No. 06-1249

IN THE
Supreme Court of the United States

WYETH,

Petitioner,

v.

DIANA LEVINE,

Respondent.

On Writ of Certiorari to
the Vermont Supreme Court

BRIEF FOR PHRMA AND BIO AS AMICI CURIAE SUPPORTING PETITIONER

DIANE E. BIERI
MAYA BERMINGHAM
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA
950 F Street, NW
Suite 300
Washington, DC 20004
(202) 835-3405

TOM DILENGE
SANDRA J.P. DENNIS
BIOTECHNOLOGY INDUSTRY ORGANIZATION
1201 Maryland Avenue, SW
Suite 900
Washington, DC 20024
(202) 962-9200

ROBERT A. LONG, JR.
Counsel of Record
MICHAEL X. IMBROSCIO
PAUL W. SCHMIDT
ERIKA LIETZAN
GREGORY M. LIPPER
COVINGTON & BURLING LLP
1201 Pennsylvania Ave, NW
Washington, D.C. 20004
(202) 662-6000

Counsel for Amici Curiae

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.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page

FEDERAL CASES

STATE CASES

FEDERAL STATUTES AND REGULATIONS

MISCELLANEOUS

INTEREST OF AMICI 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 last decade, PhRMA's members invested approximately $300 billion to develop new medicines. *See* PhRMA, *Pharmaceutical Industry Profile 2007* 42 (2007). New medicines account 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).

The Biotechnology Industry Organization ("BIO") is the world's largest biotechnology organization, providing advocacy, business developments, and

---

[1] Each party has consented to the filing of this brief and the parties' letters of consent have been lodged with the Clerk. Pursuant to Supreme Court Rule 37.6, no counsel for a party authored this brief in whole or in part, and no party or counsel for a party made a monetary contribution intended to fund the preparation or submission of this brief. A list of PhRMA's members is available at http://www.phrma.org. BIO's members are listed at http://www.BIO.org.

communications services for more than 1,150 members worldwide. BIO's mission is to champion biotechnology and advocate for its member organizations, both large and small. BIO members are involved in research and development of innovative healthcare technologies. Corporate members range from entrepreneurial companies developing a first product to Fortune 100 multinationals. BIO also represents state and regional biotechnology associations, service providers to the industry, and academic centers.

Members of PhRMA and BIO closely monitor legal issues that affect the entire industry and often offer their perspectives in cases raising such issues. The issues in this case are especially significant. Federal preemption issues arise in tens of thousands of product-liability lawsuits faced by members of PhRMA and BIO. These state-law suits undermine uniform regulation of pharmaceutical labeling by the federal Food and Drug Administration ("FDA"). Such suits also pose a threat to public health in two significant ways: *first*, by encouraging unduly risk-averse drug labeling and, at the extreme, manufacturer decisions to withdraw medicines from the market or not introduce them at all; and *second*, by discouraging physicians and patients from prescribing and using beneficial medicines because of warnings about unsubstantiated risks.

SUMMARY OF ARGUMENT

The Vermont Supreme Court, over a vigorous dissent by its Chief Justice, upheld a judgment of

nearly $7 million against the manufacturer of an FDA-approved medicine. The manufacturer was held liable because the medicine's labeling failed to contraindicate a method of injection that FDA had expressly permitted. The labeling included carefully worded instructions and warnings approved by FDA, which had reviewed the drug's risks and benefits for nearly a half-century. The Court should reverse the Vermont court's decision on the ground that Respondent's state-law claims are preempted by federal law.

1. State-law tort suits challenging the adequacy of FDA-approved prescription drug labeling pose significant risks to public health and to FDA's ability to accomplish its mission. Such suits, which have increased in number in recent years, typically focus on the very question that is a primary FDA focus in regulating medical products: evaluating and managing the risks associated with prescription medications. As a result, juries in state-law tort suits often are required to second-guess FDA's balancing of the risks and benefits of a prescription medicine. The threat of liability under state law encourages manufacturers to warn physicians and patients about risks that are speculative and scientifically unsupported. This ultimately dilutes the impact of scientifically valid warnings and discourages physicians and patients from using beneficial drugs. In addition, state-law tort actions can drive beneficial drugs off the market and deter the development of new drugs that would enhance patient health and safety.

2. The Vermont Supreme Court's decision is at odds with a core premise of the Supremacy Clause: State law cannot require what federal law prohibits. Absent new scientific information, federal regulations prohibit a manufacturer from changing prescription drug labeling without prior FDA approval. In this case, FDA knew of and considered the relevant risk over a period of decades, and approved carefully-crafted warnings and instructions designed to minimize those risks while encouraging beneficial drug use. While conceding that preemption would result "if the FDA intended . . . to prohibit any language strengthening the original warning," the Vermont Supreme Court erroneously concluded that there was no preemption because FDA had not rejected the *precise* warning sought by the plaintiff.

In addition, Respondent's state-law claims pose a serious obstacle to the objectives of the Federal Food, Drug, and Cosmetic Act by allowing a jury to second-guess FDA's careful balancing of the risks and benefits of prescription medicines. In approving drug labeling, FDA does not merely set minimum safety standards. Instead, it balances the expected therapeutic gain from a medicine against the risk entailed by its use. When juries, focusing only on the particular plaintiff before them, require warnings about unsubstantiated risks, they undermine the purpose of the FDCA by discouraging physicians and patients from using beneficial medicines.

If allowed to stand, the Vermont Supreme Court's "magic words" requirement will encourage

pharmaceutical companies to inundate FDA with requests for labeling changes to ensure that federal regulators have been presented with every potential labeling permutation. These requests, driven by the need to create a record for future litigation rather than by science, will distract agency scientists from their core mission of reviewing the safety and effectiveness of prescription medications.

ARGUMENT

I. State-Law Tort Claims Challenging Prescription Drug Labeling Undermine FDA Decisionmaking And Pose A Threat To Public Health.

A. FDA's Authority To Approve Drug Labeling Is Central To The Agency's Balancing Of Risks And Benefits.

The Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.*, creates one of the world's most demanding prescription drug approval regimes.[2] On average, it takes nearly twelve years for a new drug to be developed and approved by FDA. *See* Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development*

---

[2] In this brief, references to prescription drugs include drugs licensed as biological products pursuant to Section 351 of the Public Health Service Act, 42 U.S.C. § 262. These drugs are subject to the FDCA prohibition on misbranding, 21 U.S.C. § 352, as well as the prescription drug labeling regulations and regulations governing changes to an approved biologics license application, *see* 21 C.F.R. §§ 201.56-57, 601.12.

Costs, 22 J. Health Econ. 151, 164-66 (2003). A new drug application ("NDA") must include "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use" as well as "labeling proposed to be used for such drug." 21 U.S.C. § 355(b)(1)(A), (F). An NDA is approved only if FDA determines the drug is both safe and effective under the conditions described in the proposed labeling. *Id.* § 355(c), (d).

FDA's determination that a drug is safe and effective does not mean that the drug is risk-free. "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). Instead, just as with medical devices, the FDA confronts a more complex question in regulating medicines: "How many more lives will be saved by a [medicine] which, along with its greater effectiveness, brings a greater risk of harm?" *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1008 (2008). As the Court noted in *Riegel,* FDA answers this question by systematically evaluating all evidence of a medicine's benefits and risks; a jury, in contrast, focuses on information pertinent to an individual plaintiff. *Id.*

The centerpiece of FDA's expert weighing of risks and benefits is the medicine's labeling. *See* 21 U.S.C. § 355(d), (e). By providing a coordinated set of instructions to physicians, including warnings and contraindications calibrated to the best scientific evidence, FDA achieves a balance in communicating

information about the benefits and risks of a drug. Consistent with this approach, FDA requires the warnings in prescription drug labeling to be supported by "reasonable evidence of an association of a serious hazard with the drug." 21 C.F.R. § 201.80(e).[3]

FDA's authority over prescription drug labeling is conferred by the FDCA, which prohibits the introduction into commerce of unapproved new drugs as well s "misbranded drugs," 21 U.S.C. §§ 331(a), (d), and which provides that a drug is "misbranded" if its labeling is "false or misleading in any particular," or if its labeling lacks "adequate directions for use," *id.* § 352(a), (f). Congress has given FDA comprehensive authority to regulate drug labeling by making labeling a fundamental component of the NDA, and by requiring that approval of an NDA must be based on an FDA finding that the drug is safe and effective for use "*under the conditions prescribed, recommended, or suggested in the proposed labeling thereof*." *Id.* § 355(b)(1)(F), (d) (emphasis added). In addition,

---

[3] *See also* 21 C.F.R. § 201.57(c)(6)(i) (warnings must be supported by "reasonable evidence of a causal association with a drug."); Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3,922, 3,932 (Jan. 24, 2006) (inclusion of statement that "FDA has considered and found scientifically unsubstantiated" would "render the drug misbranded under the act (21 U.S.C. 352(a) and (f))"); *id.* at 3,935 ("additional disclosures of risk information can expose a manufacturer to liability under the act if the additional statement is unsubstantiated or otherwise false or misleading").

Congress has given FDA exclusive authority to enforce the requirement that drug labeling not be false or misleading. *See id.* § 352(a). Federal law subjects manufacturers to severe civil and criminal penalties for misbranding and for distributing a new drug without an approved NDA. *See id.* § 332 (injunctions); *id.* § 333(a) (criminal penalties, including fines and imprisonment); *id.* § 334 (seizure of product). Similar penalties apply if a manufacturer improperly withholds information from FDA or makes false statements to the agency. *Id.* §§ 332, 333.

In implementing this authority, FDA extensively regulates prescription drug labeling. The package insert for a new drug must be approved word-for-word by FDA before a drug can come to market. *See* 21 C.F.R. § 314.105(b); *see also* Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2,849, 2,849 (proposed Jan. 16, 2008) ("Supplemental Applications") ("FDA's review and prior approval of both the product and its proposed labeling is a necessary condition of lawful distribution of the product in interstate commerce"). In this case, FDA directed Petitioner that the "final printed labeling" for Phenergan "must be identical" to the labeling approved by FDA. Pet. App. 165a.

Once FDA has approved the labeling, federal law generally prohibits the manufacturer from making any "[c]hange in labeling" unless the manufacturer applies for a change and FDA approves the application. *See* 21 C.F.R. § 314.70(b)(2)(v)(A). In

limited circumstances, a manufacturer is permitted by FDA's regulations to change a drug's labeling at the same time it submits an application "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction," or "[t]o add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product." *Id.* § 314.70(c)(6)(iii)(A), (C). FDA has long interpreted this "changes being effected" (or "CBE") exception as applicable only to "concerns about *newly discovered* risks" and "important *new information* about the safe use of a drug." New Drug and Antibiotic Regulations, 47 Fed. Reg. 46,622, 46,623, 46,625 (proposed Oct. 19, 1982) (emphasis added).

When a manufacturer changes a warning without prior FDA approval, FDA reviews the revised labeling and may bring an enforcement action for making an unauthorized change or for adding statements that make the labeling false or misleading. *See* Supplemental Applications, 73 Fed. Reg. at 2,849. For these reasons, as a former FDA Chief Counsel has explained, "[t]he actual freedom of manufacturers unilaterally to change the package 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. The Volume Of State-Law Tort Litigation Challenging FDA-Approved Labeling Has Expanded Significantly.

Just as drug labeling is the centerpiece of FDA's weighing of risks and benefits, it is also the focal point of state-law tort claims against pharmaceutical companies. Nearly every state recognizes that prescription drugs inherently carry a degree of risk but also provide an essential societal benefit. Therefore, pharmaceutical liability under state law generally hinges on whether the company adequately warned of knowable risks. *See, e.g., Vitanza v. Upjohn Co.,* 778 A.2d 829, 837-38 (Conn. 2001); *Rogers v. Miles Labs., Inc.,* 802 P.2d 1346, 1353 (Wash. 1991); *Grundberg v. Upjohn Co.,* 813 P.2d 89, 92 (Utah 1991); *Feldman v. Lederle Labs.,* 479 A.2d 374, 385 (N.J. 1984) (in pharmaceutical context, "strict liability analysis becomes almost identical to negligence analysis in its focus on the reasonableness of the defendant's conduct"); *see also Brown v. Super. Court,* 751 P.2d. 470, 476 (Cal. 1988) (noting that this approach "has been adopted in the overwhelming majority of jurisdictions that have considered the matter"). The state-law approach is summarized in comment k to Section 402A of the Restatement (Second) of Torts:

> There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs . . . . The seller of such products, again with the

> qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.

Restatement (Second) Torts § 402A cmt. k (1965).

Thus, a manufacturer's liability under state tort law frequently is determined by the content of the drug's labeling — the very instructions and warnings that are carefully calibrated through FDA's regulatory process. As such, state-law claims against drug manufacturers often invite juries to second-guess FDA's decisions regarding prescription drug labeling. During the trial in this case, for instance, plaintiff's counsel explicitly asked the jury to second-guess FDA's safety determination: "Thank God we don't rely on the FDA to . . . make the safe[ty] decision. You will make the decision. . . . The FDA doesn't make the decision, you do." J.A. 211-12.

In recent years, there has been a sharp increase in the number of state-law tort suits in which juries are asked to second-guess FDA's determinations concerning the appropriate warnings and instructions about pharmaceutical risks. Rather than challenging the absence of any warning about the risk at issue, many of these state-law suits – including this case – involve situations in which FDA

has explicitly considered the risk at issue and approved labeling that expressly addresses the risk.[4]

In 2001, roughly 2,700 pharmaceutical product-liability cases asserting state-law failure to warn or related claims were litigated in federal court. Lisa Girion, *State Vioxx Trial is Set as Drug Suits Boom*, L.A. Times, June 27, 2006, at C1. That number rose to 17,000 in 2005, accounting for "more than a third of all product filings in federal courts" and "outnumbering asbestos, tobacco and auto safety claims by a widening margin since 2002." *Id.* Currently, twenty federal multidistrict litigations challenging the adequacy of FDA-approved drug labeling are pending in federal court; all but one began in 2000 or later. *See* Jud. Panel on Multidistrict Litig., *Distribution of Pending MDL Dockets* (May 13, 2008), *available at* http://www.jpml.uscourts.gov. By contrast, a recent study concluded that in the forty-year span between 1960 and 1999, there were only seven mass tort actions involving FDA-approved medicines. *See*

---

[4] *See, e.g., Kelly v. Wyeth*, No. 20033314F, 2007 WL 1302589, at *6 (Mass. Super. Ct. Apr. 12, 2007) (denying defendant's motion for summary judgment because, although labeling warned of risk of akathisia, plaintiff alleged that "the risk of akathisia was much greater than that which was represented on the label"); *Smith v. Johnson & Johnson Co.*, No. 108901/01, 2004 WL 2964419, at *5 (N.Y. Sup. Ct. Nov. 22, 2004) (denying defendant's motion for summary judgment because, although labeling warned of cardiac arrest risk, plaintiff's labeling expert opined that warning "failed to place physicians on notice" that cardiac arrest could occur in patients not taking other drugs and without preexisting heart problems).

Deborah R. Hensler, *Has the Fat Lady Sung? The Future of Mass Toxic Torts*, 26 Rev. Litig. 883, 897 tbl. 1 (2007).[5]

Challenges to FDA-approved labeling affect the entire industry and target entire classes of medicines. FDA-approved labeling has been challenged in significant litigation over nearly a dozen antidepressants and other central nervous system medicines, at least four different types of weight loss drugs, numerous hormone replacement therapies, diabetes treatments, osteoporosis medicines, and an additive used in multiple vaccines.[6]

---

[5] Similar increases have occurred in the state courts. For example, eight of the twelve 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*, *at* http://www.judiciary.state.nj.us/mass-tort/index.htm (last visited May 30, 2008) ("*NJ Mass Torts*").

[6] *See* Jud. Panel on Multidistrict Litig., *Distribution of Pending MDL Dockets* (May 13, 2008), *available at* http://www.jpml.uscourts.gov (antidepressants and CNS products Serzone, Paxil, Celexa, Lexapro, Seroquel, Mirapex, Neurontin, Zyprexa; weight loss drugs meridia, phentermine, fenfluramine, and dexfenfluramine; and hormone replacement therapy Prempro and Ortho-Evra); *NJ Mass Torts*, *supra* (anti-psychotic drugs Risperdal, Seroquel, and Zyprexa; and synthetic hormones manufactured by "several pharmaceutical companies"); *Sykes v. Glaxo-Smith Kline*, 484 F. Supp. 2d 289 (E.D. Pa. 2007) (thimerosal); *Jackson v. Pfizer*, 432 F. Supp. 2d 964 (D. Neb. 2006) (antidepressants Zoloft and Effexor); *Laisure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1163 (W.D. Wash. 2006) (antidepressant fluoxetine).

These suits are so numerous, and manufacturers' potential liability is so large and unpredictable, that the commercial liability insurance market has all but disappeared for medications. 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). "[M]ost pharmaceutical companies have extreme difficulty obtaining basic insurance coverage in the traditional liability insurance market." *Id.* 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.

The growth in state-law tort suits challenging FDA-approved labeling has posed an increasingly serious threat to public health. As demonstrated below, patients may be deterred from using a needed medicine in the face of intimidating warnings that are driven by litigation rather than science. In addition, FDA's resources may be diverted to considering proposed labeling changes intended to reduce manufacturers' exposure to state-law tort liability. To the extent such changes are included in prescription drug labeling, they dilute the effectiveness of scientifically-justified warnings. In the most extreme instances, medicines that can save lives or cure disease have been withdrawn from the market or not brought to market at all.

C. State-Law Tort Suits Encourage Labeling Statements That Are Not Based on Science, Discouraging Physicians and Patients from Using Beneficial Medicines.

State-law tort suits challenging the adequacy of prescription drug labeling – and the publicity surrounding such suits – foster a proliferation of warnings about unsubstantiated risks that drive doctors and patients away from medicines that can improve health and save lives. FDA has long cautioned 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 for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,435 (June 26, 1979). Yet as FDA observed in 2000, failure-to-warn suits have "caused manufacturers to . . . include virtually all known adverse event information, regardless of its importance or its plausible relationship to the drug." Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81,082, 81,083 (proposed Dec. 22, 2000).

The proliferation of inappropriate warnings harms patients in two ways. *First*, when labeling includes too many warnings, the warnings lose their effectiveness. As FDA has explained: "Overwarning has the effect of not warning at all. The reader stops paying attention to excess warnings." Center for Devices and Radiological Health, FDA, *Write it Right: Recommendations for Developing User*

Instruction Manuals for Medical Devices Used in Home Health Care 7 (1993). In a national survey, physicians criticized "the lack of ease in locating specific information among the extensive information presented" and labeling that "overly stresses the occurrence of extremely rare events." Requirements for Prescription Drug Product Labels, 65 Fed. Reg. at 81,083-84. In 2004, a bipartisan group of former FDA Chief Counsels stated that warnings required by state law 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, S8,657 (July 22, 2004).[7]

Second, the inclusion of inappropriate warnings about speculative risks deters medicine use that may improve patients' health or save their lives. As the California Supreme Court observed in holding that federal law preempted a conflicting state-law warning requirement for an over-the-counter drug, "the 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

---

[7] Plaintiff lawyers and other advocates now voice these same concerns, challenging warnings on the ground that they were "buried" among other warnings in the labeling, instead of being featured more prominently. *See, e.g.,* Public Citizen, Press Release, *Antibiotic Leads to Tendon Ruptures; FDA Ignores Risks* (Jan. 3, 2008) (criticizing antibiotic warning that was "far too easy to miss" given numerous other warnings surrounding it).

1, 14 (Cal. 2004). In some cases, the risk of harm is not only remote but non-existent.

These concerns are more than hypothetical. In October 2004, following an extended period of scientific discussion and media attention, FDA required pharmaceutical companies to add a "black box" warning suggesting that SSRI antidepressants may increase the risk of suicide in pediatric patients. During this period, from 2003 to 2005, SSRI prescriptions to those younger than age 15 declined by approximately 17 percent. Robert D. Gibbons, *Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in Children and Adolescents*, 164 Am. J. Psychiatry 1356, 1361 (2007). Between 2003 and 2004, "there was already a 14% increase in child adolescent suicide rates"—"the first increase of this magnitude in the child and adolescent suicide rate since the CDC began systematically collecting suicide data in 1979." *Id.* at 1358-59. As a result, the first systematic study of the effect of these new warnings concluded: "If the intent of the pediatric black box warning was to save lives, the warning failed, and in fact it may have had the opposite effect; more children and adolescents have committed suicide since it was introduced." *Id.* at 1361-62. The SSRI example involves FDA's exercise of its regulatory oversight; much greater harm can be expected from unsubstantiated warnings prompted by a deluge of state-law tort suits. Each of these lawsuits asks a jury to second-guess FDA's regulatory decisions in the context of a single patient, without giving adequate consideration to

other patients (not before the court) who would have been harmed had they *not* received the drug. *See Riegel*, 128 S. Ct. at 1008.

D. State-Law Tort Suits Can Deprive Doctors and Patients of Critical Medicines, By Inhibiting Drug Development or Driving Beneficial Drugs from the Market.

FDA is "responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health." http://www.fda.gov/opacom/morechoices/mission.html (FDA Mission Statement) (last visited May 30, 2008); *see also* 21 U.S.C. § 393(b). In fulfilling its responsibility to protect the public health, FDA works to ensure that beneficial medicines are available to patients who need them.[8]

---

[8] *See, e.g.*, 21 U.S.C. §§ 360aa-360dd (providing incentives for research, development, and marketing of drugs for treatment of rare diseases, for which costs may otherwise exceed expected profits); 21 C.F.R. §§ 316.1-316.52 (same); 21 U.S.C. § 356(a)(1) (FDA may "facilitate the development and expedite the review of [a new] drug if it is intended for the treatment of a serious or life-threatening condition and it demonstrates the potential to address unmet medical needs for such a condition"); 21 C.F.R. §§ 314.500-314.560 (same); 21 U.S.C. § 360bbb(b) (providing for patient use of investigational drugs if, among other requirements, there is "no comparable or satisfactory alternative therapy available to diagnose, monitor, or treat the disease or condition involved"); 21 C.F.R. § 312.34 (same).

Product-liability litigation challenging FDA-approved labeling can frustrate FDA's efforts to strike a balance that protects patient safety while securing the availability of needed medicines. As far back as 1988, the American Medical Association warned that "[p]roduct liability is having a profound negative impact on the development of new medical technologies." Adam R. Nelson, Amer. Med. Ass'n Bd. of Trustees, *Impact of Product Liability on the Development of New Medical Technologies* 1 (1988). In 1990, a study by the National Academy of Sciences concluded that "the net effect of the surge in liability costs has been to discourage innovation in the pharmaceutical industry." W. Kip Viscusi et al., *A Statistical Profile of Pharmaceutical Industry Liability, 1976-1989*, 24 Seton Hall L. Rev. 1418, 1419 (1994). In 1997, a peer-reviewed empirical study found that "a substantial premium exists in the U.S. pharmaceutical prices, strongly related to the prospective costs of litigation, which is absent in Canadian prices." Richard L. Manning, *Products Liability and Prescription Drug Prices in Canada and the United States*, 40 J.L. & Econ. 203, 227 (1997).

In some cases, litigation risk can drive valuable medicines entirely from the market, even when scientific research ultimately discredits the basis for the lawsuits. This is so in part because, "when a person using a prescription drug suffers a stroke or develops cancer, or her child has a birth defect, it can be quite unclear whether the injury is causally connected to use of a drug." Steven Garber, RAND, *Product Liability and the Economics of*

Pharmaceuticals and Medical Devices 46 (1993). Prescription drugs are often blamed for injuries that the patient would have suffered whether or not the patient had taken the drug. And unlike FDA scientists, jurors typically lack the medical and technical expertise to distinguish causal relationships from mere coincidence, let alone to evaluate the "complex chemical and pharmacological considerations" that go into determining whether a drug is safe and effective. *Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645, 654 (1973).[9]

Indeed, "products for patients with high rates of unexplained background injuries appear especially hazardous from a legal point of view." Garber, *supra*, at 63. As the following examples illustrate, state-law suits have the potential to drive from the market drugs that not only benefit many patients, but do not harm the plaintiffs who filed suit.

Vaccines. Experts have long asserted that second-guessing of FDA decisions has resulted in a mass exodus from the market for vaccines. "[S]ingle-product monopolies supply many of the vaccines for

---

[9] Empirical research has shown that, when evaluating risk, "the typical juror appears to be subject to a massive hindsight bias." Reid Hastie & W. Kip Viscusi, *What Juries Can't Do Well: The Jury's Performance as Risk Manager*, 40 Ariz. L. Rev. 901, 917 (1998). In addition, research has demonstrated that juries are influenced by the severity of the plaintiff's injuries: the more seriously injured the plaintiff, the more likely the jury is to find that the defendant caused the injury. *See, e.g.*, Dennis J. Devine et al., *Jury Decision Making*, 7 Psychol. Pub. Pol'y & L. 622, 699 (2001).

major illnesses, including polio, measles, rabies, mumps, and rubella." W. Kip Viscusi, *Corporate Risk Analysis: A Reckless Act?*, 52 Stan. L. Rev. 547, 583 (2000). Vaccine shortages persist despite the National Vaccine Injury Compensation Program established in 1986 by Congress to minimize the burdens of state-law failure-to-warn suits. Plaintiffs can and do opt out of the federal program. *See, e.g.*, *Sykes v. Glaxo-SmithKline*, 484 F. Supp. 2d 289, 310 (E.D. Pa. 2007) (state-law suit alleging that plaintiff was harmed by thimerosal, a vaccine preservative, even though FDA had concluded that "[t]here is no evidence of harm from the use of thimerosal as a vaccine preservative") (quotations and alterations omitted).

Starting in the late 1970s, lawsuits alleged that pharmaceutical companies failed to warn that the whooping-cough component of the DPT vaccine caused permanent brain damage. Seven companies stopped making the vaccine; the lone company that continued to produce the vaccine lost a single state-law case and was subjected to a damages award equal to half the annual sales of the vaccine. To conserve vaccine supplies, the Centers for Disease Control and Prevention were forced to ask doctors "to stop vaccinating children over age one." Linda A. Willett, *Litigation as an Alternative to Regulation: Problems Created by Follow-On Lawsuits with Multiple Outcomes*, 18 Geo. J. Legal Ethics 1477, 1488 n. 60 (2005). Claims that the vaccine caused neurological harm were subsequently "discredited." Stephen D. Sugarman, *Cases in Vaccine Court –*

Legal Battles Over Vaccines and Autism, 357 N. Eng. J. Med. 1275, 1276 (2007).

There is evidence that the threat of litigation continues to inhibit development of a vaccine for AIDS. In 1986, the medical component of the National Academy of Sciences observed that, "[g]iven the extremely high cost of vaccine development programs and the present concerns over liability for vaccine-related injuries, many manufacturers may be unwilling to initiate or pursue the derivation or distribution of a vaccine to prevent AIDS." Institute of Medicine, National Academy of Sciences, *Confronting AIDS: Directions for Public Health, Health Care and Research* 222 (1986). One company "offered to donate to the U.S. government all the data its researchers ha[d] gathered over the years on the company's AIDS vaccine" and "request[ed] in exchange only that the government assume responsibility for any future liabilities." Charles Fenyvesi, *Shift and Shield*, U.S. News & World Report, June 15, 1992, at 24.

As the AIDS crisis continued into the 1990s, commercial liability insurance companies "den[ied] coverage to HIV vaccine researchers and manufacturers and experts predict[ed] that the unavailability of liability insurance [would] delay the marketing of any future FDA-approved vaccines." Kellen F. Cloney, *Note, AIDS Vaccine Manufacturers v. Tort Regime: The Need for Alternatives*, 49 Wash. & Lee L. Rev. 559, 570 (1992). Today, more than two decades after the first documented cases of AIDS, "[e]xposure to product liability lawsuits [remains] a

significant deterrent to [HIV] vaccine development in litigious environments such as the US." John Godwin, *HIV Treatments, Vaccines, and Microbicides: Toward Coordinated Advocacy*, Canadian HIV/AIDS Pol'y & L. Rev., Apr. 2004, at 1, 10.

Drugs for Pregnant Women. Pregnant women have also suffered as a result of lawsuits that ask juries to second-guess FDA determinations. In October 1979, "the National Enquirer published a story . . . linking Bendectin, a popular morning sickness drug, with birth defects." David E. Bernstein, *The Breast Implant Fiasco*, 87 Cal. L. Rev. 457, 460 (1999). After similar media reports, "suddenly thousands of claims had been filed" alleging that Bendectin caused birth defects in plaintiffs' children. *Id.* Questionable scientific theories drove the litigation, ultimately prompting this Court's landmark decision in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).[10]

Although the manufacturer prevailed in more than two-thirds of the trials, it nevertheless "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 Testimony on Causation in*

---

[10] Dubious science continues to find its way into state tort suits, because "only a minority of state courts have wholeheartedly adopted the *Daubert* trilogy." David E. Bernstein & Jeffrey D. Jackson, *The Daubert Trilogy in the States*, 44 Jurimetrics J. 351, 365 (2004).

the Bendectin Cases, 46 Stan. L. Rev. 1, 7 (1993). Subsequent "studies 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).

The withdrawal of Bendectin increased health risks for pregnant women and babies. Without Bendectin, "hospital admission for morning sickness [has] doubled." Richard B. Stewart, *Regulatory Compliance as a Defense to Product Liability*, 88 Geo. L.J. 2167, 2171 (2000). The failure to treat severe morning sickness has an adverse effect on fetal nutrition and increases the risk of pregnancy complications. Brent, *supra*, at S264.

As the Bendectin example illustrates, liability risks would arise under state tort law even if a pregnancy drug were perfectly safe. That is so because "many pregnancies result in birth defects of unknown cause, and this leaves companies whose products were used during pregnancy vulnerable to suits." Garber, *supra*, at xxix. Indeed, "[w]ith over thirty million infants exposed to the product in utero, and a background rate of serious birth defects at perhaps 3 percent, ... [a]lmost one million babies born to mothers who used Bendectin would be expected to have had serious birth defects even if Bendectin had no such effect." *Id.* at 94-95.

Contraceptives. State-law tort litigation has also slowed contraceptive research. According to the

Institute of Medicine, "products liability litigation and the impact of that litigation on the cost and availability of liability insurance have contributed significantly to the climate of disincentives for the development of contraceptive products." Nat'l Research Council, Institute of Medicine, *Developing New Contraceptives: Obstacles and Opportunities* 141 (1990). For instance, liability costs drove the manufacturer to cease producing the Copper-7 contraceptive device – even though, at the time of withdrawal, the manufacturer had prevailed in nine of the eleven trials in which plaintiffs claimed that the device caused their injuries. *See* Garber, *supra*, at 93.

* * * *

Perversely, manufacturers' greatest liability risks tend to be associated with those patients who are most in need of beneficial medicines. For instance, "[w]ith a very substantial background rate of suicide among potential product users, the arithmetic of [antidepressants] is reminiscent of that of Bendectin." *Id.* at 99 (footnote omitted). Other essential products, used to treat common illnesses or classes of patients with high background rates of these illnesses, face the same problem. In these situations, in which the drug is crucial and the risk of a false positive is elevated, FDA's expertise is especially important.

II. Respondent's State-Law Tort Claims Are Preempted Under Well-Established Preemption Principles.

State law conflicts with federal law, and thus is preempted, when: (1) "compliance with both federal and state regulations is a physical impossibility," *Fla. Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142-43 (1963); or when (2) state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941). Both types of conflict are present in this case. As the Vermont Supreme Court recognized, an "impossibility" conflict arises when adding warnings or instructions required by state law would violate federal law. Contrary to the Vermont court's decision, however, the scope of "impossibility" preemption in the pharmaceutical context is not limited to cases in which FDA has expressly rejected the precise warnings or instructions sought by the plaintiff. It also extends to cases – including this case – in which adding such language without prior FDA approval would violate federal law. This case also presents the "obstacle" type of conflict between state and federal law, because imposing liability under state tort law would alter FDA's careful balancing of the risks and benefits of prescription medications and cause FDA to be inundated with labeling supplements.[11]

---

[11] A ruling for Petitioner in this case would not necessarily foreclose all state-law tort claims against manufacturers of prescription medicines. For example, this case does not involve

A. Respondent's State-Law Claims Are Preempted Because Adding The Instructions And Warnings At Issue Would Violate Federal Law.

1. There is no serious dispute that state law is preempted when it requires an action that is prohibited by federal law. As the Vermont Supreme Court acknowledged, if "FDA intended to prohibit defendant from strengthening the *Phenergan* label," then "it was impossible for defendant to comply with its obligations under both state and federal law." Pet. App. at 19a. *See also id.* at 17a (indicating that state-law claims would be preempted if FDA "would have rejected any attempt by [Petitioner] to strengthen its label").

Other courts agree that state law is preempted when it requires additional warnings or instructions that would violate federal law. For example, the Third Circuit recently held that federal law preempts state-law claims based on allegations that the manufacturers failed to warn of an association between antidepressants and suicide. *Colacicco v. Apotex, Inc.*, 521 F.3d 253 (3d Cir. 2008). In concluding that a suicide warning would have violated federal law, the court of appeals reasoned that "FDA has actively monitored the possible association between SSRIs and suicide for nearly twenty years, and has concluded that the suicide warnings desired by plaintiffs are without scientific

---

material new safety information that was not reported to or considered by FDA.

basis and would therefore be false and misleading." *Id.* at 269. The Third Circuit reasoned that, "[b]ecause the standard for adding a warning to drug labeling is the existence of 'reasonable evidence of an association of a serious hazard with a drug,' and the FDCA authorizes the FDA to prohibit false or misleading labeling, a state-law obligation to include a warning asserting the existence of an association between SSRIs and suicidality directly conflicts with the FDA's oft-repeated conclusion that the evidence did not support such an association." *Id.* at 271 (citation omitted).

Likewise, the California Supreme Court, in a decision involving an over-the-counter drug, held that federal law preempted a state-law requirement that the manufacturer of a nicotine patch warn consumers that the patch was "not for use by pregnant women" and that the product "contains nicotine, a chemical known to the state of California to cause reproductive harm." *Dowhal*, 88 P.3d at 3-4. Again, the court concluded that the warning required by state law was prohibited by federal law: "FDA had rejected plaintiff's claim that his data justify a different warning, and defendants d[id] not claim to have any additional data." *Id.* at 9. Other courts have also recognized that, at a minimum, preemption is required when FDA has expressly rejected the scientific basis for the proposed warning underlying the plaintiff's failure-to-warn claim.[12]

---

[12] *See, e.g.*, *Horne v. Novartis*, 541 F. Supp. 2d 768, 2008 WL 818819, at *11 (W.D.N.C. 2008); *Sykes*, 484 F. Supp. 2d at 310; *Needleman v. Pfizer Inc.*, No. Civ. A. 3:03-CV-3074N, 2004 WL

These decisions are plainly correct. A different preemption rule would subject manufacturers to a Catch-22: If they changed the labeling they would violate federal law; if they did not change the labeling they could be held liable – repeatedly – under state law and could not adjust their conduct by modifying the labeling.

2. Although the Vermont Supreme Court correctly recognized that state-law tort claims are preempted when it is impossible to comply with both federal and state law, the court defined the scope of the "impossibility" conflict too narrowly. The Vermont court erroneously concluded that it was possible for Petitioner to comply with both federal and state law in this case because federal law "allows, and arguably encourages, manufacturers to add and strengthen" FDA-approved warnings without prior FDA approval. Pet. App. 11a. The Vermont Supreme Court's ruling rests on a misinterpretation of federal law.

The Vermont Supreme Court based its ruling on its interpretation of FDA's CBE regulation, 21 C.F.R. § 314.70(c). According to the Vermont court, this regulation grants manufacturers general permission to "add and strengthen warnings" without prior FDA approval. Pet. App. 11a. Contrary to the Vermont court's view, FDA has long interpreted its regulation as creating a limited exception that applies only to

---

1773697, at *2 (N.D. Tex. Aug. 6, 2004); *Dusek v. Pfizer Inc.*, No. Civ. A H-02-3559, 2004 WL 2191804, at *6 (S.D. Tex. Feb. 20, 2004).

"concerns about *newly discovered* risks" and "important *new information* about the safe use of a drug." New Drug and Antibiotic Regulations, 47 Fed. Reg. at 46,623, 46,625 (emphasis added).[13] The agency's interpretation of the substantive meaning of its own regulation is entitled to substantial judicial deference. *See Auer v. Robbins*, 519 U.S. 452, 461 (1997).[14]

Correctly interpreted, Section 314.70(c) is a "narrow exception" to the general requirement that labeling, including labeling changes, must be approved in advance by FDA. Section 314.70(a)

---

[13] In addition, no FDA approval is required for certain minor labeling changes, so long as the manufacturer informs the FDA of the changes in its next annual report to the agency. *See* 21 C.F.R. § 314.70(d)(2)(ix) (change "concerning the description of the drug product or in the information about how the drug product is supplied, that does not involve a change in the dosage strength or dosage form"); *id.* § 314.70(d)(2)(x) ("editorial or similar minor change").

[14] It is well-settled that "[f]ederal regulations have no less preemptive effect than federal statutes." *Fidelity Fed. Sav. & Loan Ass'n v. de la Cuesta*, 458 U.S. 141, 153 (1982). Moreover, an agency's determination that a state law poses an obstacle to achieving the purposes and objectives of federal law is also entitled to a degree of judicial deference. *See Medtronic, Inc. v. Lohr*, 518 U.S. 470, 496 (1996) ("agency is uniquely qualified to determine whether a particular form of state law stands as an obstacle to accomplishment and execution of the full purposes and objectives of Congress"); *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 883 (2000) (agency "likely to have a full understanding of its own regulation and objectives, and is uniquely qualified to comprehend the likely impact of state requirements").

applies only if the manufacturer has "newly acquired safety information," *i.e.*, information that has not previously been submitted to FDA and is not cumulative of previously-submitted information. Supplemental Applications, 73 Fed. Reg. at 2850.

In this case, there was no new newly-acquired information about Phenergan relevant to the risk at issue in this case. To the contrary, it is undisputed that FDA was fully aware of the risks of IV-push administration of Phenergan and had considered those risks over a period of decades. *See* Pet'r Br. 11-18. At the time Respondent was given Phenergan, the drug's labeling expressly warned that arterial injection may cause gangrene and require amputation. *See* Pet. App. 4a. Prior to Respondent's use of Phenergen, moreover, Petitioner sought to replace the existing warning with the following warning: "INJECTION THROUGH A PROPERLY RUNNING INTRAVENOUS INFUSION MAY ENHANCE THE POSSIBILITY OF DETECTING ARTERIAL PLACEMENT." *Id.* at 4a-5a. FDA rejected the proposed change and directed Petitioner to "[r]etain verbiage in current label." *Id.* at 162a.

At trial, Respondent argued, and the jury agreed, that "the label should not have allowed IV push as a means of administration." Pet. App. 3a. But there is no dispute that FDA had before it all available information regarding Phenergen when it approved the warning that allowed IV-push administration in limited circumstances. Because there was no new information about Phenergen relevant to the risk at issue in this case, Petitioner was not authorized to

change the labeling under Section 314.70(c), and thus making the labeling change sought by Respondent without prior FDA approval would have violated federal law.

In sum, there is substantial agreement that state-law tort claims against pharmaceutical manufacturers are preempted when it is impossible for manufacturers to comply with both federal and state law. The Vermont Supreme Court erred by failing to recognize that if Petitioner had made labeling changes to comply with state law it would have violated federal law. Accordingly, the state-law claims at issue in this case are preempted.

B. Respondent's State-Law Claims Are Preempted Because They Conflict With FDA's Balancing Of Risks And Benefits.

Respondent's state-law claims also conflict with federal law for a second reason: they pose a serious obstacle to FDA's careful balancing of the risks and benefits of prescription medicines. By allowing juries to second-guess FDA's balancing of risks and benefits, state law frustrates the objective of the FDCA and its implementing regulations, which is to promote the beneficial and safe use of medicines based on reasonable scientific evidence. The Vermont Supreme Court's contrary decision rests on a fundamental misunderstanding of the structure of

the FDCA and federal regulation of prescription drugs.[15]

A new drug application must include "the labeling proposed to be used for such drug." 21 U.S.C. § 355(b)(1)(F). When it approves a new drug, FDA exercises its exclusive authority under the FDCA to determine that the drug is safe and effective when used in accordance with the labeling and that the labeling is not "false or misleading in any particular." 21 U.S.C. § 355(d)(1), (2), (4), (5), (7). In making this judgment, FDA strikes a balance, as it did here, between the benefits and risks of the drug when so labeled. *See Rutherford*, 442 U.S. at 555 (FDA "generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use.").

If FDA-approved warnings merely set a floor for additional regulation, then it would be open to States

---

[15] The Vermont Supreme Court held that the 1962 amendments to the FDCA limit preemption under the FDCA to situations in which it is impossible to comply with both federal and state law. *See* Pet. App. 21a-23a (discussing Pub. L. No. 87-781, § 202, 76 Stat. 780, 793 (1962), which provides that "[n]othing in the amendments made by this act to the [FDCA] shall be construed as invalidating any provision of State law . . . unless there is a direct and positive conflict between such amendments and such provision of State law"). As Petitioner has explained, the Vermont court's interpretation of this statutory provision is incorrect. This Court's pre-1962 opinions repeatedly used the phrase "direct and positive conflict" to describe conflict preemption in general, including both "impossibility" and "obstacle" preemption. *See* Pet'r Br. 51-54 (collecting cases).

– through legislation, regulation, or common-law tort actions – to require additional warnings. Such warnings would alter FDA's risk-benefit determinations, and thus conflict with the federal agency's determination that the drug is safe and effective when used according to its FDA-approved labeling. For this reason, state-law claims are preempted where – as in this case – FDA has considered the risk at issue and decided whether and to what extent the drug's labeling should warn of that risk.

These basic preemption principles apply to state tort claims decided by juries just as they would apply to state statutes or administrative regulations that conflict with FDA's risk-benefit determination. As the Court recently observed in a related context, it is "implausible" to conclude that "a single state jury" has "greater power to set state standards 'different from, or in addition to' federal standards" than "state officials acting through state administrative or legislative lawmaking processes." *Riegel*, 128 S. Ct. at 1008 (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 504 (Breyer, J., concurring)).[16]

---

[16] This Court has recognized that the Supremacy Clause applies "beyond [states'] positive enactments, such as statutes and regulations, to embrace common-law duties." *Bates v. Dow AgroSciences LLC*, 544 U.S. 431, 443 (2005). *See also Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1008 (2008); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 523 (1992). Although those cases involved express preemption provisions, the Court's reasoning applies equally to implied preemption: "[C]ommon-law liability is 'premised on the existence of a legal duty,' and a tort judgment therefore establishes that the defendant has violated

For all these reasons, jury verdicts in state-law pharmaceutical product liability cases frequently will conflict with FDA risk-benefit determinations reflected in a prescription drug's FDA-approved labeling. The conflict is greatly magnified when a potentially unlimited number of juries from 50 different states are asked to reach independent determinations about the appropriate balancing of risks and benefits. *See* J.A. 212 ("The FDA doesn't make the decision, you do."). These determinations can be expected to conflict with each other, as well as with FDA's determination. And because the consequences of an adverse jury verdict are so significant for the manufacturer, a relatively small number of adverse jury determinations may effectively displace FDA's risk-benefit determination.

To maintain FDA's careful balancing of risks and benefits, preemption analysis should not turn on whether FDA has disapproved the precise labeling language advocated by a particular plaintiff. Instead, the court should ask whether FDA has examined the relevant issue and approved warnings based on its review.

In this case, FDA reviewed the risks of administering Phenergan via IV push over a period of decades and approved a carefully calibrated set of

---

a state-law obligation. . . . And while the common-law remedy is limited to damages, a liability award 'can be, and indeed is designed to be, a potent method of governing conduct and controlling policy.'" *Riegel*, 128 S. Ct. at 1008 (quoting *Cipollone*, 505 U.S. at 521-22).

warnings and instructions based on its balancing of risks and benefits. The risks and benefits of IV-push administration were well known, and Petitioner had no newly-acquired information that had not been submitted to FDA. Allowing individual juries to strike their own balance between the risks and benefits conflicts with the objectives of federal law, and thus is preempted.

C. Limiting Preemption to Cases In Which FDA Has Expressly Rejected Specific Labeling Language Will Cause FDA To Be Inundated With Labeling Applications.

The Vermont court's decision effectively conditions preemption on FDA's recitation of magic words. Although Petitioner had no new information about the risks of IV-push administration, Petitioner could have avoided liability in this case if it had asked FDA to expressly disapprove every possible permutation of instructions and warnings concerning IV-push administration.

If allowed to stand, the Vermont Supreme Court's decision will encourage manufacturers to inundate FDA with requests for labeling changes that FDA has already rejected in substance. To fend off labeling criticisms from plaintiffs and their experts, manufacturers will be encouraged to submit every conceivable labeling variation to FDA so as to come within the narrow scope of preemption recognized by the Vermont Supreme Court. Such a regime would place an excessive burden on FDA.

In a related FDA preemption context, the Court has already recognized that state tort claims may give manufacturers "an incentive to submit a deluge of information that the [FDA] neither wants nor needs, resulting in additional burdens on FDA's evaluation of an application," and delaying FDA action. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 351 (2001). After considering these burdens on FDA, the Court rejected the argument that the state-law claims at issue in *Buckman* would "affect only the litigants and [would] not have the kind of direct impact on the United States, which preemption is designed to protect from undue incursion." *Id.* at 351 n.6 (quotations omitted).[17]

Indeed, the burden on FDA that is created by the Vermont Supreme Court's approach to preemption is even more serious than the burden that concerned the Court in *Buckman*. Rather than dealing with the excess information as it sees fit, FDA is *required* to respond to labeling proposals.[18] An avalanche of additional labeling requests will distract FDA from

---

[17] *See also, e.g.*, *Mason v. SmithKline Beecham Corp.*, ___ F. Supp. 2d ___, 2008 WL 1835350, at *8 n.5 (C.D. Ill. Apr. 23, 2008) (under *Buckman*, federal law preempts plaintiffs' claims to the extent they suggest manufacturer withheld studies from FDA); *Horne*, 2008 WL 818819, at *14 (same).

[18] *See* 5 U.S.C. § 555(e) (requiring agency to give notice of the denial in whole or part of a written application or petition); *see also* 21 C.F.R. § 314.70(b)(4) (authorizing applicant to request expedited review of a supplement "for public health reasons" or if a delay "would impose an extraordinary hardship on the applicant").

its core responsibility of evaluating drugs' safety and effectiveness. This burden would be imposed at the very time that Congress is attempting to *strengthen* FDA's oversight powers in order to further safeguard the public health. *See* Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823, tit. IX (2007).

FDA reporting requirements already generate "a deluge of information." Catherine T. Struve, *The FDA and the Tort System: Postmarketing Surveillance, Compensation, and the Role of Litigation*, 5 Yale J. Health Pol'y, L. & Ethics 587, 604 (2005). By creating an incentive for manufacturers to inundate FDA with labeling proposals, the state-law claim in this case poses an obstacle to the achievement of the purposes of federal law.

CONCLUSION

The judgment of the Supreme Court of Vermont should be reversed.

Respectfully submitted,

Diane E. Bieri
Maya Bermingham
Pharmaceutical Research and Manufacturers of America
950 F Street, NW
Suite 300
Washington, DC 20004
(202) 835-3405

Tom DiLenge
Sandra J.P. Dennis
Biotechnology Industry Organization
1201 Maryland Avenue, SW
Suite 900
Washington, DC 20024
(202) 962-9200

Robert A. Long, Jr.
Counsel of Record
Michael X. Imbroscio
Paul W. Schmidt
Erika Lietzan
Gregory M. Lipper
Covington & Burling LLP
1201 Pennsylvania Ave, NW
Washington, D.C. 20004
(202) 662-6000

Counsel for Amici Curiae