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 THE GENERIC PHARMACEUTICAL ASSOCIATION AS AMICUS CURIAE IN SUPPORT OF PETITIONER

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INTEREST OF THE AMICUS CURIAE[1]

The Generic Pharmaceutical Association ("GPhA") files this brief in support of petitioner Mutual Pharmaceutical Company, Inc., and in support of reversal of the United States Court of Appeals for the First Circuit's decision upholding the jury verdict against Mutual.

GPhA is a voluntary, non-profit association comprised of more than 70 manufacturers and distributors involved in the generic pharmaceutical industry. GPhA's members provide American consumers with generic medications that are as safe and effective as their brand-name counterparts, but at a fraction of the cost. "All generic drugs approved by [the Food and Drug Administration ("FDA")] have the same high quality, strength, purity, and stability as brand-name drugs."[2] Generic drugs today account for nearly 80% of prescriptions dispensed in the United States, but just 27% of prescription drug

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[1] The parties' letters of consent to the filing of *amicus* briefs have been filed with the Clerk. Under S. Ct. Rule 37.6, *amicus curiae* states that no counsel for a party wrote this brief in whole or in part, and no counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No person or entity, other than the *amicus curiae* or its counsel, has made a monetary contribution to this brief's preparation or submission.

[2] Generic Drugs: Questions and Answers, U.S. Food and Drug Administration, available at http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafe-ly/UnderstandingGenericDrugs/default.htm.

spending.[3] More than 3.2 billion prescriptions each year are filled with generic pharmaceutical products, saving the American consumer $193 billion in 2011 and more than $1 trillion over the last 10 years. ("GPhA Rpt.") GPhA's members are committed to providing safe, lower-cost medications to all Americans.

This case is one of many pending against GPhA members around the country despite this Court's decision in *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011) *reh'g denied*, 132 S. Ct. 55 (2011). In *Mensing*, this Court recognized that under federal law generic pharmaceutical manufacturers are required to produce products that are the "same as" their brand-name counterparts. *Id.* at 2474-75. Because state tort-law requirements conflict with the federal duty of "sameness," this Court held those claims are necessarily preempted. *Id.* at 2570-71, 2474-75. Recognizing *Mensing's* broad preemption of claims, plaintiffs are attempting to end run that decision.

The First Circuit accommodated plaintiffs in their search for an alternative cause of action that might avoid preemption. Left standing, the First Circuit's decision defeats Congressional goals in enacting the Hatch-Waxman Amendments (the Drug

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[3] IMS Institute for Health Care Informatics, The Use of Medicines in the United States: Review of 2011, at 26 (Apr. 2012) ("IMS 2012"); Generic Pharmaceutical Association, Generic Drug Savings in the U.S. (4th ed. 2012), available at http://www.gphaonline.org/sites/default/files/IMS%20Study%C20Aug%C202012%20WEB.pdf ("GPhA Rpt.").

Price Competition and Patent Term Restoration Act of 1984, P.L. 98-417, 98 Stat. 1585 (1984)) and the Federal Food, Drug, and Cosmetic Act ("FDCA"), undermines this Court's holding in *Mensing*, and threatens the generic drug industry's ability to sell low-cost generic drugs.

INTRODUCTION

Lawsuits involving pharmaceutical products have increased exponentially over the past few decades. In contrast to the approximately 11,000 lawsuits (total) filed in federal courts against pharmaceutical companies during the 13-year period from 1973 through 1986,[4] today it is not uncommon for hundreds of lawsuits to be filed in a single day. Yet, while the sheer number of lawsuits involving pharmaceutical products has changed dramatically, what has not changed *one iota* is the nature of those claims. From the earliest case involving a medicinal, the claim has been premised on the product's labeling. *See Thomas v. Winchester*, 2 Seld. 397, 6 N.Y. 397 (N.Y. 1852), 1852 WL 4748 (N.Y.) (recognizing claim based on labeling of medicinal product). *See also Mazetti v. Armour & Co.*, 75 Wash. 622, 135 P. 633 (1913) (same); *Darks v. Scudders-Gale Grocer Co.*, 146 Mo. App. 246, 130 S.W. 430

[4] The number of lawsuits ranged from fewer than 100 in 1974 to a high of around 1,600 in 1985. *See* Rand, Product Liability and the Business Sector, Litigation Trends in Federal Courts, 1988. Of those 11,000 lawsuits, almost 7,000 involved only two products (Dalkon Shields and Bendectin) and only two manufacturers (A.H. Robbins and Merrell Dow). *Id.* Litigation involving generic drugs was virtually unknown.

(1910) (same); *Blood Balm Co. v. Cooper*, 5 L.R.A. 612, 10 S.E. 118 (Ga. 1889) (same). That is so because even 100 years ago, it was recognized, *and accepted*, that medicinals generally have properties that can be dangerous or poisonous and, as a result, those products required adequate instructions for use – exactly what the FDCA requires today. *See, e.g.,* 21 U.S.C. 352(f) (declaring drug product misbranded where its labeling does not include "adequate directions for use").

As state product liability law developed over the years, the concept that pharmaceutical products are incapable of being made completely safe and without any risks became embedded in the law of virtually every state. The offshoot of that recognition was that pharmaceuticals that are properly prepared and accompanied with adequate directions for use are not considered defective – either in design or otherwise. *See, e.g.,* Restatement (Second) of Torts, §402(a) cmt. k (recognizing that products such as pharmaceuticals are unavoidably unsafe and not defective if properly prepared and accompanied by adequate instructions). With few exceptions not applicable to drugs with a single active ingredient (like sulindac), pharmaceutical litigation continued along that path until this Court decided *Mensing*. At that point, plaintiffs sought a cause of action they could argue did not depend on the generic drug labeling and, thus, would not be barred by the broad preemptive scope of *Mensing*.

Ms. Bartlett found herself in the same position, but for reasons unrelated to *Mensing*, which

had not been decided yet. While *Mensing* was winding its way through the courts, the district court dismissed Ms. Bartlett's failure-to-warn claim because she could not satisfy the most basic element of her claim – legal causation. As no one ever reviewed the product's labeling, Ms. Bartlett was unable to demonstrate that any inadequacy in the labeling was the proximate cause of her injury. The district court solved Ms. Bartlett's dilemma by allowing her to pursue a "defective design" claim – one that allegedly did not depend on the product's warnings. By the time Ms. Bartlett's case reached the Court of Appeals, *Mensing* had been decided, but the First Circuit chose not to apply it even though it recognized that Ms. Bartlett's claim depended on the adequacy of sulindac's labeling.

As this case clearly demonstrates, the nature of pharmaceutical products and their complex approval process have dictated that, with limited exceptions, lawsuits involving pharmaceutical products are failure-to-warn claims. Describing the claim as one for "design defect," as was done here, does not change the true nature of the claim and where those lawsuits target generic drugs, they are preempted by *Mensing*.

Yet, even if one accepts that a claim for design defect involving a generic drug does not involve the product labeling, the result is the same. Whether the basis of the claim is the generic drug's warnings or its design, the "sameness" requirement applies. Rationalizing the outcome based on the generic drug manufacturer's freedom to choose whether to sell its

product raises problems of its own, not the least of which is it subverts (indeed, inverts) the Supremacy Clause and prevents the successful application of the defense. In addition, that rationalization undermines both the Hatch-Waxman Amendments and the FDCA.

THE PROCEEDINGS BELOW

This lawsuit proceeded to trial as a purported strict liability design defect claim following the dismissal of Ms. Bartlett's other causes of action, including her failure-to-warn claim. Notably, Mutual was granted summary judgment on the failure-to-warn claim due to Ms. Bartlett's inability to establish that any alleged inadequacy in the warnings was the proximate cause of her injury because no one—not Ms. Bartlett and not her prescribing physician—ever read Mutual's sulindac package insert.

Ms. Bartlett's design defect claim suffered from a second factual roadblock: Sulindac is a molecule and, therefore, cannot be "defective" as that term is understood in state-law product liability actions; it can be only what it *is* and *cannot* be designed any differently. To solve those problems, the district court declared proximate cause "was out of the case"[5] (CA Add. 44; CA Appx. 1281-83, 1285), and (contrary to longstanding precedent[6]) eliminated

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[5] Ms. Bartlett's only burden on causation was to establish medical causation (cause-in-fact).

[6] *Compare* JA 279-80 (holding Ms. Bartlett "can prevail on a products liability claim by proving that a product was

the "defect" requirement from the claim entirely, declaring that Ms. Bartlett could succeed on her "defective design" claim merely by establishing sulindac was unreasonably dangerous.[7]

However, even under the district court's "defective design" theory, the determination of unreasonable danger necessarily turned on the adequacy of the product's warnings. The jury instructions tell the tale:

> Now, if you determine that sulindac was unreasonably dangerous, you may consider the presence and efficacy or effectiveness of a warning to avoid an unreasonable risk of danger from foreseeable uses of the product. The plaintiff must prove that the product was unreasonably dangerous even with its warning.

'unreasonably dangerous pursuant to the risk-utility balancing test'….") *with Buckingham v. R.J. Reynolds Tobacco Co.*, 142 N.H. 822, 713 A.2d 381 (1998) (holding plaintiff must allege and prove that (1) a defect existed in the product and (2) because of the defect the product was unreasonably dangerous. New Hampshire law is addressed merely to emphasize the stark contrast between the unique claim sanctioned here that required no evidence of a defect and the historically-recognized failure-to-warn claim applicable to most prescription pharmaceuticals.

[7]Under the district court's creation, "defective condition" and "unreasonably dangerous" became synonymous even though the jury was asked to decide if the "defective condition" made sulindac "unreasonably dangerous." (JA 519, 512.)

> 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 Mrs. Bartlett 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 Mutual.

(JA 513-14.) The jury, however, was not told that Mutual, as a generic drug manufacturer, could not change the sulindac labeling.[8] Furthermore, the jury was told to evaluate warnings as part of the risk/benefit analysis,[9] but was not told that Ms. Bartlett and her prescribing physician never saw Mutual's sulindac labeling. (*Id.*) In short, the district court permitted Ms. Bartlett to present a failure-to-warn claim to the jury, but without the burden of proving proximate cause.

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[8] The district court had denied Mutual's motion based on federal preemption twice before trial holding both times – incorrectly pursuant to *Mensing* – that Mutual was not precluded by federal law from changing the sulindac package insert. (PA 142a-202a; 140a.)

[9] The district court also instructed the jury that in considering the "presence and efficacy of a warning to avoid an unreasonable risk of danger" it could "consider the FDA's requirements for drug labels." (JA 516.) The court then read FDA's regulations relating to the format and content of prescription drug labeling to the jury. (JA 516-518.)

The First Circuit acknowledged that the risk/benefit evaluation at the heart of Ms. Bartlett's "design defect" claim depended on the adequacy of the sulindac labeling, (PA 18a-19a ("[T]he label was relevant to the design defect claim since, although unalterable by Mutual, its arguable inadequacies put limits on the extent to which its dangerousness was offset by adequate warnings; so the lack of clearer warning made the product itself more dangerous under the risk-benefit test…."), and recognized sulindac's design could not be changed (PA 10a ("Mutual cannot legally make sulindac in another composition (nor is it apparent how it could alter a one-molecule drug anyway)….")). Nonetheless, the First Circuit accepted the fiction that the labeling could be alternately separated from (to state the claim) and joined to (to assess the claim) the sulindac tablet as plaintiff's needs suited and ruled that *Mensing* did not preempt "design defect" claims. Rather than faithfully apply *Mensing* to the *real* claim in this case, the First Circuit relied on the "logic" of this Court's decision in *Wyeth v. Levine*, 555 U.S. 555 (2009), to conclude that the "FDCA might permit states to tell Mutual it ought not be [making or marketing its product]." (PA 10a-11a.)

SUMMARY OF ARGUMENT

The First Circuit's decision stands in stark contrast to and cannot be reconciled with the federal law governing generic drug products or this Court's decisions. The Drug Price Competition and Patent Term Restoration Act governs the approval and sale of generic drugs in the United States. Under 21

U.S.C. §355(j), a generic drug must be the same as the reference listed drug ("RLD") upon which it is based. That sameness requirement applies to the "active ingredient," the "dosage form and strength," "the route of administration," and "labeling." *See* 21 U.S.C. §355(j). In *Mensing*, this Court recognized the "federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers," and that "different federal statutes and regulations may, as here, lead to different pre-emption results." *Mensing* 131 S. Ct. at 3582. It held that the plaintiffs' lawsuits aiming state-law claims against generic drug manufacturers that conflict with those federal requirements are preempted.

To avoid the straightforward application of this Court's decision in *Mensing*, the First Circuit accepted the fiction that sulindac could be divorced from its labeling even while the jury was instructed that liability depended on the adequacy of the sulindac labeling. That the labeling was the pivotal issue of this lawsuit is not surprising. The reason is fairly evident when one considers the nature of pharmaceutical products and the long history of tort law that has developed as a result. To be more precise, a drug without its labeling has no identified benefits and no identified risks. It, therefore, is impossible to either state a claim or prove a claim that a drug product's risks outweigh its benefits (i.e., is "defective in design") without reference to and evaluation of the product's label, which leads to the conclusion that where drugs are concerned, the product liability claim is one for "failure to warn." In

the context of lawsuits against generic drug manufacturers, that means the claim is preempted.

Although recognizing that Ms. Bartlett's "design defect" claim depended on sulindac's warnings, the First Circuit tried to side-step *Mensing* by describing it as an "exception" to *Levine's* "general no-preemption rule." (PA 9a, 11a.) The First Circuit then proceeded to apply that "general no-preemption rule" to Ms. Bartlett's "design defect" claim to uphold the verdict. The First Circuit simply chose not to apply *Mensing* without any discussion of the relevant statute, even though *Mensing's* rationale applies equally to the design and labeling of generic drugs, and instead applied the "logic" of *Levine*, even though this Court acknowledged in *Mensing* that *Levine* did not apply to generic drugs. *Mensing*, 131 S. Ct. at 2581-82.

The First Circuit's ultimate rationale for concluding that Ms. Bartlett's claim was not preempted; i.e., that Mutual did not have to sell its product, sidesteps the preemption analysis. There cannot be a conflict between federal law and state law if no law applies. Under the First Circuit's rationale, the preemption issue never arises. That analysis is no analysis at all. Moreover, if, as the First Circuit held, a state might be permitted to tell a manufacturer it ought not sell its federally-approved product, either directly or by imposing damages, state law effectively would preempt federal law.

The First Circuit's rationale carried to its conclusion would thwart Congress's objectives in

enacting not only the Hatch-Waxman Amendments but also the FDCA. While Congress intended to increase the availability of low-cost generic drugs, the First Circuit's suggestion that a state might, through a jury, prohibit the sale of generic drugs or assess damages based on the sale of the federally-approved product would have the effect of decreasing the availability of low-cost generic drugs, either because those drugs are no longer sold, or because they are available only at significantly increased prices.

The First Circuit's decision also threatens the drug approval process – one that has been in place for many decades. Years ago, Congress decided to centralize approval decisions relating to drug products in FDA. The First Circuit advocates that lay jurors who likely will have little to no relevant education or experience should be permitted to second-guess FDA's analysis and make the complex scientific decisions involved in assessing the risks and benefits of drug products and whether they should be sold in interstate commerce. It ignores the disparity of information a jury will have available to it to make that decision from the information available to FDA and offers no justification for wresting that decision from the agency Congress, decades ago, vested with responsibility for making it.

The First Circuit would leave manufacturers to the whims of state-law juries, who will be asked to, and will decide, based on limited cherry-picked information, whether a drug product's risks outweigh its benefits. It takes years for FDA to assess a drug's

safety profile. In contrast, a jury trial involving pharmaceutical products is measured in days or weeks, during which time not only is testimony related to the actual drug presented, but also testimony related to the plaintiff's injury, life, and medical history. In sum, two or three days, maybe less or maybe a little more, of that trial *may* be devoted to testimony regarding the drug and its alleged benefits and risks.[10] The First Circuit would have a jury, who receives two to three days of information in the context of hearing only a single plaintiff's tale, second-guess a decision an expert agency developed over several years. That result flies in the face of the FDCA.

Without the ability to change the design of the drug or to change the drug's labeling, the First Circuit's decision subjects generic drug manufacturers to absolute liability if they choose to sell generic drugs. The First Circuit's alternative, withdrawing from the market to avoid damages, would inevitably result in the unavailability of low-cost generic drugs to the detriment of the American public.

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[10] The trial in this case lasted slightly less than three weeks, and a significant amount of that time was spent on issues outside the presence of the jury. (*See generally* District Court's Transcript of Proceedings.)

ARGUMENT

A. "DESIGN DEFECT" CLAIMS ARE DIRECTED TO THE PRODUCT'S WARNINGS

Last term, this Court explained that the design of a product and its warnings are connubial concepts. In rejecting the plaintiffs' contention in *Kurns* that "[t]he basis of liability for failure to warn ... is not the 'design' or 'manufacture' of a product," but rather "the failure to provide adequate warnings regarding the product's risks," this Court recognized that

> [a] failure-to-warn claim imposes liability on a particular design of [a product] unless warnings deemed sufficient under state law are given. This duty to warn and the accompanying threat of liability will inevitably influence a manufacturer's choice whether to use that particular design. By influencing design decisions in that manner, failure-to-warn liability has a "'direct and substantial effect' on the "physical elements" of a [product].

Kurns v. Railroad Friction Products Corp., 132 S. Ct. 1261 (2012).

The relationship between a product's design and its labeling is particularly germane to pharmaceuticals. A drug's initial risk profile is developed during clinical trials conducted to support

approval of the new drug application ("NDA"), and the risk profile is defined in the product's labeling. Unlike many products, a drug's risks cannot be altered or improved by changing the design, i.e., its active pharmaceutical ingredient ("API")[11], for the simple reason that a drug with a different API is a different drug – one that has its own risk profile. *See, e.g., Sprague v. Upjohn Co.*, No. 91-40035, 1995 WL 376 934, at *1 (D. Mass. May 10, 1994) ("Halcion is incapable of being … redesigned. To alter the chemistry of the [t]riazolam molecule, would be to create a new … product."). Therefore, with respect to pharmaceutical products, the "physical element"[12] (the API) necessarily defines the warnings. Indeed, the warnings for a pharmaceutical product are drafted for a product with a specific API – and none other. As a result, claims involving a pharmaceutical product necessarily arise from the product's labeling; they allege either that the pharmaceutical product labeling failed to adequately disclose the risks inherent in the product when the NDA was approved or failed to account for new data after approval.

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[11]References to the "design" of a drug are to API because it is the relevant constituent of a drug that is the subject of state-law claims. While inactive ingredients can be changed, they seldom are the subject of personal injury lawsuits, and were not the subject of this lawsuit.

[12]Generic drug manufacturers have no "choice" in the "particular design" of their products. The "design" is limited to the approved API for the reference listed drug.

Attempts to selectively untether the design of a prescription drug from its labeling by allowing a claim that "the drug's risks outweighed its benefits" making it unreasonably dangerous ignore one very salient fact: The FDA-approved "benefit" is derived only by reference to the approved indications in the product labeling, and the source of the "risks" to which the benefits are compared also is the FDA-approved labeling. In other words, a pharmaceutical product cannot be divorced from its label as it is not possible to conduct a risk/benefit (i.e., design defect) evaluation without the product labeling.

The concept that a drug is nothing without its label is both a practical and a legal concept. Imagine being handed a small round pill. One cannot hold that pill in the palm of one's hand and know its active ingredient, what benefit it might deliver, and what risks it may present. The pill is given meaning only by the label that identifies that ingredient. However, knowledge of the ingredient itself is not sufficient to give the product utility. One must know the product's uses, the dose at which it should be administered, its contraindications, the risks associated with its administration, as well as the other information in the labeling.[13] None of that is evident without the labeling. In fact, drug products are approved for sale by the FDA as safe and effective for use as recommended in the submitted labeling. (*See, e.g.,* CA 2169 (Defendant's Ex. 188, Letter from R. Williams to Mutual, April 17, 1991

[13] It is exactly for that reason that Congress entered the field of drug regulation over a century ago.

(approving Mutual's sulindac as "safe and effective for use"); *see also* 21 U.S.C. §355(d) (requiring FDA to refuse approval of new drug application where application does not include data to show drug is "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling").) In that regard, drugs are unique. One can look at a ladder and surmise its purpose and its benefits – to help humans reach higher places than they could without it; one cannot look at that small round pill and know its purpose or its benefits. Reference to the approved labeling is required as the use of the product is a function of its approved labeling. As a result, it is impossible to allege the risks of a pharmaceutical product outweigh its benefits without implicating the labeling. Ms. Bartlett's allegation is a case in point.

Ms. Bartlett's design defect claim was that "sulindac was in a defective condition unreasonably dangerous to the user/consumer … in that its foreseeable risks exceeded the benefits." (JA 104-105, ¶¶53, 55.) Sulindac's benefits (its approved uses as indicated on the product labeling) are that it treats osteoarthritis, rheumatoid arthritis, acute gouty arthritis, ankylosing spondylitis, and acute painful shoulder (acute subacromial bursitis/supraspinatus tendinitis).[14] (JA 553.) The foreseeable risk Ms. Bartlett targeted was an alleged

[14] Sulindac is the only NSAID approved to treat acute painful shoulder (acute subacromial bursitis/supraspinatus tendinitis) (the condition for which it was prescribed to Ms. Bartlett (JA 82, ¶8)) and acute gouty arthritis. (PA 46a.)

potential to cause rare, idiosyncratic allergic reactions – Stevens Johnson Syndrome ("SJS") and toxic epidermal necrolysis ("TEN") – both identified in the sulindac labeling. (JA 554.) In other words, she claimed that sulindac did not have the efficacy disclosed in the package insert, or that it presented risks greater than those set forth in the package insert. Plaintiffs' allegations make that much clear. That is why the First Circuit ultimately acknowledged that the product's warnings are an integral part of the analysis. (PA 18a-19a.)

There can be no doubt that design defect claims involving a pharmaceutical product directly target the product warnings and in substance are failure-to-warn claims. That conclusion is inescapable given that part and parcel of the drug's approval is the approval of the drug's labeling. One is not, and cannot, be approved without the other. *See* 21 U.S.C. §355.

That is not to say that drug product labeling is static; it is not. The risk profile of a drug continues to develop over the course of the years it is marketed. When, and if, new risks are identified, either the brand-name drug manufacturer or FDA will institute a label change to reflect the changed risk profile. Generic drug manufacturers then will follow suit, changing their labels to be the same as the reference listed drug. Those facts do not detract from the maxim that a drug and its label must be evaluated together. Rather, they reinforce that the underlying premise of the claim against a drug manufacturer remains a failure-to-warn claim. Under this Court's

decision in *Levine* and *Mensing*, a brand-name manufacturer may be subjected to state-law liability for a failure to warn, but a generic drug manufacturer may not.

B. THE FIRST CIRCUIT'S DECISION IS IN DIRECT CONFLICT WITH BOTH THE HOLDING AND RATIONALE OF *MENSING*

Recognizing the inseparability of the label from the evaluation of a drug's design, it is clear Ms. Bartlett's claim was merely a disguised failure-to-warn claim. The First Circuit decision not to apply *Mensing* directly conflicts with both the holding and the rationale of *Mensing*.

The First Circuit understood that Ms. Bartlett's claim depended on sulindac's warnings: "[T]he label was relevant to the design defect claim since, although unalterable by Mutual, its arguable inadequacies put limits on the extent to which its dangerousness was offset by adequate warnings; so the lack of clearer warning made the product itself more dangerous under the risk-benefit test…." (PA 18a-19a.) In other words, the First Circuit recognized that the *only* change that could be made to alter sulindac's risk/benefit equation was a change to the labeling. That recognition should have ended the analysis because it identified that the true nature of the claim before it was based on the product's warnings and *Mensing* bars that claim. The First Circuit, however, discounted the significance of the labeling by asserting that the claim was not a failure-to-warn claim, as though

Mensing did not apply if the failure-to-warn claim simply was given a different name.

Ignoring the fact that "federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers," and that "different federal statutes and regulations may … lead to different pre-emption results," *Mensing*, 131 S. Ct. at 2582, the First Circuit chose to apply the "logic" of *Levine* rather than the "logic" of *Mensing*. According to the First Circuit, this Court adopted a "general no-preemption rule" in *Levine* to which *Mensing* was merely an exception that applied to claims premised on inadequate warnings involving generic drugs. (PA 8a-11a.) The First Circuit recognized that *Levine* involved brand-name drugs and that its "holding was technically limited to failure-to-warn claims," but nonetheless concluded that *Levine's* "logic applies to design defect claims" involving both brand-name and generic drugs. (*Id.* 9a and n.2.) Yet, it chose not to apply the "logic" in *Mensing* because *Mensing* merely "carved out an exception to *Wyeth*, finding that the FDCA preempts failure-to-warn claims against generic drug manufacturers" (*id.*), and that the question of whether the FDCA similarly preempts "design defect claims against generic drug manufacturers … has yet to [be] decide[d]." (*Id.* 8a.)

However, even if the design defect claim did not depend on the product labeling, the "same as" requirement in 21 U.S.C. §355(j), applies to much more than labeling—it applies to the generic drug's

design; i.e., its "active ingredient," "route of administration," "dosage form," and "strength." The First Circuit never referenced the statute and offered absolutely no explanation of why the analysis should differ for a design defect claim.

C. REMOVING THE PRODUCT FROM THE MARKET DOES NOT RESOLVE THE CONFLICT AND RAISES CONFLICTS OF ITS OWN

Acknowledging, as they must, that Mutual could not change the sulindac molecule (either physically or legally), the district court, and ultimately the First Circuit, concluded that the claim was not preempted because Mutual could have chosen not to sell its product. (PA 10a, 11a.) Fundamentally, that solution ignores necessary elements of the preemption analysis and elevates state law over federal law. Moreover, it is irreconcilable with Congress's purposes and objectives in enacting Hatch-Waxman as well as Congress's purposes and objectives in enacting the FDCA.

1. The First Circuit's Decision Ignores Necessary Elements of the Preemption Analysis and Elevates State Law over Federal Law

"The Supremacy Clause establishes that federal law 'shall be the supreme Law of the Land … any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.'" *Mensing*, 131 S. Ct. at 2577 (quoting U.S. Const. Art. VI, cl. 2.) The First

Circuit decided Ms. Bartlett's state-law claim is not preempted because Mutual could avoid state law damage awards by merely choosing not to sell its federally-approved product. (PA 10a, 11a.)

The First Circuit's analysis and decision ignores a basic, fundamental premise: If the product is not on the market there are no applicable laws. With respect to the sale of products that are federally regulated that means there is no applicable federal law and, concomitantly, there is no applicable state law. It is not until the manufacturer sells a product that the laws and the Supremacy Clause become applicable.

In the case of generic drugs that means the manufacturer must comply with the requirements in 21 U.S.C. §355(j). On the state level, the manufacturer must ensure its product is safe and adequately labeled. As a result, the preemption analysis requires: (1) the product to be on the market; (2) an applicable federal law – here the Hatch-Waxman Amendments to the FDCA and FDA's regulations governing generic drugs; and (3) an applicable state law – here state product liability law.

If those facts do not exist, there is no federal law that can be supreme to the law of any state. If Mutual had not sold sulindac, there would be no lawsuit and this case would not be before this Court. The Supremacy Clause anticipates – in fact, requires – an applicable federal law and an applicable state law. The First Circuit's rationale

would simply eliminate the need to apply the Supremacy Clause—a result this Court rejected. *See Mensing*, 131 S. Ct. at 2579 ("We do not read the *Supremacy* Clause to permit an approach to preemption that renders conflict pre-emption all but meaningless.").

Moreover, the First Circuit's conclusion that it was appropriate to assess damages against Mutual because it chose to sell its federally-approved product – a product whose design and labeling it could not change – elevates state law over federal law. Rather than avoiding the conflict, the First Circuit's solution heightens it.

2. The First Circuit's Decision Conflicts with Congress's Purposes and Objectives in Enacting Hatch-Waxman

In 1984, in recognition of the need for a less-costly procedure for approval of generic drugs, Congress passed the Hatch-Waxman Amendments. The overriding purpose of the Amendments was to increase the availability of low cost generic drugs. *See* "P.L. 98-417, Drug Price Competition and Patent Term Restoration Act," H.R. Rep. No. 857(I), 98th Cong., 2d Sess. (1984), reprinted in 1984 U.S.C.C.A.N. 2647; *New Drug Application: Hearings on H.R. 3605 Before the Subcomm. On Health and the Environment of the House Comm. on Energy and Commerce*, 98th Cong., 1st Sess. (1983); Drug Price Competition and Patent Term Restoration Act of 1984, Committee Notes, 130 Cong. Rec. 24416, H.R.

3605 (daily ed. Sept. 6, 1984); Drug Price Competition and Patent Term Restoration Act, Committee Notes, 130 Cong. Rec. 24970, S. 1538 (daily ed. Sept. 12, 1984). One would be hard-pressed to conjure a more frontal attack on Congressional objectives than the suggestion that generic drug companies avoid state-law liability by either withdrawing their products or not selling them in the first instance.[15] While Congress intended to promote and make low-cost generic drugs more readily available, the First Circuit advocates generic drug companies unilaterally withdraw those same drugs from the market thereby decreasing their availability.

The alternative of simply paying damages for selling the generic drug is no better. The First Circuit would have juries assess large and repeated damages against generic drug companies for selling the drugs Congress sought to have approved and sold. The higher prices that would result again subvert Congressional objectives.

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[15] Likewise, it would be contrary to the purposes of the expedited approval process applicable to generic drugs to place companies in the untenable position of extensively researching marketed pharmaceuticals to second guess the FDA's conclusions whether they are safe and effective before making generic versions of those drugs.

3. Permitting Juries to Second-Guess FDA's Risk-Benefit Determinations Conflicts with Congress's Purposes and Objectives in Enacting the FDCA

In 1938, Congress revamped the Pure Drug and Food Act passed in 1906, and vested authority in a federal agency to review and approve drug products before they could be sold in the United States. The passage of the FDCA marks the advent of the requirement that drugs be approved before they can be sold. The 1938 Act placed exclusive authority in FDA to determine whether a drug product was safe for sale in interstate commerce. That exclusive authority remains in FDA today.

However, in the wake of *Mensing*, plaintiffs are inviting and encouraging courts to wrest that authority from FDA's hands and place it in the hands of juries across the country – an invitation the First Circuit accepted. Rather than having the agency designated by Congress, which is staffed with highly trained physicians and scientists who have access to neutral outside expert advisory committees determine whether drugs may be sold, the First Circuit advocates placing that function in the hands of jurors with access only to incomplete, biased information. Instead of having the agency that possesses all the information regarding a drug – the original clinical studies, all adverse events reported since the initial sale of the drug (from all sources), the worldwide medical literature, and all the data regarding other marketed drugs − decide its safety

for sale, the First Circuit favors placing that determination in a jury's hands.

Yet, a jury is provided only that small subset of data that counsel chooses to present through experts it chooses. The data will be limited to that which focuses on the injury or risk at issue in the lawsuit. The expert will be biased. An untrained jury of the plaintiffs' peers will be asked to decide whether the limited information they are given warrants the withdrawal of the drug product from that state's market – for all people and for all purposes. Ultimately one state-law jury's determination effectively could result in withdrawal of the drug product throughout the country, placing inappropriate and unauthorized burdens on interstate commerce.

This Court recognized that potential in *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 325 (2008), when it observed that juries are ill-equipped to regulate medical products.

> A state statute, or a regulation adopted by a state agency, could at least be expected to apply cost-benefit analysis similar to that applied by the experts at the FDA: How many more lives will be saved by the [drug] which, along with its greater effectiveness, brings a greater risk of harm? A jury, on the other hand, 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.

The Eighth Circuit Court of Appeals made a similar observation in *Brooks v. Howmedica, Inc.,* 273 F.3d 785, 797 (8th Cir. 2001): "It would be difficult for a jury focused on a single case to take into account 'the cumulative, systemic effects' of a series of verdicts. In contrast, the FDA possesses a broader perspective." That is why courts, including this one, have rejected attempts by plaintiffs to usurp FDA's powers and authority. *See, e.g., Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 348-53 (2001) (finding tort claim prohibited because it conflicts with FDA's authority to police fraud according to its own "delicate balance of statutory objectives"); *Robinson v. McNeil Consumer Healthcare*, 2010 WL 3156548 (7th Cir. Aug. 11, 2010) (holding claims for selling over-the-counter drug without stronger warnings of prescription version prohibited because "[t]he decision whether to permit a drug to be sold over the counter rather than just be prescription is for the FDA…. The agency bases its decision on whether the drug is safe and effective for use without a doctor's permission … and it has decided not to require [the drug] be sold by prescription only"); *Autin v. Solvay Pharms., Inc.*, 2006 U.S. Dist. LEXIS 19507 (W.D. Tenn. Mar. 31, 2006) (concluding "court cannot usurp FDA's power to evaluate the effectiveness of a drug or to approve a drug").

The verdict in this case bears out those concerns. Even though the potential risk of developing SJS/TEN (an idiosyncratic, allergic

reaction that cannot be predicted), according to Ms. Bartlett's experts, occurs only in between one to two patients per million (JA 424), a lay jury of ten members, presented with limited information (far less than FDA possesses), determined that sulindac should not be marketed at all. In other words, they decided based on their purported risk/benefit analysis that the risk to those few exceeded the benefits for the 999,998 patients per million who used the drug beneficially. And, they reached that conclusion despite the fact that FDA concluded after extensive analysis that sulindac should not be withdrawn from the market.

In enacting the FDCA, Congress established a uniform, feasible, safe, and economically sound set of rules implemented by experts at a single agency to determine drug safety and approve drugs for sale. Approval of drugs for sale belongs in FDA's hands and not a jury's.

Indeed, the First Circuit recognized that permitting juries to evaluate whether the risks of a drug product outweighed its benefits and whether a drug should be sold amounted to "second-guessing the FDA," but concluded that "*Wyeth* resolved the conflict against general preemption." (PA 10a.) While FDA approval alone has never found favor as a grounds for preempting state-law claims, it is an unwarranted extension of *Levine* to sanction the substitution of a jury's risk/benefit analysis for that of FDA, especially in the circumstance where a generic pharmaceutical company has no choice in either the risks or benefits it discloses and where the

only alternative is removal of the product from the market in direct contrast to the statute's core objectives. Indeed, for the branded drug company, the conclusion that a product's labeling does not accurately describe the drug's potential risks is remedied through a revised package insert, rather than through the draconian conclusion that the product should not be sold.

It also raises the specter of why Congress enacted the FDCA and centralized the safety and efficacy determination regarding drugs and whether or not they should be sold in interstate commerce in FDA. Had Congress intended lay juries to make that decision, it simply could have left matters as they stood. The complexity of drug products, however, counseled the development of a single agency staffed with professionals who have both the training and experience to make informed decisions. Those decisions should not be placed in the hands of juries.

D. LEFT STANDING, THE FIRST CIRCUIT'S DECISION WOULD SEVERELY IMPACT THE GENERIC DRUG INDUSTRY AND THE AVAILABILITY OF GENERIC DRUGS

The savings to American consumers and federal and state governments since the Hatch Waxman Amendments were enacted are not subject to debate. (*See* GPhA Rpt. (noting sale of generic drugs has saved American consumers more than $1 trillion over the last 10 years.) Generic drugs do not pose additional risk to patients because FDA already

has determined that the drug is safe and effective when accompanied by the FDA-approved labeling.

The landscape will change dramatically if the First Circuit's "defective design" type claim is allowed. No longer will generic drug manufacturers and the public be able to rely on FDA's safety and efficacy determination. No longer will they be able to rely on the sufficiency of the package insert. Instead, generic drug manufacturers will be faced with the prospect of absolute liability for every drug they sell – drugs for which they cannot change the warnings or other aspects of the design. The unprecedented imposition of absolute liability will force them (and others who may bear the risk such as insurance companies) to reassess the wisdom of being a market participant.[16]

The American public will feel the impact as generic drug prices inevitably will rise. The strides that have been achieved since the Hatch-Waxman Amendments were enacted will be lost. While today nearly 80% of all prescriptions are filled with generic drugs at only 27% of prescription drug costs (*see* IMS 2012), tomorrow's tale could be far different.

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[16] The First Circuit's decision makes the environment even more hostile for generic drug manufacturers by removing causation from the elements a plaintiff is required to prove in order to prevail on a "design defect" claim. It affirmed the district court's decision that a "design defect" claim could be submitted to the jury based on alleged deficiencies in Mutual's labeling even though neither Ms. Bartlett nor her prescribing physician ever saw Mutual's labeling.

In short, the First Circuit's "defective design" claim threatens to turn back the clock, decrease competition, and increase prescription drug costs.

CONCLUSION

The First Circuit's decision should be reversed.

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