No. 06-1249

In the Supreme Court of the United States

WYETH, PETITIONER

v.

DIANA LEVINE

ON PETITION FOR A WRIT OF CERTIORARI TO THE SUPREME COURT OF VERMONT

BRIEF FOR THE UNITED STATES AS AMICUS CURIAE

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QUESTION PRESENTED

Whether state-law tort claims are preempted to the extent that they would impose liability for a drug manufacturer's use of labeling that the Food and Drug Administration approved after being informed of the relevant risk.

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This brief is filed in response to the Court's order inviting the Solicitor General to express the views of the United States. In the view of the United States, the petition for a writ of certiorari should be held pending this Court's decisions in *Riegel* v. *Medtronic, Inc.*, No. 06-179 (argued Dec. 4, 2007), and *Warner-Lambert Co., LLC* v. *Kent*, cert. granted, No. 06-1498 (Sept. 25, 2007), and then disposed of as appropriate in light of the decisions in those cases.

STATEMENT

1. Under the Federal Food, Drug, and Cosmetic Act (FDCA or Act), 21 U.S.C. 301 *et seq.*, a drug manufacturer may not market a new drug unless it has submitted a new drug application to the Food and Drug Administration (FDA) and received the agency's approval. 21 U.S.C. 355(a). An application must contain, among other things, "the labeling proposed to be used for such drug,"

21 U.S.C. 355(b)(1)(F) (Supp. V 2005); see 21 C.F.R. 314.50(c)(2)(i) and (e)(2)(ii); "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," 21 U.S.C. 355(b)(1)(A) (Supp. V 2005); and "a discussion of why the benefits exceed the risks [of the drug] under the conditions stated in the labeling," 21 C.F.R. 314.50(d)(5)(viii); see 21 C.F.R. 314.50(c)(2)(ix).

The FDCA also requires that drugs not be misbranded. 21 U.S.C. 331(a) and (b). A drug is misbranded if, among other things, the drug's "labeling is false or misleading in any particular;" the labeling does not provide "adequate directions for use" or certain "adequate warnings;" the drug "is dangerous to health when used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof;" or the labeling does not comply with certain FDA regulations. 21 U.S.C. 352(a), (f) and (j). FDA has established specific requirements for prescription drug labeling. 21 C.F.R. Pt. 201.

FDA will approve a new drug application if it finds, among other things, that (i) the drug is "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof," (ii) there is "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 thereof," and (iii) the proposed labeling is not "false or misleading in any particular." 21 U.S.C. 355(d).

After a drug has been approved and marketed, the manufacturer must investigate and report to FDA any adverse events associated with use of the drug in humans, 21 C.F.R. 314.80, and must periodically submit

any new information that may affect FDA's previous conclusions about the safety, effectiveness, or labeling of the drug, 21 C.F.R. 314.81. See 21 U.S.C. 355(k) (post-approval reporting and record-keeping requirements); Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901 *et seq.*, 121 Stat. 922 (enhancing FDA's authority to require postmarket studies and surveillance). FDA "shall" withdraw its approval of an application if it finds, among other things, that the drug is not safe or effective under the conditions of use specified in the drug's labeling. 21 U.S.C. 355(e).

Following FDA's approval of an application, the manufacturer generally may not make changes to the drug, including "[c]hanges in labeling," without first submitting a supplemental application to FDA and securing the agency's prior approval for the change. 21 C.F.R. 314.70(b)(2)(v)(A). A manufacturer must submit such a supplemental application "to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug." 21 C.F.R. 201.57(c)(6). "An applicant may ask FDA to expedite its review of a supplement for public health reasons." 21 C.F.R. 314.70(b)(4). In addition, a manufacturer may change a drug's labeling at the same time that it submits a supplemental application to FDA, without waiting for the agency's approval of the change, if, among other things, the change "add[s] or strengthen[s]" a warning or a statement about administration of the drug in order to promote safety. 21 C.F.R. 314.70(c)(6)(iii)(A) and (C). FDA interprets that regulation to permit changes without prior approval only to address "newly discovered risks." 47 Fed. Reg. 46,623 (1982). If a manufacturer makes a change before receiving FDA's approval, the agency may later reject the

change and order the manufacturer to cease distribution of the changed product. 21 C.F.R. 314.70(c)(7).

2. After FDA approved petitioner's new drug application for the anti-nausea drug Phenergan, petitioner informed FDA of adverse events in which Phenergan apparently was inadvertently injected intra-arterially, resulting in gangrene and amputation. See, *e.g.*, Pet. App. 139a-140a (1967 report). Over the ensuing years, FDA and petitioner engaged in back-and-forth communications concerning the appropriate labeling to address the risks presented by inadvertent intra-arterial injection. See, *e.g.*, *id.* at 141a-166a. As part of its deliberations, FDA convened an expert advisory committee to consider that question. *Id.* at 144a, 147a-148a.

As of 2000 (when the events giving rise to this suit occurred), the FDA-approved labeling stated, in part, that "[u]nder no circumstances should Phenergan Injection be given by intra-arterial injection due to the likelihood of severe arteriospasm and the possibility of subsequent gangrene." Pet. App. 167a. The labeling went on to explain that the "preferred" method of administering the drug is "by deep intramuscular injection," because intravenous administration can result, in some circumstances, in inadvertent intra-arterial injection. *Ibid.* For circumstances in which the drug is injected intravenously, the labeling described in detail how such injection should be done, in order "to avoid * * * inadvertent intra-arterial injection." *Ibid.*

3. In April 2000, respondent sought treatment at a health center for headache and nausea. Pet App. 2a. The health center's staff first administered Phenergan to respondent by intra-muscular injection. *Ibid.* When respondent's nausea continued, the staff administered a second dose of Phenergan by intravenous injection into

her arm. *Ibid.* The intravenous injection was made by a procedure the parties refer to as IV push, whereby the Phenergan solution was not dripped through a free-flowing bag, but instead was directly injected into respondent's arm. See *id.* at 2a, 52a. The IV push apparently resulted in inadvertent arterial injection, which damaged respondent's arteries, caused gangrene, and required amputation of her hand and forearm. *Id.* at 2a.

Respondent brought and settled an action against the health center where she had received the injection of Phenergan. Pet. App. 50a. She also sued petitioner in a Vermont state court, asserting negligence and failure-to-warn claims premised on alleged inadequacies in the drug's labeling. *Id.* at 3a. Respondent asserted that "the label should not have allowed IV push as a means of administration, as it was safer to use other available options, such as intramuscular injection or administration through the tubing of a hanging IV bag." *Ibid.* After the trial court rejected petitioner's preemption defense, *id.* at 49a-74a, the jury found in respondent's favor, and the trial court entered judgment in the amount of $6,774,000, *id.* at 3a.

4. a. The Vermont Supreme Court affirmed. Pet. App. 1a-34a. It interpreted 21 C.F.R. 314.70(c) to "allow unilateral changes to drug labels whenever the manufacturer believes it will make the product safer." *Id.* at 13a. In the court's view, Section 314.70(c) was crucial to the preemption analysis: "While specific federal labeling requirements and state common-law duties might otherwise leave drug manufacturers with conflicting obligations, [Section] 314.70(c) allows manufacturers to avoid state failure-to-warn claims without violating federal law" by making unilateral changes to FDA-approved labeling. *Id.* at 11a.

The Vermont Supreme Court also relied on a provision in the 1962 amendments to the FDCA that states that "[n]othing in th[ose] amendments * * * 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." Drug Amendments of 1962, Pub. L. No. 87-781, § 202, 76 Stat. 793. The court construed that provision to limit preemption to circumstances in which it would be physically impossible for a manufacturer to comply with both federal and state law. Pet. App. 21a. Here, the court determined, there was no such impossibility because there was no indication that FDA would have rejected a supplemental application seeking to strengthen the warning under Section 314.70(c). *Id.* at 17a.

b. Chief Judge Reiber dissented. Pet. App. 35a-48a. He explained that respondent's state-law claims conflict with federal law because, while "FDA concluded that the drug—with its approved methods of administration and as labeled—was both safe and effective," the "jury concluded that the same drug—with its approved methods of administration and as labeled—was 'unreasonably dangerous.'" *Id.* at 35a (quoting *Town of Bridport* v. *Sterling Clark Lurton Corp.*, 693 A.2d 701, 704 (Vt. 1997)). Supporting that conclusion, in the Chief Judge's view, is the fact that FDA does not merely establish minimum safety standards, but instead "balances its assessment of a drug's safety against concerns for the drug's efficacy, taking into account that a safer but less effective drug is not necessarily best for the public health overall." *Id.* at 47a. With respect to drug labels, the Chief Judge explained, "FDA considers not only what information to include, but also what to exclude,"

in part because overwarning can do more harm than good. *Ibid.*

The Chief Judge also took issue with the majority's understanding of Section 314.70(c). Pet. App. 39a-41a. He explained that the regulation "allow[s] manufacturers to address newly discovered risks," but "does not allow manufacturers to simply reassess and draw different conclusions regarding the same risks and benefits already balanced by the FDA." *Id.* at 40a.

DISCUSSION

Petitioners' claims are impliedly preempted by the FDCA because they challenge labeling that FDA approved, after being informed of the relevant health risk, based on its expert weighing of the risks and benefits of requiring additional or different warnings. The Vermont Supreme Court's contrary conclusion rests on its mistaken view that an FDA regulation, 21 C.F.R. 314.70(c), "allow[s] unilateral changes to drug labels whenever the manufacturer believes [the changes] will make the product safer." Pet. App. 13a. That interpretation of the regulation is wrong, because Section 314.70(c) permits unilateral changes based only on newly available information, not based on information that was previously available to FDA, such as the risk at issue here.

While the Vermont Supreme Court's decision is wrong, it does not warrant plenary review at this time. The decision below does not squarely conflict with any decision of a federal court of appeals or another state supreme court. Moreover, this Court's decisions in two pending FDA preemption cases—*Riegel* v. *Medtronic, Inc.*, No. 06-179 (argued Dec. 4, 2007), and *Warner-Lambert, LLC* v. *Kent*, cert. granted, No. 06-1498 (Sept.

25, 2007)—may shed significant light on the question presented in this case. Accordingly, the Court should hold the petition in this case pending its decisions in *Riegel* and *Warner-Lambert*, and then dispose of the petition as appropriate in light of its disposition of those cases.

A. Respondent's Claims Are Impliedly Preempted

Federal law preempts state laws that conflict with federal law, including state laws that either "make it 'impossible' for private parties to comply with both state and federal law," *Geier* v. *American Honda Motor Co.*, 529 U.S. 861, 873 (2000), or that "stand[] 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). Because respondent's claims challenge labeling that FDA approved after being informed of the relevant risk, they conflict with FDA's approval of the labeling and are therefore preempted.

1. FDA's approval of a drug, including its labeling, generally preempts state law claims challenging the drug's safety, efficacy, or labeling

a. FDA may approve a new drug application only if it determines, among other things, that (i) the drug is "safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof," (ii) there is "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 thereof," and (iii) the proposed labeling is not "false or misleading in any particular." 21 U.S.C. 355(d). Thus, FDA specifically considers and approves a drug's labeling. Indeed, the agency's consideration of safety and effectiveness is di-

rectly tied to its consideration of "the proposed labeling," *ibid.*, in part because a drug's safety and effectiveness depend on the conditions under which it is used (*e.g.*, its dosage, its method of administration, and its intended use). Labeling is "[t]he centerpiece of risk management," as it "communicates to health care practitioners the agency's formal, authoritative conclusions regarding the conditions under which the product can be used safely and effectively." 71 Fed. Reg. 3934 (2006).

FDA's review of a new drug application is similar to its premarket approval process for Class III medical devices, see 60 Fed. Reg. 39,180 (1995), which this Court has correctly described as "rigorous," *Medtronic, Inc.* v. *Lohr*, 518 U.S. 470, 477 (1996). As part of the approval process, an applicant must submit "the labeling proposed to be used for such drug," 21 U.S.C. 355(b)(1)(F) (Supp. V 2005), as well as extensive information about the composition, manufacture, and specification of the drug, any studies of the drug's pharmacological actions and toxicological effects in animals, any studies of the drug's bioavailability and pharmacokinetics in humans, any clinical investigations of the drug, and "any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source." 21 C.F.R. 314.50(d); see 21 U.S.C. 355(b)(1)(A) (Supp. V 2005).

If FDA is not ultimately satisfied that a drug is safe for use under the conditions of its labeling and that there is substantial evidence that the drug is effective when used according to the labeling, FDA cannot approve the application. 21 U.S.C. 355(d). Thus, FDA's approval reflects its expert determination, based on a careful review of extensive scientific and technical infor-

mation, that a drug is safe and effective when used according to its labeling, and that the labeling satisfies federal requirements.

b. In making those determinations, FDA does not merely police minimum standards of safety, as the Vermont Supreme Court thought. See Pet. App. 19a. Instead, FDA *weighs* health benefits against health risks. See 71 Fed. Reg. at 3934; 60 Fed. Reg. at 39,180. As this Court has explained, FDA "generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use." *United States* v. *Rutherford*, 442 U.S. 544, 555 (1979); accord *FDA* v. *Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 140 (2000). FDA has, for example, approved cancer treatments that are highly toxic and thus not "safe" as that term is ordinarily used, but that are nonetheless safe in the relevant sense under the FDCA because the potential benefits to health outweigh the risks. 61 Fed. Reg. 44,413 (1996); see *Brown & Williamson*, 529 U.S. at 142.

FDA also weighs the overall health consequences of including particular instructions or warnings in a drug's labeling. As explained above, a drug's safety and effectiveness are not determined in the abstract, divorced from its labeling. See 71 Fed. Reg. at 3934. Rather, FDA requires each new drug application to contain "a discussion of why the benefits exceed the risks [of the drug] *under the conditions stated in the labeling*." 21 C.F.R. 314.50(d)(5)(viii) (emphasis added); see 21 C.F.R. 314.50(c)(2)(ix). If FDA then concludes that a drug's benefits outweigh its risks only under certain conditions, the agency may require appropriate labeling to reflect that determination. See, *e.g.*, 21 C.F.R. 314.110(a).

Moreover, a warning in a drug's labeling must strike a balance between notifying users of potential dangers

and not unnecessarily deterring beneficial uses. 71 Fed. Reg. at 3935. "Exaggeration of risk could discourage appropriate use of a beneficial drug," and thereby harm the public health. *Ibid.* In addition, excessive warnings can cause more meaningful risk information to "lose its significance." 44 Fed. Reg. 37,447 (1979); accord 71 Fed. Reg. at 3935; 65 Fed. Reg. 81,083 (2000). "Warnings about dangers with less basis in science or fewer hazards could take attention away from those that present confirmed, higher risks." *Brooks* v. *Howmedica, Inc.*, 273 F.3d 785, 796 (8th Cir. 2001), cert. denied, 535 U.S. 1056 (2002). Thus, as the dissent explained, there are "a number of sound reasons why the FDA may prefer to limit warnings on product labels." Pet. App. 47a (quoting *Brooks*, 273 F.3d at 796).

For those reasons, "FDA interprets the [FDCA] to establish both a 'floor' and a 'ceiling'" with respect to drug labeling. 71 Fed. Reg. at 3935. FDA's approval of labeling for a new drug reflects FDA's expert judgment that the labeling strikes the appropriate balance. *Ibid.* Where, as here, FDA was presented with information concerning the relevant risk, a jury's imposition of liability based on a drug's FDA-approved labeling would interfere with FDA's expert judgment.

That conflict is especially clear in this case because, as the dissent explained, any recovery under state law would be predicated on a finding that Phenergan, as labeled, was "unreasonably dangerous." Pet. App. 35a (quoting *Town of Bridport* v. *Sterling Clark Lurton Corp.*, 693 A.2d at 704). That finding would directly conflict with FDA's determination that the drug, as labeled, was safe and effective. *Id.* at 35a-36a. As such, respondent's claims are preempted. See, *e.g.*, *Geier*, 529 U.S. at 881-883 (holding that state suit seeking to impose

liability for failure to use a particular type of restraint system would stand as an obstacle to the federal agency's decision to encourage the use of a range of restraint systems); *Buckman Co.* v. *Plaintiffs' Legal Comm.*, 531 U.S. 341, 348 (2001) (holding that state-law fraud-on-FDA claim was impliedly preempted because it would interfere with FDA's ability to strike a "somewhat delicate balance of statutory objectives").

2. Federal law precluded petitioner from unilaterally changing the FDA-approved labeling

The Vermont Supreme Court erroneously interpreted 21 C.F.R. 314.70(c) to "allow unilateral changes to drug labels whenever the manufacturer believes it will make the product safer." Pet. App. 13a. As discussed above, however, the FDCA requires a manufacturer to receive FDA's approval for a new drug's labeling. 21 U.S.C. 355(a) and (d). And because FDA's approval strikes an important balance between, among other things, warning of risks and not overdeterring beneficial uses, manufacturers may *not* ordinarily modify labeling approved by FDA without first obtaining FDA's approval for the change. See 21 C.F.R. 314.70. Here, for example, FDA instructed petitioner that the "final printed labeling * * * must be identical" to the approved labeling. Pet. App. 165a. If manufacturers were free to make unilateral changes to labeling the day after FDA's approval, based on information that was previously available to FDA, the approval process would be greatly undermined and the agency's careful balancing of risks and benefits thwarted. The Vermont Supreme Court's view that "FDA approval of a drug label" is nothing more than "a first step," *id.* at 15a, is there-

fore fundamentally inconsistent with the federal regulatory framework.

Consistent with the stringent statutory and regulatory requirements for approval of a new drug in the first place, a manufacturer ordinarily must submit a supplemental application before making any changes to the drug, including changes in labeling. 21 C.F.R. 314.70(a)(2)(v). As a general rule, the manufacturer must obtain prior approval by FDA before making such changes. Section 314.70(c) provides a limited exception to that rule permitting "the holder of an approved [new drug] application [to] commence distribution of the [changed] drug product involved upon receipt by the agency of a supplement for the change" if, among other things, the change "add[s] or strengthen[s]" a warning or a statement about administration of the drug in order to promote safety. 21 C.F.R. 314.70(c)(6)(iii)(A) and (C).

As FDA explained when it proposed that regulation in 1982, however, changes may be made without prior FDA approval only "to correct concerns about *newly discovered risks* from the use of the drug." 47 Fed. Reg. at 46,623 (emphasis added). FDA explained that, "[a]lthough most changes in labeling would require the applicant to submit a supplement and obtain FDA approval before making a change," some changes that "would make available *important new information* about the safe use of a drug product" could be made upon submission of a supplemental application. *Id.* at 46,635 (emphasis added); compare FDA, *Draft Guidance for Industry and FDA Staff, Modifications to Devices Subject to Premarket Approval* (*PMA*) 19 (Mar. 9, 2007) <http://www.fda.gov/cdrh/ode/guidance/1584.pdf> (explaining that a manufacturer may make unilateral changes to a device subject to FDA's premarket approval only if "the

manufacturer has newly acquired safety-related information" that "was not previously considered by the FDA").

Thus, any changes to a drug's labeling without prior FDA approval still must be the subject of a supplemental application, which FDA can approve or reject, and must be based on material new information—not information that was previously available to FDA, nor even cumulative new information that does not add materially to the information that was previously available to the agency. As the dissent explained, Section 314.70(c) does not "allow manufacturers to simply reassess and draw different conclusions regarding the same risks and benefits already balanced by the FDA." Pet. App. 40a. FDA's interpretation of its own regulation is entitled to significant deference. See *Auer* v. *Robbins*, 519 U.S. 452, 461 (1997).

In this case, it does not appear that respondent relies on any material new information that was not available to FDA. The parties dispute whether FDA specifically and expressly rejected the stronger warning that respondent asserts should have been included in the labeling. See, *e.g.*, Br. in Opp. 15-17. There is and can be no dispute, however, that FDA was presented with extensive information about the dangers of accidental intra-arterial injection from intravenous administration of the drug, and that Phenergan's FDA-approved labeling provided specific guidance on how to inject the drug, either intramuscularly or intravenously, so as to reduce that risk. See p. 4, *supra*. Nor did the Vermont Supreme Court point to any marked change in the number or type of reported cases of accidental intra-arterial injection from intravenous administration that might have suggested that the risk was of a magnitude that was not

previously known at the time that FDA approved labeling that addressed that risk. Under a correct reading of Section 314.70, therefore, petitioner could not have changed the labeling without prior FDA approval, and respondent's claims are preempted.

Moreover, even when a manufacturer may make a change at the same time that it submits a supplemental application to FDA under Section 314.70(c), the supplemental application must "give a full explanation of the basis for the change." 21 C.F.R. 314.70(c)(3). The agency may then reject the change based on its own balancing of the relevant health risks and benefits. See 21 C.F.R. 314.70(c)(7). If FDA rejects the change, it may order the manufacturer to cease further distribution of the changed product. *Ibid.* Changed labeling also "remains subject to enforcement action" if FDA finds that the change "makes the labeling false or misleading." 71 Fed. Reg. at 3934; see 21 U.S.C. 352 (2000 & Supp. V 2005). Thus, whether to authorize a change is, in the end, "squarely and solely FDA's" decision. 71 Fed. Reg. at 3934. For these reasons, in practice manufacturers typically consult with FDA before making labeling changes that the manufacturer believes could appropriately be made unilaterally under 21 C.F.R. 314.70(c) while a supplemental application was pending before FDA. See 71 Fed. Reg. at 3934.

3. The 1962 amendments to the FDCA did not displace ordinary conflict-preemption principles

The Vermont Supreme Court mistakenly thought that Section 202 of the 1962 amendments to the FDCA precludes the application of ordinary conflict preemption principles in this case. See Pet. App. 21a-23a. That provision states as follows:

> Nothing in the amendments made by this Act to the Federal Food, Drug, and Cosmetic Act 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.

Pub. L. No. 87-781, § 202, 76 Stat. 780, 793 (1962).

At the outset, it is not clear to what extent Section 202 applies here. It is limited to "the amendments made by" the 1962 legislation. § 202, 76 Stat. 793. While those amendments broadened the scope of FDA's new drug approval process by requiring the agency to consider the efficacy as well as the safety of a drug, see § 102(b), 76 Stat. 781, FDA's new drug approval process predated the amendments, see 21 U.S.C. 355(a) and (d) (1958). Indeed, FDA approved Phenergan before 1962. See Pet. 6; Br. in Opp. 23 n.8.

Even assuming *arguendo* that Section 202 is relevant in this case, however, that provision means only that Congress did not intend the 1962 amendments to preempt the *field* of drug regulation; it does not manifest an intent to displace ordinary principles of *conflict* preemption. 71 Fed. Reg. at 3935 n.8. Indeed, Section 202 expressly contemplates preemption in circumstances involving "a direct and positive conflict." § 202, 76 Stat. 793.

The Vermont Supreme Court read that phrase to refer only to situations in which it would be impossible to comply with both federal and state law, as distinguished from situations in which state law would frustrate the purpose of the federal scheme. Pet. App. 21a-23a. That interpretation is incorrect. Before 1962, this Court had long used the phrase "direct and positive con-

flict" to refer to conflict preemption generally, not to a mere subset of such preemption. See, *e.g.*, *United Constr. Workers* v. *Laburnum Constr. Corp.*, 347 U.S. 656, 663 n.5 (1954); *Sinnot* v. *Davenport*, 63 U.S. 227, 243 (1859). In so doing, the Court contrasted "direct and positive" conflict preemption to "field" preemption, not to some subset of conflict preemption. *E.g.*, *Kelly* v. *Washington ex rel. Foss Co.*, 302 U.S. 1, 9-10 (1937). More generally, this Court has never "driven a legal wedge—only a terminological one—between 'conflicts' that prevent or frustrate the accomplishment of a federal objective and 'conflicts' that make it 'impossible' for private parties to comply with both state and federal law." *Geier*, 529 U.S. at 873.

In any event, "[t]he Court has * * * refused to read general 'saving' provisions to tolerate actual conflict both in cases involving impossibility and in 'frustration-of-purpose' cases." *Geier*, 529 U.S. at 873-874 (citation omitted). That would appear to apply, *a fortiori*, to a provision that addresses only the effect of particular amendments, not the overall permanent code. See p. 16, *supra*. Moreover, even when a statute contained a savings clause providing that "[c]ompliance with" a federal safety standard "does not exempt any person from *any* liability under common law," 15 U.S.C. 1397(k) (1988) (emphasis added), this Court held that the savings clause did not preclude the application of ordinary conflict preemption principles, including frustration of purpose principles. *Geier*, 529 U.S. at 868, 873-874. The savings clause here, which expressly provides for conflict preemption, likewise does not displace ordinary conflict preemption principles.

In the preamble to its January 2006 rule concerning the labeling of drugs, FDA explained that the govern-

ment's "long standing view[]" is that "FDA approval of labeling under the [FDCA] * * * preempts conflicting or contrary State law," especially considering that "FDA interprets the [FDCA] to establish both a 'floor' and a 'ceiling'" for labeling. 71 Fed. Reg. at 3934, 3935. The agency also "recognized[] that FDA's regulation of drug labeling will not preempt all State law actions." *Id.* at 3936. FDA then provided some specific examples of circumstances in which state laws are preempted, but it did not attempt to exhaust such circumstances. See *id.* at 3935-3936 (noting that "at least" those examples would be preempted). In this brief, the government has articulated a more generally applicable rule of decision, consistent with the framework and examples set forth in the preamble, that reflects FDA's explanation in that preamble that (i) the labeling requirements are not a mere minimum safety standard, but rather strike a balance between risks and benefits, and (ii) FDA's regulations permit changes in labeling without prior approval only in narrow circumstances. See *id.* at 3934-3935.[*]

[*] While respondent argues (Br. in Opp. 8, 28) that FDA's 2006 preamble reflected a change in the agency's position, she relies solely on snippets from Federal Register notices that did not squarely address, much less discuss, the preemption question here. See 65 Fed. Reg. at 81,103 (stating that proposed *changes* to existing labeling rules would not have federalism implications); 63 Fed. Reg. 66,384 (1998) (response to comments concerning Medication Guides for "a small number of products," *id.* at 66,379); 44 Fed. Reg. at 37,437 (responding to comment that FDA should use different administrative procedures).

B. This Court Should Hold The Petition For A Writ Of Certiorari Pending The Decisions in *Riegel* and *Warner-Lambert*

Although the Vermont Supreme Court's decision is wrong, it does not warrant this Court's plenary review at this time.

1. Petitioner asserted (Reply 1) for the first time in its reply brief that the decision below conflicts with *Dowhal* v. *Smithkline Beecham Consumer Healthcare*, 88 P.3d 1 (Cal. 2004). There is no conflict. In *Dowhal*, California law required over-the-counter stop-smoking products containing nicotine to provide a specific health warning. *Id.* at 3-4. When the drug companies asked FDA for permission to change their labels to comply with the California law, FDA repeatedly denied their requests, told them to continue to use a different FDA-approved warning, and stressed that "*[a]ny additional or modified warning may render the product misbranded*." *Id.* at 5-6. FDA was concerned that a stronger warning against the use of stop-smoking products would harm the public health by causing pregnant women to continue smoking instead of using the (less harmful) stop-smoking products. *Id.* at 4-5. Even when FDA ultimately permitted the companies to modify their warning labels, it prohibited them from using the particular labels required by the California law. *Id.* at 10-11. Against that unusual backdrop, the California Supreme Court correctly held that the state law was preempted. *Id.* at 11.

There is no square conflict because the *Dowhal* court tied its holding, not to FDA's approval of a new drug application, but to the agency's subsequent, specific prohibition of the warnings that would have complied with

California law. 88 P.3d at 10-11. On the facts of this case, in contrast, the Vermont Supreme Court determined that "FDA has not indicated that a stronger warning would be misleading." Pet. App. 13a; see *id.* at 16a-19a. While FDA had rejected alternative labeling proposed by petitioner, the court below determined that there was no indication that FDA did so "to preserve the use of IV push as a method of administering Phenergan." *Id.* at 17a. Thus, the two decisions are reconcilable based on the differing findings of fact in each case, and the Vermont Supreme Court might have found preemption in a case like *Dowhal* even under its erroneous impossibility standard of conflict preemption. To be sure, petitioner may dispute the Vermont Supreme Court's interpretation of the record in this case. And the United States submits that respondent's claims are preempted regardless of whether FDA explicitly rejected the specific warning now proposed by respondent, because the agency nonetheless balanced the relevant considerations in approving the product's labeling after being informed of the relevant risks. But those disagreements with the decision below do not amount to a conflict in legal authority.

2. Petitioner also relies (Reply 1-2) on a circuit split concerning the preemptive effect of FDA's premarket approval of Class III medical devices. That conflict is real, but is not directly implicated here because this case involves implied preemption based on FDA's approval of a new drug application and regulations governing changes in labeling, not express preemption based on FDA's premarket approval of a medical device. Cf. 21 U.S.C. 360k(a) (expressly preempting certain requirements with respect to medical devices). Most importantly, this Court already granted review in *Riegel* to determine the

preemptive scope of FDA's premarket approval of a Class III medical device, and the Court heard argument in that case on December 4, 2007.

As petitioner's reliance (Reply 1-2) on the medical-device cases reflects, there is significant overlap between the preemption question in this case and the preemption question in *Riegel*. While the FDCA contains an express preemption provision concerning devices (but not drugs), see 21 U.S.C. 360k, this Court has determined that implied preemption principles are relevant to the interpretation of that provision. See *Lohr*, 518 U.S. at 500; *id.* at 508 (Breyer, J., concurring).

Moreover, FDA's review of new drug applications and its premarket approval process for Class III devices are similar. See 60 Fed. Reg. at 39,180-39,181. In both instances, FDA conducts an extensive review of a product's safety and efficacy, balances health benefits against health risks in determining whether to grant approval, and generally precludes the manufacturer from making changes without the agency's prior approval. See U.S. Br. at 10-14, *Riegel*, *supra* (No. 06-179); pp. 8-14, *supra*. Under each regulatory regime, the manufacturer can make unilateral changes in labeling only in narrow circumstances while its supplemental application is pending with FDA. See *ibid.* Accordingly, this Court's resolution of *Riegel* is likely to be instructive on the question presented here.

In addition, the petition in *Warner-Lambert* (which the Court granted after inviting the views of the Solicitor General in this case) poses the related question whether the FDCA impliedly preempts state tort claims that require a court to determine, as a condition for imposing damages liability, whether a drug manufacturer defrauded FDA in a new drug application and whether

FDA would have denied or withdrawn approval of the drug but for that fraud. See Pet. at (i), *Warner-Lambert*, *supra*. That case differs from this one because the question there involves preemption of state-law determinations of fraud on FDA, while the question here involves preemption of common-law tort claims based on FDA's approval of a new drug application. Nonetheless, because *Warner-Lambert* involves implied preemption of claims involving FDA's approval of a new drug application, the decision in *Warner-Lambert* may also shed light on the proper resolution of the question in this case. For that reason as well, the Court should hold the petition in this FDA preemption case pending its resolution of the two FDA preemption petitions it has already granted for this Term.

CONCLUSION

The Court should hold the petition for a writ of certiorari pending its disposition of *Riegel* v. *Medtronic, Inc.*, No. 06-179 (argued Dec. 4, 2007), and *Warner-Lambert Co., LLC* v. *Kent*, cert. granted, No. 06-1498 (Sept. 25, 2007), and then dispose of the petition as appropriate in light of its disposition of those cases.

Respectfully submitted.

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