[3]

Respondent's design-defect claim under New Hampshire law is premised on a manufacturer's duty to design a product that is not "unreasonably dangerous." *Vautour* v. *Body Masters Sports Indus., Inc.*, 784 A.2d 1178, 1181-1182 (N.H. 2001). That duty, however, does not focus only on physical characteristics of the product itself. In New Hampshire, "[t]he duty to warn is part of the general duty to design * * * products that are reasonably safe." *Chellman* v. *Saab-Scania AB*, 637 A.2d 148, 150 (N.H. 1993). For that reason, a "product design" is "unreasonably dangerous" if "the magnitude of the danger outweighs the utility of the product" in light of the "usefulness and desirability of the product to the public as a whole" *and* "the presence and efficacy of a warning to avoid an unreasonable risk of harm." *Vautour,* 784 A.2d at 1182 (citation omitted). State law that turns on the adequacy of a generic drug's labeling conflicts with federal law under *Mensing*, quite aside from issues concerning the design of the product itself.

Because "[t]he duty to warn *is part of* the general duty to design" non-defective products in New Hampshire, *Chellman*, 637 A.2d at 150 (emphasis added), the jury had to consider "the presence and efficacy of a warning

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[3] Whether a State chooses to define the scope of its tort duties as elements of a plaintiff's cause of action, a defendant's defense, or a combination thereof is immaterial. "When a person has a substantive defense in law to an action," that legal defense simply establishes that "the conduct of which complaint is made is not a breach of duty." Glanville Williams, *The Concept of Legal Liberty*, 56 Colum. L. Rev. 1129, 1129 (1956).

to avoid an unreasonable risk of harm" when deciding whether petitioner's generic sulindac *as labeled* was unreasonably dangerous. See *Vautour*, 784 A.2d at 1182. Thus, the state-law duty to design a non-defective product *includes* a duty to provide an adequate warning. But with respect to generic drugs, any state-law demand to "use a different, stronger label" for a generic drug to avoid liability is preempted by federal regulations currently forbidding generic-drug manufacturers from independently changing their labeling. *Mensing*, 131 S. Ct. at 2577, 2579.

The record shows that the hybrid design-and-warning nature of New Hampshire design-defect law underlies the verdict below. The district court specifically instructed the jury that a "defect in design" exists only if "a warning was not present and effective to avoid [an] unreasonable danger" from use and that, if "a warning was present and effective to avoid that unreasonable danger, then [the jury] must find for [petitioner]." J.A. 514. Respondent's counsel likewise argued at length to the jury that petitioner's labeling was insufficient to warn of the risk of SJS/TEN at the time of respondent's injury and that the subsequent FDA-approved labeling change itself showed that respondent's labeling was ineffective. See p. 10, *supra*; cf. p. 7, *supra* (explaining labeling change for all prescription NSAIDs, not just sulindac).

Nor is this feature of product-liability law unique to New Hampshire. A defective-drug-design claim often overlaps with a failure-to-warn claim, and whether a drug is unreasonably dangerous is typically considered in light of the adequacy of accompanying warnings. See Restatement (Second) of Torts § 402A cmt. k, at 353-354 (1965) (it is "especially common in the field of drugs" for

products to be "incapable of being made safe for their intended and ordinary use" and "for this very reason cannot be legally sold except * * * under the prescription of a physician"; "[s]uch a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous"); *Bruesewitz* v. *Wyeth*, 131 S. Ct. 1068, 1077 n.41 (2011) (noting that, as of 1986, "a large number of courts" took comment *k* to mean that manufacturers "did not face strict liability for side effects of properly manufactured prescription drugs that were accompanied by adequate warnings"); *Kurns* v. *Railroad Friction Prods. Corp.*, 132 S. Ct. 1261, 1268 (2012) (discussing Restatement (Third) of Torts: Products Liability § 2(c), at 14 (1998) (*Third Restatement*)); Pet. Br. Addendum B (listing States that follow comment *k*).

2. The court of appeals concluded that impossibility preemption of respondent's design-defect claim was defeated because petitioner could comply simultaneously with state and federal law simply by deciding not "to make the drug and market it in New Hampshire." Pet. App. 10a-11a. But that reasoning cannot be reconciled with *Mensing*'s conclusion that it was "impossible" for the manufacturer to comply with a state-law duty to change its labeling because federal law prohibited the change. *Mensing*'s reasoning presupposed that the generic product would be on the market and that the relevant question for preemption purposes was whether state law could require the manufacturer to change the labeling of the drug it was selling.

In fact, the Eighth Circuit in *Mensing* had grounded its no-impossibility-preemption holding in part on the rationale that generic-drug manufacturers "were not compelled to market [the drug at issue]" and thus "could

have simply stopped selling the product" in order to comply with different state-law labeling duties. *Mensing* v. *Wyeth*, 588 F.3d 603, 611 (8th Cir. 2009), rev'd, 131 S. Ct. 2567 (2011). This Court's decision reversing the Eighth Circuit's judgment did not expressly address that reasoning, but the Court presumably was aware of it.[4] Although the Court sometimes grants review "to decide particular legal issues while assuming without deciding the validity of antecedent propositions," *Domino's Pizza, Inc.* v. *McDonald*, 546 U.S. 470, 478-479 (2006) (citation omitted), *Mensing* is reasonably understood as reflecting an implicit judgment that a manufacturer's ability simply to withdraw from marketing the drug was not a sufficient basis to defeat impossibility preemption of the failure-to-warn claim there.[5]

This conclusion is reinforced by the fact that *Wyeth* also appears to have rested on a similar assumption. Were the court of appeals' stop-selling rationale valid, *Wyeth*'s analysis of FDA's changes-being-effected (CBE) regulation, which allows brand-name-drug manufacturers to make certain labeling changes without prior FDA approval, would have been unnecessary to reject the manufacturer's impossibility-preemption argument.

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[4] Cf. *Mensing*, 131 S. Ct. at 2587 n.8 (Sotomayor, J., dissenting) (noting that "the Eighth Circuit suggested that the Manufacturers could not show impossibility because federal law merely permitted them to sell generic drugs" and "did not require them to do so," but that the respondents "ha[d] not advanced this argument" and the dissent found it unnecessary to consider it).

[5] The *Mensing* respondent petitioned this Court for rehearing specifically on the ground that the Court's analysis was flawed because drug manufacturers "could have satisfied their duty under state tort law by suspending sales." Pet. for Reh'g, at 2-3, *Mensing*, *supra* (No. 09-993) (citing *Mensing*, 588 F.3d at 611). The Court denied rehearing. 132 S. Ct. 55 (2011).

See 555 U.S. at 568-573. In particular, the Court stressed that Wyeth had not demonstrated that it was impossible to comply with a state-law duty to change the label because it had not clearly shown that FDA would not have approved such a change, *id.* at 571, 573, thereby implying that impossibility preemption would have been established if Wyeth had made such a showing.

B. Pure Design-Defect Claims Are Preempted Unless Based On New And Scientifically Significant Information That Rendered The Product Misbranded Under Federal Law

Because respondent's design-defect claim under New Hampshire law necessarily turns on the adequacy of the labeling for sulindac, it is preempted under *Mensing*. This Court therefore need not decide whether a "pure" design-defect claim under another State's law that did not consider labeling would be preempted. That is a much more difficult question.

The Restatement (Third) of Torts identifies such a design-defect claim as one assuming the existence of a "reasonable health-care provider[]" who knows all the "foreseeable risks and therapeutic benefits" of the drug. *Third Restatement* § 6(c) & cmts. b and f, at 145, 147, 149. If such a provider, in the exercise of expert medical judgment, would "not prescribe the drug * * * for any class of patients" because its "foreseeable risks of harm" are "sufficiently great in relationship to its foreseeable therapeutic benefits," the drug will provide "net benefits to no class of patients" and is deemed defectively designed. *Id.* § 6(c) & cmt. f, at 145, 149. That test imposes a "very demanding objective standard" that could be met only under "unusual circumstances." *Id.* cmt. f, at 149.

It does not appear that this approach has been accepted in the States to any significant degree, and it has

not been adopted in New Hampshire. See *Vautour*, 784 A.2d at 1182-1184. But if New Hampshire's design-defect tort law were to be reformulated in that manner, it might apply a safety standard triggered when an objective health-care provider knowing all the drug's foreseeable risks and benefits would conclude that "the magnitude of the danger [from using the drug] outweighs the utility of the product" not for "the public as a whole," *id.* at 1182 (citation omitted), but for any class of patients. That test would require a jury to revisit FDA's expert scientific determination, made for the brand-name drug after extensive undertakings by the manufacturers and extensive scrutiny by FDA, that the approved uses of the drug are, in fact, "safe" for the indicated population because the drug's "therapeutic benefits * * * outweigh its risk of harm." *FDA* v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 140 (2000). Although the question is close, the government concludes that such a claim would be preempted unless the claim was based on new and scientifically significant information that rendered the drug misbranded under 21 U.S.C. 352(j).

Several factors do weigh in favor of finding no preemption even in that context. First, the FDCA makes FDA approval a prerequisite for, *inter alia*, "introduc[ing] or deliver[ing] for introduction into interstate commence" any "new drug." 21 U.S.C. 355(a). That text does not expressly require that an approved drug be made available in any particular State or that the manufacturer be guaranteed the ability to make it so. Second, Congress in 1976 adopted an express preemption provision in the FDCA for medical devices (21 U.S.C. 360k(a)) but has not enacted a similar provision for drugs. Congress's failure to do so, "coupled

with its certain awareness of the prevalence of state tort litigation," reflects a willingness to allow at least certain types of tort actions against drug manufacturers. *Wyeth*, 555 U.S. at 574-575; see *Riegel*, 552 U.S. at 327. Third, design-defect actions are not inherently inconsistent with federal regulation of product safety, and Congress has preserved at least some such actions (and other tort claims) when enacting express preemption provisions in certain other contexts. See, *e.g.*, 21 U.S.C. 379r(e) (FDCA provision governing over-the-counter drugs); *Bates* v. *Dow Agroscis. LLC*, 544 U.S. 431, 439, 447-449 (2005) (pesticide regulation); *Sprietsma* v. *Mercury Marine*, 537 U.S. 51, 59, 63 (2002) (boat design); *Geier* v. *American Honda Motor Co.*, 529 U.S. 861, 867-870 (2000) (automobile safety); cf. *Bruesewitz*, 131 S. Ct. at 1075-1082 (finding a defective-vaccine-design claim expressly preempted by Vaccine Act without addressing whether the claim would otherwise have been viable). Finally, certain language in *Wyeth* supports the proposition that at least certain state-law tort actions have long been understood to complement FDA drug-safety regulation. See 555 U.S. at 574-579.

Although the foregoing considerations are significant, we nevertheless conclude that in the context of FDA's regulation of new drugs under the FDCA, "pure" state-law design-defect claims would be preempted where state law does not require the plaintiff to prove that the manufacturer knew or should have known of new and scientifically significant evidence that rendered the drug misbranded under federal law. In those circumstances, the ability of a manufacturer to withdraw its product from the market altogether in order to avoid a violation of state law—despite the commitment of resources by the manufacturers of the brand-name and generic prod-

ucts and FDA's extensive evaluations and approvals for the product to enter the national market—should not be deemed sufficient to defeat impossibility preemption. And the application of state law to require that result would "stand[] as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Crosby*, 530 U.S. at 372-373 (citation omitted).

Our conclusion that the FDCA preempts state-law defective-drug-design claims does not, however, suggest that all state tort claims are preempted. To the contrary, state tort law remains vital in several FDA-approved drug contexts.

First, as *Wyeth* held, state-law failure-to-warn claims may be brought against a brand-name manufacturer that fails to update its labeling in light of newly acquired information as permitted by FDA's CBE regulation. "Failure to instruct or warn is *the* major basis of liability for manufacturers of prescription drugs," *Third Restatement* § 6 cmt. d, at 147 (emphasis added), and that primary basis for liability exists when changes are permitted by FDA's CBE regulation. Cf. p. 16 n.2, *supra* (noting that regulatory change could also allow failure-to-warn actions against generic-drug manufacturers).

Second, appropriate state-law actions that parallel the FDCA's drug "misbranding" prohibition would not be preempted. Under that prohibition, a manufacturer has a federal duty not to market a drug if, *inter alia*, it is "dangerous to health" when used as provided in the labeling. 21 U.S.C. 352(j); see 21 U.S.C. 331(a). A state-law duty not to market the drug in the same circumstances would not conflict with federal law if it appropriately accounted for FDA's role under the FDCA. Cf. *Bates*, 544 U.S. at 447 (state-law pesticide labeling requirement not preempted under express preemption

provision if it is "equivalent to, and fully consistent with, [federal] misbranding provisions"); *Lohr*, 518 U.S. at 495 (express preemption under FDCA in medical-device context). But the jury was not required to find in this case that, notwithstanding FDA's approval of sulindac and its review of its safety in 2005, new evidence concerning the rare occurrence of SJS/TEN rendered sulindac so dangerous as to be misbranded under that federal standard.[6]

Neither of the foregoing theories is available here. And as explained below, a pure design-defect claim, even if New Hampshire law provided for one, would be preempted if not based on new, scientifically significant evidence.

1. Congress has vested FDA with the responsibility to determine when a new drug is "safe" and "effective" under the conditions of use stated in its labeling, so as to warrant the drug entering the interstate market. 21 U.S.C. 355. Because no drug is entirely safe, FDA makes an expert judgment that "a drug [is] safe when the expected therapeutic gain justifies the risk entailed by its use," *United States* v. *Rutherford*, 442 U.S. 544, 555 (1979), *i.e.*, that the drug's likely "therapeutic benefits * * * outweigh its risk of harm." *Brown & Williamson Tobacco Corp.*, 529 U.S. at 140; see 71 Fed. Reg. 3934 (2006); 60 Fed. Reg. 39,180 (1995); 47 Fed. Reg. 39,149 (1982).

FDA must conduct a robust scientific analysis of a new drug's safety and efficacy, which correspondingly

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[6] FDA's approval of a new-drug application reflects FDA's determination that the drug is safe and effective "under the conditions, prescribed, recommended, or suggested" in its labeling. 21 U.S.C. 355(d). Thus, preemption based on the approval of a drug does not extend to unapproved uses.

entails a substantial commitment of resources by the brand-name manufacturer and follow-on commitments by generic manufacturers. The FDCA requires extensive non-clinical and clinical scientific research to support an NDA. See pp. 2-3, *supra*. FDA approval may be granted only if FDA determines that it has "[]sufficient information to determine whether [the] drug is safe" for its labeled uses; concludes that the relevant investigations "include[d] adequate [safety] tests by all methods reasonably applicable"; and finds "substantial evidence" of efficacy, *i.e.*, "adequate and well-controlled investigations" by scientific experts "on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have." 21 U.S.C. 355(d), (d)(1) and (4).

FDA's "rigorous evaluation process" is executed by an "FDA review team—medical doctors, chemists, statisticians, microbiologists, pharmacologists, and other experts"—which determines whether the "drug is safe and effective for its proposed use" by "scrutiniz[ing] everything about the drug—from the design of clinical trials to the severity of side effects to the conditions under which the drug is manufactured." FDA, *The FDA's Drug Review Process* (May 1, 2012), http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm. FDA may consult with independent panels of scientific experts, 21 U.S.C. 355(n), and "usually communicates often with sponsors about scientific, medical, and procedural issues that arise during the review process." FDA, *The CDER Handbook* 24 (1998) http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM198415.pdf; see 21 C.F.R. 314.50(f)(4), 314.102(a), (c), (d), and (e).

If FDA finds a drug safe and effective, the subsequent ANDA process for generic-drug approval builds upon FDA's determination of the safety and efficacy of the brand-name counterpart. 21 U.S.C. 355(j)(2)(A)(ii)-(iv); see pp. 3-4, *supra*. That ANDA process is designed to ensure that each generic drug is "therapeutically equivalent" to a drug that has passed FDA's rigorous examination and therefore is itself considered to be safe and effective. See p. 4, *supra*.

Congress has further charged FDA with monitoring post-marketing drug safety. A manufacturer must maintain extensive clinical records and make numerous reports to FDA, 21 U.S.C. 355(k)(1), including reports that disclose adverse events associated with the use of its drug, 21 C.F.R. 314.80(a) and (c), 314.81, and all "significant new information * * * that might affect the safety, effectiveness, or labeling of the drug," 21 C.F.R. 314.81(b)(2)(i), (v), and (vi). Those duties apply to manufacturers of generic drugs as well as the brand-name drug. 21 C.F.R. 314.98. In addition, FDA independently receives spontaneous adverse-event reports from health professionals and members of the public. FDA, *Postmarketing Surveillance Programs* (Aug. 19, 2009), http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/ucm090385.htm.

The Act provides that FDA shall withdraw approval of a drug if, *inter alia*, it finds that the drug is not safe for the uses identified at the time of the drug's approval or is not effective as claimed for those uses. 21 U.S.C. 355(e)(1)-(3). Approval may be withdrawn only following procedures that afford the manufacturer due process and the opportunity for a hearing. 21 U.S.C. 355(e).

Since 2007, FDA may also require (not merely request) labeling changes. 21 U.S.C. 355(*o*)(4) (Supp. V 2011).[7]

FDA's ongoing risk-benefit analysis will sometimes take into account the availability of more effective or less risky alternatives, which may change over time. For example, in 2005, when FDA reviewed the risk/benefit profiles of all NSAIDs (p. 7, *supra*), it requested that Bextra be withdrawn from the market because it presented greater safety risks (including of SJS/TEN) than other NSAIDs for the same indication with comparable efficacy. J.A. 560, 579-580 & n.8, 588-591. The manufacturer promptly complied. FDA, *Information for Healthcare Professionals, Valdecoxib (marketed as Bextra)* (July 27, 2010), http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124649.htm. But FDA did not request withdrawal of sulindac or other NSAIDs. J.A. 297-298, 364 (explaining that FDA "specifically considered" the research and data on which respondent relies). FDA did withdraw its approval of terfenadine when a safer alternative became available. See 63 Fed. Reg. 53,444 (1998); 62 Fed. Reg. 1889 (1997); cf. 47 Fed. Reg. 22,547-22,548 (1982) (declining to withdraw approval of erythromycin estolate despite lower-risk alternatives because higher risks were "offset by" greater efficacy in certain circumstances).

In the face of this elaborate regulatory regime instituted to safeguard the national market and protect consumers throughout the United States, and the extensive commitment of public and private resources to those

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[7] In 2007, Congress also granted additional FDA authority to ensure the ongoing safety of FDA-approved brand-name and generic drugs. See, *e.g.*, 21 U.S.C. 355(k)(3)-(4), (*o*) and (p), 355-1 (Supp. V 2011).

ends, it would be inconsistent with the FDCA to conclude that a manufacturer must abandon a market it has been approved by FDA to enter in order to avoid violating a duty recognized by a jury under state tort law that deems its product unsafe.

2. By requiring a jury independently to balance the health risks and benefits of FDA-approved uses of a drug and to determine if the drug is "unreasonably dangerous" for those uses, a State with a pure design-defect product-liability law would force the jury to "second-guess[]" FDA's safety determination (Pet. App. 10a), which balances the drug's therapeutic risks and benefits for its labeled uses. Such ad-hoc reconsiderations on a State-by-State and lawsuit-by-lawsuit basis would undermine FDA's drug-safety determinations, which are made based on sound scientific judgments by an expert federal agency with appropriate access to pertinent safety data, and the assurance that FDA's approval provides for all participants in the market.

Federal laws establishing merely minimum safety standards do not normally preempt state-law standards because they do not ordinarily render compliance with federal law impossible or frustrate the federal objective of ensuring minimum levels of safety. See, *e.g.*, *Sprietsma*, 537 U.S. at 57 n.6, 64-68. But where federal regulation is designed to strike a balance between competing considerations, state laws that interfere with the federal balance are impliedly preempted. *Bonito Boats, Inc.* v. *Thunder Craft Boats, Inc.*, 489 U.S. 141, 152 (1989); *Chicago & N.W. Transp. Co.* v. *Kalo Brick & Tile Co.*, 450 U.S. 311, 321, 326-327, 330 (1981). In *Geier*, for example, an agency determined that public safety was best served by affording manufacturers the choice to install a variety of different passive restraint systems in

their vehicles. 529 U.S. at 874-875, 881. A state suit seeking to impose liability for a manufacturer's decision not to use a particular type of restraint system thus stood as an obstacle to the federal agency's decision. *Id.* at 881-883; see also, *e.g.*, *International Paper Co.* v. *Ouellette*, 479 U.S. 481, 494 (1987) (state nuisance law preempted because it would "upset[] the balance of public and private interests so carefully addressed by" the federal permitting regime for water pollution).

Moreover, state tort liability is "designed to be[] a potent method of governing conduct and controlling policy," *Riegel*, 552 U.S. at 324 (citation omitted), and that very potency can be at odds with FDA's approval of a drug for the interstate market. Tort judgments that second-guess FDA's expert determination have the potential to materially increase a drug's price and/or cause its withdrawal, depriving individuals of access to a drug that FDA has determined is safe and effective for sale in the national market under the approved conditions for use. As this Court recognized in *Reigel*, a jury tends to focus on the risk of a particular design that arguably contributed to a particular plaintiff's injury, not the design's overall benefits, because "the patients who reaped those benefits are not represented in court." *Id.* at 325. FDA, by contrast, has access to extensive safety data and employs scientific experts who impartially analyze drugs' health risks and benefits. That federal regulatory function accounts "for those who would suffer without new [drugs] if juries were allowed" to determine whether a drug was "unreasonably unsafe" under "the tort law of 50 States," *id.* at 326.

In this case, for example, the district court instructed the jury to give FDA's determinations whatever weight it thought appropriate (see p. 10, *supra*), and respond-

ent relied on the *absence* of evidence in the record before the jury indicating whether FDA was aware of data on sulindac's relative safety risks. 9/2/2010 p.m. Tr. 107-108; cf. J.A. 366. But in fact the underlying data came from FDA, and FDA had considered the relevant publication addressing spontaneous reporting rates of SJS/TEN for NSAIDs on which respondent principally rested her design-defect claim. J.A. 297-298, 364; Pet. App. 42a. Indeed, FDA in 2005 conducted a "comprehensive review" of the risks and benefits of all NSAIDs but did not conclude that sulindac or other NSAIDs (aside from Bextra) should be withdrawn from the market based on incidents of SJS/TEN. J.A. 364; cf. Pet. App. 47a n.12 (noting that Bextra had 189 spontaneous adverse-event reports of SJS/TEN in a short, 3.5-year period).

3. As the foregoing discussion shows, brand-name and generic drugs should be treated the same for purposes of design-defect claims. A manufacturer must submit an ANDA and obtain FDA approval before marketing a generic drug. As the court of appeals correctly recognized, the active ingredient in a generic drug must be the same as that in the brand-name drug. Pet. App. 10a. The generic manufacturer may not alter that ingredient without prior FDA approval. See pp. 4-5, *supra*.[8] But the same is true of the manufacturer of a brand-name drug. For both, any change that created a new active ingredient would require prior FDA approval of a new NDA for the resulting new drug product. See pp. 4-5, *supra*.

In light of the statutory purpose of the Hatch-Waxman Amendments to accelerate the availability of

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[8] This case does not involve allegations or evidence regarding the dangerousness or usefulness of any of the inactive ingredients of petitioner's sulindac.

low-cost generic alternatives to brand-name drugs, see *House Report* 14-15, preemption in the generic-drug context, just as in the brand-name-drug context, should not be defeated on the rationale that the manufacturer could always comply with state law by declining to provide the very drug whose availability Congress sought to provide in generic form to the public. In both situations, a state-law design-defect claim would lie only if it rested on new, scientifically significant information that rendered the drug misbranded.

4. The court of appeals supported its contrary conclusion by reading *Wyeth* as "adopt[ing] a general no-preemption rule" logically covering all drug-design-defect claims. Pet. App. 11a. That reading is incorrect. "[G]eneral expressions, in every opinion, are to be taken in connection with the case in which those expressions are used," *Cohens* v. *Virginia*, 19 U.S. (6 Wheat.) 264, 399 (1821) (Marshall, C.J.), and the passages in *Wyeth* must be read in context.

The passages in *Wyeth* on which the court of appeals relied were in Part IV of the Court's opinion addressing obstacle preemption. Pet. App. 9a (quoting 555 U.S. at 574-575, 578). By that point, the Court, in Part III of its opinion, had already rejected impossibility preemption on the ground that FDA's CBE regulation affirmatively authorized a manufacturer to change the labeling unilaterally, subject only to later FDA review. It is not surprising in that context that the Court rejected the manufacturer's further contention that the Act's purposes would be frustrated by subjecting to liability under state law a brand-name-drug manufacturer that had newly acquired information undermining its drug's safety but that failed to strengthen its labeling as specifically contemplated by FDA's CBE regulation.

In rejecting obstacle preemption, the Court observed that Congress's failure to enact an express preemption provision for prescription drugs, as it had done for medical devices in 1976 (see 555 U.S. at 567)—when combined with Congress's "certain awareness of the prevalence of state court litigation"—indicated that Congress would not have believed such "state-law suits posed an obstacle to its objectives," or that "FDA oversight [was] the exclusive means of ensuring drug safety and effectiveness." *Id.* at 574-575. *Wyeth* accordingly declined to accept the view that FDA's labeling approvals, and the mere possibility that FDA would disapprove a manufacturer's subsequent enhanced warning on safety grounds under the CBE regulation, necessarily preempt a state-law failure-to-warn suit when the manufacturer did not make such a change, because the government failed in that situation to explain "how state law has interfered with FDA's regulation of drug labeling during decades of coexistence." *Id.* at 577.

That analysis does not categorically extend to all claims that the design of a drug's active ingredient is defective, because a manufacturer cannot unilaterally alter the design (unlike the labeling) of a drug. A defective-design claim would lie only if based on significant new evidence that triggered a duty under federal law not to market a misbranded drug. Significantly, moreover, the Court in *Wyeth* rested its preemption ruling in large part on criticism of the preamble to a 2006 FDA labeling rule for what the Court regarded as the novel proposition that when FDA approves an NDA that includes particular labeling, it must be presumed to have performed a precise balancing of risks and benefits with respect to labeling and established a specific labeling standard that leaves no room for different state-law

judgments. See 555 U.S. 575-581. In this case, by contrast, the proposition that FDA's approval of a drug as safe and effective does reflect an expert judgment that the drug's therapeutic benefits outweigh its risks for the uses identified in the labeling is based on FDA's longstanding interpretation of the Act, affirmed by this Court in *Brown & Williamson Tobacco Corp.*, 529 U.S. at 140, and *Rutherford*, 442 U.S. at 555.

It is also instructive that *Wyeth* supported its view that tort suits "continued unabated despite . . . FDA regulation" by citing the decisions collected at footnote 11 in Justice Ginsburg's dissenting opinion in *Riegel*, 552 U.S. at 340 n.11. See *Wyeth*, 555 U.S. at 567. Those decisions primarily involved failure-to-warn claims; and the four that addressed attempts to extend general product-liability design-defect principles to prescription drugs did not deem the drugs' designs defective per se, but rather conditioned recovery on proof of inadequate warnings.[9] That pattern reflects that courts "traditional[ly] refus[ed]" to "impose tort liability for defective designs of prescription drugs" and allowed liability "only" for "manufacturing defects" and "[in]adequate instructions and warnings." *Third Restatement* § 6 cmts. a and b, at 145-146; Pet. App. 5a. Although some courts in the 1980s began to recognize pure design-defect claims for prescription drugs without labeling deficiencies, such strict-liability claims continued to be unusual: As of the late 1990s, it was "relatively rare" for

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[9] See *Reyes* v. *Wyeth Labs.*, 498 F.2d 1264, 1273-1275 (5th Cir.) (Texas law), cert. denied, 419 U.S. 1096 (1974); *Basko* v. *Sterling Drug, Inc.*, 416 F.2d 417, 425-426 (2d Cir. 1969) (Connecticut law); *Davis* v. *Wyeth Labs., Inc.*, 399 F.2d 121, 126-129 (9th Cir. 1968) (Montana law); *Cunningham* v. *Charles Pfizer & Co.*, 532 P.2d 1377, 1380-1381 (Okla. 1974).

FDA-approved drugs to be held defectively designed. Robert B. Leflar & Robert S. Adler, *The Preemption Pentad*, 64 Tenn. L. Rev. 691, 715 & n.128 (1997); see James A. Henderson, Jr. & Aaron D. Twerski, *A Proposed Revision of Section 402A of the* Restatement (Second) of Torts, 77 Cornell L. Rev. 1512, 1537 n.40 (1992) (1981 decision "is widely believed to be the first case directly raising a defective drug design claim").

For these reasons, *Wyeth*'s conclusion that "Congress did not intend FDA oversight" to preempt state tort litigation reflects that *certain* state-law claims traditionally have been understood as "a complementary form of drug regulation." 555 U.S. at 575, 578. *Wyeth* thus "recognize[d] that some state-law claims might well frustrate the achievement of congressional objectives" even as it concluded that the failure-to-warn action before it was "not such a case." *Id.* at 581 (emphasis added). By contrast, federal law would preempt a pure defective-drug-design claim that required a jury to second-guess FDA's safety determination, without any further need to find the existence of new and scientifically significant evidence that rendered the product misbranded under federal law.

CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

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