No. 12-142

IN THE
Supreme Court of the United States

MUTUAL PHARMACEUTICAL COMPANY, INC.,
Petitioner,
v.
KAREN L. BARTLETT,
Respondent.

On Writ of Certiorari to the
United States Court of Appeals for the First Circuit

BRIEF OF *AMICUS CURIAE* DRI – THE VOICE OF THE DEFENSE BAR IN SUPPORT OF PETITIONER

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INTEREST OF THE *AMICUS CURIAE*[*]

Amicus curiae DRI–The Voice of the Defense Bar ("DRI") is an international membership organization of more than 23,000 attorneys engaged in the defense of clients in civil litigation. DRI is committed to enhancing the skills, effectiveness, and professionalism of defense attorneys in furtherance of their clients' interests. Because of this commitment, DRI seeks to address issues germane to defense attorneys and the civil justice system. DRI has long been a voice in the ongoing effort to make the civil justice system more fair, efficient, and consistent. To promote its objectives, DRI participates as *amicus curiae* in cases that raise issues of vital concern to its members, their clients, and the judicial system.

DRI members represent pharmaceutical manufacturers, distributors, wholesalers, and retailers in product-liability suits in state and federal courts around the country. Members have considerable familiarity with the interplay between state products liability law and the federal regulations that govern prescription drug marketing. Not only are members well versed in how prescription-drug cases are pleaded, briefed, and argued, they also witness first-hand how the parties' legal arguments are distilled into jury arguments

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[*] The parties' blanket consents to the filing of *amicus curiae* briefs are on file with the Clerk. No counsel for a party authored any part of this brief, and no such counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No person other than *amicus curiae*, its members, or its counsel made a monetary contribution to the brief's preparation or submission.

and presentations at trial. This experience has shown that prescription-drug product-liability trials are inevitably about a drug's warnings—what is in them, what is not in them, and how they have evolved over time.

DRI members are also very familiar with the challenges that arise when juries must evaluate complex decisions regarding the safety and efficacy of prescription drugs. For example, some evidence, such as anecdotal "adverse event" reports, tends to carry disproportionate weight with juries, compared with clinical-study evidence that may be more scientifically rigorous but less readily comprehensible to the layperson. This first-hand experience gives DRI a fuller understanding of the problems that would arise from allowing lay juries to second-guess the Food and Drug Administration ("FDA") on the core public-health decision of whether a particular drug should be available on the market.

SUMMARY OF ARGUMENT

A. There is no principled basis for distinguishing this case from *PLIVA, Inc.* v. *Mensing*, 131 S. Ct. 2567 (2011).

Like the plaintiff in *Mensing*, respondent asserted and argued below that a generic drug was defective—not in some abstract sense, but because the warnings it bore were inadequate to convey the risks that the drug's formulation entails. And like the defendants in *Mensing*, petitioner was prohibited by federal law from giving a different warning. Yet respondent now asserts that this case requires a different result because it was pleaded as a "design

defect" case (even though the plaintiff in *Mensing also* pleaded design defect).

It is worth noting what is not at issue in this case. It is undisputed that federal law prohibited petitioner from changing the design of its drug. A generic drug must be the "same as" a brand-name drug and its design cannot differ in any clinically relevant way. See 21 U.S.C. § 355(j)(2)(A). Any tort theory that would require a generic manufacturer to adopt an alternative design is plainly preempted because state law cannot mandate what federal law prohibits.

Indeed, alternative design in a drug product liability case is a legal fiction. As the court below readily recognized, there is no way to "alter a one-molecule drug." Pet. App. 10a. Further, if one were to alter a drug's molecular make-up, those alterations would result in a *different drug*, with *different clinical effects*, both in efficacy and in safety. See Bernard D. Goldstein & Mary Sue Henifin, "Reference Guide on Toxicology," at 664 n.82, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (Fed. Judicial Center 3d ed. 2011) ("[M]olecules with minor structural differences can produce very different biological effects.") (internal quotation marks omitted).

Thus, what this case truly comes down to is the drug's warnings. Indeed, product-liability cases against drug products invariably come down to the warnings. As the law, medical science, and common sense recognize, no drug is one-hundred percent safe. To the extent respondent now argues that this case is about something other than warnings, that argument is belied by the record, which shows that

the adequacy of sulindac's warnings was a central issue at trial, and the jury was instructed to consider their adequacy during deliberations. J.A. 514.

Respondent attempts to decouple this appeal from the record and argue that this case is not about sulindac's warnings, but instead is about whether sulindac belongs on the market at all. See, *e.g.*, Br. in Opp. 22-23. In other words, respondent contends that even if federal law prohibits state law from forcing petitioner to adopt a different label or a different design, it can force it to adopt *no* design whatsoever. The Eighth Circuit made the same error in *Mensing* v. *Wyeth, Inc.*, 588 F.3d 603 (8th Cir. 2009), which this Court reversed in *Mensing*. The Eighth Circuit had reasoned that generic drug defendants "could have simply stopped selling the product" to avoid being held liable for allegedly inadequate warnings federal law prevented them from changing. *Id.* at 611. This Court nonetheless held the tort claim preempted. As the court of appeals recognized (yet disregarded) in this case, accepting a "stop selling" theory would deprive *Mensing*'s holding of any effect, because "a generic maker can avoid defective warning lawsuits as well as design defect lawsuits by not making the drug at all." Pet. App. 11a; see also *In re Darvocet, Darvon & Propoxyphene Prods. Liab. Litig.*, MDL No. 2226, 2012 WL 718618, at *3 (E.D. Ky. Mar. 5, 2012) ("And as the Generic Defendants observe, the idea that they should have simply stopped selling propoxyphene is an oversimplified solution that could apply anytime the issue of impossibility preemption arises: avoid a conflict between state and federal law by withdrawing from the regulated conduct altogether.").

B. Even if respondent were advancing a theory truly independent of sulindac's warning and thus not squarely preempted under *Mensing*, she would fare no better. Respondent would allow a state jury to conduct its own balancing of risks and benefits, indistinguishable from the one FDA makes in approving a drug or declining to withdraw it from the market, and to expressly contradict FDA's judgment as to the outcome. That usurpation of FDA's role is preempted in its own right.

Congress gave FDA sole authority both to approve drugs for market *and to withdraw that approval*, and it erected substantive and procedural protections to guide that FDA decision-making process. The statutory framework does not allow state-court juries to second-guess FDA's judgment on the most fundamental question entrusted to that agency: which drugs shall be available to doctors and patients. Such "directly conflicting commands," *Wyeth* v. *Levine*, 555 U.S. 555, 590 (2009) (Thomas, J., concurring in the judgment), are preempted by federal law.

Even as respondent portrays it, therefore, the jury verdict in this case impossibly conflicts with federal law, replaces the expert judgment of an agency with the verdict of a lay jury, and endangers the health and safety of the American public.

C. Moreover, permitting this type of state-law tort claim to proceed despite FDA's sole authority over drug approval would put defendants at a serious disadvantage at trial. A claim focused on the mere act of selling an FDA-approved drug puts FDA's decision-making process on trial. Yet by virtue of federal law, generic drug manufacturers,

distributors, and retailers do not have access to all the studies performed and all the safety information reported on any one drug. Even brand-name drug manufacturers do not have access to the full scientific record relevant to a decision to maintain or withdraw a drug's approval; they are not privy to safety data on the universe of drugs plaintiffs inevitably argue would have been safer than the drug at issue. Yet federal law erects considerable barriers to private litigants that seek this information (and critical testimony) from the sole body with all the relevant data—FDA. Federal regulations requiring agency officials to refuse to comply with otherwise lawful third-party subpoenas thwart defendants' access to information critical to their defense.

ARGUMENT

The opinion below held petitioner liable for the design and labeling of its generic drug despite the court's recognition that under federal law petitioner could change neither. The court's decision thus is directly contrary to this Court's decision in *Mensing*. Indeed, even the First Circuit recognized that holding petitioner liable for the design of generic sulindac was inconsistent with the rationale of *Mensing* since it could no more "legally make sulindac in another composition" than change its labeling. Pet. App. 10a. The court of appeals' effort to distinguish *Mensing* as covering failure-to-warn but not design-defect claims is unpersuasive because products-liability cases involving pharmaceuticals inevitably turn on the adequacy of the warnings, as in fact occurred at trial. Respondent's effort to recast the jury's decision as simply a determination that

sulindac is defective because its risks outweigh its benefits, divorced from the warnings, is, as the opinion below correctly recognized, nothing but second-guessing FDA. The decision to approve, and also the decision to withdraw, a drug is committed to the expertise of FDA, under a prescribed standard and with procedural safeguards, and allowing a state-court jury to usurp FDA's role impossibly conflicts with federal law. Permitting juries to determine that a drug approved by FDA as safe and effective under prescribed conditions of use should not be available to physicians and their patients would undermine FDA's role and authority and endanger public health.

A. State-Law Design-Defect Cases Against Generic Drugs Invariably Turn on a Drug's Warnings and Are Preempted by Federal Law

Drugs come with warnings because no drug can be designed to be completely safe. Some drugs entail serious risks, including permanent, debilitating injuries, or even death. The chance of a particular class of persons experiencing an adverse effect from a drug can sometimes be predicted with some certainty, and therefore mitigated by warnings. Sometimes it is impossible to know who is at risk, only that the risk exists. In both situations, the information conveyed to doctors in warnings enables them to make informed judgments in the clinical setting as to whether the risks to a particular patient are or are not outweighed by the expected therapeutic benefits.

No drug molecule can be examined in a vacuum: under federal law, a drug is not a drug without

accompanying labeling, and the drug's formulation cannot be divorced from its labeling for tort-law purposes. Under the federal Food, Drug, and Cosmetic Act ("FDCA"), which governs drug approval, safety monitoring, and marketing withdrawal in the United States, applicants must submit proposed product labeling even to be considered for drug approval. See 21 U.S.C. § 355(b)(1)(F). And no drug may be approved for sale in the United States without an accompanying set of warnings. See 21 U.S.C. § 355(d). The labeling provides essential context—telling doctors what medical conditions a drug can treat, the effective dose, the types of patients who may benefit, the known risks, and how a doctor can minimize and monitor for those risks.

The same is true under state product-liability law: a drug is analyzed under a design-defect theory not based solely on the molecule, but also based on whether the labeling properly disclosed the known risks. That is because drugs are recognized as "unavoidably unsafe" products. Restatement (Second) of Torts § 402A, cmt. k (1965). The Restatement provides that

> 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.

Id.

In DRI members' experience, under both federal and state law, drug safety is intertwined with a drug's labeling. DRI members are keenly aware from their trials across the country that whether based explicitly on a "failure-to-warn" theory or called simply "design defect," product-liability trials that involve pharmaceuticals inevitably sweep in the drug's warnings.

It should be no surprise, then, that the trial below—despite ostensibly being focused on a single theory of "defective design"—was not confined to a discussion of the molecular makeup of sulindac, but instead turned on whether sulindac's warnings adequately conveyed the risk of Stevens Johnson Syndrome ("SJS"). Respondent's experts disputed the adequacy of sulindac's FDA-approved warnings, see App. to Cert. Reply 6a-7a, 9a, 12a; J.A. 480, and the jury was charged with determining whether those warnings were adequate:

> If you determine that Sulindac was unreasonably dangerous and that a warning was not present and effective to avoid that unreasonable danger, then you must find [respondent] has proven this element of her claim, a defect in design. However, if you determine that Sulindac was unreasonably dangerous, but that a warning was present and effective to avoid that unreasonable danger, then you must find for [petitioner].

J.A. 514. As the jury instructions so pointedly show, the trial court held petitioner liable for selling a drug that a jury found to be unreasonably dangerous *as labeled*. That finding punishes petitioner for doing exactly what federal law required: giving its generic

drug the same labeling as the brand-name drug Clinoril®. See 21 U.S.C. § 355(j)(2)(A)(v).

As this Court recognized just two Terms ago, a generic drug defendant cannot be held liable under state law for giving an allegedly inadequate warning because federal law does not permit the company to take any unilateral step to minimize the drug's risks. *Mensing*, 131 S. Ct. at 2579. Thus, it cannot strengthen the warnings, clarify the population of patients who may benefit from the drug, or mandate, or even recommend, closer medical monitoring or registration. All these actions would require changes to the package insert or related warnings information (defined broadly as "labeling"), see 21 U.S.C. § 321(m); 21 C.F.R. § 202.1(*l*)(2) (2012), none of which can be accomplished independently by a generic drug company. In other words, all the potential avenues the FDCA affords to drug manufacturers to minimize the risks of a drug while maintaining its place on the market were unavailable to petitioner.

The same conflict arises whether a plaintiff argues that a generic drug defendant should have (1) changed its warnings, (2) changed the design of its drug, or (3) simply stopped selling the product. *Mensing* confirms that the first two options are directly preempted by federal law. Federal law requires generic drugs to be the "same as" their brand-name counterparts, in both design and labeling. 21 U.S.C. § 355(j)(2)(A); see *Mensing*, 131 S. Ct. at 2575.

The third option—to "stop selling"—is no less invalid; it is no option at all. Such a theory asks a jury to find that, *at least absent some change in the*

FDA-approved labeling or design, the drug as currently designed and labeled may not be sold or used in that state without incurring liability. That still amounts to state-law punishment for the very features that, under federal law, the generic manufacturer is powerless to change: the labeling and the design. See *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig. (No. II)*, MDL No. 2243, 2011 WL 5903623, at *6 n.5 (D.N.J. Nov. 21, 2011) ("Plaintiffs insist that Generic Defendants could have simply removed [the drug] from the market. . . . [I]t is essentially a re-argument of *Mensing*. The Supreme Court unequivocally held that failure-to-warn claims against generic drug manufacturers are preempted by federal law.").

Contrary to the opinion below, *Mensing* was not just a case about claims pleaded as failure-to-warn. Mensing herself alleged—just like respondent argues here—that "defendants developed, marketed, and distributed," *i.e.*, *sold the drug*, "even after learning of the design and manufacturing defects." J.A., *PLIVA, Inc.* v. *Mensing*, No. 09-993, 2011 WL 1209890, at *106-113 (U.S. Jan. 24, 2011). The clear holding of *Mensing* is that punishing a manufacturer for selling a drug it had no opportunity to design or label differently places the manufacturer in an impossible position. The Supremacy Clause requires that the state-law rule must yield, whether the state demands that the manufacturer choose a different design or *no* design at all.

B. A State-Law Tort Regime That Permits Juries To Overrule FDA's Decision To Allow a Drug To Be Available to Doctors and Patients Is Not Permissible Under the Supremacy Clause

Even if respondent could successfully disentangle her tort claim from the plainly preempted design-defect and failure-to-warn theories on which the case was tried, her post-hoc "stop-selling" theory would still be preempted. Respondent maintains that the 50 states, or any of them, may ban the sale or use of any drug that they deem "unreasonably dangerous" on the ground that "the [drug's] risks outweigh its benefits." Br. in Opp. 22. The scheme respondent proposes is contrary to federal law. Under federal law, a single decision-maker decides whether a drug's risks outweigh its benefits: that is FDA, based on defined criteria, a fair process, and—above all—a capacity to understand the science at issue that far exceeds a lay jury's. When FDA approves a drug, it does not simply remove federal obstacles to its manufacture and marketing; rather, it decides that the drugs it approves shall be available to healthcare providers and their patients for the benefit of the public health. Under the system Congress created, FDA's judgment about safety and efficacy cannot be second-guessed by the States, or any one of them, or a jury in one of their courtrooms.

Furthermore, for a state to remove a generic equivalent to a branded drug that remains on the market would undermine the goals of the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman"), Pub. L. No. 98-417, 98 Stat. 1585 (1984), which created the system that allows

generic drugs to be readily available at low cost to consumers. If petitioner were to stop selling generic sulindac, the reference-listed drug Clinoril® would remain available for sale in New Hampshire, and the net result would be only that consumers would pay more. The vital purpose of Hatch-Waxman, as this Court recognized in *Mensing*, was to allow "the generic drug market to expand, bringing more drugs more quickly and cheaply to the public." 131 S. Ct. at 2582. It is precisely for that purpose that Hatch-Waxman requires generic manufacturers to make their designs and labels the "same as" those of the brand drugs that FDA has already approved as safe and effective. 21 U.S.C. § 355(j)(2)(A). To permit juries, acting under state law, to find that a generic drug is unsafe and should not be sold because the manufacturer adheres to its federal duty of sameness under Hatch-Waxman would impermissibly conflict with Congress's objective to facilitate the availability of lower cost generic substitutes for previously approved brand drugs.

1. FDA Exercises Its Sole Power To Approve and Withdraw Drugs Based on Rigorous Procedures and Scientific Evidence

a. Congress vested in FDA the sole power to approve drugs for market and to remove them from the market. The FDCA expressly prohibits marketing a drug without FDA approval. See 21 U.S.C. § 331(d) (prohibiting "introduction or delivery for introduction into commerce of any article in violation of section . . . 355"); *id.* § 355(a) ("No person shall introduce or deliver for introduction into interstate commerce any new drug" without FDA

approval); see also *id.* §§ 332, 333, 334 (severe penalties for marketing a drug without that approval). And even after it approves a drug, FDA retains the express and sole authority to *withdraw* a drug's approval. See 21 U.S.C. § 355(e); see also 21 C.F.R. § 314.150 (2012).

Congress prescribed precise standards and procedures for FDA to apply in making its approval and withdrawal decisions. FDA must decide within specified time periods whether the standard for approval of a new drug application is met, see 21 U.S.C. § 355(c)(1), and if so, that is the end of the matter: FDA "shall issue an order approving the application." *Id.* § 355(d). And it shall remain approved unless and until FDA concludes, generally "after due notice and opportunity for hearing," that the (distinct) statutory standard for withdrawing a drug is met. *Id.* § 355(e).

The FDCA requires that the decision to approve a drug be based on a careful balancing of its risks and benefits. This balancing is an important concept that underpins the Act's drug approval regime. Manufacturers must provide FDA with clinical data that a drug "is safe for use" *and* that it is "effective in use" to obtain marketing approval. 21 U.S.C. § 355(b)(1)(A). FDA is tasked with deciding whether the benefits of a drug outweigh its risks based on all readily ascertainable information about that drug and its effects on a particular class of patients under prescribed conditions of use. If a manufacturer does not provide "substantial evidence" that a drug is "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof," or if "there is a lack of substantial evidence

that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended or suggested in the proposed labeling," FDA may not approve that application. See 21 U.S.C. § 355(d)(1), (5).

The FDCA also specifies the level of scientific evidence required for FDA to approve a drug. Drug approval must be based on "substantial evidence." 21 U.S.C. § 355(d). The Act defines "substantial evidence" as

> evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, 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 under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

21 U.S.C. § 355(d)(7).

The decision to withdraw a drug from the market requires comparable scientific analysis and policy choices by FDA. See *Warner-Lambert Co.* v. *Heckler*, 787 F.2d 147, 151 (D.C. Cir. 1986) ("The statute mandates the same [substantial evidence] standard when the Commissioner is deciding whether to withdraw approval for a drug that previously received FDA approval."). Pursuant to the Act, FDA's withdrawal decision must be based on "clinical or other experience, tests, or other scientific data," and evaluated in conjunction with the "conditions of

use" on which the drug was approved. See 21 U.S.C. § 355(e). In other words, FDA must answer the question: Does the best science available counsel in favor of permitting a drug to be marketed, given what is known about its risks and benefits?

Critical to both the approval and withdrawal decision is the statutory phrase "conditions of use." No drug is safe for all people, for all purposes, for all time. Thus, when FDA approves a drug (or later reexamines its safety), it approves it only in conjunction with specific, approved labeling, which includes both warnings about risks and directions about which patients may benefit from the drug. See 21 U.S.C. § 355(b)(1)(F). As a result, any decision on the continued marketing of a drug cannot be made in isolation without considering (1) what has been done and what could be done to better educate physicians and patients about the particular risks of a drug, (2) which patients are most likely to benefit from a drug, (3) how much and how long a drug should be administered, and (4) how a physician and patient can best monitor the patient to ensure any adverse effects are caught early and properly addressed. *Cf.* 21 U.S.C. § 355-1(e), (f) (listing potential risk mitigation strategies such as direct-to-patient warnings, written informed consent forms, and medical monitoring).

b. Withdrawing a drug from the market is a serious decision that requires a close and unbiased look at the science and an eye to the broader public health. A decision to withdraw a drug's approval ends the ability of doctors to prescribe that drug for any patient under any condition. Accordingly, just as with the approval process, FDA does not exercise

its authority to *withdraw* a drug's approval in isolation. FDA convenes Advisory Committees at which leading scientists in the relevant fields hear testimony, discuss evidence, and make recommendations to the agency. FDA hears testimony not just from agency and company officials, but also from practicing clinicians, patient advocacy groups, and often patients themselves.

If the evidence demonstrates problems with an approved drug, FDA seeks solutions to minimize the risks of a drug short of withdrawing approval. People suffering from debilitating and life-threatening diseases may face limited options. There are some diseases for which only one or two drugs are approved. Some patients fail to respond to conventional therapies and require different drugs, which have a different risk profile. Some patients are allergic to drugs used as conventional therapies, and doctors must resort to second-line drugs. FDA places great reliance on doctors to use their best professional judgment to determine when a treatment, though of a higher risk, is nonetheless the right treatment for an individual. "All drugs have risks, and prescribers must balance the risks and benefits of a drug when making judgments about an individual patient's therapy." FDA, Draft Guidance for Industry on the FDA's "Drug Watch" for Emerging Drug Safety Information, 70 Fed. Reg. 24606, 24606 (May 10, 2005); see also FDA, Guidance on Drug Safety Information – FDA's Communication to the Public, 72 Fed. Reg. 10224, 10224 (Mar. 7, 2007) (implementing the draft guidance).

The FDCA gives FDA many options short of withdrawal to mitigate the risks of a drug without pulling it from the market. See 21 U.S.C. § 355-1(e), (f) (giving FDA authority, *inter alia*, to mandate new warnings, require that patients sign an informed consent, receive patient-focused literature on a drug, or view a video, and require registries for doctors and patients). For example, in 2008, FDA received a petition from an advocacy group requesting that FDA withdraw its approval for Avandia, a diabetes drug. FDA decided to maintain the drug's approval because its benefits outweighed its risks for a class of patients. But to mitigate the drug's risks, FDA implemented stricter procedures for prescribing and use, and required the manufacturer to complete an additional clinical trial on the drug. See Memorandum from Janet Woodcock, Director, Center for Drug Evaluation and Research, on Decision on continued marketing of rosiglitazone (Avandia, Avandamet, Avandaryl) (Sept. 22, 2010), available at http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM226959.pdf.

c. Despite the array of mechanisms FDA has to minimize the risks of a drug while keeping it available for those who benefit from it, in some cases scientific evidence develops and changes the risk/benefit profile of a drug. In those cases where a drug's benefits no longer outweigh its risks for a given indication, FDA exercises its authority to withdraw that drug's approval.

FDA's decision on whether to maintain the cancer drug Avastin's approval for metastatic breast cancer patients is a case in point, illustrating the vital role

FDA plays in balancing scientific data and public safety for critical decisions to deny access to a drug. On February 25, 2008, FDA granted accelerated approval to Avastin for use in certain advanced-stage breast cancer patients because of evidence that the drug stopped the progression of cancer in some patients for close to six months. See FDA, Proposal To Withdraw Approval for the Breast Cancer Indication for Bevacizumab, 76 Fed. Reg. 27332, 27333 (May 11, 2011). It granted accelerated approval on the condition that the manufacturer conduct certain additional clinical studies to determine to a greater degree whether the efficacy of the drug outweighed its potential risks. *Id.*

In July 2010, FDA convened a meeting of the Oncologic Drugs Advisory Committee to review results of those studies. Due to the members' assessment that it was not possible to predict which group of breast cancer patients would benefit from the drug, and given reports of severe side effects, the Advisory Committee recommended withdrawing Avastin's breast cancer indication. See Tr. for the Oncologic Drugs Advisory Committee (July 20, 2010), available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/UCM221998.pdf. Several months later, the Office of Oncology Products at FDA announced its decision to withdraw the drug's approval for breast cancer patients, and FDA wrote a letter to the breast cancer community explaining its decision. See Letter from Janet Woodcock, FDA, to Breast Cancer Community (Dec. 16, 2012), available at www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM237286.pdf.

Avastin's manufacturer—and many patient advocacy groups—objected to FDA's decision, and the manufacturer requested an opportunity for a formal hearing. That hearing took place in June 2011 before the Oncologic Drugs Advisory Committee, and was presided over by an FDA representative. See Tr. of FDA Public Hearing on Proposal To Withdraw Approval for the Breast Cancer Indication for Bevacizumab (Avastin) [hereinafter "Tr. of Avastin Hr'g"] (June 28-29, 2011), available at http://www.fda.gov/downloads/NewsEvents/MeetingsConferencesWorkshops/UCM261611.pdf and http://www.fda.gov/downloads/NewsEvents/MeetingsConferencesWorkshops/UCM261697.pdf. The Advisory Committee was composed of medical experts from the M.D. Anderson Cancer Center in Houston, Texas, the Cleveland Clinic of Ohio, and the National Cancer Institute, a patient advocate representative, and a (non-voting) industry representative. Tr. of Avastin Hr'g 2-4 (June 28, 2011). Over two days, FDA and Avastin's manufacturer made statements and presented expert testimony through witnesses. FDA, the manufacturer, and the Advisory Committee were also given an opportunity to ask and respond to questions about the evidence. The hearing was also open to the public, and several dozen patients, doctors, and advocacy groups made statements about people whose breast cancer was unresponsive to all other conventional therapies yet remarkably responsive to Avastin. *Id.* at 19-124.

At the conclusion of the hearing, the Advisory Committee made a non-binding recommendation to FDA to withdraw approval. See Tr. of Avastin Hr'g 204-268 (June 29, 2011). The manufacturer and all interested parties then submitted written comments

to FDA. In November 2011, the FDA Commissioner issued her final decision to withdraw the breast cancer indication for Avastin. The Commissioner—in a seventy-page decision—recognized that there may be individuals who have benefited from Avastin, but found that due to the inability to reliably predict who those women are, and in combination with what she deemed "considerable" risks of the drug, the benefits of Avastin in combating breast cancer do not outweigh its risks for any identifiable population. See FDA, Decision of the Comm'r, Proposal to Withdraw Approval for Breast Cancer Indication for AVASTIN, Dkt. No. FDA-2010-N-0621, at 44-45, 48 (Nov. 18, 2011), available at http://www.regulations.gov/#!documentDetail;D=FDA-2010-N-0621-0544.

FDA did not withdraw Avastin from the market altogether. Rather, its decision took note of the fact that while Avastin was no longer FDA-approved for breast cancer, the drug would still be approved for other types of cancer—for which its benefits did outweigh its risks—and thus still on the market. *Id.* at 4.

As the Avastin example illustrates, FDA's decision whether to withdraw approval of a previously approved drug is a complex and nuanced determination, balancing many considerations beyond the ken of a lay jury, or the ability of private litigants to replicate.

2. The FDCA's Approval and Withdrawal Framework Does Not Allow State Juries To Declare an FDA-Approved Drug Unreasonably Dangerous

When the availability of a proven medicine is at stake, a single jury should not be making the decision for all. But allowing tort suits like the one below to proceed essentially permits just that outcome. Death by a thousand cuts, or a thousand jury verdicts, is still death. See *Riegel* v. *Medtronic, Inc.*, 552 U.S. 312, 325 (2008) ("[E]xcluding common-law duties from the scope of pre-emption would make little sense. State tort law that requires a manufacturer's catheters to be safer, but hence less effective, than the model the FDA has approved disrupts the federal scheme no less than state regulatory law to the same effect."). And it is one that is prohibited by the FDCA, which places these decisions in the hands of FDA, an expert agency that—unlike a jury—has a national public-health responsibility and is politically accountable for its discharge of that responsibility.

FDA's rigorous withdrawal procedure, as illustrated by the Avastin example, stands in stark contrast to the process leading to the jury's determination in this case that sulindac as labeled should not have been sold. That jury was composed of lay persons, not experts. It heard evidence about sulindac, but not the full record before FDA. While it heard testimony from experts hired by counsel, it also heard the testimony of close to a dozen friends, family members, and caregivers of respondent, who all spoke about the effect of plaintiff's injuries. Not a single FDA official testified. After sitting in a

courtroom for three weeks, facing a single plaintiff with visible and severe injuries, the jury decided that sulindac (as labeled) should not have been sold.

Juries, unlike FDA, are not constrained by public health considerations, nor even by the standards that the FDCA requires of FDA upon approving a drug—and, critically for the purposes of this case, upon withdrawing that drug's approval. Juries, unlike FDA, do not have to weigh the risks and benefits of a drug in light of the conditions of use *and other options, if any, for all consumers of the drug*, as FDA must do. See 21 U.S.C. §§ 355(e)(1)-(3); 21 C.F.R. §§ 314.150(2)(i)-(iii) (2012). They do not have to read or analyze all the available scientific literature about a drug and defend their decision on appeal based on "substantial evidence" or even a review of the "whole record," as is required of FDA. 21 U.S.C. § 355(h); 5 U.S.C. § 556(d) (requiring agency adjudication to be based upon a review of the "whole record" and supported by "substantial evidence"). Juries do not have to convene hearings with FDA officials; in fact, they do not have to hear any testimony from FDA at all, as happened in this case. A jury must only listen to the evidence before it, look to a single, injured plaintiff and decide after-the-fact whether the drug should have been available for use by that plaintiff, whom the drug concededly injured. That is a stacked deck and does not result in wise public-health decisions.

That is not the system created by the FDCA. Allowing states to impose tort-law duties like the one upheld below conflicts with the careful statutory regime that Congress enacted to ensure that drugs that "substantial evidence" shows to be beneficial to

the public are available, and those that are not are either not approved, or withdrawn. See *Geier* v. *Am. Honda Motor Co.*, 529 U.S. 861, 886 (2000) (state-tort law may not declare unlawful an act that the responsible federal agency prescribed should remain lawful); *Wyeth*, 555 U.S. at 590 (Thomas, J., concurring in the judgment) ("[I]f federal law gives an individual the right to engage in certain behavior that state law prohibits," the state law is preempted, "notwithstanding the fact that an individual could comply with both by electing to refrain from the covered behavior."); accord, *e.g., Arizona* v. *United States*, 132 S. Ct. 2492, 2506-07 (2012) (holding that federal law prescribing that a decision "is entrusted to the discretion of the Federal Government" preempts state attempts to interfere with that discretion); *Chi. & N.W. Transp. Co.* v. *Kalo Brick & Tile Co.*, 450 U.S. 311, 324, 331 (1981) (reversing a decision "holding that a State can impose sanctions upon a regulated carrier for doing that which only the [federal agency], acting pursuant to the will of Congress, has the power to declare unlawful or unreasonable").

The FDCA answers the question Justice Breyer asked during oral argument in *Warner-Lambert Co.* v. *Kent*:

> Now, who would you rather have make the decision as to whether this drug is, on balance, going to save people or, on balance, going to hurt people? An expert agency, on the one hand, or 12 people pulled randomly for a jury role who see before them only the people whom the drug hurt and don't see those who need the drug to cure them? Now, it seems to

> me that is Congress's fundamental choice, and Congress has opted for the agency.

Tr. of Oral Arg. 30-31, *Warner-Lambert* (Feb. 25, 2008) (No. 06-1498). The FDCA entrusts that decision to FDA.

Individuals who believe that a drug's risk-benefit profile does not warrant marketing approval are not left without a remedy. They have an established pathway under federal law for pursuing a drug's withdrawal from the market. Consumers can—and regularly do—file Citizen's Petitions seeking a drug's withdrawal from the market. See 21 C.F.R. § 10.30 (2012) (providing process for citizens to petition FDA to "issue, amend, or revoke a regulation or order or take or refrain from taking any other form of administrative action"). In response, FDA institutes comprehensive reviews of the scientific evidence and, at times, convenes Advisory Committees to consider issues presented by such petitions. FDA responds regularly to Citizen's Petitions seeking changes to a drug's warnings or seeking a drug's withdrawal, and FDA can and has withdrawn drug approvals in response to those petitions. See, *e.g.*, Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, to Sidney Wolfe, Director, Public Citizen's Health Research Group (Jan. 3, 2011), available at http://www.regulations.gov/#!documentDetail;D=FDA-2009-P-0595-0005 (granting petition to ban weight-loss drug Meridia, due to cardiovascular risks); FDA, Withdrawal of Approval of New Drug Application, 68 Fed. Reg. 1469, 1469 (Jan. 10, 2003) (announcing withdrawal of diabetes drug Rezulin's approval due to the introduction of new diabetes treatments with lower risk profiles).

The remedy given to citizens by the FDCA also prevents the practical and public-health problems raised by the 50-state drug-approval and withdrawal system that respondent envisions. From a public health standpoint, the Citizen's Petition process ensures that drugs that entail severe risks but nonetheless are important to make available to those patients who would benefit from them, remain an option for doctors to prescribe where appropriate. And FDA's uniform resolution of such petitions avoids the significant practical consequences of having a drug on sale in some states, but not others, due to unfavorable state-court verdicts (or even positive enactments). Such a legal patchwork would pose serious problems for drug companies seeking to avoid tort liability. For example, even if drug companies were able to prevent a drug from being sold within New Hampshire, no company can prevent a New Hampshire resident from filling his prescription across the river in Vermont (and then suing the company in New Hampshire). Allowing jury decisions that a drug is not safe enough to be marketed has the potential to bind large sections of the country, thereby nullifying the federal approval.

C. A Rule Permitting States To Put FDA's Approval Process on Trial Compromises Drug Defendants' Ability To Erect a Full Defense

Under the decision below, drug-defect litigation would proceed in a way that deprives FDA's expert judgment of even *evidentiary* effect, much less the conclusive effect that Congress intended it to have. If every state, and every state jury, were permitted to operate as a mini-FDA and to declare drugs

unsafe, pharmaceutical defendants would be left unable to draw on the views and actions of the *real* FDA to assert a robust defense to state-law tort actions.

The decision whether to approve or withdraw approval for a drug goes to the heart of federal drug regulation. At the center of that decision is FDA. State-tort lawsuits that assert a drug is defective inevitably put FDA's decision-making on trial.

Yet defendants are severely hamstrung in their ability to put on a full defense to these claims because the only party with full information is FDA—and FDA is not a party to a state-law product-liability action concerning a drug.

FDA is the only entity with all the data and other scientific information about a drug, and thus the only entity with the ability to conduct a true risk/benefit analysis on the continued marketing of a drug. It receives the full initial application to approve a new drug, an application that includes years of pre-clinical research, pharmacology profiles, animal studies, and the methodology and results for clinical studies. See 21 C.F.R. § 314.50 (2012). That application is not made public, and as a result, is only available to the initial applicant—and not later manufacturers of generic drugs (like petitioner), nor distributors of the drug, nor wholesalers. After the drug is on the market, FDA collects quarterly, annual, and periodic adverse event reports on the drug. See, *e.g.*, 21 C.F.R. §§ 312.85, 314.80, 314.81(b)(2)(i) (2012). FDA also has authority to order manufacturers to conduct new and follow-up studies to track certain safety issues. See 21 C.F.R. § 312.85 (2012). Most of this information is

unavailable to follow-on manufacturers of a drug, and other entities.

FDA is also the only entity that is charged with analyzing—and that has the ability to analyze—a drug in combination with other available drugs for a given subset of patients. Even a company that submits the original application to sell a new drug is missing this vital piece of information that is necessary to determine whether a drug should be on the market. The decision, as FDA readily acknowledges, cannot be made in a vacuum. See, *e.g.*, Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research, FDA, to Sidney Wolfe, Director, Public Citizen's Health Research Group, at 17 (Nov. 6, 2012), available at http://www.regulations.gov/#!documentDetail;D=FDA-2011-P-0455-0005 (denying a request from a consumer advocacy group to remove a high-dose Alzheimer's drug from the market, reasoning that it "is one of only two drugs indicated for treating the severe stage of" Alzheimer's and "a physician may determine that an improvement in a patient's cognition justifies the risk of additional side effects"). A drug with serious risks might remain on the market despite those risks because only one other, or perhaps no other, drug treats the disease that drug is designed to target. Only FDA can analyze the safety data of the drug at issue in litigation against the safety data of other drugs designed to treat the same disease, if any.

For example, there are dozens of different antibiotics on the market. A jury may see the variety of antibiotics available, and that a plaintiff was injured by one with a higher incidence of side

effects than, for example, penicillin. That jury may very well decide that the drug plaintiff took should never have been sold. However, when FDA examines that same drug, it may determine that it should be marketed because allergies may prevent a class of people from taking penicillin, or because that antibiotic has unique benefits such that some people who do not respond to other antibiotics are healed by that one. See *Riegel*, 552 U.S. at 325 ("A jury . . . sees only the cost of a more dangerous design, and is not concerned with its benefits; the patients who reaped those benefits are not represented in court.").

Given that FDA is at the center of the decision about a drug's efficacy and safety profile, it follows that FDA's analyses, conclusions, and underlying data are of primary relevance at a trial about whether a drug's benefits outweigh its risks. But for a drug manufacturer, there are serious roadblocks to accessing this information.

This Court has held that private litigants may not obtain testimony from federal employees simply by obtaining and serving a valid subpoena. See *U.S.* ex rel. *Touhy* v. *Ragen*, 340 U.S. 462 (1951). In *Touhy*, the Court held that the Department of Justice may lawfully promulgate regulations that restrict, or even prevent, private litigants from obtaining agency documents and/or testimony through otherwise valid subpoenas. Many other agencies, including FDA, have responded by promulgating comparable regulations of their own. For example, FDA regulations prohibit any FDA employee from giving "testimony before any tribunal pertaining to any function of the [FDA] or with respect to any information acquired in the discharge of his official

duties" without specific authorization from the Commissioner. 21 C.F.R. § 20.1(a) (2012). The Commissioner has asserted broad authority to grant or deny requests for testimony, based on her own conception of "the public interest" and "the objectives of the [FDCA] and [FDA]." *Id.* § 20.1(c) (2012). Even if an employee is lawfully subpoenaed, without the Commissioner's authorization, the employee can only "respectfully decline to testify on the grounds that it is prohibited." *Id.* § 20.1(b) (2012).

As a result, defendants who would benefit from FDA's considered expertise and far greater wealth of data on not just the drug at issue in a product-liability lawsuit, but the entire class of drugs considered along with that drug, are often blocked from obtaining FDA memoranda, internal meeting notes, and other indicia of the agency's reasoning for awarding and maintaining a drug's approval. Further, it is exceedingly rare when FDA permits an official to testify in a product-liability lawsuit about the internal agency decision-making process about any given drug.

These roadblocks to third-party discovery exist for sound policy reasons. FDA is not tasked with defending its approval decisions in state courts around the country; it is tasked with analyzing and monitoring the safety of drugs on the market. FDA has provided a procedural mechanism for individuals to challenge its decisions through filing Citizen's Petitions, of which there have been many (and some of which have led to a drug's withdrawal from market). But because the FDCA does not provide for state-tort actions challenging FDA drug approval decisions, it does not provide equivalent procedural

mechanisms to safeguard a defendant's ability to defend FDA's approval decision in court.

CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

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