131 S.Ct. 2567 (2011)

PLIVA, INC., et al., Petitioners,
v.
Gladys MENSING.
Actavis Elizabeth, LLC, Petitioner,
v.
Gladys Mensing.
Actavis, Inc., Petitioner,
v.
Julie Demahy.

Nos. 09-993, 09-1039, 09-1501.

Supreme Court of United States.

Argued March 30, 2011.
Decided June 23, 2011.

2571*2571 Jay P. Lefkowitz, New York, NY, for Petitioners.

Louis M. Bograd, Washington, DC, for Respondents.

Edwin S. Kneedler, for United States as amicus curiae, by special leave of the Court, supporting the Respondents.

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Michael K. Johnson, Lucia J. W. McLaren, Goldenberg & Johnson, P.L.L.C., Minneapolis, MN, Daniel J. McGlynn, McGlynn, Glisson & Mouton, Baton Rouge, LA, Claire Prestel, Washington, DC, for Respondent Gladys Mensing.

Louis M. Bograd, Washington, DC, for Respondents Gladys Mensing & Julie Demahy.

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Justice THOMAS delivered the opinion of the Court, except as to Part III-B-2.[*]

These consolidated lawsuits involve state tort-law claims based on certain drug manufacturers' alleged failure to provide adequate warning labels for generic metoclopramide. The question presented is whether federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, these state-law claims. We hold that they do.

I

Metoclopramide is a drug designed to speed the movement of food through the digestive system. The Food and Drug Administration (FDA) first approved metoclopramide tablets, under the brand name Reglan, in 1980. Five years later, generic manufacturers also began producing metoclopramide. The drug is commonly used to treat digestive tract problems such as diabetic gastroparesis and gastroesophageal reflux disorder.

Evidence has accumulated that long-term metoclopramide use can cause tardive dyskinesia, a severe neurological disorder. Studies have shown that up to 29% of patients who take metoclopramide for several years develop this condition. *McNeil v. Wyeth,* 462 F.3d 364, 370, n. 5 (C.A.5 2006); see also Shaffer, Butterfield, Pamer, & Mackey, Tardive Dyskinesia Risks and Metoclopramide Use Before and After U.S. Market Withdrawal of Cisapride, 44 J. Am. Pharmacists Assn. 661, 663 (2004) (noting 87 cases of metoclopramide-related tardive dyskinesia reported to the FDA's adverse event reporting system by mid-2003).

Accordingly, warning labels for the drug have been strengthened and clarified several times. In 1985, the label was modified to warn that "tardive dyskinesia ... may develop in patients treated with metoclopramide," and the drug's package insert added that "[t]herapy longer than 12 weeks has not been evaluated and cannot be

recommended." Physician's Desk Reference 1635-1636 (41st ed.1987); see also Brief for Petitioner PLIVA et al. 21-22 (hereinafter PLIVA Brief). In 2004, the brand-name Reglan manufacturer requested, and the FDA approved, a label change to add that "[t]herapy should not exceed 12 weeks in duration." Brief for United 2573*2573 States as *Amicus Curiae* 8 (hereinafter U.S. Brief). And in 2009, the FDA ordered a black box warning—its strongest—which states: "Treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible .... Treatment with metoclopramide for longer than 12 weeks should be avoided in all but rare cases." See Physician's Desk Reference 2902 (65th ed.2011).

Gladys Mensing and Julie Demahy, the plaintiffs in these consolidated cases, were prescribed Reglan in 2001 and 2002, respectively. Both received generic metoclopramide from their pharmacists. After taking the drug as prescribed for several years, both women developed tardive dyskinesia.

In separate suits, Mensing and Demahy sued the generic drug manufacturers that produced the metoclopramide they took (Manufacturers). Each alleged, as relevant here, that long-term metoclopramide use caused her tardive dyskinesia and that the Manufacturers were liable under state tort law (specifically, that of Minnesota and Louisiana) for failing to provide adequate warning labels. They claimed that "despite mounting evidence that long term metoclopramide use carries a risk of tardive dyskinesia far greater than that indicated on the label," none of the Manufacturers had changed their labels to adequately warn of that danger. *Mensing v. Wyeth, Inc.,*588 F.3d 603, 605 (C.A.8 2009); see also *Demahy v. Actavis, Inc.,* 593 F.3d 428, 430 (C.A.5 2010).

In both suits, the Manufacturers urged that federal law pre-empted the state tort claims. According to the Manufacturers, federal statutes and FDA regulations required them to use the same safety and efficacy labeling as their brand-name counterparts. This means, they argued, that it was impossible to simultaneously comply with both federal law and any state tort-law duty that required them to use a different label.

The Courts of Appeals for the Fifth and Eighth Circuits rejected the Manufacturers' arguments and held that Mensing and Demahy's claims were not pre-empted. See588 F.3d, at 614, 593 F.3d, at 449. We granted certiorari, 562 U.S. ___, 131 S.Ct. 817, 178 L.Ed.2d 550 (2010), consolidated the cases, and now reverse each.

II

Pre-emption analysis requires us to compare federal and state law. We therefore begin by identifying the state tort duties and federal labeling requirements applicable to the Manufacturers.

A

It is undisputed that Minnesota and Louisiana tort law require a drug manufacturer that is or should be aware of its product's danger to label that product in a way that renders it reasonably safe. Under Minnesota law, which applies to Mensing's lawsuit, "where the manufacturer... of a product has actual or constructive knowledge of danger to users, the ... manufacturer has a duty to give warning of such dangers."*Frey v. Montgomery Ward & Co.,* 258 N.W.2d 782, 788 (Minn. 1977). Similarly, under Louisiana law applicable to Demahy's lawsuit, "a manufacturer's duty to warn includes a duty to provide adequate instructions for safe use of a product." *Stahl v. Novartis Pharmaceuticals Corp.,* 283 F.3d 254, 269-270 (C.A.5 2002); see also La.Rev.Stat. Ann. § 9:2800.57 (West 2009). In both States, a duty to warn falls specifically on the manufacturer. See *Marks v. OHMEDA, Inc.,* 2003-1446, pp. 8-9 (La.App.3/31/04), 871 So.2d 1148, 1155; *Gray v. Badger Min. Corp.,* 676 N.W.2d 268, 274 (Minn.2004).

2574*2574 Mensing and Demahy have pleaded that the Manufacturers knew or should have known of the high risk of tardive dyskinesia inherent in the long-term use of their product. They have also pleaded that the Manufacturers knew or should have known that their labels did not adequately warn of that risk. App. 437-438, 67-69, 94-96. The parties do not dispute that, if these allegations are true, state law required the Manufacturers to use a different, safer label.

B

Federal law imposes far more complex drug labeling requirements. We begin with what is not in dispute. Under the 1962 Drug Amendments to the Federal Food, Drug, and Cosmetic Act, 76 Stat. 780, 21 U.S.C. § 301 *et seq.,* a manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate.[1] See, *e.g.,* 21 U.S.C. §§ 355(b)(1), (d); *Wyeth v. Levine,* 555 U.S. 555, 567, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009). Meeting those requirements involves costly and lengthy clinical testing. §§

355(b)(1)(A), (d); see also D. Beers, Generic and Innovator Drugs: A Guide to FDA Approval Requirements § 2.02[A] (7th ed.2008).

Originally, the same rules applied to all drugs. In 1984, however, Congress passed the Drug Price Competition and Patent Term Restoration Act, 98 Stat. 1585, commonly called the Hatch-Waxman Amendments. Under this law, "generic drugs" can gain FDA approval simply by showing equivalence to a reference listed drug that has already been approved by the FDA.[2] 21 U.S.C. § 355(j)(2)(A). This allows manufacturers to develop generic drugs inexpensively, without duplicating the clinical trials already performed on the equivalent brand-name drug. A generic drug application must also "show that the [safety and efficacy] labeling proposed ... is the same as the labeling approved for the [brand-name] drug." § 355(j)(2)(A)(v); see also § 355(j)(4)(G); Beers §§ 3.01, 3.03[A].

As a result, brand-name and generic drug manufacturers have different federal drug labeling duties. A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. See, *e.g.,* 21 U.S.C. §§ 355(b)(1), (d); *Wyeth, supra,* at 570-571, 129 S.Ct. 1187. A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's. See, *e.g.,* § 355(j)(2)(A)(v); § 355(j)(4)(G); 21 CFR §§ 314.94(a)(8), 314.127(a)(7).

The parties do not disagree. What is in dispute is whether, and to what extent, generic manufacturers may change their labels *after* initial FDA approval. Mensing and Demahy contend that federal law provided several avenues through which the Manufacturers could have altered their metoclopramide labels in time to prevent the injuries here. The FDA, however, tells us that it interprets its regulations to require that the warning labels 2575*2575 of a brand-name drug and its generic copy must always be the same—thus, generic drug manufacturers have an ongoing federal duty of "sameness." U.S. Brief 16; see also 57 Fed.Reg. 17961 (1992) ("[T]he [generic drug's] labeling must be the same as the listed drug product's labeling because the listed drug product is the basis for [generic drug] approval"). The FDA's views are "controlling unless plainly erroneous or inconsistent with the regulation[s]" or there is any other reason to doubt that they reflect the FDA's fair and considered judgment.*Auer v. Robbins,* 519 U.S. 452, 461, 462, 117 S.Ct. 905, 137 L.Ed.2d 79 (1997)(internal quotation marks omitted).[3]

First, Mensing and Demahy urge that the FDA's "changes-being-effected" (CBE) process allowed the Manufacturers to change their labels when necessary. See Brief for Respondents 33-35; see also 593 F.3d, at 439-444; *Gaeta v. Perrigo Pharmaceuticals Co.,* 630 F.3d 1225, 1231 (C.A.9 2011); *Foster v. American Home Prods. Corp.,* 29 F.3d 165, 170 (C.A.4 1994). The CBE process permits drug manufacturers to "add or strengthen a contraindication, warning, [or] precaution," 21 CFR § 314.70(c)(6)(iii)(A) (2006), or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," § 314.70(c)(6)(iii)(C). When making labeling changes using the CBE process, drug manufacturers need not wait for preapproval by the FDA, which ordinarily is necessary to change a label. *Wyeth, supra,* at 568, 129 S.Ct. 1187. They need only simultaneously file a supplemental application with the FDA. 21 CFR § 314.70(c)(6).

The FDA denies that the Manufacturers could have used the CBE process to unilaterally strengthen their warning labels. The agency interprets the CBE regulation to allow changes to generic drug labels only when a generic drug manufacturer changes its label to match an updated brand-name label or to follow the FDA's instructions. U.S. Brief 15, 16, n. 7 (interpreting 21 CFR § 314.94(a)(8)(iv)); U.S. Brief 16, n. 8. The FDA argues that CBE changes unilaterally made to strengthen a generic drug's warning label would violate the statutes and regulations requiring a generic drug's label to match its brand-name counterpart's. *Id.,* at 15-16; see also 21 U.S.C. § 355(j)(4)(G); 21 CFR §§ 314.94(a)(8)(iii), 314.150(b)(10) (approval may be withdrawn if the generic drug's label "is no longer consistent with that for [the brand-name]").

We defer to the FDA's interpretation of its CBE and generic labeling regulations. Although Mensing and Demahy offer other ways to interpret the regulations, see Brief for Respondents 33-35, we do not find the agency's interpretation "plainly erroneous or inconsistent with the regulation." *Auer, supra,* at 461, 117 S.Ct. 905 (internal quotation marks omitted). Nor do Mensing and Demahy suggest there is any other reason to doubt the agency's reading. We therefore conclude that the CBE process was not open to the Manufacturers 2576*2576 for the sort of change required by state law.

2

Next, Mensing and Demahy contend that the Manufacturers could have used "Dear Doctor" letters to send additional warnings to prescribing physicians and other

healthcare professionals. See Brief for Respondents 36; 21 CFR § 200.5. Again, the FDA disagrees, and we defer to the agency's views.

The FDA argues that Dear Doctor letters qualify as "labeling." U.S. Brief 18; see also 21 U.S.C. § 321(m); 21 CFR § 202.1(*l*)(2). Thus, any such letters must be "consistent with and not contrary to [the drug's] approved ... labeling." 21 CFR § 201.100(d)(1). A Dear Doctor letter that contained substantial new warning information would not be consistent with the drug's approved labeling. Moreover, if generic drug manufacturers, but not the brand-name manufacturer, sent such letters, that would inaccurately imply a therapeutic difference between the brand and generic drugs and thus could be impermissibly "misleading." U.S. Brief 19; see 21 CFR § 314.150(b)(3) (FDA may withdraw approval of a generic drug if "the labeling of the drug ... is false or misleading in any particular").

As with the CBE regulation, we defer to the FDA. Mensing and Demahy offer no argument that the FDA's interpretation is plainly erroneous. See *Auer,* 519 U.S., at 461, 117 S.Ct. 905. Accordingly, we conclude that federal law did not permit the Manufacturers to issue additional warnings through Dear Doctor letters.

3

Though the FDA denies that the Manufacturers could have used the CBE process or Dear Doctor letters to strengthen their warning labels, the agency asserts that a different avenue existed for changing generic drug labels. According to the FDA, the Manufacturers could have proposed— indeed, were required to propose—stronger warning labels to the agency if they believed such warnings were needed. U.S. Brief 20; 57 Fed.Reg. 17961. If the FDA had agreed that a label change was necessary, it would have worked with the brand-name manufacturer to create a new label for both the brand-name and generic drug. *Ibid.*

The agency traces this duty to 21 U.S.C. § 352(f)(2), which provides that a drug is "misbranded ... [u]nless its labeling bears... adequate warnings against ... unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users." See U.S. Brief 12. By regulation, the FDA has interpreted that statute to require that "labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e).

According to the FDA, these requirements apply to generic drugs. As it explains, a "`central premise of federal drug regulation is that the manufacturer bears responsibility for the content of its label at all times.'" U.S. Brief 12-13 (quoting *Wyeth,*555 U.S., at 570-571, 129 S.Ct. 1187). The FDA reconciles this duty to have adequate and accurate labeling with the duty of sameness in the following way: Generic drug manufacturers that become aware of safety problems must ask the agency to work toward strengthening the label that applies to both the generic and brand-name equivalent drug. U.S. Brief 20.

The Manufacturers and the FDA disagree over whether this alleged duty to request a strengthened label actually existed. 2577*2577 The FDA argues that it explained this duty in the preamble to its 1992 regulations implementing the Hatch-Waxman Amendments. *Ibid.;* see 57 Fed.Reg. 17961 ("If a [generic drug manufacturer] believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised"). The Manufacturers claim that the FDA's 19-year-old statement did not create a duty, and that there is no evidence of any generic drug manufacturer ever acting pursuant to any such duty. See Tr. of Oral Arg. 19-24; Reply Brief for Petitioner PLIVA et al. 18-22. Because we ultimately find pre-emption even assuming such a duty existed, we do not resolve the matter.

C

To summarize, the relevant state and federal requirements are these: State tort law places a duty directly on all drug manufacturers to adequately and safely label their products. Taking Mensing and Demahy's allegations as true, this duty required the Manufacturers to use a different, stronger label than the label they actually used. Federal drug regulations, as interpreted by the FDA, prevented the Manufacturers from independently changing their generic drugs' safety labels. But, we assume, federal law also required the Manufacturers to ask for FDA assistance in convincing the brand-name manufacturer to adopt a stronger label, so that all corresponding generic drug manufacturers could do so as well. We turn now to the question of pre-emption.

III

The Supremacy Clause establishes that federal law "shall be the supreme Law of the Land ... any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const., Art. VI, cl. 2. Where state and federal law "directly

conflict," state law must give way. *Wyeth, supra,* at 583, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment); see also *Crosby v. National Foreign Trade Council,* 530 U.S. 363, 372, 120 S.Ct. 2288, 147 L.Ed.2d 352 (2000) ("[S]tate law is naturally preempted to the extent of any conflict with a federal statute"). We have held that state and federal law conflict where it is "impossible for a private party to comply with both state and federal requirements."[4] *Freightliner Corp. v. Myrick,* 514 U.S. 280, 287, 115 S.Ct. 1483, 131 L.Ed.2d 385 (1995) (internal quotation marks omitted).[5]

A

We find impossibility here. It was not lawful under federal law for the Manufacturers to do what state law required of them. And even if they had fulfilled their federal duty to ask for FDA 2578*2578 assistance, they would not have satisfied the requirements of state law.

If the Manufacturers had independently changed their labels to satisfy their state-law duty, they would have violated federal law. Taking Mensing and Demahy's allegations as true, state law imposed on the Manufacturers a duty to attach a safer label to their generic metoclopramide. Federal law, however, demanded that generic drug labels be the same at all times as the corresponding brand-name drug labels. See, *e.g.,* 21 CFR § 314.150(b)(10). Thus, it was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal law duty to keep the label the same.

The federal duty to ask the FDA for help in strengthening the corresponding brand-name label, assuming such a duty exists, does not change this analysis. Although requesting FDA assistance would have satisfied the Manufacturers' federal duty, it would not have satisfied their state tort-law duty to provide adequate labeling. State law demanded a safer label; it did not instruct the Manufacturers to communicate with the FDA about the possibility of a safer label. Indeed, Mensing and Demahy deny that their state tort claims are based on the Manufacturers' alleged failure to ask the FDA for assistance in changing the labels. Brief for Respondents 53-54; cf. *Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) (holding that federal drug and medical device laws pre-empted a state tort-law claim based on failure to properly communicate with the FDA).

B

1

Mensing and Demahy contend that, while their state-law claims do not turn on whether the Manufacturers asked the FDA for assistance in changing their labels, the Manufacturers' federal affirmative defense of pre-emption does. Mensing and Demahy argue that if the Manufacturers had asked the FDA for help in changing the corresponding brand-name label, they might eventually have been able to accomplish under federal law what state law requires. That is true enough. The Manufacturers "freely concede" that they could have asked the FDA for help. PLIVA Brief 48. If they had done so, and if the FDA decided there was sufficient supporting information, and if the FDA undertook negotiations with the brand-name manufacturer, and if adequate label changes were decided on and implemented, then the Manufacturers would have started a Mouse Trap game that eventually led to a better label on generic metoclopramide.

This raises the novel question whether conflict pre-emption should take into account these possible actions by the FDA and the brand-name manufacturer. Here, what federal law permitted the Manufacturers to do could have changed, even absent a change in the law itself, depending on the actions of the FDA and the brand-name manufacturer. Federal law does not dictate the text of each generic drug's label, but rather ties those labels to their brand-name counterparts. Thus, federal law would permit the Manufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so.

Mensing and Demahy assert that when a private party's ability to comply with state law depends on approval and assistance from the FDA, proving pre-emption requires that party to demonstrate that the FDA would not have allowed compliance 2579*2579 with state law. Here, they argue, the Manufacturers cannot bear their burden of proving impossibility because they did not even *try* to start the process that might ultimately have allowed them to use a safer label. Brief for Respondents 47. This is a fair argument, but we reject it.

The question for "impossibility" is whether the private party could independently do under federal law what state law requires of it. See *Wyeth,* 555 U.S., at 573, 129 S.Ct. 1187 (finding no pre-emption where the defendant could "unilaterally" do what state law required). Accepting Mensing and Demahy's argument would render conflict pre-emption largely meaningless because it would make most conflicts between state and federal law illusory. We can often imagine that a third party or the Federal Government *might* do something that makes it lawful for a private party to accomplish under federal law what state law requires of it. In these cases, it is

certainly possible that, had the Manufacturers asked the FDA for help, they might have eventually been able to strengthen their warning label. Of course, it is also*possible* that the Manufacturers could have convinced the FDA to reinterpret its regulations in a manner that would have opened the CBE process to them. Following Mensing and Demahy's argument to its logical conclusion, it is also *possible* that, by asking, the Manufacturers could have persuaded the FDA to rewrite its generic drug regulations entirely or talked Congress into amending the Hatch-Waxman Amendments.

If these conjectures suffice to prevent federal and state law from conflicting for Supremacy Clause purposes, it is unclear when, outside of express pre-emption, the Supremacy Clause would have any force.[6] We do not read the Supremacy Clause to permit an approach to pre-emption that renders conflict pre-emption all but meaningless. The Supremacy Clause, on its face, makes federal law "the supreme Law of the Land" even absent an express statement by Congress. U.S. Const., Art. VI, cl. 2.

2

Moreover, the text of the Clause—that federal law shall be supreme, "any Thing in the Constitution or Laws of any State to the Contrary notwithstanding"—plainly contemplates conflict pre-emption by describing federal law as effectively repealing contrary state law. *Ibid.;* see Nelson, Preemption, 86 Va. L.Rev. 225, 234 (2000); *id.,*at 252-253 (describing discussion of the Supremacy Clause in state ratification debates as concerning whether federal law could repeal state law, or vice versa). The phrase "any [state law] to the Contrary notwithstanding" is a *non obstante*provision. *Id.,* at 238-240, nn. 43-45. Eighteenth-century legislatures used *non obstante* provisions to specify the degree to which a new statute was meant to repeal older, potentially conflicting statutes in the same field. *Id.,* at 238-240 (citing dozens of statutes from the 1770's and 1780's with similar provisions). A *non obstante* provision "in a new statute acknowledged that the statute might contradict prior law and instructed courts not to apply the general presumption against implied repeals." *Id.,* at 241-242; 4 M. Bacon, A New Abridgment of the Law 639 (4th ed. 1778) ("Although 2580*2580 two Acts of Parliament are *seemingly* repugnant, yet if there be no Clause of *non Obstante* in the latter, they shall if possible have such Construction, that the latter may not be a Repeal of the former by Implication"). The*non obstante* provision in the Supremacy Clause therefore suggests that federal law should be understood to impliedly repeal conflicting state law.

Further, the provision suggests that courts should not strain to find ways to reconcile federal law with seemingly conflicting state law. Traditionally, courts went to great lengths attempting to harmonize conflicting statutes, in order to avoid implied repeals.*Warder v. Arell,* 2 Va. 282, 296 (1796) (opinion of Roane, J.) ("[W]e ought to seek for such a construction as will reconcile [the statutes] together"); *Ludlow's Heirs v. Johnston,* 3 Ohio 553, 564 (1828) ("[I]f by any fair course of reasoning the two [statutes] can be reconciled, both shall stand"); *Doolittle v. Bryan,* 14 How. 563, 566, 14 L.Ed. 543 (1853) (requiring "the repugnance be quite plain" before finding implied repeal). A *non obstante* provision thus was a useful way for legislatures to specify that they did not want courts distorting the new law to accommodate the old. Nelson,*supra,* at 240-242; see also J. Sutherland, Statutes and Statutory Construction § 147, p. 199 (1891) ("[W]hen there is inserted in a statute a provision [of *non obstante*] .... It is to be supposed that courts will be less inclined against recognizing repugnancy in applying such statutes"); *Weston's Case,* 73 Eng. Rep. 780, 781 (K.B.1576) ("[W]hen there are two statutes, one in appearance crossing the other, and no clause of *non obstante* is contained in the second statute... the exposition ought to be that both should stand in force"); G. Jacob, A New Law Dictionary (J. Morgan ed., 10th ed. 1782) (definition of "statute," ¶ 6: "[W]hen there is a seeming variance between two *statutes,* and no clause of *non obstante* in the latter, such construction shall be made that both may stand"). The *non obstante* provision of he Supremacy Clause indicates that a court need look no further than "the ordinary meanin[g]" of federal law, and should not distort federal law to accommodate conflicting state law. *Wyeth,* 555 U.S., at 588, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment) (internal quotation marks omitted).

To consider in our pre-emption analysis the contingencies inherent in these cases— in which the Manufacturers' ability to comply with state law depended on uncertain federal agency and third-party decisions— would be inconsistent with the *non obstante* provision of the Supremacy Clause. The Manufacturers would be required continually to prove the counterfactual conduct of the FDA and brand-name manufacturer in order to establish the supremacy of federal law. We do not think the Supremacy Clause contemplates that sort of contingent supremacy. The *non obstante* provision suggests that pre-emption analysis should not involve speculation about ways in which federal agency and third-party actions could potentially reconcile federal duties with conflicting state duties. When the "ordinary meaning" of federal law blocks a private party from independently accomplishing what state law requires, that party has established pre-emption.

3

To be sure, whether a private party can act sufficiently independently under federal law to do what state law requires may sometimes be difficult to determine. But this is not such a case. Before the Manufacturers could satisfy state law, the FDA—a federal agency—had to undertake special effort permitting them to do so. To decide these cases, it is enough to hold 2581*2581 that when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes.

Here, state law imposed a duty on the Manufacturers to take a certain action, and federal law barred them from taking that action. The only action the Manufacturers could independently take—asking for the FDA's help—is not a matter of state-law concern. Mensing and Demahy's tort claims are pre-empted.

C

Wyeth is not to the contrary. In that case, as here, the plaintiff contended that a drug manufacturer had breached a state tort-law duty to provide an adequate warning label. 555 U.S., at 559-560, 129 S.Ct. 1187. The Court held that the lawsuit was not pre-empted because it was possible for Wyeth, a brand-name drug manufacturer, to comply with both state and federal law. *Id.,* at 572-573, 129 S.Ct. 1187.[7]Specifically, the CBE regulation, 21 CFR § 314.70(c)(6)(iii), permitted a brand-name drug manufacturer like Wyeth "to unilaterally strengthen its warning" without prior FDA approval. 555 U.S., at 573, 129 S.Ct. 1187; cf. *supra,* at 2575-2576. Thus, the federal regulations applicable to Wyeth allowed the company, of its own volition, to strengthen its label in compliance with its state tort duty.[8]

We recognize that from the perspective of Mensing and Demahy, finding pre-emption here but not in *Wyeth* makes little sense. Had Mensing and Demahy taken Reglan, the brand-name drug prescribed by their doctors, *Wyeth* would control and their lawsuits would not be pre-empted. But because pharmacists, acting in full accord with state law, substituted generic metoclopramide instead, federal law pre-empts these lawsuits. See, *e.g.,* Minn.Stat. § 151.21 (2010) (describing when pharmacists may substitute generic drugs); La. Rev.Stat. Ann. § 37:1241(A)(17) (West 2007) (same). We acknowledge the unfortunate hand that federal drug regulation has dealt Mensing, Demahy, and others similarly situated.[9]

2582*2582 But "it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre." *Cuomo v. Clearing House*

Assn., L.L. C., 557 U.S. ___, ___, 129 S.Ct. 2710, 2733, 174 L.Ed.2d 464 (2009) (THOMAS, J., concurring in part and dissenting in part) (internal quotation marks and brackets omitted). It is beyond dispute that the federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers. Indeed, it is the special, and different, regulation of generic drugs that allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public. But different federal statutes and regulations may, as here, lead to different pre-emption results. We will not distort the Supremacy Clause in order to create similar pre-emption across a dissimilar statutory scheme. As always, Congress and the FDA retain the authority to change the law and regulations if they so desire.

* * *

The judgments of the Fifth and Eighth Circuits are reversed, and the cases are remanded for further proceedings consistent with this opinion.

It is so ordered.

Justice SOTOMAYOR, with whom Justice GINSBURG, Justice BREYER, and Justice KAGAN join, dissenting.

The Court today invokes the doctrine of impossibility pre-emption to hold that federal law immunizes generic-drug manufacturers from all state-law failure-to-warn claims because they cannot unilaterally change their labels. I cannot agree. We have traditionally held defendants claiming impossibility to a demanding standard: Until today, the mere possibility of impossibility had not been enough to establish pre-emption.

The Food and Drug Administration (FDA) permits—and, the Court assumes, requires—generic-drug manufacturers to propose a label change to the FDA when they believe that their labels are inadequate. If it agrees that the labels are inadequate, the FDA can initiate a change to the brand-name label, triggering a corresponding change to the generic labels. Once that occurs, a generic manufacturer is in full compliance with both federal law and a state-law duty to warn. Although generic manufacturers may be able to show impossibility in some cases, petitioners, generic manufacturers of metoclopramide (Manufacturers), have shown only that they *might* have been unable to comply with both federal law and their state-

law duties to warn respondents Gladys Mensing and Julie Demahy. This, I would hold, is insufficient to sustain their burden.

The Court strains to reach the opposite conclusion. It invents new principles of pre-emption law out of thin air to justify its dilution of the impossibility standard. It effectively rewrites our decision in *Wyeth v. Levine,* 555 U.S. 555, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009), which holds 2583*2583 that federal law does not pre-empt failure-to-warn claims against brand-name drug manufacturers. And a plurality of the Court tosses aside our repeated admonition that courts should hesitate to conclude that Congress intended to pre-empt state laws governing health and safety. As a result of today's decision, whether a consumer harmed by inadequate warnings can obtain relief turns solely on the happenstance of whether her pharmacist filled her prescription with a brand-name or generic drug. The Court gets one thing right: This outcome "makes little sense." *Ante,* at 2581.

I

A

Today's decision affects 75 percent of all prescription drugs dispensed in this country. The dominant position of generic drugs in the prescription drug market is the result of a series of legislative measures, both federal and state.

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, 98 Stat. 1585—commonly known as the Hatch-Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA)—to "make available more low cost generic drugs by establishing a generic drug approval procedure," H.R.Rep. No. 98-857, pt. 1, p. 14 (1984). As the majority explains, to accomplish this goal the amendments establish an abbreviated application process for generic drugs. *Ante,* at 2574-2575; see also 21 U.S.C. § 355(j)(2)(A). The abbreviated approval process implements the amendments' core principle that generic and brand-name drugs must be the "same" in nearly all respects: To obtain FDA approval, a generic manufacturer must ordinarily show, among other things, that its product has the same active ingredients as an approved brand-name drug; that "the route of administration, the dosage form, and the strength of the new drug are the same" as the brand-name drug; and that its product is "bioequivalent" to the brand-name drug. §§ 355(j)(2)(A)(ii), (iii), (iv). By eliminating the need for generic manufacturers to prove their drugs' safety and efficacy independently, the Hatch-Waxman

Amendments allow generic manufacturers to bring drugs to market much less expensively.

The States have also acted to expand consumption of low-cost generic drugs. In the years leading up to passage of the Hatch-Waxman Amendments, States enacted legislation authorizing pharmacists to substitute generic drugs when filling prescriptions for brand-name drugs. Christensen, Kirking, Ascione, Welage, & Gaither, Drug Product Selection: Legal Issues, 41 J. Am. Pharmaceutical Assn. 868, 869 (2001). Currently, all States have some form of generic substitution law. See*ibid.* Some States require generic substitution in certain circumstances. Dept. of Health and Human Servs., ASPE Issue Brief: Expanding the Use of Generic Drugs 7 (2010) (hereinafter Expanding the Use of Generic Drugs);[1] see, *e.g.,* N.Y. Educ. Law Ann. § 6816-a (West 2010). Others permit, but do not require, substitution. Expanding the Use of Generic Drugs 7; see, *e.g.,* Cal. Bus. & Prof.Code Ann. § 4073 (West Supp.2011). Some States require patient consent to substitution, and all States "allow the physician to specify that the brand name must be prescribed, although with different levels of effort from the physician." Expanding the 2584*2584 Use of Generic Drugs 7.[2]

These legislative efforts to expand production and consumption of generic drugs have proved wildly successful. It is estimated that in 1984, when the Hatch-Waxman Amendments were enacted, generic drugs constituted 19 percent of drugs sold in this country. Congressional Budget Office, How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry 27 (1998).[3]Today, they dominate the market. See Expanding the Use of Generic Drugs 2 (generic drugs constituted 75 percent of all dispensed prescription drugs in 2009). Ninety percent of drugs for which a generic version is available are now filled with generics. *Id.,* at 3-4. In many cases, once generic versions of a drug enter the market, the brand-name manufacturer stops selling the brand-name drug altogether. See Brief for Marc T. Law et al. as *Amici Curiae* 18 (citing studies showing that anywhere from one-third to one-half of generic drugs no longer have a marketed brand-name equivalent). Reflecting the success of their products, many generic manufacturers, including the Manufacturers and their *amici,* are huge, multinational companies. In total, generic drug manufacturers sold an estimated $66 billion of drugs in this country in 2009. See *id.,* at 15.

B

As noted, to obtain FDA approval a generic manufacturer must generally show that its drug is the same as an approved brand-name drug. It need not conduct clinical trials to prove the safety and efficacy of the drug. This does not mean, however, that a generic manufacturer has no duty under federal law to ensure the safety of its products. The FDA has limited resources to conduct postapproval monitoring of drug safety. See *Wyeth,* 555 U.S., at 578, 129 S.Ct. 1187. Manufacturers, we have recognized, "have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge." *Id.,* at 578-579, 129 S.Ct. 1187. Federal law thus obliges drug manufacturers—both brand-name and generic—to monitor the safety of their products.

Under federal law, generic manufacturers must "develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences" to the FDA.[4] 21 CFR § 314.80(b);[5] see also § 314.98 (making § 314.80 applicable to generic manufacturers); Brief for United States as *Amicus Curiae* 6, and n. 2 (hereinafter U.S. Brief). They must review all reports of adverse drug experiences received from "any source." § 314.80(b). If a manufacturer receives a report of a serious and unexpected 2585*2585 adverse drug experience, it must report the event to the FDA within 15 days and must "promptly investigate." §§ 314.80(c)(1)(i)-(ii); see also Tr. of Oral Arg. 8. Most other adverse drug experiences must be reported on a quarterly or yearly basis.[6] § 314.80(c)(2). Generic manufacturers must also submit to the FDA an annual report summarizing "significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product," including a "description of actions the [manufacturer] has taken or intends to take as a result of this new information." § 314.81(b)(2)(i); see also § 314.98(c).

Generic manufacturers, the majority assumes, also bear responsibility under federal law for monitoring the adequacy of their warnings. I agree with the majority's conclusion that generic manufacturers are not permitted unilaterally to change their labels through the "changes-being-effected" (CBE) process or to issue additional warnings through "Dear Doctor" letters. See *ante,* at 2574-2576. According to the FDA, however, that generic manufacturers cannot disseminate additional warnings on their own does not mean that federal law permits them to remain idle when they conclude that their labeling is inadequate. FDA regulations require that labeling "be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e) (2006), currently codified at 21 CFR § 201.80(e) (2010); see also *Wyeth,* 555 U.S., at 570-571, 129 S.Ct. 1187. The FDA construes this regulation to oblige generic manufacturers "to

seek to revise their labeling and provide FDA with supporting information about risks" when they believe that additional warnings are necessary.[7] U.S. Brief 20.

2586*2586 The Manufacturers disagree. They read the FDA regulation to require them only to ensure that their labels match the brand-name labels. See Brief for Petitioner PLIVA et al. 38-41. I need not decide whether the regulation in fact obliges generic manufacturers to approach the FDA to propose a label change. The majority assumes that it does. And even if generic manufacturers do not have a duty to propose label changes, two points remain undisputed. First, they do have a duty under federal law to monitor the safety of their products. And, second, they may approach the FDA to propose a label change when they believe a change is required.

II

This brings me to the Manufacturers' pre-emption defense. State law obliged the Manufacturers to warn of dangers to users. See *Hines v. Remington Arms Co.,* 94-0455, p. 10 (La.12/8/94), 648 So.2d 331, 337; *Frey v. Montgomery Ward & Co.,* 258 N.W.2d 782, 788 (Minn.1977). The Manufacturers contend, and the majority agrees, that federal law pre-empts respondents' failure-to-warn claims because, under federal law, the Manufacturers could not have provided additional warnings to respondents without the exercise of judgment by the FDA. I cannot endorse this novel conception of impossibility pre-emption.

A

Two principles guide all pre-emption analysis. First, "`the purpose of Congress is the ultimate touchstone in every pre-emption case.'" *Wyeth,* 555 U.S., at 565, 129 S.Ct. 1187 (quoting *Medtronic, Inc. v. Lohr,* 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996)). 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.'" *Wyeth,* 555 U.S., at 565, 129 S.Ct. 1187 (quoting*Lohr,* 518 U.S., at 485, 116 S.Ct. 2240; some internal quotation marks omitted; alterations in original).

These principles find particular resonance in these cases. The States have traditionally regulated health and safety matters. See *id.,* at 485, 116 S.Ct. 2240.

Notwithstanding Congress' "certain awareness of the prevalence of state tort litigation" against drug manufacturers, *Wyeth,* 555 U.S., at 575, 129 S.Ct. 1187,Congress has not expressly pre-empted state-law tort actions against prescription drug manufacturers, whether brand-name or generic. To the contrary, when Congress amended the FDCA in 1962 to "enlarg[e] the FDA's powers to `protect the public health' and `assure the safety, effectiveness, and reliability of drugs,' [it] took care to preserve state law." *Id.,* at 567, 129 S.Ct. 1187 (quoting 76 Stat. 780); see Pub.L. 87-781, § 202, 76 Stat. 793 ("Nothing in the amendments made by this Act to the [FDCA] shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law"). Notably, although Congress enacted an express pre-emption provision for medical devices in 1976, see Pub.L. 94-295, § 521, 90 Stat. 574, 21 U.S.C. § 360k(a), it included no such provision in the Hatch-Waxman Amendments eight years later. Cf. *Wyeth,* 555 U.S., at 567, 574-575, 129 S.Ct. 1187. Congress' "silence on the issue ... is powerful evidence that [it] did not intend FDA oversight to be the exclusive means 2587*2587 of ensuring drug safety and effectiveness." *Id.,* at 575, 129 S.Ct. 1187.

B

Federal law impliedly pre-empts state law when state and federal law "conflict"—*i.e.,*when "it is impossible for a private party to comply with both state and federal law" or when state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Crosby v. National Foreign Trade Council,* 530 U.S. 363, 372-373, 120 S.Ct. 2288, 147 L.Ed.2d 352 (2000) (internal quotation marks omitted). The Manufacturers rely solely on the former ground of pre-emption.

Impossibility pre-emption, we have emphasized, "is a demanding defense." *Wyeth,*555 U.S., at 573, 129 S.Ct. 1187. Because pre-emption is an affirmative defense, a defendant seeking to set aside state law bears the burden to prove impossibility. See*ibid.; Silkwood v. Kerr-McGee Corp.,* 464 U.S. 238, 255, 104 S.Ct. 615, 78 L.Ed.2d 443 (1984). To prevail on this defense, a defendant must demonstrate that "compliance with both federal and state [law] is a physical impossibility." *Florida Lime & Avocado Growers, Inc. v. Paul,* 373 U.S. 132, 142-143, 83 S.Ct. 1210, 10 L.Ed.2d 248 (1963); see also *Wyeth,* 555 U.S., at 573, 129 S.Ct. 1187. In other words, there must be an "inevitable collision" between federal and state law. *Florida Lime,* 373 U.S., at 143, 83 S.Ct. 1210. "The existence of a

hypothetical or potential conflict is insufficient to warrant" pre-emption of state law. *Rice v. Norman Williams Co.,* 458 U.S. 654, 659, 102 S.Ct. 3294, 73 L.Ed.2d 1042 (1982); see also *Gade v. National Solid Wastes Management Assn.,* 505 U.S. 88, 110, 112 S.Ct. 2374, 120 L.Ed.2d 73 (1992) (KENNEDY, J., concurring in part and concurring in judgment). In other words, the mere possibility of impossibility is not enough.

The Manufacturers contend that it was impossible for them to provide additional warnings to respondents Mensing and Demahy because federal law prohibited them from changing their labels unilaterally.[8] They concede, however, that they could have asked the FDA to initiate a label change. If the FDA agreed that a label change was required, it could have asked, and indeed pressured, the brand-name manufacturer to change its label, triggering a corresponding change to the Manufacturers' generic labels.[9] Thus, had the Manufacturers invoked the available mechanism for initiating label changes, they may well have been able to change their labels in sufficient time to warn respondents. 2588*2588 Having failed to do so, the Manufacturers cannot sustain their burden (at least not without further factual development) to demonstrate that it was impossible for them to comply with both federal and state law. At most, they have demonstrated only "a hypothetical or potential conflict." *Rice,* 458 U.S., at 659, 102 S.Ct. 3294.

Like the majority, the Manufacturers focus on the fact that they cannot change their labels unilaterally—which distinguishes them from the brand-name-manufacturer defendant in *Wyeth.* They correctly point out that in *Wyeth* we concluded that the FDA's CBE regulation authorized the defendant to strengthen its warnings before receiving agency approval of its supplemental application describing the label change. 555 U.S., at 568-571, 129 S.Ct. 1187; see also 21 CFR § 314.70(c)(6). But the defendant's label change was contingent on FDA acceptance, as the FDA retained "authority to reject labeling changes made pursuant to the CBE regulation."*Wyeth,* 555 U.S., at 571, 129 S.Ct. 1187. Thus, in the long run, a brand-name manufacturer's compliance with a state-law duty to warn required action by two actors: The brand-name manufacturer had to change the label and the FDA, upon reviewing the supplemental application, had to agree with the change.[10] The need for FDA approval of the label change did not make compliance with federal and state law impossible in every case. Instead, because the defendant bore the burden to show impossibility, we required it to produce "clear evidence that the FDA would not have approved a change to [the] label." *Ibid.*

I would apply the same approach in these cases. State law, respondents allege, required the Manufacturers to provide a strengthened warning about the dangers of long-term metoclopramide use.[11] Just like the brand-name manufacturer in *Wyeth,*the Manufacturers had available to them a mechanism for attempting to comply with their state-law duty to warn. Federal law thus "accommodated" the Manufacturers' state-law duties. See *ante,* at 2581, n. 8. It was not necessarily impossible for the Manufacturers to comply with both federal and state law because, had they approached the FDA, the FDA may well have agreed that a label change was necessary. Accordingly, as in *Wyeth,* I would require the Manufacturers to show that the FDA would not have approved a proposed label change. They have not made such a showing: They do "not argue that [they] attempted to give the kind of warning required by [state law] but [were] prohibited from doing so by the FDA." *Wyeth,* 555 U.S., at 572, 129 S.Ct. 1187.

This is not to say that generic manufacturers could never show impossibility. If a generic-manufacturer defendant proposed a label change to the FDA but the FDA rejected the proposal, it would be impossible for that defendant to comply with a state-law duty to warn. Likewise, impossibility would be established if the FDA had not yet responded to a generic manufacturer's request for a label change at the 2589*2589time a plaintiff's injuries arose. A generic manufacturer might also show that the FDA had itself considered whether to request enhanced warnings in light of the evidence on which a plaintiff's claim rests but had decided to leave the warnings as is. (The Manufacturers make just such an argument in these cases. See, *e.g.,* Brief for Petitioner Actavis et al. 11.) But these are questions of fact to be established through discovery. Because the burden of proving impossibility falls on the defendant, I would hold that federal law does not render it impossible for generic manufacturers to comply with a state-law duty to warn as a categorical matter.

This conclusion flows naturally from the overarching principles governing our pre-emption doctrine. See *supra,* at 2586. Our "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.'" *Wyeth,* 555 U.S., at 565-566, n. 3, 129 S.Ct. 1187 (quoting *Lohr,* 518 U.S., at 485, 116 S.Ct. 2240). It is for this reason that we hold defendants asserting impossibility to a "demanding" standard. *Wyeth,*555 U.S., at 573, 129 S.Ct. 1187. This presumption against pre-emption has particular force when the Federal Government has afforded defendants a mechanism for complying with state law, even when that mechanism requires federal agency action. (The presumption has even greater force when federal law requires defendants to invoke that mechanism, as the majority assumes in these

cases.) In such circumstances, I would hold, defendants will usually be unable to sustain their burden of showing impossibility if they have not even attempted to employ that mechanism. Any other approach threatens to infringe the States' authority over traditional matters of state interest—such as the failure-to-warn claims here—when Congress expressed no intent to pre-empt state law.

C

The majority concedes that the Manufacturers might have been able to accomplish under federal law what state law requires. *Ante,* at 2578-2579. To reach the conclusion that the Manufacturers have nonetheless satisfied their burden to show impossibility, the majority invents a new pre-emption rule: "The question for `impossibility' is whether the private party could *independently* do under federal law what state law requires of it." *Ante,* at 2579 (emphasis added). Because the Manufacturers could not have changed their labels without the exercise of judgment by the FDA, the majority holds, compliance with both state and federal law was impossible in these cases.[12]

The majority's new test has no basis in our precedents. The majority cites only*Wyeth* in support of its test. As discussed above, however, *Wyeth* does not stand for the proposition that it is impossible to comply with both federal and state law whenever federal agency approval is required. To the contrary, label changes by brand-name manufacturers such as Wyeth are subject to FDA review and acceptance. See *supra,* at 2588. And, even if *Wyeth* could be characterized as turning on the fact that the brand-name manufacturer could change its label unilaterally, the possibility 2590*2590 of unilateral action was, at most, a sufficient condition for rejecting the impossibility defense in that case. *Wyeth* did not hold that unilateral action is a necessary condition in every case.

With so little support in our case law, the majority understandably turns to other rationales. None of the rationales that it offers, however, makes any sense. First, it offers a *reductio ad absurdum:* If the possibility of FDA approval of a label change is sufficient to avoid conflict in these cases, it warns, as a "logical conclusion" so too would be the possibility that the FDA might rewrite its regulations or that Congress might amend the Hatch-Waxman Amendments. *Ante,* at 2581-2582. The logic of this conclusion escapes me. Conflict analysis necessarily turns on existing law. It thus would be ridiculous to conclude that federal and state law do not conflict on the ground that the defendant could have asked a federal agency or Congress to change the law. Here, by contrast, the Manufacturers' compliance with their state-

law duty to warn did not require them to ask for a change in federal law, as the majority itself recognizes. See *ante,* at 2578 ("[F]ederal law would permit the Manufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so"). The FDA already afforded them a mechanism for attempting to comply with their state-law duties. Indeed, the majority assumes that FDA regulations *required* the Manufacturers to request a label change when they had "reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e).

Second, the majority suggests that any other approach would render conflict pre-emption "illusory" and "meaningless." *Ante,* at 2579. It expresses concern that, without a robust view of what constitutes conflict, the Supremacy Clause would not have "any force" except in cases of express pre-emption. *Ibid.* To the extent the majority's purported concern is driven by its *reductio ad absurdum,* see *ante,* at 2579, n. 6, that concern is itself illusory, for the reasons just stated. To the extent the majority is concerned that our traditionally narrow view of what constitutes impossibility somehow renders conflict pre-emption as a whole meaningless, that concern simply makes no sense: We have repeatedly recognized that conflict pre-emption may be found, even absent impossibility, where state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Crosby,* 530 U.S., at 373, 120 S.Ct. 2288 (internal quotation marks omitted); see, *e.g., Geier v. American Honda Motor Co.,* 529 U.S. 861, 886, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000); *Barnett Bank of Marion Cty., N.A. v. Nelson,*517 U.S. 25, 31, 116 S.Ct. 1103, 134 L.Ed.2d 237 (1996); *Hines v. Davidowitz,* 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941). The majority's expansive view of impossibility is thus unnecessary to prevent conflict pre-emption from losing all meaning.[13]

Third, a plurality of the Court adopts the novel theory that the Framers intended for the Supremacy Clause to operate as a so-called *non obstante* provision. See 2591*2591*ante,* at 2579-2580 (citing Nelson, Preemption, 86 Va. L.Rev. 225 (2000)). According to the plurality, *non obstante* provisions in statutes "instruc[t] courts not to apply the general presumption against implied repeals." *Ante,* at 2579 (internal quotation marks omitted); see also *ante,* at 2580 (stating that when a statute contains a *non obstante*provision, "`courts will be less inclined against recognizing repugnancy in applying such statutes'" (quoting J. Sutherland, Statutes and Statutory Construction § 147, p. 199 (1891)). From this understanding of the Supremacy Clause, the plurality extrapolates the principle that "courts should not

strain to find ways to reconcile federal law with seemingly conflicting state law." *Ante,* at 2580.

This principle would have been news to the Congress that enacted the Hatch-Waxman Amendments in 1984: Our precedents hold just the opposite. For more than half a century, we have directed courts to presume that congressional action does*not* supersede "the historic police powers of the States ... unless that was the clear and manifest purpose of Congress." *Rice v. Santa Fe Elevator Corp.,* 331 U.S. 218, 230, 67 S.Ct. 1146, 91 L.Ed. 1447 (1947); see also *Gade,* 505 U.S., at 111-112, 112 S.Ct. 2374 (KENNEDY, J., concurring in part and concurring in judgment). We apply this presumption against pre-emption both where Congress has spoken to the pre-emption question and where it has not. See *Wyeth,* 555 U.S., at 566, n. 3, 129 S.Ct. 1187. In the context of express pre-emption, we read federal statutes whenever possible not to pre-empt state law. See *Altria Group, Inc. v. Good,* 555 U.S. 70, 77, 129 S.Ct. 538, 172 L.Ed.2d 398 (2008) ("[W]hen the text of a pre-emption clause is susceptible of more than one plausible reading, courts ordinarily `accept the reading that disfavors pre-emption'" (quoting *Bates v. Dow Agrosciences LLC,* 544 U.S. 431, 449, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005))); see also *Cipollone v. Liggett Group, Inc.,* 505 U.S. 504, 518, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992). And, when the claim is that federal law impliedly pre-empts state law, we require a "strong" showing of a conflict "to overcome the presumption that state and local regulation ... can constitutionally coexist with federal regulation." *Hillsborough County v. Automated Medical Laboratories, Inc.,* 471 U.S. 707, 716, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985).

The plurality's new theory of the Supremacy Clause is a direct assault on these precedents.[14] Whereas we have long presumed that federal law does not pre-empt, or repeal, state law, the plurality today reads the Supremacy Clause to operate as a provision instructing courts "*not* to apply the general presumption against implied repeals." *Ante,* at 2579 (internal quotation marks omitted; emphasis added). And whereas we have long required evidence of a "clear and manifest" purpose to pre-empt, *Rice,* 331 U.S., at 230, 67 S.Ct. 1146, the plurality now instructs courts to "look no further than the ordinary meaning of federal law" before concluding that Congress must have intended to cast aside state law, *ante,* at 2580 (internal quotation marks and alteration omitted).

That the plurality finds it necessary to resort to this novel theory of the Supremacy Clause—a theory advocated by no party 2592*2592 or *amici* in these cases—is telling. Proper application of the longstanding presumption *against* pre-emption

compels the conclusion that federal law does not render compliance with state law impossible merely because it requires an actor to seek federal agency approval. When federal law provides actors with a mechanism for attempting to comply with their state-law duties, "respect for the States as `independent sovereigns in our federal system'" should require those actors to attempt to comply with state law before being heard to complain that compliance with both laws was impossible. *Wyeth,* 555 U.S., at 565-566, n. 3, 129 S.Ct. 1187 (quoting *Lohr,* 518 U.S., at 485, 116 S.Ct. 2240).

III

Today's decision leads to so many absurd consequences that I cannot fathom that Congress would have intended to pre-empt state law in these cases.

First, the majority's pre-emption analysis strips generic-drug consumers of compensation when they are injured by inadequate warnings. "If Congress had intended to deprive injured parties of [this] long available form of compensation, it surely would have expressed that intent more clearly." *Bates,* 544 U.S., at 449, 125 S.Ct. 1788. Given the longstanding existence of product liability actions, including for failure to warn, "[i]t is difficult to believe that Congress would, without comment, remove all means of judicial recourse for those injured by illegal conduct." *Silkwood,*464 U.S., at 251, 104 S.Ct. 615; see also *Bruesewitz v. Wyeth LLC,* 562 U.S. ___, ___, 131 S.Ct. 1068, 1080, 179 L.Ed.2d 1 (2011) (noting our previously expressed "doubt that Congress would quietly preempt product-liability claims without providing a federal substitute"). In concluding that Congress silently immunized generic manufacturers from all failure-to-warn claims, the majority disregards our previous hesitance to infer congressional intent to effect such a sweeping change in traditional state-law remedies.

As the majority itself admits, a drug consumer's right to compensation for inadequate warnings now turns on the happenstance of whether her pharmacist filled her prescription with a brand-name drug or a generic. If a consumer takes a brand-name drug, she can sue the manufacturer for inadequate warnings under our opinion in*Wyeth.* If, however, she takes a generic drug, as occurs 75 percent of the time, she now has no right to sue. The majority offers no reason to think—apart from its new articulation of the impossibility standard—that Congress would have intended such an arbitrary distinction. In some States, pharmacists must dispense generic drugs absent instruction to the contrary from a consumer's physician. Even when consumers can request brand-name drugs, the price of the brand-name drug or the

consumers' insurance plans may make it impossible to do so. As a result, in many cases, consumers will have no ability to preserve their state-law right to recover for injuries caused by inadequate warnings.

Second, the majority's decision creates a gap in the parallel federal-state regulatory scheme in a way that could have troubling consequences for drug safety. As we explained in *Wyeth,* "[s]tate tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly." 555 U.S., at 579, 129 S.Ct. 1187. Thus, we recognized, "state law offers an additional, and important, layer of consumer protection that complements FDA regulation." *Ibid.*Today's decision eliminates the traditional state-law incentives for generic manufacturers to monitor and disclose safety risks. When a generic drug has a brand-name equivalent on the market, the brand-name 2593*2593 manufacturer will remain incentivized to uncover safety risks. But brand-name manufacturers often leave the market once generic versions are available, see *supra,* at 2573-2574, meaning that there will be no manufacturer subject to failure-to-warn liability. As to those generic drugs, there will be no "additional ... layer of consumer protection." *Wyeth,* 555 U.S., at 579, 129 S.Ct. 1187.

Finally, today's decision undoes the core principle of the Hatch-Waxman Amendments that generic and brand-name drugs are the "same" in nearly all respects.[15] See Brief for Rep. Henry A. Waxman as *Amicus Curiae* 9. The majority pins the expansion of the generic drug market on "the special, and different, regulation of generic drugs," which allows generic manufacturers to produce their drugs more cheaply. *Ante,* at 2582. This tells only half the story. The expansion of the market for generic drugs has also flowed from the increased acceptance of, and trust in, generic drugs by consumers, physicians, and state legislators alike.

Today's decision introduces a critical distinction between brand-name and generic drugs. Consumers of brand-name drugs can sue manufacturers for inadequate warnings; consumers of generic drugs cannot. These divergent liability rules threaten to reduce consumer demand for generics, at least among consumers who can afford brand-name drugs. They may pose "an ethical dilemma" for prescribing physicians. Brief for American Medical Association et al. as *Amici Curiae* 29. And they may well cause the States to rethink their longstanding efforts to promote generic use through generic substitution laws. See Brief for National Conference of State Legislators as*Amicus Curiae* 15 (state generic substitution laws "have proceeded on the premise that... generic drugs are not, from citizens' perspective, materially different from brand ones, except for the lower price"). These

consequences are directly at odds with the Hatch-Waxman Amendments' goal of increasing consumption of generic drugs.

Nothing in the Court's opinion convinces me that, in enacting the requirement that generic labels match their corresponding brand-name labels, Congress intended these absurd results. The Court certainly has not shown that such was the "*clear and manifest* purpose of Congress." *Wyeth,* 555 U.S., at 565, 129 S.Ct. 1187(internal quotation marks omitted; emphasis added). To the contrary, because federal law affords generic manufacturers a mechanism for attempting to comply with their state-law duties to warn, I would hold that federal law does not categorically pre-empt state-law failure-to-warn claims against generic manufacturers. Especially in light of the presumption against pre-emption, the burden should fall on generic manufacturers to show that compliance was impossible on the particular facts of their case. By holding that the "possibility of *possibility*" is insufficient to "defea[t]" pre-emption in these cases, *ante,* at 2581, n. 8, the Court contorts our pre-emption doctrine and exempts defendants from their burden to establish impossibility. With respect, I dissent.

[*] Justice KENNEDY joins all but Part III-B-2 of this opinion.

[1] All relevant events in these cases predate the Food and Drug Administration Amendments Act of 2007, 121 Stat. 823. We therefore refer exclusively to the pre-2007 statutes and regulations and express no view on the impact of the 2007 Act.

[2] As we use it here, "generic drug" refers to a drug designed to be a copy of a reference listed drug (typically a brand-name drug), and thus identical in active ingredients, safety, and efficacy. See, *e.g.,United States v. Generix Drug Corp.,* 460 U.S. 453, 454-455, 103 S.Ct. 1298, 75 L.Ed.2d 198 (1983); 21 CFR § 314.3(b) (2006) (defining "reference listed drug").

[3] The brief filed by the United States represents the views of the FDA. Cf. *Talk America, Inc. v. Michigan Bell Telephone Co.,* 564 U.S. ___, ___, n. 1, 131 S.Ct. 2254, 2257, n. 1, ___ L.Ed.2d ___, 2011 WL 2224429, at *3, n. 1 (2011); *Chase Bank USA, N.A. v. McCoy,* 562 U.S. ___, ___, 131 S.Ct. 871, 877-78, 178 L.Ed.2d 716 (2011). Although we defer to the agency's interpretation of its regulations, we do not defer to an agency's ultimate conclusion about whether state law should be pre-empted. *Wyeth v. Levine,* 555 U.S. 555, 576, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009).

[4] We do not address whether state and federal law "directly conflict" in circumstances beyond "impossibility." See *Wyeth,* 555 U.S., at 582, 590-591, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment) (suggesting that they might).

[5] The Hatch-Waxman Amendments contain no provision expressly pre-empting state tort claims. See *post,* at 2586-2587, 2592 (SOTOMAYOR, J., dissenting). Nor do they contain any saving clause to expressly preserve state tort claims. Cf. *Williamson v. Mazda Motor of America, Inc.,* 562 U.S. ___, ___, 131 S.Ct. 1131, 1141-43, 179 L.Ed.2d 75 (2011) (THOMAS, J., concurring in judgment)(discussing the saving clause in the National Traffic and Motor Vehicle Safety Act of 1966, 49 U.S.C. § 30103(e)). Although an express statement on pre-emption is always preferable, the lack of such a statement does not end our inquiry. Contrary to the dissent's suggestion, the absence of express pre-emption is not a reason to find no *conflict* pre-emption. See *post,* at 2592.

[6] The dissent asserts that we are forgetting "purposes-and-objectives" pre-emption. *Post,* at 2586-2587. But as the dissent acknowledges, purposes-and-objectives pre-emption is a form of conflict pre-emption. *Post,* at 2586-2587, 2590-2591. If conflict pre-emption analysis must take into account hypothetical federal action, including possible changes in Acts of Congress, then there is little reason to think that pre-emption based on the purposes and objectives of Congress would survive either.

[7] Wyeth also urged that state tort law "creat[ed] an unacceptable `obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'" 555 U.S., at 563-564, 129 S.Ct. 1187(quoting *Hines v. Davidowitz,* 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941)). The Court rejected that argument, and that type of pre-emption is not argued here. Cf. *post,* at 2590, n. 13 (opinion of SOTOMAYOR, J.).

[8] The FDA, however, retained the authority to eventually rescind Wyeth's unilateral CBE changes. Accordingly, the Court noted that Wyeth could have attempted to show, by "clear evidence," that the FDA would have rescinded any change in the label and thereby demonstrate that it would in fact have been impossible to do under federal law what state law required. *Wyeth, supra,* at 571, 129 S.Ct. 1187. Wyeth offered no such evidence.

That analysis is consistent with our holding today. The Court in *Wyeth* asked what the drug manufacturer could independently do under federal law, and in the absence of clear evidence that Wyeth could not have accomplished what state law required of it, found no pre-emption. The *Wyeth*Court held that, because federal law accommodated state law duties, "the possibility of impossibility" was "not enough." *Post,* at 2587; see also *Rice v. Norman Williams Co.,* 458 U.S. 654, 659, 102 S.Ct. 3294, 73 L.Ed.2d 1042 (1982) (rejecting "hypothetical" impossibility). But here, "existing" federal law directly conflicts with state law. *Post,* at 2590 ("Conflict analysis necessarily turns on existing law"). The question in these cases is not whether the possibility of *impossibility* establishes pre-emption, but rather whether the possibility of *possibility* defeats pre-emption. *Post,* at 2587.

[9] That said, the dissent overstates what it characterizes as the "many absurd consequences" of our holding. *Post,* at 2592. First, the FDA informs us that "[a]s a practical matter, genuinely new information about drugs in long use (as generic drugs typically are) appears infrequently." U.S. Brief 34-35. That is because patent protections ordinarily prevent generic drugs from arriving on the market for a number of years after the brand-name drug appears. Indeed, situations like the one alleged here are apparently so rare that the FDA has no "formal regulation" establishing generic drug manufacturers' duty to initiate a label change, nor does it have any regulation setting out that label-change process. *Id.,* at 20-21. Second, the dissent admits that, even under its approach, generic drug manufacturers could establish pre-emption in a number of scenarios. *Post,* at 2588-2589.

[1] Online at http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib.pdf (all Internet materials as visited June 17, 2011, and available in Clerk of Court's case file).

[2] In addition, many insurance plans are structured to promote generic use. See Congressional Budget Office, Effects of Using Generic Drugs on Medicare's Prescription Drug Spending 9 (2010), online at http://www.cbo.gov/ftpdoc/118xx/doc11838/09-15-PrescriptionDrugs.pdf. State Medicaid programs similarly promote generic use. See Kaiser Comm'n on Medicaid and the Uninsured, State Medicaid Outpatient Prescription Drug Policies: Findings from a National Survey, 2005 Update 10 (2005), online at www.kff.org/medicaid/upload/state-medicaid-outpatient-prescription-drug-policies-findings-from-a-national-survey-2005-update-report.pdf.

[3] Online at http://www.cbo.gov/ftpdocs/6xx/doc655/pharm.pdf.

[4] An adverse drug experience is defined as "[a]ny adverse event associated with the use of a drug in humans, whether or not considered drug related." 21 CFR § 314.80(a) (2006).

[5] Like the majority, I refer to the pre-2007 statutes and regulations. See *ante,* at 2574, n. 1.

[6] At congressional hearings on the Hatch-Waxman Amendments, representatives of the generic drug manufacturers confirmed both their obligation and their ability to conduct postapproval investigation of adverse drug experiences. See Drug Legislation: Hearings on H.R. 1554 et al. before the Subcommittee on

Health and the Environment of the House Committee on Energy and Commerce, 98th Cong., 1st Sess., 45 (1983) (statement of Kenneth N. Larsen, chairman of the Generic Pharmaceutical Industry Association (GPhA)) (generic manufacturers "are sensitive to the importance of looking at adverse reactions"); *id.,* at 47-48 ("[W]e will do and provide whatever is required to be performed to meet the regulatory requirement to provide for the safety and well-being of those that are using the drug, this is our role and responsibility. This is an obligation to be in this business"); *id.,* at 50-51 (statement of Bill Haddad, executive officer and president of GPhA) ("Every single generic drug company that I know has a large research staff. It not only researches the drug that they are copying, or bringing into the market but it researches new drugs, researches adverse reaction[s]").

[7] The FDA's construction of this regulation mirrors the guidance it provided to generic manufacturers nearly 20 years ago in announcing the final rule implementing the abbreviated application process for generic drugs:

"If an ANDA [*i.e.,* application for approval of a generic drug] applicant believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised. After approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised." 57 Fed.Reg. 17961 (1992).

FDA's internal procedures recognize that the Office of Generic Drugs will have to consult with other FDA components on "some labeling reviews." Manual of Policies and Procedures 5200.6, p. 1 (May 9, 2001). Consultations involving "possible serious safety concerns" receive the highest priority. *Id.,* at 3.

[8] In its decision below, the Eighth Circuit suggested that the Manufacturers could not show impossibility because federal law merely permitted them to sell generic drugs; it did not require them to do so. See *Mensing v. Wyeth, Inc.,* 588 F.3d 603, 611 (2009) ("The generic defendants were not compelled to market metoclopramide. If they realized their label was insufficient but did not believe they could even propose a label change, they could have simply stopped selling the product"); see also *Geier v. American Honda Motor Co.,* 529 U.S. 861, 873, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000)(describing "a case of impossibility" as one "in which state law penalizes what federal law *requires*" (emphasis added)). Respondents have not advanced this argument, and I find it unnecessary to consider.

[9] At the time respondents' cause of action arose, the FDA did not have authority to require a brand-name manufacturer to change its label. (It received that authority in 2007. See Pub.L. 110-85, § 901, 121 Stat. 924-926, 21 U.S.C. § 355(*o*)(4) (2006 ed., Supp. III). It did, however, have the equally significant authority to withdraw the brand-name manufacturer's permission to market its drug if the manufacturer refused to make a requested labeling change. See 21 U.S.C. § 355(e) (2006 ed.); 21 CFR § 314.150(b)(3).

[10] A brand-name manufacturer's ability to comply with a state-law duty to warn would depend on its own unilateral actions only during the period after it should have changed its label but before the FDA would have approved or disapproved the label change. The claim in *Wyeth* does not appear to have arisen during that period.

[11] Respondents' state-law claim is not that the Manufacturers were required to ask the FDA for assistance in changing the labels; the role of the FDA arises only as a result of the Manufacturers' pre-emption defense.

[12] These cases do not involve a situation where a brand-name manufacturer itself produces generic drugs. See Okie, Multinational Medicines—Ensuring Drug Quality in an Era of Global Manufacturing, 361 N. Eng. J. Med. 737, 738 (2009); see also GPhA, Frequently Asked Questions About Generics, http://www.gphaonline.org/about-gpha/about-generics/faq ("Brand-name companies make about half of generic drugs"). In that case, the manufacturer could independently change the brand-name label under the CBE regulation, triggering a corresponding change to its own generic label.

[13] Justice THOMAS, the author of today's opinion, has previously expressed the view that obstacle pre-emption is inconsistent with the Constitution. See *Williamson v. Mazda Motor of America, Inc.,* 562 U.S. ___, ___, 131 S.Ct. 1131, 1141-43, 179 L.Ed.2d 75 (2011) (opinion concurring in judgment);*Wyeth v. Levine,* 555 U.S. 555, 604, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009) (opinion concurring in judgment). That position,

however, has not been accepted by this Court, and it thus should not justify the majority's novel expansion of impossibility pre-emption.

[14] The author of the law review article proposing this theory of the Supremacy Clause acknowledges as much. See Nelson, Preemption, 86 Va. L.Rev. 225, 304 (2000) ("The *non obstante* provision rejects an artificial presumption that Congress did not intend to contradict any state laws and that federal statutes must therefore be harmonized with state law"). The plurality, on the other hand, carefully avoids discussing the ramifications of its new theory for the longstanding presumption against pre-emption.

[15] According to the GPhA, both the FDA and the generic drug industry "spend millions of dollars each year . . . seeking to reassure consumers that affordable generic drugs really are—as federal law compels them to be—*the same as* their pricier brand-name counterparts." Brief for GPhA as *Amicus Curiae* on Pet. for Cert. in Nos. 09-993, 09-1039, pp. 2-3.