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 FOR DR. JOHN T. SCHULZ, III AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENT

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INTEREST OF *AMICUS CURIAE* [1]

Amicus curiae Dr. John T. Schulz, III is a surgeon specializing in burn trauma and critical care and the head of the burn unit at Bridgeport Hospital in Connecticut, which is part of the Yale-New Haven health system and associated with Yale Medical School. He has a Ph.D. from Harvard in Biochemistry, a medical degree from Yale, is on the faculty of the Yale School of Medicine, and has taught at Harvard Medical School. In addition to his surgical practice, Dr. Schulz is a research scientist who has conducted clinical and basic research in a number of areas, including research on toxic epidermal necrolysis, one of the conditions caused by sulindac and suffered by Respondent Karen Bartlett. He has researched, published on, and treated patients with TEN for over 14 years.

Dr. Schulz was one of Respondent's treating physicians at the Mass. General Hospital burn unit. He testified at the trial below regarding the nature and extent of Respondent's injuries and his treatment of Respondent.

Dr. Schulz is interested in this case because of his personal experience with the harm that sulindac caused to one of his patients, his extensive knowledge of the dangers of sulindac and of Stevens-Johnson

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[1] No counsel for a party authored this brief in whole or in part, nor did any person or entity, other than *amicus* or his counsel, make a monetary contribution intended to fund the preparation or submission of this brief. This brief is submitted pursuant to the blanket consent letters from all parties, on file with this Court.

syndrome and toxic epidermal necrolysis in general, and his concern that FDA is not capable of acting as the sole bulwark against the dangers of drugs like sulindac.

SUMMARY OF ARGUMENT

1. The regulatory history of sulindac – a non-steroidal anti-inflammatory drug ("NSAID") – is an unfortunate example of how FDA is not capable of being the sole guardian of public safety in connection with drugs. First cleared for sale in 1978, previously unappreciated threats from sulindac emerged in subsequent decades, including the severe, though infrequent and unpredictable, threat of Stevens-Johnson syndrome and toxic epidermal necrolysis ("SJS/TEN"). Almost all NSAIDs carry some risk of SJS/TEN, but the risk from sulindac was higher than all other NSAIDs on the market from 1980 through 1997. Although FDA eventually required the labels of NSAIDs to carry warnings of this threat, it did not request sulindac's removal from the market or withdraw its consent for the sale of the drug.

In 2005, by contrast, FDA asked that Bextra – a then relatively new COX-2 selective NSAID – to be withdrawn from the market based on 7 reported deaths from SJS/TEN, a supposedly higher reporting rate of SJS/TEN for Bextra than for other COX-2 selective NSAIDs, and the lack of unique medical advantage for Bextra compared to other NSAIDs. At the same time, however, FDA essentially ignored equally or more damning evidence against sulindac. In fact, sulindac was associated with significantly more deaths from SJS/TEN than Bextra, had the

highest adjusted reporting rate of SJS/TEN compared to any other NSAID between 1980 and 1997, had a higher death rate per reported case than Bextra, and there was more compelling evidence of a causal link between sulindac and SJS/TEN than there was for Bextra. Sulindac thus raised safety concerns comparable to or greater than Bextra and similarly had no offsetting medical advantages relative to the numerous other NSAIDs on the market.

FDA's inconsistent treatment of the serious dangers of Bextra and sulindac illustrates that FDA is not an omniscient and unerring arbiter of drug safety, as Petitioner and its *amici* seem to suggest. Rather, it is a body with limited time, resources, and expertise that is not capable of being the exclusive judge of drug safety in the United States. While it performs an important function as a first-line safety hurdle and a last-ditch safety backstop, it cannot replace the decentralized operation of state common law as a means of addressing drug safety issues above the inconsistently implemented federal minimum standards.

2. In addition to being *incapable* of performing the role of an exclusive and centralized arbiter of drug safety or hazard, FDA was never designed nor intended to assume such a role. Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 310, *et seq.*, FDA approval is not the *final* say on whether a drug is safe, and it does not confer a *right* to sell any particular drug throughout the United States. Rather, it is only the *first* determination regarding drug safety and a condition precedent to avoiding a preemptive congressional bar on the sale

of a drug. And there certainly is nothing in the FDCA giving FDA authority to decide how to allocate responsibility for the risks and consequences of various drugs that have overcome the minimum federal hurdle and made it onto the market. It is perfectly consistent with the role of FDA and its actual operations in this area for it to determine that a drug may be safe enough to avoid a preemptive congressional bar on its sale, yet for various States to determine that the remaining dangers of the drug are such that responsibility for the risks from its use should be allocated to the manufacturer. Such potential state-law liability does not second-guess FDA's enforcement of federal minimum safety standards; it addresses a wholly separate question that FDA lacks authority to answer.

2. The Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984), likewise does far less than Petitioner and its *amici* suggest. To start with, this case has nothing to do with any differences between generic and brand-name manufacturers. Strict liability would apply equally to *any* manufacturer of sulindac, and the so-called "sameness" requirement imposes no unique burden on generic manufactures in this context. Furthermore, the Act does not grant generics unique legal and economic immunity in the market. Rather, it merely provides expedited and simplified means for additional companies seeking to sell generic versions of drugs already on the market to clear the FDA-approval hurdle. The Act does so by lowering unnecessary barriers to entry if a drug is the same as one already on the market, thus allowing for increased competition on equal footing with the brand-

name manufacturers that could recoup their initial FDA approval costs during their period of patent exclusivity.

Contrary to Petitioner's repeated suggestion, the Hatch-Waxman Act does not *require* any manufacturer to produce a drug that is the "same" as an existing drug on the market. "Sameness" is merely a condition precedent to the simplified procedures designed to put generics on equal competitive footing with their branded alternatives. Hatch-Waxman never sought to insulate them from *all* state-law liability, much less from the "same" strict liability that would be faced by their branded competitors. If any given drug is deemed unreasonably dangerous and hence subject to strict liability, that determination would apply equally to the branded and generic versions of the drug (assuming the generics were, in fact, the "same" as the branded version in all material respects). Liability such as found in this case thus puts no unique burdens on generics, puts them to the exact same choices as their branded competitors, and thus is entirely consistent with the purposes and terms of the Hatch-Waxman Act.

ARGUMENT

I. FDA's Failure Concerning the Dangers of Sulindac Illustrates the Inappropriateness of Enthroning FDA as the Exclusive Arbiter of Drug Safety.

Sulindac is a non-steroidal anti-inflammatory drug ("NSAID") used to relieve pain resulting from a variety of conditions. [JA553] It was first approved by FDA for sale in 1978. After the patent on Sulindac

expired, it was approved for sale in generic form in 1988, and approved for sale by Petitioner in 1991. [CAA2169]

Although pre-marketing clinical trials of sulindac "indicated the occurrence of only relatively mild adverse effects, * * * during postmarketing clinical experience, reports began to accumulate describing serious adverse reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, hepatotoxicity, pancreatitis, granulocytopenia, aplastic anemia, and thrombocytopenia." Glen D. Park, Reynold Spector, Thomas Headstream, and Mark Goldberg, *Serious Adverse Reactions Associated with Sulindac*, 142 ARCH. INTERN. MED. 1292 (1982). [JA596] While those reports influenced sulindac's label, which by 2002 warned that adverse "[d]ermatologic" reactions including TEN and SJS, along with other "[h]ypersensitivity reactions," were "potentially fatal" [JA554], the drug remained on the market.

FDA's failure to pull sulindac's approval for marketing is particularly surprising given that medical reports throughout the 1980s and 1990s regularly listed sulindac as a leading cause of SJS/TEN.[2] In fact, from 1980 to 1997, sulindac had more reported cases of SJS/TEN in FDA's reporting system than

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[2] *See, e.g.*, Michael Bigby, Robert S. Stern, and Kenneth A. Arndt, *Allergic Cutaneous Reactions to Drugs*, 16 PRIMARY CARE 713, 719 (1989) ("Two large series of cases [of TEN] have been reported. The drugs most commonly implicated are the NSAIDs (especially phenylbutazone, oxyphenbutazone, sulindac, and piroxicam), antibiotics (especially trimethoprim-sulfamethoxazole), the barbiturates, phenytoin, and allopurinol."). [JA613]

any other NSAID. Robert S. Stern, Maja Mockenhaupt, Judith Parsells, and David Kaufman, *Analysis and Prevention of Data that assess the risk of Stevens-Johnson Syndrome and toxic epidermal necrolysis associated with nonsteroidal anti-inflamatory drugs* 10-11 (Final Report to Pharmacia, Inc., Oct. 2001) ("The NSAIDs with the most reports coded as SJS or TEN, (sulindac (89 reports)) ranked fifth among all drugs on the basis of total reports."). [JA627-28] By 2004, the number of reports for sulindac had grown to 134. [Pet. App. 44a (district court discussion of the testimony)]

Not only did sulindac have the highest total number of reports among the NSAIDs, it also had the highest adjusted rate of reports and, along with the next closest NSAID, had "*significantly and substantially higher rates* of reports [of] SJS/TEN reactions relative to office visits with a prescription than other NSAIDs." *Id*. at 12 (emphasis added). [JA629]; *see also* Maja Mockenhaupt, Judith Parsells Kelly, David Kaufman, Robert S. Stern, and the SCAR Study Group, *The Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Associated with Nonsteroidal Anti-inflammatory Drugs: A Multinational Perspective*, 30 J. RHEUMATOLOGY 2234, 2237 (2003) (sulindac in the U.S. had reporting rates comparable to the high-risk NSAID piroxicam, used widely in Europe).

In addition to having a high rate of reported SJS/TEN reactions, sulindac may create a risk of more severe reactions because it has a long half-life in the body. *See* Pierre E. Wolkenstein, Jean C. Roujeau, Jean Revus, Drug-Induced Toxic Epidermal

Necrolysis, 16 CLINICS IN DERMATOLOGY 399, 403 (1998) ("NSAIDs with long half-lives (pyrazolones, oxicams, fenbufen, sulindac) are suspected to have higher risks [of TEN].") [JA623]; Tr. Testimony (Dr. Tackett) (longer half-life drugs have a higher risk of producing SJS/TEN) [JA480]. Patients "exposed to causative drugs with long half-lives had an increased risk of dying." Ignacio Garcia-Doval, Laurence LeCleach, Helene Bocquet, Xose-LuisOtero, Jean-Claude Roujeau, *Toxic epidermal necrolysis and Stevens-Johnson syndrome: does early withdrawal of causative drugs decrease the risk of death?* 136 ARCH. DERMATOL. 323 (2000).

That increased risk of death is borne out with sulindac. During the 1980s alone, there were at least 13 deaths reported in the literature for sulindac-associated SJS/TEN. *See* Kristina E. Ward, Raoul Archambault, Tracey L. Mersfelder, *Severe Adverse Skin Reactions to Nonsteroidal Antiinflammatory Drugs: A Review of the Literature*, 67 AM. J. HEALTH SYS. PHARM. 206 (2010) (reviewing articles from the 1980s reporting deaths from sulindac-associated SJS/TEN) (available at http://www.medscape.com/viewarticle/717043_4). Through 1997, reported deaths from sulindac-associated SJS/TEN totaled at least 38, with 32 in the United States. Tr. Testimony (Dr. Salisbury) [JA425]; *see also* Tr. Testimony (Dr. Tackett) (at least 39 reported deaths from sulindac-associated SJS/TEN) [JA 466]; Pet. App. 44a-45a (39 deaths out of 134 reported cases through 2004).

And if the reported incidents of, and deaths from, sulindac-associated SJS/TEN were not troubling

enough, it is well-known that drug-related SJS/TEN is notoriously under-reported, meaning that the reported cases actually vastly underestimate the true rate of drug-associated SJS/TEN. *See* Mittman, N., *et al.*, *Evaluation of the Extent of Under-Reporting of Serious Adverse Drug Reactions, The Case of Toxic Epidermal Necrolysis*, 27 DRUG SAFETY 477 (2004) (study in Canada concluding that only 4% to 10% of TEN cases are reported); Lois La Grenade, Lauren Lee, Joyce Weaver, Renan Bonnel, Claudia Karwoski, Laura Governale and Allen Brinker, *Comparison of Reporting of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Association with Selective COX-2 Inhibitors*, 28 DRUG SAFETY 917, 922 (2005) (because of substantial under-reporting, "reporting rates cannot be equated with incidence rates") [JA637]. In fact, *amicus* Dr. Schulz's own extensive experience with SJS/TEN cases at burn centers, and his knowledge of their general lack of reporting of such cases to FDA, suggests that FDA's database likely contains only 5%, or one-twentieth, of the actual cases of drug-associated SJS/TEN.

FDA's failure to recognize and respond adequately to the dangers from sulindac is particularly mystifying given its relatively timely reaction to the SJS/TEN dangers from Bextra – a more recent COX-2 selective NSAID. As part of its review of the cardiovascular risks of the newer COX-2 selective NSAIDs Celebrex, Vioxx, and Bextra, an FDA Committee also reviewed reports of SJS/TEN associated with Bextra. As a result of that review, the Committee concluded that "the overall risk versus benefit profile for Bextra is unfavorable at this time" and recommended "that

Bextra be withdrawn from the U.S. market." Memorandum, Apr. 6, 2005 ("FDA Memo."). [JA588] The Committee based this recommendation on its conclusion that although it found "no data showing that Bextra is worse than other NSAIDs with regard to CV risk," and despite the boxed warning for Bextra regarding SJS/TEN, the FDA had "received 7 spontaneous reports of deaths from these reactions" and that the "reporting rate for these serious skin reactions appears to be greater for Bextra than other COX-2 selective agents." *Id.* [JA589] The Committee found particularly notable that "the risk of these serious skin reactions in individual patients is unpredictable, * * * which makes risk management efforts difficult." *Id.* [JA589]

Based on such heightened risks, and the lack of evidence that Bextra had any advantage over other NSAIDs in terms of "a GI safety benefit, better efficacy compared to other products, or efficacy in a setting of patients who are refractory to treatment with other products," there was nothing to offset the heightened risk and thus withdrawal from the market was appropriate. *Id.* [JA589]

Comparing sulindac to Bextra makes the disparate treatment of the two drugs more than surprising. Sulindac was associated with a higher number of reported incidents of SJS/TEN than was Bextra – at least 134 versus 63. Sulindac was associated with a higher number of *fatalities* from SJS/TEN than was Bextra – at least 13 during only a fraction of its time on the market, and 39 deaths through the early 2000s, versus 7 for Bextra. Sulindac had the highest adjusted reporting rate for SJS/TEN of *any* NSAID on

the market between 1980 and 1997. Stern, *et al.*, Final Report to Pharmacia, *supra*, at 12 [JA629].[3] Sulindac had a higher fatality rate per reported incident than Bextra (39/134 versus 7/63, respectively), suggesting more serious and dangerous reactions from sulindac. And the evidence of a causal relationship between sulindac and SJS/TEN was stronger than it was for Bextra: while the reported Bextra incidents all involved a correlation between use and SJS/TEN, for sulindac there were reported cases in which a re-challenge with the drug led to a recurrence of SJS. Tr. Testimony (Dr. Tackett) (noting positive rechallenges in the sulindac literature) [JA480].

Indeed, the testimony at trial was "that sulindac had * * * a safety profile similar to other drugs deemed dangerous enough to have been withdrawn from the market," including Bextra. Pet. App. 4a-5a; *see also* Pet. App. 39a-58a, 65a (district court discussing evidence on risks and benefits; discussing expert

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[3] Although Bextra's SJS/TEN reports occurred over a shorter time period than did sulindac's reports, Bextra's usage rate was considerably higher and occurred at a time when awareness of the link between drugs and SJS/TEN had improved and reporting rates in general were higher. *See* Stern, *et al.*, Final Report to Pharmacia, *supra*, at 12 [JA629]. Indeed, that sulindac's reports were as high as they were, given the timeframe of its introduction, its lower usage rate, and the under-reporting of SJS/TEN drug reactions in general, makes it all the more remarkable that those high numbers did not trigger significant red-flags at FDA.

testimony that sulindac carried higher risk and no greater benefits than other NSAIDs).

Petitioner's suggestion, at 19, that FDA's review of Bextra, its subsequent strengthening of the warnings for other NSAIDs, and its failure to also remove sulindac from the market somehow constitute an affirmative endorsement of sulindac's safety and net benefit seriously misreads FDA's limited actions and information. There is no indication that FDA actually reviewed evidence regarding the SJS/TEN risk from sulindac and its review of Bextra was limited to a comparison to other COX-2 selective NSAIDs, not the non-selective NSAIDs such as sulindac. *See* Resp. Br. 6-7, 52-53; FDA Memo. (comparing risk to other COX-2 selective agents) [JA589]; Tr. Testimony (FDA lacked study regarding sulindac risks) [JA429-31]. Any further suggestion that FDA specifically endorsed sulindac after a "comprehensive analysis," Generic Pharm. Ass'n Amicus Br. 28, thus seems palpably false, is not backed by any evidence of such a review, and, if true, merely shows that the review was woefully deficient in that FDA did not even discuss the substantial red-flags related to sulindac. In short, nothing FDA did could possibly be deemed a considered decision that sulindac *should* stay on the market, that its cost-benefit ratio was favorable, or that state-law decisions to the contrary should be preempted.

What is actually more interesting and relevant about FDA's review of Bextra is that its reasons for why Bextra lacks any unique therapeutic benefit to offset its greater risks all apply equally to sulindac. *See* FDA Memo. (no data to distinguish NSAIDs on

other risks or unique therapeutic benefits) [JA577-79]. Furthermore, FDA found that Bextra was unfit for marketing notwithstanding that it already had a black-box warning –the strongest type available – for SJS/TEN reactions. *Id*. [JA579-81]. That treatment demonstrates that unreasonable danger can exist regardless of available warnings or even in the face of the maximum possible warning. Such a warning could not save Bextra and equally could not rehabilitate sulindac. The FDA's treatment of Bextra thus flatly contradicts Petitioner's attempts to frame this case as implicitly involving a failure-to-warn claim.

FDA's review of sulindac and related drugs illustrates that FDA is not remotely capable of adequately policing the all drugs on the market, or of responding to emerging threats in a reliable and consistent manner. Indeed, FDA's failure regarding sulindac should come as no surprise to this Court, which has already recognized FDA's "limited resources to monitor the 11,000 drugs on the market." *Wyeth v. Levine,* 555 U.S. 555, 578-79 (2009). Given such limitations, this Court should decline Petitioner's efforts to characterize FDA as more than a limited gatekeeper or to elevate it to the role of exclusive and omnipotent arbiter of all matters drug-related. FDA is not fit for that role and was not intended for that role.

II. FDA Is Not Intended To Be the Sole Bulwark Against the Dangers of Prescription Drugs Sold by Branded or Generic Manufacturers.

A. The FDCA Only Empowers FDA to Enforce Federal Minimum Safety Standards, Not to Impose Preemptive Maximum Safety Standards.

As the First Circuit recognized and Respondent further explains, FDA was never intended to be the sole arbiter of drug safety, and particular not the arbiter of the maximum level of safety that can be expected from prescription drugs. *See* Pet. App. 9a; Resp. Br. 43-45. Respondent correctly observes that the FDCA, as amended, creates a federal bar on the marketing of drugs and then provides a mechanism, via FDA approval, for escaping that federal bar. *Id*. But the lifting of the federal prior restraint on marketing a drug is not the same as granting manufacturers blanket and preemptive authorization or immunity from other constraints that may operate at the state level.[4]

Petitioner thus is flatly wrong in its repeated mischaracterization of the FDCA and FDA as having conferred upon it "the right to engage in interstate commerce free from state-law liability" Pet Br. at 40;

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[4] For example, there is no federal law *forbidding* individuals from driving at 100 mph, but there is likewise no federal right to do so. The absence of a federal prohibition does not imply a federal right. States may forbid that which federal law merely permits, but does not compel or grant a right to do.

see also id. (quoting case discussing " 'the exercise of * * * federally protected rights.' ") (citation omitted).[5]

One further point of note regarding the role of FDA is that when a court or jury applying state law imposes liability for the sale of a drug permitted on the market by FDA, it is not "second guess[ing]" FDA. Pet. Br. 56. Rather, it is answering an entirely different question. FDA is and remains the exclusive authority on whether a drug has satisfied the minimum *federal* standards necessary to remove the federal bar to marketing. If FDA determines that a drug has not met those standards, marketing remains prohibited, and no State or jury applying state law could change that result and lift the federal ban. But FDA has no authority to opine on anything beyond whether federal minimum standards are met, is never asked whether a drug meets a higher or different standard, and thus has not even offered a *first* guess on the state-law question put to the jury in this case. That is the very nature of deciding minimum rather than maximum safety – while States or juries applying state law cannot decide that *less* safety is appro-

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[5] Petitioner's suggestion, at 58, that the FDCA's procedural protections surrounding the *withdrawal* of FDA approval of a drug application demonstrates a supervening right to market drugs once initially approved is likewise wrong. Those procedural protections expressly operate against, and only against, a federal entity and are notably silent regarding any state restrictions on, or liability for, drug sales. Statutory limits on the authority delegated to a federal agent are not even remotely sufficient to grant manufacturers a free-standing right as against the sovereign authority of the States.

priate, they are free to decide that minimum federal safety is insufficient. FDA thus cannot be "second" guessed on a question that it has not answered and lacks the authority to answer.

B. The Hatch-Waxman Act Only Provides an Alternative Path for Meeting Federal Minimum Safety Requirements, Not Blanket Immunity from State Law.

In addition to misconceiving the purposes and operation of the FDCA and the role and authority of FDA, Petitioner also misconceives the purposes and operation of the Hatch-Waxman Act and even the relevance of that Act to this case. While this case happens to involve a manufacturer of a generic drug, it has *nothing* to do with any differences between generic and branded manufacturers. For purposes of strict liability, both types of manufacturers face identical risks and have identical options on how to respond to such risks. Any suggestion that the Hatch-Waxman Act provides generic manufacturers with unique immunity relative to their branded counterparts is absurd.

As explained by Respondent, at 54-55, compliance with the Act merely puts generic manufacturers in the same position as branded manufacturers – approval of an application to market a generic version of a drug is not blanket authority or a federal "right" to market that drug, but rather just the removal of the pre-existing federal impediment to such marketing.

The purpose of Hatch-Waxman was to eliminate unnecessary obstacles to competition and put generic

manufacturers on comparable footing with brand manufacturers, who had the opportunity to amortize their up-front NDA expenses over the life of their patent monopoly. But the notion that Hatch-Waxman gives generics a *greater* right to sell drugs free from state-law liability than their branded counterparts is nowhere to be found in the Act or elsewhere.[6]

The nature of New Hampshire's strict liability cause of action illustrates why there is nothing in the Hatch-Waxman Act that would distinguish generic manufacturers in this area.

Strict liability in New Hampshire makes a company financially responsible for the injuries resulting from products that are unreasonably dangerous notwithstanding the presence of a warning. As the district court recognized, under New Hampshire law, "the plaintiff must prove that the product was unreasonably dangerous *despite* any warning in place at the time of its sale." [JA343 (emphasis in original)] Indeed, it is irrelevant to the tort whether the warn-

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[6] The supposed "sameness" requirement on which Petitioner rests so much actually has nothing to do with this case and does not impose any unique constraints on generic manufacturers. Faced with an unreasonably dangerous drug, branded manufacturers are no more capable of changing the composition of the drug than are generic manufacturers. In either case a change would create a new drug and require a new NDA. The issue here thus has nothing to do with any unique restrictions on generics, as in failure-to-warn cases, but on a straight-forward reading of the FDCA and the fact that it grants no federal *right* to market an unreasonably dangerous drug – whether branded or generic – free from state-law liability.

ing is legally or factually adequate to apprise doctors or patients of the danger, and a "jury could conclude that a product is unreasonably dangerous even if its warning is adequate, or better than adequate." [JA344 (citations omitted)]

The removal of Bextra from the market perfectly illustrates why this case is not about the adequacy of the warnings and does not implicate any difference in generic manufacturers' ability to change their warnings. Bextra had the strongest warning available – a black-box warning – yet FDA still deemed its dangers to outweigh its limited to non-existent benefits in light of the many other NSAIDs on the market. The precise same reasoning is true with sulindac as well – higher risk than other drugs in its class, and no comparative advantage to such drugs, makes it unreasonably dangerous.

By permitting liability for the injuries caused by certain unreasonably dangerous drugs notwithstanding the adequacy of the warning and notwithstanding any notions of "fault" – *i.e.*, *strict* liability – this area of the common law is quite different than most other torts. Rather than being designed to deter and compensate for blameworthy conduct, it merely seeks to internalize and hence spread the cost of unavoidably dangerous products. Much like worker compensation programs, it essentially constitutes a limited insurance program recognizing that while there will be inevitable adverse consequences from certain activities, the costs of those consequences for drugs with an unfavorable cost-benefit ratio should be built into the price and borne by all, rather than borne primarily by

the few individuals unfortunate enough to suffer the consequences directly.[7]

Petitioner and its *amici* make much of the notion that by imposing such financial responsibility on generic drug-makers, strict liability might drive them out of the business of selling certain drugs or at least raise the prices they must charge for such drugs. But to the extent that being required to internalize the costs of injuries would make a drug more expensive and potentially unprofitable, that economic truism applies equally to branded and generic manufacturers, reflects the efficient operation of the market, and certainly does not conflict with anything in the Hatch-Waxman Act.

As long as a product continues to be in demand and profitable at its true (fully-cost-internalized) price, manufacturers – both generic and branded – have every incentive to sell it at the lowest competitive price possible. However, if the fully internalized cost of a product is such that there is no demand for, or profit from, such product, then it is indeed likely that *all* manufacturers would cease to sell such a product. But that is a consequence of the market and

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[7] Strict liability is not really a design defect claim, it is an inherent danger claim where the danger is unreasonable. Petitioner's claim that the design of a generic drug must be "the same" as the branded drug thus is a red herring. A finding of unreasonable danger would apply equally to the branded and generic versions of a drug, assuming they were in fact the same. Neither manufacturer has any relative advantage in how to respond to the conclusion that the drug they are selling is unreasonably dangerous.

competition from numerous other drugs with a better cost-benefit ratio and hence a lower internalized cost.

Because branded and generic manufacturers face the same cost structure and choices under strict liability, they will continue to face competition on equal footing and thus drive the price down as close to marginal cost as is economically feasible. And if the answer is the drug is not economically viable in light of its costs and dangers, then nothing in federal law insists that such a drug remain on the market absent unique circumstances not applicable here.

Finally, Petitioner argues that the "stop-selling-or-pay" theory of the court of appeals below would have led to a different result in *PLIVA, Inc.* v. *Mensing*, 131 S. Ct. 2567 (2011), and hence is untenable. Apart from the fact that generic and branded manufacturers were not on equal footing in connection with their ability to change their warnings, there is nothing wrong with the notion that a different legal argument could have led to a different result in *Mensing*. Many cases decide narrow issues as they are presented to the Court, with the clear possibility that some other, un-argued, issue, might have led to a different outcome. Whether by waiver, failure to include an argument in the Questions Presented, or otherwise, earlier cases often reach a result that would not survive later cases deciding different, yet supervening, issues. *Compare, e.g.*, *United States* v. *United Foods, Inc.*, 533 U.S.405, 416-17 (2001) (holding that compelled support of commodity advertising violated the First Amendment and declining to address government speech argument because not timely raised by the government), *with Johanns* v. *Livestock Market-*

ing Ass'n, 544 U.S. 550, 562-65 (2005) (holding that compelled support of commodity advertising involved government speech not subject to First Amendment compelled-subsidy challenge). Although there are ample grounds for distinguishing the causes of action here and in *Mensing*, even if there were not, that is entirely untroubling given the supervening answer given by the First Circuit in this case, but not presented to, or decided by, this Court in Mensing.

CONCLUSION

For the reasons above, this Court should affirm the decision below.

Respectfully submitted,

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