SUPREME COURT OF THE UNITED STATES

No. 06–1249

WYETH, PETITIONER *v.* DIANA LEVINE

ON WRIT OF CERTIORARI TO THE SUPREME COURT OF VERMONT

[March 4, 2009]

JUSTICE STEVENS delivered the opinion of the Court.

Directly injecting the drug Phenergan into a patient's vein creates a significant risk of catastrophic consequences. A Vermont jury found that petitioner Wyeth, the manufacturer of the drug, had failed to provide an adequate warning of that risk and awarded damages to respondent Diana Levine to compensate her for the amputation of her arm. The warnings on Phenergan's label had been deemed sufficient by the federal Food and Drug Administration (FDA) when it approved Wyeth's new drug application in 1955 and when it later approved changes in the drug's labeling. The question we must decide is whether the FDA's approvals provide Wyeth with a complete defense to Levine's tort claims. We conclude that they do not.

I

Phenergan is Wyeth's brand name for promethazine hydrochloride, an antihistamine used to treat nausea. The injectable form of Phenergan can be administered intramuscularly or intravenously, and it can be administered intravenously through either the "IV-push" method, whereby the drug is injected directly into a patient's vein,

or the "IV-drip" method, whereby the drug is introduced into a saline solution in a hanging intravenous bag and slowly descends through a catheter inserted in a patient's vein. The drug is corrosive and causes irreversible gangrene if it enters a patient's artery.

Levine's injury resulted from an IV-push injection of Phenergan. On April 7, 2000, as on previous visits to her local clinic for treatment of a migraine headache, she received an intramuscular injection of Demerol for her headache and Phenergan for her nausea. Because the combination did not provide relief, she returned later that day and received a second injection of both drugs. This time, the physician assistant administered the drugs by the IV-push method, and Phenergan entered Levine's artery, either because the needle penetrated an artery directly or because the drug escaped from the vein into surrounding tissue (a phenomenon called "perivascular extravasation") where it came in contact with arterial blood. As a result, Levine developed gangrene, and doctors amputated first her right hand and then her entire forearm. In addition to her pain and suffering, Levine incurred substantial medical expenses and the loss of her livelihood as a professional musician.

After settling claims against the health center and clinician, Levine brought an action for damages against Wyeth, relying on common-law negligence and strict-liability theories. Although Phenergan's labeling warned of the danger of gangrene and amputation following inadvertent intra-arterial injection,[1] Levine alleged that the

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[1]The warning for "Inadvertent Intra-arterial Injection" stated: "Due to the close proximity of arteries and veins in the areas most commonly used for intravenous injection, extreme care should be exercised to avoid perivascular extravasation or inadvertent intra-arterial injection. Reports compatible with inadvertent intra-arterial injection of Phenergan Injection, usually in conjunction with other drugs intended for intravenous use, suggest that pain, severe chemical irritation, severe

labeling was defective because it failed to instruct clinicians to use the IV-drip method of intravenous administration instead of the higher risk IV-push method. More broadly, she alleged that Phenergan is not reasonably safe for intravenous administration because the foreseeable risks of gangrene and loss of limb are great in relation to the drug's therapeutic benefits. App. 14–15.

Wyeth filed a motion for summary judgment, arguing that Levine's failure-to-warn claims were pre-empted by federal law. The court found no merit in either Wyeth's field pre-emption argument, which it has since abandoned, or its conflict pre-emption argument. With respect to the contention that there was an "actual conflict between a specific FDA order," *id.*, at 21, and Levine's failure-to-warn action, the court reviewed the sparse correspondence between Wyeth and the FDA about Phenergan's labeling and found no evidence that Wyeth had "earnestly attempted" to strengthen the intra-arterial injection warning or that the FDA had "specifically disallowed" stronger language, *id.*, at 23. The record, as then developed,

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spasm of distal vessels, and resultant gangrene requiring amputation are likely under such circumstances. Intravenous injection was intended in all the cases reported but perivascular extravasation or arterial placement of the needle is now suspect. There is no proven successful management of this condition after it occurs. . . . Aspiration of dark blood does not preclude intra-arterial needle placement, because blood is discolored upon contact with Phenergan Injection. Use of syringes with rigid plungers or of small bore needles might obscure typical arterial backflow if this is relied upon alone. When used intravenously, Phenergan Injection should be given in a concentration no greater than 25 mg per mL and at a rate not to exceed 25 mg per minute. When administering any irritant drug intravenously, it is usually preferable to inject it through the tubing of an intravenous infusion set that is known to be functioning satisfactorily. In the event that a patient complains of pain during intended intravenous injection of Phenergan Injection, the injection should be stopped immediately to provide for evaluation of possible arterial placement or perivascular extravasation." App. 390.

"lack[ed] any evidence that the FDA set a ceiling on this matter." *Ibid.*

The evidence presented during the 5-day jury trial showed that the risk of intra-arterial injection or perivascular extravasation can be almost entirely eliminated through the use of IV-drip, rather than IV-push, administration. An IV drip is started with saline, which will not flow properly if the catheter is not in the vein and fluid is entering an artery or surrounding tissue. See *id.*, at 50–51, 60, 66–68, 75. By contrast, even a careful and experienced clinician using the IV-push method will occasionally expose an artery to Phenergan. See *id.*, at 73, 75–76. While Phenergan's labeling warned against intra-arterial injection and perivascular extravasation and advised that "[w]hen administering any irritant drug intravenously it is usually preferable to inject it through the tubing of an intravenous infusion set that is known to be functioning satisfactorily," *id.*, at 390, the labeling did not contain a specific warning about the risks of IV-push administration.

The trial record also contains correspondence between Wyeth and the FDA discussing Phenergan's label. The FDA first approved injectable Phenergan in 1955. In 1973 and 1976, Wyeth submitted supplemental new drug applications, which the agency approved after proposing labeling changes. Wyeth submitted a third supplemental application in 1981 in response to a new FDA rule governing drug labels. Over the next 17 years, Wyeth and the FDA intermittently corresponded about Phenergan's label. The most notable activity occurred in 1987, when the FDA suggested different warnings about the risk of arterial exposure, and in 1988, when Wyeth submitted revised labeling incorporating the proposed changes. The FDA did not respond. Instead, in 1996, it requested from Wyeth the labeling then in use and, without addressing Wyeth's 1988 submission, instructed it to "[r]etain verbiage in

current label" regarding intra-arterial injection. *Id.*, at 359. After a few further changes to the labeling not related to intra-arterial injection, the FDA approved Wyeth's 1981 application in 1998, instructing that Phenergan's final printed label "must be identical" to the approved package insert. *Id.*, at 382.

Based on this regulatory history, the trial judge instructed the jury that it could consider evidence of Wyeth's compliance with FDA requirements but that such compliance did not establish that the warnings were adequate. He also instructed, without objection from Wyeth, that FDA regulations "permit a drug manufacturer to change a product label to add or strengthen a warning about its product without prior FDA approval so long as it later submits the revised warning for review and approval." *Id.*, at 228.

Answering questions on a special verdict form, the jury found that Wyeth was negligent, that Phenergan was a defective product as a result of inadequate warnings and instructions, and that no intervening cause had broken the causal connection between the product defects and the plaintiff's injury. *Id.*, at 233–235. It awarded total damages of $7,400,000, which the court reduced to account for Levine's earlier settlement with the health center and clinician. *Id.*, at 235–236.

On August 3, 2004, the trial court filed a comprehensive opinion denying Wyeth's motion for judgment as a matter of law. After making findings of fact based on the trial record (supplemented by one letter that Wyeth found after the trial), the court rejected Wyeth's pre-emption arguments. It determined that there was no direct conflict between FDA regulations and Levine's state-law claims because those regulations permit strengthened warnings without FDA approval on an interim basis and the record contained evidence of at least 20 reports of amputations similar to Levine's since the 1960's. The court also found

that state tort liability in this case would not obstruct the FDA's work because the agency had paid no more than passing attention to the question whether to warn against IV-push administration of Phenergan. In addition, the court noted that state law serves a compensatory function distinct from federal regulation. *Id.*, at 249–252.

The Vermont Supreme Court affirmed. It held that the jury's verdict "did not conflict with FDA's labeling requirements for Phenergan because [Wyeth] could have warned against IV-push administration without prior FDA approval, and because federal labeling requirements create a floor, not a ceiling, for state regulation." ___ Vt. ___, ___ 944 A. 2d 179, 184 (2006). In dissent, Chief Justice Reiber argued that the jury's verdict conflicted with federal law because it was inconsistent with the FDA's conclusion that intravenous administration of Phenergan was safe and effective.

The importance of the pre-emption issue, coupled with the fact that the FDA has changed its position on state tort law and now endorses the views expressed in Chief Justice Reiber's dissent, persuaded us to grant Wyeth's petition for certiorari. 552 U. S. ___ (2008). The question presented by the petition is whether the FDA's drug labeling judgments "preempt state law product liability claims premised on the theory that different labeling judgments were necessary to make drugs reasonably safe for use." Pet. for Cert. *i.*

II

Wyeth makes two separate pre-emption arguments: first, that it would have been impossible for it to comply with the state-law duty to modify Phenergan's labeling without violating federal law, see *Fidelity Fed. Sav. & Loan Assn.* v. *De la Cuesta*, 458 U. S. 141, 153 (1982), and second, that recognition of Levine's state tort action creates an unacceptable "obstacle to the accomplishment and

execution of the full purposes and objectives of Congress," *Hines* v. *Davidowitz*, 312 U. S. 52, 67 (1941), because it substitutes a lay jury's decision about drug labeling for the expert judgment of the FDA. As a preface to our evaluation of these arguments, we identify two factual propositions decided during the trial court proceedings, emphasize two legal principles that guide our analysis, and review the history of the controlling federal statute.

The trial court proceedings established that Levine's injury would not have occurred if Phenergan's label had included an adequate warning about the risks of the IV-push method of administering the drug. The record contains evidence that the physician assistant administered a greater dose than the label prescribed, that she may have inadvertently injected the drug into an artery rather than a vein, and that she continued to inject the drug after Levine complained of pain. Nevertheless, the jury rejected Wyeth's argument that the clinician's conduct was an intervening cause that absolved it of liability. See App. 234 (jury verdict), 252–254. In finding Wyeth negligent as well as strictly liable, the jury also determined that Levine's injury was foreseeable. That the inadequate label was both a but-for and proximate cause of Levine's injury is supported by the record and no longer challenged by Wyeth.[2]

The trial court proceedings further established that the critical defect in Phenergan's label was the lack of an adequate warning about the risks of IV-push administra-

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[2]The dissent nonetheless suggests that physician malpractice was the exclusive cause of Levine's injury. See, *e.g.*, *post*, at 1 (opinion of ALITO, J.) ("[I]t is unclear how a 'stronger' warning could have helped respondent"); *post*, at 16–18 (suggesting that the physician assistant's conduct was the sole cause of the injury). The dissent's frustration with the jury's verdict does not put the merits of Levine's tort claim before us, nor does it change the question we must decide—whether federal law pre-empts Levine's state-law claims.

tion. Levine also offered evidence that the IV-push method should be contraindicated and that Phenergan should never be administered intravenously, even by the IV-drip method. Perhaps for this reason, the dissent incorrectly assumes that the state-law duty at issue is the duty to contraindicate the IV-push method. See, *e.g.*, *post*, at 8, 25. But, as the Vermont Supreme Court explained, the jury verdict established only that Phenergan's warning was insufficient. It did not mandate a particular replacement warning, nor did it require contraindicating IV-push administration: "There may have been any number of ways for [Wyeth] to strengthen the Phenergan warning without completely eliminating IV-push administration." ___ Vt., at ___, n. 2, 944 A. 2d, at 189, n. 2. We therefore need not decide whether a state rule proscribing intravenous administration would be pre-empted. The narrower question presented is whether federal law pre-empts Levine's claim that Phenergan's label did not contain an adequate warning about using the IV-push method of administration.

Our answer to that question must be guided by two cornerstones of our pre-emption jurisprudence. First, "the purpose of Congress is the ultimate touchstone in every pre-emption case." *Medtronic, Inc.* v. *Lohr*, 518 U. S. 470, 485 (1996) (internal quotation marks omitted); see *Retail Clerks* v. *Schermerhorn*, 375 U. S. 96, 103 (1963). Second, "[i]n all pre-emption cases, and particularly in those in which Congress has 'legislated . . . in a field which the States have traditionally occupied,' . . . we 'start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.'" *Lohr*, 518 U. S., at 485 (quoting *Rice* v. *Santa Fe Elevator Corp.*, 331 U. S. 218, 230 (1947)).[3]

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[3] Wyeth argues that the presumption against pre-emption should not

In order to identify the "purpose of Congress," it is appropriate to briefly review the history of federal regulation of drugs and drug labeling. In 1906, Congress enacted its first significant public health law, the Federal Food and Drugs Act, ch. 3915, 34 Stat. 768. The Act, which prohibited the manufacture or interstate shipment of adulterated or misbranded drugs, supplemented the protection for consumers already provided by state regulation and common-law liability. In the 1930's, Congress became increasingly concerned about unsafe drugs and fraudulent marketing, and it enacted the Federal Food, Drug, and Cosmetic Act (FDCA), ch. 675, 52 Stat. 1040, as amended, 21 U. S. C. §301 *et seq.* The Act's most substantial innovation was its provision for premarket approval of new drugs. It required every manufacturer to submit a new drug application, including reports of investigations and specimens of proposed labeling, to the FDA for review. Until its application became effective, a manufacturer was

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apply to this case because the Federal Government has regulated drug labeling for more than a century. That argument misunderstands the principle: We rely on the presumption because respect for the States as "independent sovereigns in our federal system" leads us to assume that "Congress does not cavalierly pre-empt state-law causes of action." *Medtronic, Inc.* v. *Lohr*, 518 U. S. 470, 485 (1996). The presumption thus accounts for the historic presence of state law but does not rely on the absence of federal regulation.

For its part, the dissent argues that the presumption against pre-emption should not apply to claims of implied conflict pre-emption at all, *post*, at 21, but this Court has long held to the contrary. See, *e.g.*, *California* v. *ARC America Corp.*, 490 U. S. 93, 101–102 (1989); *Hillsborough County* v. *Automated Medical Laboratories, Inc.*, 471 U. S. 707, 716 (1985); see also *Rush Prudential HMO, Inc.* v. *Moran*, 536 U. S. 355, 387 (2002). The dissent's reliance on *Buckman Co.* v. *Plaintiffs' Legal Comm.*, 531 U. S. 341 (2001), see *post*, at 21, and n. 14, is especially curious, as that case involved state-law fraud-on-the-agency claims, and the Court distinguished state regulation of health and safety as matters to which the presumption does apply. See 531 U. S., at 347–348.

prohibited from distributing a drug. The FDA could reject an application if it determined that the drug was not safe for use as labeled, though if the agency failed to act, an application became effective 60 days after the filing. FDCA, §505(c), 52 Stat. 1052.

In 1962, Congress amended the FDCA and shifted the burden of proof from the FDA to the manufacturer. Before 1962, the agency had to prove harm to keep a drug out of the market, but the amendments required the manufacturer to demonstrate that its drug was "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling" before it could distribute the drug. §§102(d), 104(b), 76 Stat. 781, 784. In addition, the amendments required the manufacturer to prove the drug's effectiveness by introducing "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling." §102(d), *id.*, at 781.

As it enlarged the FDA's powers to "protect the public health" and "assure the safety, effectiveness, and reliability of drugs," *id.*, at 780, Congress took care to preserve state law. The 1962 amendments added a saving clause, indicating that a provision of state law would only be invalidated upon a "direct and positive conflict" with the FDCA. §202, *id.*, at 793. Consistent with that provision, state common-law suits "continued unabated despite . . . FDA regulation." *Riegel* v. *Medtronic, Inc.*, 552 U. S. ___, ___ (2008) (slip op., at 8) (GINSBURG, J., dissenting); see *ibid.*, n. 11 (collecting state cases). And when Congress enacted an express pre-emption provision for medical devices in 1976, see §521, 90 Stat. 574 (codified at 21 U. S. C. §360k(a)), it declined to enact such a provision for prescription drugs.

In 2007, after Levine's injury and lawsuit, Congress again amended the FDCA. 121 Stat. 823. For the first

time, it granted the FDA statutory authority to require a manufacturer to change its drug label based on safety information that becomes available after a drug's initial approval. §901(a), *id.*, at 924–926. In doing so, however, Congress did not enact a provision in the Senate bill that would have required the FDA to preapprove all changes to drug labels. See S. 1082, 110th Cong., 1st Sess., §208, pp. 107–114 (2007) (as passed) (proposing new §506D). Instead, it adopted a rule of construction to make it clear that manufacturers remain responsible for updating their labels. See 121 Stat. 925–926.

III

Wyeth first argues that Levine's state-law claims are pre-empted because it is impossible for it to comply with both the state-law duties underlying those claims and its federal labeling duties. See *De la Cuesta*, 458 U. S., at 153. The FDA's premarket approval of a new drug application includes the approval of the exact text in the proposed label. See 21 U. S. C. §355; 21 CFR §314.105(b) (2008). Generally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application. There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency's approval. Among other things, this "changes being effected" (CBE) regulation provides that if a manufacturer is changing a label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval. §§314.70(c)(6)(iii)(A), (C).

Wyeth argues that the CBE regulation is not implicated in this case because a 2008 amendment provides that a

manufacturer may only change its label "to reflect newly acquired information." 73 Fed. Reg. 49609. Resting on this language (which Wyeth argues simply reaffirmed the interpretation of the regulation in effect when this case was tried), Wyeth contends that it could have changed Phenergan's label only in response to new information that the FDA had not considered. And it maintains that Levine has not pointed to any such information concerning the risks of IV-push administration. Thus, Wyeth insists, it was impossible for it to discharge its state-law obligation to provide a stronger warning about IV-push administration without violating federal law. Wyeth's argument misapprehends both the federal drug regulatory scheme and its burden in establishing a pre-emption defense.

We need not decide whether the 2008 CBE regulation is consistent with the FDCA and the previous version of the regulation, as Wyeth and the United States urge, because Wyeth could have revised Phenergan's label even in accordance with the amended regulation. As the FDA explained in its notice of the final rule, "'newly acquired information'" is not limited to new data, but also encompasses "new analyses of previously submitted data." *Id.*, at 49604. The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments: "[I]f the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for 'newly acquired information.'" *Id.*, at 49607; see also *id.*, at 49606.

The record is limited concerning what newly acquired information Wyeth had or should have had about the risks of IV-push administration of Phenergan because Wyeth did not argue before the trial court that such information was required for a CBE labeling change. Levine did,

however, present evidence of at least 20 incidents prior to her injury in which a Phenergan injection resulted in gangrene and an amputation. See App. 74, 252.[4] After the first such incident came to Wyeth's attention in 1967, it notified the FDA and worked with the agency to change Phenergan's label. In later years, as amputations continued to occur, Wyeth could have analyzed the accumulating data and added a stronger warning about IV-push administration of the drug.

Wyeth argues that if it had unilaterally added such a warning, it would have violated federal law governing unauthorized distribution and misbranding. Its argument that a change in Phenergan's labeling would have subjected it to liability for unauthorized distribution rests on the assumption that this labeling change would have rendered Phenergan a new drug lacking an effective application. But strengthening the warning about IV-push administration would not have made Phenergan a new drug. See 21 U. S. C. §321(p)(1) (defining "new drug"); 21 CFR §310.3(h). Nor would this warning have rendered Phenergan misbranded. The FDCA does not provide that a drug is misbranded simply because the manufacturer has altered an FDA-approved label; instead, the misbranding provision focuses on the substance of the label and, among other things, proscribes labels that fail to include "adequate warnings." 21 U. S. C. §352(f). Moreover, because the statute contemplates that federal juries will resolve most misbranding claims, the FDA's belief that a drug is misbranded is not conclusive. See §§331, 332, 334(a)–(b). And the very idea that the FDA would bring an enforcement action against a manufacturer for

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[4] Levine also introduced evidence that Pfizer had withdrawn Vistaril, another antinausea drug, from intravenous use several decades earlier because its intravenous injection had resulted in gangrene and amputations. See App. 79.

strengthening a warning pursuant to the CBE regulation is difficult to accept—neither Wyeth nor the United States has identified a case in which the FDA has done so.

Wyeth's cramped reading of the CBE regulation and its broad reading of the FDCA's misbranding and unauthorized distribution provisions are premised on a more fundamental misunderstanding. Wyeth suggests that the FDA, rather than the manufacturer, bears primary responsibility for drug labeling. Yet through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market. See, *e.g.*, 21 CFR §201.80(e) (requiring a manufacturer to revise its label "to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug"); §314.80(b) (placing responsibility for postmarketing surveillance on the manufacturer); 73 Fed. Reg. 49605 ("Manufacturers continue to have a responsibility under Federal law . . . to maintain their labeling and update the labeling with new safety information").

Indeed, prior to 2007, the FDA lacked the authority to order manufacturers to revise their labels. See 121 Stat. 924–926. When Congress granted the FDA this authority, it reaffirmed the manufacturer's obligations and referred specifically to the CBE regulation, which both reflects the manufacturer's ultimate responsibility for its label and provides a mechanism for adding safety information to the label prior to FDA approval. See *id.*, at 925–926 (stating that a manufacturer retains the responsibility "to maintain its label in accordance with existing requirements, including subpart B of part 201 and *sections 314.70* and 601.12 of title 21, Code of Federal Regulations (or any successor regulations)" (emphasis added)). Thus, when

the risk of gangrene from IV-push injection of Phenergan became apparent, Wyeth had a duty to provide a warning that adequately described that risk, and the CBE regulation permitted it to provide such a warning before receiving the FDA's approval.

Of course, the FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application, just as it retains such authority in reviewing all supplemental applications. But absent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with both federal and state requirements.

Wyeth has offered no such evidence. It does not argue that it attempted to give the kind of warning required by the Vermont jury but was prohibited from doing so by the FDA.[5] See Tr. of Oral Arg. 12–13; see also Brief for United States as *Amicus Curiae* 25. And while it does suggest that the FDA intended to prohibit it from strengthening the warning about IV-push administration because the

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[5]The record would not, in any event, support such an argument. In 1988, Wyeth did propose different language for Phenergan's warning about intra-arterial injection, adapted from revisions the FDA proposed in 1987. See App. 339–341, 311–312. When the FDA approved Wyeth's application, it instructed Wyeth to retain the wording in its current label. During the trial court proceedings, Levine indicated that the language proposed in 1988 would have more strongly warned against IV-push administration. But the trial court and the Vermont Supreme Court found that the 1988 warning did not differ in any material respect from the FDA-approved warning. See ___ Vt. ___, ___, 944 A. 2d 179, 189 (2006) ("Simply stated, the proposed warning was different, but not stronger. It was also no longer or more prominent than the original warning . . ."); App. 248–250. Indeed, the United States concedes that the FDA did not regard the proposed warning as substantively different: "[I]t appears the FDA viewed the change as non-substantive and rejected it for formatting reasons." Brief for United States as *Amicus Curiae* 25; see also ___ Vt., at ___, 944 A. 2d, at 189.

agency deemed such a warning inappropriate in reviewing Phenergan's drug applications, both the trial court and the Vermont Supreme Court rejected this account as a matter of fact. In its decision on Wyeth's motion for judgment as a matter of law, the trial court found "no evidence in this record that either the FDA or the manufacturer gave more than passing attention to the issue of" IV-push versus IV-drip administration. App. 249. The Vermont Supreme Court likewise concluded that the FDA had not made an affirmative decision to preserve the IV-push method or intended to prohibit Wyeth from strengthening its warning about IV-push administration. ___ Vt., at ___, 944 A. 2d, at 188–189. Moreover, Wyeth does not argue that it supplied the FDA with an evaluation or analysis concerning the specific dangers posed by the IV-push method. We accordingly cannot credit Wyeth's contention that the FDA would have prevented it from adding a stronger warning about the IV-push method of intravenous administration.[6]

Impossibility pre-emption is a demanding defense. On the record before us, Wyeth has failed to demonstrate that it was impossible for it to comply with both federal and state requirements. The CBE regulation permitted Wyeth to unilaterally strengthen its warning, and the mere fact that the FDA approved Phenergan's label does not establish that it would have prohibited such a change.

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[6]The dissent's suggestion that the FDA intended to prohibit Wyeth from strengthening its warning does not fairly reflect the record. The dissent creatively paraphrases a few FDA orders—for instance by conflating warnings about IV-push administration and intra-arterial injection, see, *e.g.*, *post*, at 9, 11–12, 15–16—to suggest greater agency attention to the question, and it undertakes a study of Phenergan's labeling that is more elaborate than any FDA order. But even the dissent's account does not support the conclusion that the FDA would have prohibited Wyeth from adding a stronger warning pursuant to the CBE regulation.

IV

Wyeth also argues that requiring it to comply with a state-law duty to provide a stronger warning about IV-push administration would obstruct the purposes and objectives of federal drug labeling regulation. Levine's tort claims, it maintains, are pre-empted because they interfere with "Congress's purpose to entrust an expert agency to make drug labeling decisions that strike a balance between competing objectives." Brief for Petitioner 46. We find no merit in this argument, which relies on an untenable interpretation of congressional intent and an overbroad view of an agency's power to pre-empt state law.

Wyeth contends that the FDCA establishes both a floor and a ceiling for drug regulation: Once the FDA has approved a drug's label, a state-law verdict may not deem the label inadequate, regardless of whether there is any evidence that the FDA has considered the stronger warning at issue. The most glaring problem with this argument is that all evidence of Congress' purposes is to the contrary. Building on its 1906 Act, Congress enacted the FDCA to bolster consumer protection against harmful products. See *Kordel* v. *United States*, 335 U. S. 345, 349 (1948); *United States* v. *Sullivan*, 332 U. S. 689, 696 (1948). Congress did not provide a federal remedy for consumers harmed by unsafe or ineffective drugs in the 1938 statute or in any subsequent amendment. Evidently, it determined that widely available state rights of action provided appropriate relief for injured consumers.[7] It may

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[7] Although the first version of the bill that became the FDCA would have provided a federal cause of action for damages for injured consumers, see H. R. 6110, 73d Cong., 1st Sess., §25 (1933) (as introduced), witnesses testified that such a right of action was unnecessary because common-law claims were already available under state law. See Hearings on S. 1944 before a Subcommittee of the Senate Committee on Commerce, 73d Cong., 2d Sess., 400 (1933) (statement of W. A. Hines); see *id.*, at 403 (statement of J. A. Ladds) ("This act should not

also have recognized that state-law remedies further consumer protection by motivating manufacturers to produce safe and effective drugs and to give adequate warnings.

If Congress thought state-law suits posed an obstacle to its objectives, it surely would have enacted an express pre-emption provision at some point during the FDCA's 70-year history. But despite its 1976 enactment of an express pre-emption provision for medical devices, see §521, 90 Stat. 574 (codified at 21 U. S. C. §360k(a)), Congress has not enacted such a provision for prescription drugs. See *Riegel*, 552 U. S., at ___ (slip op., at 14) ("Congress could have applied the pre-emption clause to the entire FDCA. It did not do so, but instead wrote a pre-emption clause that applies only to medical devices").[8] Its silence on the issue, coupled with its certain awareness of the prevalence of state tort litigation, is powerful evidence that Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness. As Justice O'Connor explained in her opinion for a unanimous Court: "The case for federal pre-emption is particularly weak where Congress has indicated its awareness of the operation of state law in a field of federal interest, and has nonetheless decided to stand by both concepts and to tolerate whatever tension there [is] between them." *Bonito Boats, Inc.* v. *Thunder Craft Boats, Inc.*, 489 U. S. 141, 166–167 (1989) (internal quotation marks omitted); see also *supra*, at 8 (discussing the presumption against pre-

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attempt to modify or restate the common law with respect to personal injuries").

[8] In 1997, Congress pre-empted certain state requirements concerning over-the-counter medications and cosmetics but expressly preserved product liability actions. See 21 U. S. C. §§379r(e), 379s(d) ("Nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State").

emption).

Despite this evidence that Congress did not regard state tort litigation as an obstacle to achieving its purposes, Wyeth nonetheless maintains that, because the FDCA requires the FDA to determine that a drug is safe and effective under the conditions set forth in its labeling, the agency must be presumed to have performed a precise balancing of risks and benefits and to have established a specific labeling standard that leaves no room for different state-law judgments. In advancing this argument, Wyeth relies not on any statement by Congress, but instead on the preamble to a 2006 FDA regulation governing the content and format of prescription drug labels. See Brief for Petitioner 8, 11, 42, 45, and 50 (citing 71 Fed. Reg. 3922 (2006)). In that preamble, the FDA declared that the FDCA establishes "both a 'floor' and a 'ceiling,'" so that "FDA approval of labeling . . . preempts conflicting or contrary State law." *Id.*, at 3934–3935. It further stated that certain state-law actions, such as those involving failure-to-warn claims, "threaten FDA's statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs." *Id.*, at 3935.

This Court has recognized that an agency regulation with the force of law can pre-empt conflicting state requirements. See, *e.g.*, *Geier* v. *American Honda Motor Co.*, 529 U. S. 861 (2000); *Hillsborough County* v. *Automated Medical Laboratories*, *Inc.,* 471 U. S. 707, 713 (1985). In such cases, the Court has performed its own conflict determination, relying on the substance of state and federal law and not on agency proclamations of pre-emption. We are faced with no such regulation in this case, but rather with an agency's mere assertion that state law is an obstacle to achieving its statutory objectives. Because Congress has not authorized the FDA to pre-empt state law directly, cf. 21 U. S. C. §360k (authorizing the FDA to determine the scope of the Medical Devices Amendments' pre-emption

clause),[9] the question is what weight we should accord the FDA's opinion.

In prior cases, we have given "some weight" to an agency's views about the impact of tort law on federal objectives when "the subject matter is technica[l] and the relevant history and background are complex and extensive." *Geier*, 529 U. S., at 883. Even in such cases, however, we have not deferred to an agency's *conclusion* that state law is pre-empted. Rather, we have attended to an agency's explanation of how state law affects the regulatory scheme. While agencies have no special authority to pronounce on pre-emption absent delegation by Congress, they do have a unique understanding of the statutes they administer and an attendant ability to make informed determinations about how state requirements may pose an "obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Hines*, 312 U.S, at 67; see *Geier*, 529 U. S., at 883; *Lohr*, 518 U. S., at 495–496. The weight we accord the agency's explanation of state law's impact on the federal scheme depends on its thoroughness, consistency, and persuasiveness. Cf. *United States* v. *Mead Corp.*, 533 U. S. 218, 234–235 (2001); *Skidmore* v. *Swift & Co.*, 323 U. S. 134, 140 (1944).

Under this standard, the FDA's 2006 preamble does not merit deference. When the FDA issued its notice of pro-

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[9] For similar examples, see 47 U. S. C. §§253(a), (d) (2000 ed.) (authorizing the Federal Communications Commission to pre-empt "any [state] statute, regulation, or legal requirement" that "may prohibit or have the effect of prohibiting the ability of any entity to provide any interstate or intrastate telecommunications service"); 30 U. S. C. §1254(g) (2006 ed.) (pre-empting any statute that conflicts with "the purposes and the requirements of this chapter" and permitting the Secretary of the Interior to "set forth any State law or regulation which is preempted and superseded"); and 49 U. S. C. §5125(d) (2000 ed. and Supp. V) (authorizing the Secretary of Transportation to decide whether a state or local statute that conflicts with the regulation of hazardous waste transportation is pre-empted).

posed rulemaking in December 2000, it explained that the rule would "not contain policies that have federalism implications or that preempt State law." 65 Fed. Reg. 81103; see also 71 *id.*, at 3969 (noting that the "proposed rule did not propose to preempt state law"). In 2006, the agency finalized the rule and, without offering States or other interested parties notice or opportunity for comment, articulated a sweeping position on the FDCA's preemptive effect in the regulatory preamble. The agency's views on state law are inherently suspect in light of this procedural failure.

Further, the preamble is at odds with what evidence we have of Congress' purposes, and it reverses the FDA's own longstanding position without providing a reasoned explanation, including any discussion of how state law has interfered with the FDA's regulation of drug labeling during decades of coexistence. The FDA's 2006 position plainly does not reflect the agency's own view at all times relevant to this litigation. Not once prior to Levine's injury did the FDA suggest that state tort law stood as an obstacle to its statutory mission. To the contrary, it cast federal labeling standards as a floor upon which States could build and repeatedly disclaimed any attempt to preempt failure-to-warn claims. For instance, in 1998, the FDA stated that it did "not believe that the evolution of state tort law [would] cause the development of standards that would be at odds with the agency's regulations." 63 *id.*, at 66384. It further noted that, in establishing "minimal standards" for drug labels, it did not intend "to preclude the states from imposing additional labeling requirements." *Ibid.*[10]

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[10] See also 44 Fed. Reg. 37437 (1979) ("It is not the intent of the FDA to influence the civil tort liability of the manufacturer"); 59 Fed. Reg. 3948 (1994) ("[P]roduct liability plays an important role in consumer protection"); Porter, The *Lohr* Decision: FDA Perspective and Position, 52 Food & Drug L. J. 7, 10 (1997) (former chief counsel to the FDA

In keeping with Congress' decision not to pre-empt common-law tort suits, it appears that the FDA traditionally regarded state law as a complementary form of drug regulation. The FDA has limited resources to monitor the 11,000 drugs on the market,[11] and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge.

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stating that the FDA regarded state law as complementing the agency's mission of consumer protection).

[11] In 1955, the same year that the agency approved Wyeth's Phenergan application, an FDA advisory committee issued a report finding "conclusively" that "the budget and staff of the Food and Drug Administration are inadequate to permit the discharge of its existing responsibilities for the protection of the American public." Citizens Advisory Committee on the FDA, Report to the Secretary of Health, Education, and Welfare, H. R. Doc. No. 227, 84th Cong., 1st Sess., 53. Three recent studies have reached similar conclusions. See FDA Science Board, Report of the Subcommittee on Science and Technology: FDA Science and Mission at Risk 2, 6 (2007), online at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf (all Internet materials as visited Feb. 23, 2009, and available in Clerk of Court's case file) ("[T]he Agency suffers from serious scientific deficiencies and is not positioned to meet current or emerging regulatory responsibilities"); National Academies, Institute of Medicine, The Future of Drug Safety: Promoting and Protecting the Health of the Public 193–194 (2007) ("The [FDA] lacks the resources needed to accomplish its large and complex mission . . . . There is widespread agreement that resources for postmarketing drug safety work are especially inadequate and that resource limitations have hobbled the agency's ability to improve and expand this essential component of its mission"); GAO, Drug Safety: Improvement Needed in FDA's Postmarket Decision-making and Oversight Process 5 (GAO–06–402, 2006), http://www.gao.gov/new.items/d06402.pdf ("FDA lacks a clear and effective process for making decisions about, and providing management oversight of, postmarket safety issues"); see also House Committee on Oversight and Government Reform, Majority Staff Report, FDA Career Staff Objected to Agency Preemption Policies 4 (2008) ("[T]he Office of Chief Counsel ignored the warnings from FDA scientists and career officials that the preemption language [of the 2006 preamble] was based on erroneous assertions about the ability of the drug approval process to ensure accurate and up-to-date drug labels").

State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. Failure-to-warn actions, in particular, lend force to the FDCA's premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times. Thus, the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation.[12] The agency's 2006 preamble represents a dramatic change in position.

Largely based on the FDA's new position, Wyeth argues that this case presents a conflict between state and federal law analogous to the one at issue in *Geier*. There, we held that state tort claims premised on Honda's failure to install airbags conflicted with a federal regulation that did not require airbags for all cars. The Department of Transportation (DOT) had promulgated a rule that provided car manufacturers with a range of choices among passive restraint devices. *Geier*, 529 U. S., at 875. Rejecting an "'all airbag'" standard, the agency had called for a gradual phase-in of a mix of passive restraints in order to spur technological development and win consumer acceptance. *Id.,* at 879. Because the plaintiff's claim was that car manufacturers had a duty to install airbags, it presented an obstacle to achieving "the variety and mix of devices that the federal regulation sought." *Id.*, at 881.

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[12] See generally Brief for Former FDA Commissioners Drs. Donald Kennedy and David Kessler as *Amici Curiae;* see also Kessler & Vladeck, A Critical Examination of the FDA's Efforts To Preempt Failure-To-Warn Claims, 96 Geo. L. J. 461, 463 (2008); *Bates* v. *Dow Agrosciences LLC*, 544 U. S. 431, 451 (2005) (noting that state tort suits "can serve as a catalyst" by aiding in the exposure of new dangers and prompting a manufacturer or the federal agency to decide that a revised label is required).

Wyeth and the dissent contend that the regulatory scheme in this case is nearly identical, but, as we have described, it is quite different. In *Geier*, the DOT conducted a formal rulemaking and then adopted a plan to phase in a mix of passive restraint devices. Examining the rule itself and the DOT's contemporaneous record, which revealed the factors the agency had weighed and the balance it had struck, we determined that state tort suits presented an obstacle to the federal scheme. After conducting our own pre-emption analysis, we considered the agency's explanation of how state law interfered with its regulation, regarding it as further support for our independent conclusion that the plaintiff's tort claim obstructed the federal regime.

By contrast, we have no occasion in this case to consider the pre-emptive effect of a specific agency regulation bearing the force of law. And the FDA's newfound opinion, expressed in its 2006 preamble, that state law "frustrate[s] the agency's implementation of its statutory mandate," 71 Fed. Reg. 3934, does not merit deference for the reasons we have explained.[13] Indeed, the "complex and extensive" regulatory history and background relevant to this case, *Geier*, 529 U. S., at 883, undercut the FDA's recent pronouncements of pre-emption, as they reveal the longstanding coexistence of state and federal law and the FDA's traditional recognition of state-law remedies—a recognition in place each time the agency reviewed Wyeth's Phenergan label.[14]

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[13] The United States' *amicus* brief is similarly undeserving of deference. Unlike the Government's brief in *Geier* v. *American Honda Motor Co.*, 529 U. S. 861 (2000), which explained the effects of state law on the DOT's regulation in a manner consistent with the agency's prior accounts, see *id.*, at 861, the Government's explanation of federal drug regulation departs markedly from the FDA's understanding at all times relevant to this case.

[14] Wyeth's more specific contention—that this case resembles *Geier*

In short, Wyeth has not persuaded us that failure-to-warn claims like Levine's obstruct the federal regulation of drug labeling. Congress has repeatedly declined to pre-empt state law, and the FDA's recently adopted position that state tort suits interfere with its statutory mandate is entitled to no weight. Although we recognize that some state-law claims might well frustrate the achievement of congressional objectives, this is not such a case.

V

We conclude that it is not impossible for Wyeth to comply with its state and federal law obligations and that Levine's common-law claims do not stand as an obstacle to the accomplishment of Congress' purposes in the FDCA. Accordingly, the judgment of the Vermont Supreme Court is affirmed.

It is so ordered.

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because the FDA determined that no additional warning on IV-push administration was needed, thereby setting a ceiling on Phenergan's label—is belied by the record. As we have discussed, the FDA did not consider and reject a stronger warning against IV-push injection of Phenergan. See also App. 249–250 ("[A] tort case is unlikely to obstruct the regulatory process when the record shows that the FDA has paid very little attention to the issues raised by the parties at trial").