No. 06-1249

IN THE
Supreme Court of the United States

WYETH,

Petitioner,

v.

DIANA LEVINE,

Respondent.

On Petition for a Writ of Certiorari
to the Supreme Court of Vermont

BRIEF FOR THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AS AMICUS CURIAE SUPPORTING PETITIONER

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QUESTION PRESENTED

Whether the prescription drug labeling judgments imposed on manufacturers by the Food and Drug Administration ("FDA") pursuant to FDA's comprehensive safety and efficacy authority under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq*., preempt state law product liability claims premised on the theory that different labeling judgments were necessary to make drugs reasonably safe for use.

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INTEREST OF AMICUS CURIAE

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is a voluntary, nonprofit association that represents the country's leading research-based pharmaceutical and biotechnology companies.[1] PhRMA's members are dedicated to discovering medicines that enable patients to lead longer, healthier, and more productive lives. Member companies are the source of a majority of all new medicines that are discovered and marketed. In the past decade alone, PhRMA's members invested approximately $300 billion to develop new medicines. *See* PhRMA, *Pharmaceutical Industry Profile 2007* 42 (2007). New medicines accounted for 40% percent of the lifespan increase between 1986 and 2000. *See* Frank R. Lichtenberg, *The Impact of New Drug Launches on Longevity: Evidence From Longitudinal, Disease-Level Data From 52 Countries, 1982-2001* 21 (Nat'l Bureau of Econ. Research, Working Paper No. 9754, 2003).

PhRMA's members closely monitor legal issues that affect the entire industry, and PhRMA often offers its perspective in cases raising such issues. The issues in this case are especially significant. Unlike cases that address the law of an individual state, this case presents federal preemption issues that arise across the tens of thousands of product-liability lawsuits faced by PhRMA's members. When these state-law suits undermine FDA's regulation of pharmaceutical labeling, patients are deterred from using beneficial medicines and PhRMA's members are deterred from developing new ones.

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[1] Each party has consented to the filing of this brief and each party's letter of consent has been lodged with the Clerk. Pursuant to Supreme Court Rule 37.6, no party authored this brief in whole or in part, and no person or entity other than PhRMA or its members contributed money to the preparation or submission of the brief. A list of PhRMA's members is available at http://www.phrma.org.

STATEMENT

In this case, over the dissent of its Chief Justice, the Vermont Supreme Court upheld a nearly $7 million judgment against a manufacturer of an injectable medicine. The manufacturer was held liable because the medicine's labeling failed to disclaim a method of injection that FDA had expressly permitted after reviewing the drug's risks and benefits.

A. Before a new drug may be introduced into U.S. commerce, FDA must conclude that the drug is safe and effective for its proposed uses. *See* 21 U.S.C. § 355, *reprinted in* Pet. App. 84a-110a. In practice, FDA approves new drugs after a "sponsor demonstrates that their benefits outweigh their risks for a specific population and a specific use." *Examining Food and Drug Administration's (FDA) Drug Approval Process*: *Hearing Before the S. Comm. on Health, Education, Labor, and Pensions*, 109th Cong. 9 (2005) (joint prepared statement of Sandra L. Kweder, M.D., Deputy Dir., Office of New Drugs at Ctr. for Drug Eval. & Resrch., U.S. FDA & Janet Woodcock, M.D., FDA's Acting Deputy Comm'r for Operations).

Congress has entrusted FDA with the exclusive responsibility for making these scientific determinations. When it evaluates new drugs, "FDA considers not only complex clinical issues related to the use of the product in study populations, but also important and practical public health issues pertaining to the use of the product in day-to-day clinical practice." *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products*, 71 Fed. Reg. 3922 (Jan. 24, 2006), *reprinted in* Pet. App. 128a-129a ("*2006 FDA Labeling Regulations*").

"Few if any drugs are completely safe in the sense that they may be taken by all persons in all circumstances without risk." *United States v. Rutherford*, 442 U.S. 544, 555 (1979). Thus, a prescription drug must bear "labeling" for physicians that, based on all available scientific information, accurately and fairly describes the drug's intended uses and potential risks. *See* 21 U.S.C. § 355(d), *reprinted in* Pet. App. 107a-108a. A drug's labeling is the "centerpiece of [its] risk management." *2006 FDA Labeling Regulations*, *reprinted in* Pet. App. 129a. The labeling "reflects thorough FDA review of the pertinent scientific evidence and communicates to health care practitioners the agency's formal, authoritative conclusions regarding the conditions under which the product can be used safely and effectively." *Id.*

Federal law prohibits the introduction into commerce of drugs that are "misbranded," and federal law grants to FDA the exclusive authority to enforce the statutory prohibition against misbranding. *See* 21 U.S.C. § 331(a), (b), (k). "Misbranding" occurs when the labeling is "false or misleading in any particular." *Id.* § 352(a).

A manufacturer may propose revisions to its FDA-approved labeling at any time and must propose revisions in certain situations. But FDA intends for revisions to reflect new information—not to revisit the agency's scientific evaluation of existing information. FDA "may later deny approval of the [revised labeling], and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading." *2006 FDA Labeling Regulations*, *reprinted in* Pet. App. 130a.

Thus, "manufacturers typically consult with FDA before [revising the labeling] to avoid implementing labeling changes with which the agency ultimately might disagree (and that therefore might subject the manufacturer to en-

forcement action)." *Id.* at 132a. As explained by a former FDA Chief Counsel, "[t]he actual freedom of manufacturers unilaterally to change the packet insert is minimal." Richard M. Cooper, *Drug Labeling & Products Liability: The Role of the Food & Drug Administration*, 41 Food Drug Cosm. L.J. 233, 236 (1986).

B. State-law product-liability suits typically turn on the adequacy of the drug's FDA-approved labeling. Because no drug can be made perfectly safe, pharmaceutical manufacturers generally discharge their duties under state law if "prescribing health-care providers are adequately informed of the [drug's] relevant benefits and risks." Restatement (Third) Torts § 6 cmt. b (1998); *see also* Restatement (Second) Torts § 402A cmt. k (1965) (similar). When seeking to hold a manufacturer liable under state law, a plaintiff will argue either that the drug's labeling omitted a warning about an alleged side effect or that the drug's labeling included a statement that was affirmatively misleading.

In response to claims that their drugs' FDA-approved labeling is inadequate under state law, some defendants have argued that federal law preempts such state-law claims. Courts have considered a range of preemption arguments, which depend upon how directly FDA has considered the language at issue. Some courts have considered whether mere FDA approval of the labeling preempts state-law claims that the labeling was inadequate. *See, e.g.*, *Peters v. Astrazeneca, LP*, 417 F. Supp. 2d 1051, 1055 (W.D. Wis. 2006) (addressing whether "the FDA drug labeling process so thoroughly occupies the legislative field that it may be reasonably inferred that Congress left no room for state product liability law to supplement it") (quotations omitted). Other courts have considered whether state-law claims are preempted when FDA has considered the specific health and safety issues or warn-

ing proposal implicated by the claim at issue. *See, e.g.*, *Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d. 964, 968-69 (D. Neb. 2006) (considering whether failure-to-warn claim was preempted because defendant attempted to include warning at issue and "FDA did not insert those warnings").

The claim at issue in this case implicates the latter scenario. Plaintiff received her drug through an "IV-push"—"direct intravenous injection into her arm." Pet. App. 2a. After the drug accidentally entered her artery, she suffered gangrene, and doctors were forced to amputate her hand and forearm. *See id.* At the time Plaintiff received the drug, its labeling warned physicians that arterial injection causes gangrene and requires amputation. *See id.* at 4a. The labeling also advised that it is "USUALLY PREFERABLE TO INJECT [THE DRUG] THROUGH THE TUBING OF AN INTRAVENOUS INFUSION SET." *Id.*

Before Plaintiff received her injection, Wyeth sought to enhance the existing warning about the preferred use of an intravenous infusion set over IV-push. Wyeth proposed the following warning: "INJECTION THROUGH A PROPERLY RUNNING INTRAVENOUS INFUSION MAY ENHANCE THE POSSIBILITY OF DETECTING ARTERIAL PLACEMENT." *Id.* at 4a-5a. FDA rejected Wyeth's enhanced warning and directed the company to "[r]etain [the] verbiage in [the] current label." *Id.* at 162a.

C. The arguments for preemption in this case are especially strong because Wyeth was held liable for failing to disclaim a particular method of administering the drug. FDA had expressly determined that the labeling should endorse this particular method of administration in at least some circumstances.

Notwithstanding the warning about the potential risks of direct intravenous injection, Plaintiff argued, and the jury agreed, that "the label should not have allowed IV push as a means of administration." Pet. App. 3a. Although FDA has long recognized the risks of direct intravenous injection, *see id.* at 53a, the agency has never sought to bar this method of administration. As Wyeth explains in its petition for certiorari, in some circumstances direct intravenous injection may be desirable. Direct intravenous injection delivers the drug more quickly and thus is more likely to prevent dehydration in cases of severe nausea. In addition, direct intravenous injection may be necessary to deliver the drug to patients who are overweight or to patients whose muscles receive diminished blood flow. *See* Pet. for Cert. at 8 & n.3. Moreover, FDA has long considered the risks of direct intravenous injection, and Plaintiff did not present any new information that had escaped FDA's attention.

Thus, the state-law requirement here directly contradicts an informed FDA decision about the appropriate use of the drug. Wyeth was held liable for failing to disavow an approved method of administration that FDA has determined benefits the health of at least some patients.

SUMMARY OF ARGUMENT

The Vermont Supreme Court's decision significantly affects the pharmaceutical industry and the public health, and the decision conflicts with a decision of another state's highest court. Accordingly, this Court should grant the petition for certiorari.

First, the Vermont Supreme Court's decision profoundly affects the pharmaceutical industry and the public health. Federal preemption is perhaps the single most important product-liability issue confronting PhRMA's

members. Pharmaceutical companies face an unprecedented number of state-law suits in which plaintiffs seek to revisit FDA decisions about a drug's labeling. These lawsuits encourage manufacturers to include warnings that are scientifically unsupported, discourage physicians and patients from using beneficial drugs, and deter the development of new drugs that would enhance patient health and safety. FDA itself has recognized that the public health suffers when state law imposes liability for compliance with FDA decisions.

Second, the Vermont Supreme Court's decision conflicts with a decision of the California Supreme Court. In both cases, plaintiffs sought to hold defendants liable for failing to warn against a specific use, even though FDA had approved those uses based on its scientific review of their risks and benefits. Each court based its decision on the doctrine of implied conflict preemption, and each court was asked to address both the "impossibility" and "obstacle" strands of conflict preemption. But whereas the California Supreme Court held that the plaintiffs' claims conflicted with federal law, the Vermont Supreme Court held that they did not.

ARGUMENT

I. The Vermont Supreme Court's Decision Significantly Affects The Pharmaceutical Industry And The Public Health.

This case presents legal questions that directly and significantly affect both the pharmaceutical industry and the public health. Pharmaceutical manufacturers face tens of thousands of state-law suits challenging the adequacy and truthfulness of FDA-approved labeling. Many of these lawsuits seek to hold defendants liable for failing to adopt labeling that FDA specifically rejected or for fail-

ing to deviate from warning language that FDA approved after scrutinizing the drug's safety and effectiveness. These suits threaten the public health by deterring innovation and by interfering with FDA's regulation of drug safety and efficacy.

A. An Unprecedented Number of State-Law Suits Seek to Hold Defendants Liable for Complying with FDA's Labeling Decisions.

Numerous plaintiffs seek to hold manufacturers liable under state law for adhering to warnings that FDA approved or for failing to adopt warnings that FDA rejected. Many of these lawsuits implicate the preemption defenses at issue in this case.

For example, there are currently eighteen federal multidistrict litigations in which plaintiffs challenge the adequacy or truthfulness of FDA-approved drug labeling. Twelve involve more than two-hundred plaintiffs; nine involve more than five-hundred plaintiffs; and six involve more than a thousand plaintiffs. *See* Jud. Panel on Multidistrict Litig., *Distribution of Pending MDL Dockets* (Mar. 12, 2007) ("*Pending MDL Dockets*"), *available at* http://www.jpml.uscourts.gov. "Such suits now account for more than a third of all product filings in federal courts, outnumbering asbestos, tobacco and auto safety claims by a widening margin since 2002." Lisa Girion, *State Vioxx Trial is Set as Drug Suits Boom*, L.A. Times, June 27, 2006, at C1.

State courts are equally inundated with mass-tort suits in which plaintiffs challenge the adequacy of FDA-approved labeling. For instance, eight of the thirteen consolidated actions designated as Mass Torts by the New Jersey courts involve challenges to FDA-approved labeling for prescription drugs. *See* N.J. Judiciary, *Mass Tort*

Information Center ("*NJ Mass Torts*"), *at* http://www.judiciary.state.nj (last visited Apr. 19, 2007). Several of these suits involve hundreds of plaintiffs, and two involve thousands. *See id.*

Challenges to FDA-approved labeling affect the entire industry and target entire classes of medicines. For example, Bristol-Myers Squibb faces multiple product-liability suits in connection with at least two of its FDA-approved medicines; Merck and Novartis in connection with at least three; Pfizer and GlaxoSmithKline in connection with at least five; and Wyeth in connection with at least six.[2] FDA-approved labeling is at issue in litigation over at least seven different antidepressants, at least three different antipsychotic medications, at least four different types of diet drugs, several different hormone-replacement therapies, and an additive used in multiple vaccines.[3] Collectively, these suits will cost individual companies billions of dollars. *See, e.g.*, Karen Gullo & Margaret Cronin Fisk, *Drug Maker Faces Thousands of*

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[2] *See* Bristol-Myers Squibb Co., Annual Report (Form 10-K), at 136 (Feb. 26, 2007); Merck & Co., Annual Report (Form 10-K)), at 22, 29, 31 (Feb. 28, 2007); Novartis AG, Registration of Securities of Foreign Private Issuers (Form 20-F), at F-54-55 (Jan. 31, 2007); Pfizer Inc., Annual Report (Form 10-K) (Mar. 1, 2007), Ex. 13 at 68-71; GlaxoSmithKline PLC, Registration of Securities of Foreign Issuers (Form 20-F), at 159-60 (Mar. 2, 2007); Wyeth, Annual Report (Form 10-K), at 43-46 (Feb. 26, 2007).

[3] *See Pending MDL Dockets*, *supra* (antidepressants Serzone, Paxil, Celexa, Lexapro; diet drugs Meridia, Phentermine, Fenfluramine, and Dexfenfluramine; and hormone-replacement therapy Prempro); *NJ Mass Torts*, *supra* (anti-psychotic drugs Risperdal, Seroquel, and Zyprexa; and synthetic hormones manufactured by "several pharmaceutical companies"); *Sykes v. Glaxo-SmithKline*, – F. Supp. 2d – , 2007 WL 957337 (E.D. Pa. Mar. 28, 2007) (thimerosal); *Jackson v. Pfizer*, 432 F. Supp. 2d 964 (D. Neb. 2006) (antidepressants Zoloft and Efexor); *Lasure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1163 (W.D. Wash. 2006) (antidepressant fluoxetine).

New Claims, Int'l Herald Trib., Apr. 21, 2006, at 19 (Eli Lilly has reserved $1 billion for Zyprexa lawsuits); Pfizer Inc., Annual Report (Form 10-K) (Mar. 1, 2007), Ex. 13 at 68 (in 2003, Pfizer spent $975 million on Rezulin lawsuits); Merck & Co., Annual Report (Form 10-K)), at 28-29 (Feb. 28, 2007) (Merck has reserved $858 million for Vioxx lawsuits).

These suits are so prevalent and their results so unpredictable that many pharmaceutical companies are unable to implement basic safeguards against catastrophic financial harm. "[M]ost pharmaceutical companies have extreme difficulty obtaining basic insurance coverage in the traditional liability insurance market." Rochelle Chodock, et al., *"Insuring" The Continued Solvency of Pharmaceutical Companies in the Face of Product Liability Class Actions*, 40 Tort Trial & Ins. Prac. L.J. 997, 1000 (2005). Insurance experts have observed that "the pharmaceutical industry presents one of the most volatile risk management challenges in the world of business today." Mindy W. Toran, *Industry Risk Report: The Life Sciences*, Risk & Ins., Dec. 2003, at 1.

Manufacturers' inability to obtain the basic financial safeguard of insurance demonstrates that state-law actions present an intolerable level of risk. The insurance industry has literally determined that the risk associated with these lawsuits is so volatile and unpredictable that it cannot be measured or managed.

Preemption questions like the one at issue in *Levine* often determine the scope and viability of these individual and mass tort suits. *See, e.g.*, *In re Aredia & Zometa Prods. Liab. Litig.*, No. 3:06-MD-1760, 2007 WL 649266, at *4 (M.D. Tenn. Feb. 27, 2007) (discussing potential preemption defenses); *In re Zyprexa Prods. Liab. Litig.*, 238 F.R.D. 539, 539-40 (E.D.N.Y. 2006) (requesting sup-

plemental briefing on FDA preemption). For example, in many cases plaintiffs seek to hold defendants liable for declining to adopt warnings that FDA specifically rejected. *See, e.g.*, *Jackson*, 432 F. Supp. 2d at 968 (rejecting defendant's preemption argument even though FDA rejected warning at issue); *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 527-28 (E.D. Pa. 2006) (accepting defendant's preemption argument because FDA rejected warning at issue), *appeal docketed*, No. 06-3107 (3d Cir. June 21, 2006). In these cases, the defendant can avoid liability only by violating federal law and subjecting itself to federal penalties for misbranding.

B. These Lawsuits Harm The Public Health.

While ostensibly motivated by concern for patients' safety, the proliferation of state-law challenges to FDA-approved labeling actually harms the public health. "State actions are not characterized by centralized expert evaluation of drug regulatory issues. Instead, they encourage, and in fact require, lay judges and juries to second-guess the assessment of benefits versus risks of a specific drug to the general public—the central role of FDA—sometimes on behalf of a single individual or group of individuals." *2006 FDA Labeling Regulations*, *reprinted in* Pet. App. 134a. The resulting distortion of risk-benefit assessment drives beneficial drugs from the market, distracts FDA from promoting health and safety, and produces labeling that is inaccurate and confusing.

1. State-law actions like *Levine* may force valuable drugs from the market and stifle the development of new ones. "Tort litigation may drive from the market not just individual manufacturers of multi-source drugs but also entire product lines." Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. Rev. 371, 392 (2002).

The scholarly literature supplies several examples:

- **Vaccines:** "Liability hazards led many firms to exit the vaccine market." W. Kip Viscusi, *Corporate Risk Analysis: A Reckless Act?*, 52 Stan. L. Rev. 547, 583 (2000). The result has been "recent shortages of five routinely recommended childhood vaccines, and the well-publicized annual shortages of the influenza vaccine." Elissa Levy, Note, *The Health Act's FDA Defense to Punitive Damages: A Gift to Drug Makers or to the Public?*, 74 Fordham L. Rev. 2425, 2447 (2006).

- **Contraceptives:** "Pharmaceutical companies have moved out of contraceptive research because of fear of product liability lawsuits. . . ." William M. Brown, *Déjà Vu All Over Again: The Exodus from Contraceptive Research and How to Reverse It*, 40 Brandeis L.J. 1, 32 (2001).

- **Drugs for Rare Diseases:** "[L]iability concerns serve to deter treatment of persons with rare diseases, delay development of drugs, and increase insurance costs." Gregory C. Jackson, *Pharmaceutical Product Liability May Be Hazardous to Your Health: A No-Fault Alternative to Concurrent Regulation*, 42 Am. U. L. Rev. 199, 208 n.61 (1992).

The litigation-induced demise of the morning-sickness drug Bendectin is illustrative. Questionable scientific theories drove the litigation and ultimately informed this Court's landmark ruling in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993). Along the way, the manufacturer "voluntarily withdrew Bendectin from the market, citing an increasing number of lawsuits and declining sales due to negative publicity." Joseph Sanders, *From Science to Evidence*: *The Testi-*

mony on Causation in the Bendectin Cases, 46 Stan. L. Rev. 1, 7 (1993). No comparable drug has replaced it.

Experts have since discredited the purported connection to birth defects that drove Bendectin from the market: "[S]tudies clearly demonstrate that Bendectin has no measurable reproductive risks to the mother or the fetus." Robert Brent, *Medical, Social, and Legal Implications of Treating Nausea and Vomiting of Pregnancy*, 186 Am. J. Obstetrics & Gynecology S262, S262-63 (2002). Because untreated morning sickness can cause dehydration, Bendectin's absence has actually increased threats to fetal health. *See id.* at S264 (treatment of severe morning sickness improves "nutrition for mother and fetus" and "decrease[s] risk of some pregnancy complications").

2. Decisions like the Vermont Supreme Court's will encourage companies to "submit a deluge of information that [FDA] neither wants nor needs." *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 351 (2001). This consequence, which partly motivated the Court's recent FDA-preemption holding in *Buckman*, will distract FDA officials from their core responsibilities of protecting health and safety.

Levine will actually impose greater burdens than contemplated in *Buckman*. Whereas the Court in *Buckman* preempted state-law claims based on a concern that they would encourage companies to burden FDA with excessive information, the *Levine* decision encourages companies to burden FDA with unscientific proposals for labeling changes. Unnecessary proposals for labeling changes will interfere with FDA's operations more than will mere submissions of information: whereas the agency may respond to excess information as it deems fit, it *must* respond to actual proposals.

Moreover, in denying any weight to FDA's rejection of Wyeth's attempt to strengthen the labeling, the court refused to "interpret the FDA's statement as evidence that it would have rejected *any* attempt by defendant to strengthen its label." Pet. App. 17a (emphasis added). This hairsplitting encourages manufacturers to inundate FDA with repeated and duplicative for labeling changes that FDA has already rejected in substance. Such duplicative requests will further distract FDA scientists from policing drug safety. They will also raise the already "high costs of regulatory approval and compliance [that] deter even large, well-financed drug and medical device companies from investing in research and development." Charles J. Walsh, *Rationalizing the Regulation of Prescription Drugs & Medical Devices: Perspectives on Private Certification & Tort Reform*, 48 Rutgers L. Rev. 883, 931 (1996).

3. Regulatory bottlenecks aside, FDA has long recognized that "it would be inappropriate to require statements in drug labeling that do not contribute to the safe and effective use of the drug, but instead are intended solely to influence civil litigation in which the agency has no part." *Content and Format for Labeling of Human Prescription Drugs*, 44 Fed. Reg. 37434, 37435 (June 26, 1979). Yet decisions like *Levine* encourage manufacturers to base warnings on litigation risk rather than on science.

Unnecessary warnings deter doctors and patients from using beneficial drugs. "[T]he risk of harm may be so remote that it is outweighed by the greater risk that a warning will scare consumers into foregoing use of a product that in most cases will be to their benefit." *Dowhal v. SmithKline Beecham Consumers Healthcare*, 88 P.3d 1, 14 (Cal. 2004).

Extra warnings also obscure existing ones. According to a bipartisan group of former FDA Chief Counsels, state-imposed warnings erode "FDA's ability to advance the public health by allocating scarce space in product labeling to the most important information." 150 Cong. Rec. S8,657 (July 22, 2004). Ultimately, "[w]arnings about dangers with less basis in science or fewer hazards could take attention away from those that present confirmed, higher risks." *Brooks v. Howmedica, Inc.*, 273 F.3d 785, 796 (8th Cir. 2001).

These effects are more than hypothetical. During the 1990s, FDA conducted "two initial focus groups and a national physician survey." *Requirements for Prescription Drug Product Labels*, 65 Fed. Reg. 81082, 81083 (Dec. 22, 2000). Physicians lamented "the lack of ease in locating specific information among the extensive information presented," and they complained that "labeling overly stresses the occurrence of extremely rare events." *Id.* at 81084. Rulings like *Levine* will make risk-related information even muddier.

C. FDA Has Recognized These Threats to the Public Health.

FDA itself recognizes that the public health suffers when state law undermines the agency's regulation of prescription drug labeling. The agency has attempted to address this concern, albeit with limited success.

In 2000, upon proposing new regulations designed to make drug warnings clearer, FDA observed that "the use of labeling in product liability and medical malpractice lawsuits, together with increasing litigation costs, has caused manufacturers to become more cautious and include virtually all known adverse event information, re-

gardless of its importance or its plausible relationship to the drug." *Id.* at 81083.

In January 2006, in the preamble to its final labeling regulations, FDA identified specific ways in which state-law requirements can undermine federal goals. First, "they can erode and disrupt the careful and truthful representation of benefits and risks that prescribers need to make appropriate judgments about drug use." *2006 FDA Labeling Regulations*, *reprinted in* Pet. App. 133a. Second, they can "pressure . . . manufacturers to expand labeling warnings to include speculative risks and, thus, to limit physician appreciation of potentially far more significant contraindications and side effects." *Id.* Third, they can "discourag[e] safe and effective use of approved products or encourag[e] inappropriate use." *Id.*

FDA has also identified "several instances in which product liability lawsuits have directly threatened the agency's ability to regulate manufacturer dissemination of risk information for prescription drugs." *Id.* at 130a. Thus, the agency has urged courts nationwide to dismiss, on grounds of federal preemption, certain state-law claims that directly undermine the agency's ability to protect public health.[4] In many of its briefs, FDA has observed that the plaintiffs, like the plaintiff here, sought to hold

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[4] *See, e.g.*, Brief for United States as Amicus Curiae Supporting Appellees at 1, *Colacicco v. Apotex, Inc.*, No. 06-3107 (3d Cir. Dec. 4, 2006) (arguing that federal law should preempt claim, given FDA's conclusion "that the existing scientific knowledge did not support such a warning"); Brief for United States as Amicus Curiae Supporting Appellee & Cross-Appellant at 1, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004) (Nos. 02-55372/55498) (same, given FDA's "determination that there is no scientific basis for such warning"); Brief for United States as Amicus Curiae Supporting Defendant at 2, *Kallas v. Pfizer, Inc.*, No. 2:04cv0998 PGC (D. Utah Sept. 15, 2005) (same, given that desired labeling "would have misbranded the drug").

defendants liable under state law for failing to include a warning that FDA had rejected.

II. The Vermont Supreme Court's Decision Conflicts With A Decision Of The California Supreme Court.

The Vermont Supreme Court's decision exacerbates the public-health concerns discussed above and reflects the wider legal debate about whether and when state-law suits may revisit FDA's scientific judgments about pharmaceutical labeling. In this regard, the decision conflicts with a decision from the California Supreme Court and presents an excellent vehicle for this Court to clarify the scope of FDA preemption and preserve FDA's ability to protect the public health.

A. The Vermont Supreme Court's decision conflicts with the California Supreme Court's decision in *Dowhal v. SmithKline Beecham Consumer Healthcare*, 88 P.3d 1 (Cal. 2004). Although *Dowhal* involved an over-the-counter drug, in both *Levine* and *Dowhal* the plaintiffs sought to hold the defendant liable for failing to warn against an FDA-approved use of a pharmaceutical. Moreover, in both *Levine* and *Dowhal* the courts based their decisions on the doctrine of implied conflict preemption. Whereas the Vermont Supreme Court dismissed FDA's scientific judgment and allowed the claim to proceed, the California Supreme Court deferred to FDA's scientific views and held that the claim was preempted.

In *Levine*, the defendant was held liable for failing to warn physicians that the drug should not be directly intravenously injected into patients. The court rejected Wyeth's argument that inclusion of the state-law warning would have violated federal law. FDA, the court acknowledged, had not restricted the method by which the drug

could be injected and had specifically rejected Wyeth's attempt to strengthen the warning about the risks of direct intravenous injection. *See* Pet. App. 54a-55a. But the court did not defer to FDA's scientific judgment and instead asserted that Wyeth "could have warned against [direct intravenous] administration without prior FDA approval." *Id.* at 6a.

The court also rejected Wyeth's argument that state-law liability in this case would pose an obstacle to the fulfillment of federal regulatory objectives. Pointing to federal statutory language that forecloses preemption absent a "direct and positive conflict between [federal law] and state law," the court held that this language "essentially removes from our consideration the question of whether common-law tort claims present an obstacle to the purposes and objectives of Congress." *Id.* at 21a.

In reaching the opposite conclusion in *Dowhal*, the California Supreme Court respected FDA's determinations. The court addressed a preemption challenge to a state law (1) providing that the defendant's product, an over-the-counter nicotine patch, was "not for use by pregnant women," and (2) requiring the defendant to warn patients that the product "contains nicotine, a chemical known to the state of California to cause reproductive harm." 88 P.3d at 3-4. As did the court in *Levine*, the court in *Dowhal* based its decision on the doctrine of "conflict preemption." *Id.* at 7.

Like the court in *Levine*, the court in *Dowhal* acknowledged that manufacturers may, in certain circumstances, change their FDA-approved labeling without prior FDA approval (but subject to FDA approval or disapproval after the change). Unlike the court in *Levine*, however, the court in *Dowhal* acknowledged the importance of FDA's prior scientific decision: "FDA had re-

jected plaintiff's claim that his data justify a different warning, and defendants do not claim to have any additional data." *Id.* at 9.

The court in *Dowhal* also held that the state-law requirement was preempted because it would pose an obstacle to FDA's health-related objectives by deterring pregnant women from using the patch to quit smoking. *See id.* at 4 ("[T]he purpose of the products is to help individuals stop smoking, and smoking is even more dangerous to the fetus."). Unlike the Vermont Supreme Court, the California Supreme Court held that the federal statute's limitation on preemption did not foreclose preemption "if state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Id.* at 11 (quotations omitted).[5]

B. This case presents an ideal vehicle for this Court to alleviate the judicial conflict over FDA preemption and curb the ability of state law to undermine FDA's regulation of health and safety. *Levine* comes to the Court after a final judgment—a significant feat, given the pressure on pharmaceutical defendants to settle high-stakes personal-injury suits. *See* David E. Bernstein, *The Breast Implant Fiasco*, 87 Cal. L. Rev. 457, 493 (1999) ("[I]f a defendant loses just one major lawsuit, . . . that loss can stimulate an avalanche of copycat lawsuits.").

Moreover, in addressing the dissent's arguments, the Vermont Supreme Court recognized that courts continue

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[5] The non-prescription-labeling provision at issue in *Dowhal* exempted, from an express-preemption provision, any "State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997." 21 U.S.C. § 379r(d)(2). California's requirement was adopted by referendum in 1986 and was thus immune from express preemption. *See Dowhal*, 88 P.3d at 3.

to disagree about whether states may second-guess express FDA judgments about the uses and labeling of pharmaceuticals:

> We recognize that our dissenting colleague has reached the opposite conclusion. There is little to say, beyond what we have already said, except that we respectfully disagree with his analysis . . . . While the dissent cites favorably the minority view, we agree with the majority view.

Pet. App. 23a. These disagreements persist, moreover, even though FDA has repeatedly asked courts to foreclose state-law suits in which plaintiffs seek to revisit the agency's scientific decisions. Only this Court can reconcile these conflicting views.

CONCLUSION

PhRMA respectfully requests that the Court grant the petition.

Respectfully submitted,

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