No. 17-290

IN THE

Supreme Court of the United States

MERCK SHARP & DOHME CORP.,
Petitioner,

v.

DORIS ALBRECHT, ET AL.,
Respondents.

On Writ of Certiorari to
the United States Court of Appeals
for the Third Circuit

BRIEF OF *AMICUS CURIAE* AMERICAN ASSOCIATION FOR JUSTICE IN SUPPORT OF RESPONDENTS

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INTEREST OF *AMICUS CURIAE*[1]

The American Association for Justice ("AAJ") is a national voluntary bar association founded in 1946 to safeguard the right of all Americans to seek legal recourse for wrongful injury. AAJ's members primarily represent plaintiffs in personal injury actions, employment rights cases, consumer cases, and other civil actions. AAJ works to protect the ability of plaintiffs to vindicate their rights under state tort laws.

As this brief details, in the years since this Court's decision in *Wyeth v. Levine*, 555 U.S. 555 (2009), drug manufacturers have attempted to curtail plaintiffs' state-law rights by arguing for an expansive theory of conflict-preemption that would preempt state laws based on only a hypothetical conflict with federal law. Based on its members' experience with pharmaceutical tort litigation—and its organizational concern for the development of the law in this area—AAJ is well-positioned to explain why such an expansion of federal preemption doctrine is both ill-conceived and contrary to precedent.

INTRODUCTION AND SUMMARY OF ARGUMENT

Over the last decade, this Court has on three separate occasions affirmed that state-law failure-to-warn claims are not preempted where federal law permits a drug manufacturer "to unilaterally strengthen its warning without prior FDA approval." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 624 (2011) (citing *Wyeth v. Levine*, 555 U.S.

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[1] No counsel for a party authored this brief in whole or in part and no person other than *amicus* and its counsel made a monetary contribution to its preparation or submission. The parties' letters consenting to the filing of amicus briefs are on file with the Clerk.

555, 573 (2009) (internal quotation marks omitted); *see also Mut. Pharm. Co., Inc. v. Bartlett*, 570 U.S. 472, 490 (2013).

Despite this clarity, drug manufacturers have repeatedly urged lower courts to divine a rule from *Wyeth* that state-law claims are preempted in cases where the law permitted a company to strengthen its drug's warning label so long as the FDA hypothetically might have rejected that new warning later. This argument not only runs counter to both *Wyeth* and *Mensing*, but also to the cornerstone principle that a state's law is only preempted "to the extent that it *actually* conflicts with federal law." *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 (1990) (emphasis added).

This case presents an opportunity for this Court to reaffirm that there is no such thing as "hypothetical preemption." This Court should clarify that *Wyeth* requires a drug manufacturer to show that the FDA actually rejected the warning at issue—not just that the FDA could or would likely have rejected it. This bright-line rule for impossibility preemption claims is straightforward, easily applied across the entire range of failure-to-warn cases, and faithful to the fundamental rule that state law only gives way when it actually conflicts with federal law. It also avoids any need for the kind of freewheeling speculation about the FDA's hypothetical views that is required by drug manufacturers' reading of *Wyeth*.

Under an actual-rejection standard, preemption does not turn on what the FDA might have done with a particular proposed warning. But if this Court concludes that a defendant's preemption defense in the failure-to-warn context *does* require such an inquiry (as drug manufacturers contend), the final determination should

be submitted to a jury when that defense involves contested questions of fact. Our drug-safety laws frequently require juries to examine complex scientific evidence regarding safety and causation. The inquiry here would be no different: A manufacturer may add a new warning to its label so long as "there is reasonable evidence of a causal association" between a drug and "a clinically significant hazard." 21 C.F.R. § 201.57(c)(6)(i). Determining, based on a weighing of the evidence, whether a sufficient basis for a claimed causal association has been met rests firmly within the jury's traditional realm of competence. The Court should affirm the Third Circuit's decision below denying preemption.

ARGUMENT

I. A state-law failure-to-warn claim should not be preempted on impossibility grounds unless the FDA actually rejected the warning at issue.

This Court has long held that federal conflict preemption will not be found where there is only "a hypothetical or potential conflict" between state and federal law. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982). Instead, where conflict preemption is alleged, a state's law is only preempted "to the extent that it *actually* conflicts with federal law." *English*, 496 U.S. at 79 (emphasis added). When a party asserts that its state-law obligations were preempted because it was impossible to comply with both state and federal law, the party must demonstrate that it was *actually* "not lawful under federal law . . . to do what state law required." *Mensing*, 564 U.S. at 618.

That rule takes its cue from the text of the Supremacy Clause and our federalist system. Under the Supremacy Clause, state law is preempted only by federal law "made in Pursuance" of the Constitution—

not by extratextual considerations that may require speculation or hypothesis. U.S. const., art. VI, cl. 2. That is why preemption analysis "should not be [a] freewheeling judicial inquiry into whether a state statute is in tension with federal objectives, but an inquiry into whether the ordinary meanings of state and federal law conflict.'" *Wyeth*, 555 U.S. at 588 (Thomas, J., concurring in judgment) (internal quotation marks and citation omitted). When it comes to impossibility preemption, in other words, "state and federal law conflict where it is 'impossible for a private party to comply with both state and federal requirements.'" *Mensing*, 564 U.S. at 618 (quoting *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995)).

Despite these longstanding principles, litigants in the lower courts have seized on a few sentences from this Court's decision in *Wyeth* to argue for what is effectively a doctrine of hypothetical conflict preemption. In *Wyeth*, this Court held that impossibility preemption does not apply to a failure-to-warn claim where federal law permitted a pharmaceutical company to add the relevant warning to its label. 555 U.S. at 568–73. There, the plaintiff had sued the drug manufacturer Wyeth to argue that it should have adopted a warning regarding the risk of gangrene developing from a particular way of administering a drug. *Id.* at 571. Wyeth argued that it could not have adopted the warning because federal regulations prevented it from changing its drug's label. The Court rejected Wyeth's "cramped reading" of the regulation, and held that the failure-to-warn claim was not preempted. *Id.* at 570–71. The Court noted that the FDA's "changes being effected" process permits drug manufacturers to add new warnings to their labels, which meant that Wyeth "could have . . . added a stronger warning" about the drug in question. *Id.* at 568, 570. In so

holding, the Court briefly noted that even though FDA regulations permit drug companies to add new warnings to their labels, the FDA can later act to reject those changes. *Id.* at 571. But, the Court said, that would not lead to preemption in a failure-to-warn case unless there was "clear evidence that the FDA would not have approved [the] change" in question. *Id.* at 571.

In the years since *Wyeth*, that observation has sparked a novel breed of "hypothetical impossibility" preemption. Drug manufacturers in post-*Wyeth* failure-to-warn cases have advanced a theory of preemption that does not turn on actual impossibility—whether a drug manufacturer could *actually* have added particular warnings to its label—but instead on hypothetical impossibility—whether the manufacturer was right not to include the warning because the FDA *could have and would have* rejected it. *See, e.g.*, *Forst v. SmithKline Beecham Corp.*, 639 F. Supp. 2d 948 (E.D. Wis. 2009); *Dorsett v. Sandoz*, 699 F. Supp. 2d 1142 (C.D. Cal. 2010); *Lofton v. McNeil Consumer & Specialty Pharms.*, 682 F. Supp. 2d 662 (N.D. Tex. 2010); *Hunt v. McNeil Consumer Healthcare*, 6 F. Supp. 3d 694 (E.D. La. 2014); *Koho v. Forest Labs.*, 17 F. Supp. 3d 1109 (W.D. Wash. 2014).

But impossibility preemption does not deal in hypotheticals. This Court should make clear that *Wyeth* did not create a new form of hypothetical conflict preemption. To the contrary, under settled principles of conflict preemption, to win preemption under *Wyeth*'s "clear evidence" standard, a drug manufacturer must show that (1) it attempted to adopt a warning appropriate for the specific injury at issue in the case, (2) the FDA rejected that warning, and (3) no new material evidence arose after that rejection that would have enabled the company

to attempt to add the warning again. As we explain, this standard aligns with this Court's case law, establishes a bright-line rule for preemption claims, and avoids enmeshing lower courts in the type of freewheeling speculation about what the FDA would have done that is called for by drug manufacturers' reading of *Wyeth*.

First, a standard that rejects an inquiry into the FDA's hypothetical actions squares with the Supremacy Clause and this Court's preemption jurisprudence as a whole. As noted above, this Court has rejected the notion of preemption based on "a hypothetical or potential conflict" between state and federal law. *Rice*, 458 U.S. at 659. When it comes to impossibility preemption, "the existence of . . . potential conflicts is entirely too speculative" to warrant preemption. *Exxon Corp. v. Governor of Maryland*, 437 U.S. 117, 131 (1978). Consistent with the text of the Supremacy Clause, for purposes of impossibility preemption state and federal law conflict only "where it is 'impossible for a private party to comply with both state and federal requirements.'" *Mensing*, 564 U.S. at 618 (internal quotations omitted). And "delv[ing] into hypothetical situations" posed by defendants seeking to dodge state-law liability does not present a court with a scenario in which compliance with a state law "requires a violation" of federal law. *Exxon Corp.*, 437 U.S. at 131 (internal quotations omitted); *see also Rice*, 458 U.S. at 659 ("A state regulatory scheme is not pre-empted by the federal antitrust laws simply because in a hypothetical situation a private party's compliance with the statute might cause him to violate the antitrust laws.").

This Court's approach to preemption in the FDA context in particular reinforces this understanding. In *Mensing*, for instance, this Court specifically confirmed

that "[t]he question for 'impossibility' is whether the private party could independently do under federal law what state law requires of it." *Mensing*, 564 U.S. at 620. Impossibility preemption turns, in other words, on what the company "could independently do" at the time in question, not on what might have been the case "depending on the actions of the FDA." *Id.* In *Mensing*, that meant that there was a conflict, and thus preemption, because the drug manufacturer could not have added a warning without express FDA action—so it could not exercise independent authority to comply with state law without running afoul of federal law. *Id.* at 620–21.

But in other contexts, the federal regulatory scheme imposes no similar concrete prohibitions. In cases where the "changes being effected" process is available, for example, there is no conflict *unless and until* the FDA acts—companies are permitted to add a warning to their labels and FDA action is required to remove or prohibit the warning. *See Wyeth*, 555 U.S. at 571; 21 C.F.R. § 314.70(c). In such a case, no conflict preemption exists until the FDA acts because until that point a drug company can "independently" comply with state law by adding a warning to its label. And this is true even if it suspects that the FDA *might* decide not to permit such a warning down the road. *Mensing*, 564 U.S. at 620.

Anchoring conflict preemption to the FDA's actual rejection of a manufacturer's proposed label also advances the aims of the broader regulatory scheme for commercial drugs. As this Court has explained, the principal "premise" of the Food, Drug, and Cosmetic Act is that "manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times." *Wyeth*, 555 U.S. at 579. Given that understanding, "state law

offers an additional, and important, layer of consumer protection that complements FDA regulation"—in the absence of specific FDA regulation, state law (often through common-law tort claims) steps in to supply additional consumer protections. *Id.*

A standard that permits manufacturers to claim preemption even in the absence of FDA action undermines this framework. Restricting preemption to cases where the FDA has actually rejected a manufacturer's proposed warning promotes the incentives for manufacturers to submit new labels with proposed warnings to the FDA—the only way to guarantee either compliance with state law or a valid defense based on conflict preemption. But if manufacturers can claim preemption based on actions the FDA *might* have taken, the incentive to comply with state law is diminished: if a manufacturer believes it has a good argument that the FDA *might* reject the proposed warning, it can avoid complying with state law and reap the benefits of federal preemption, all without risking the possibility that the FDA would, in fact, permit the new warning to issue.

Second, restricting the availability of preemption to cases in which the FDA has acted would provide an administrable bright line for lower courts, avoiding the need for intensive fact development and speculation about the FDA's likely course of conduct.

Post-*Wyeth* cases involving hypothetical-conflict arguments demonstrate just how far some courts have strayed from this Court's "counsel of restraint" when it comes to hypothetical preemption conflicts. *Exxon Corp.*, 437 U.S. at 131. Because a drug manufacturer seeking preemption cannot point to an actual rejection by the FDA that prevented it from adopting the warning at issue, it must ask a court to speculate on what the FDA

would have done had the manufacturer attempted to comply with its alleged state-law duty. In making these arguments, companies have asked courts to consider a wide range of evidence to evaluate whether there might have been a conflict between state and federal law. Among other things, defendants have pointed to:

- The fact that no relevant warning was required for the drug at issue, against a backdrop of periodic reviews by the FDA of evidence with respect to the relevant risks, *Forst*, 639 F. Supp. 2d at 954;
- The fact that a similar warning was required for a similar drug around the time in question, but no new warning was required for the drug at issue, *Hunt*, 6 F. Supp. 3d at 701–02;
- The FDA's decision to require a warning for the prescription version of a drug but not for the over-the-counter version, *Lofton*, 682 F. Supp. 2d at 677;
- A manufacturer's repeated interactions with the FDA in which the FDA did not require an enhanced warning with respect to the drug at issue, *Forst*, 639 F. Supp. 2d at 954;
- The FDA's decision to aim for consistent labels across a particular class of drugs, *Koho*, 17 F. Supp. 3d at 1118–19;
- The FDA's implementation of minor changes in phrasing for required warnings for the drug at issue, *Dorsett*, 669 F. Supp. 2d at 1158 n.14;
- The FDA's rejection of a request to remove a drug from the marketplace, *Lofton*, 682 F. Supp. 2d at 677;

- The FDA's decision to require warnings of the specific symptoms of a disorder, but not a warning that named the disorder itself, *Id.* at 677–78;
- General statements and memoranda issued by the FDA regarding the category of risk at issue, *Dorsett*, 699 F. Supp. 2d at 1157;
- The FDA's responses to citizen petitions addressing the same or related risks for the same or related drugs, *Id.* at 1157; *Lofton*, 682 F. Supp. 2d at 677–78.

Embracing a form of impossibility preemption that turns on these sorts of facts would inevitably open the door to uncabined speculation based on a wide—and ever-increasing—assortment of contextual clues. That transforms *Wyeth*'s passing statement about "clear evidence" into a license to construct elaborate counterfactual scenarios in which the whole range of the FDA's actions—sometimes spanning the course of decades, *see, e.g.*, *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 392–96 (7th Cir. 2010)—is mined for hints of regulatory intent. No principled view of conflict preemption supports such an approach.

Indeed, construing facts like these to ascertain preemption demands extensive guesswork. How should a factfinder square, for instance, a statement by the FDA that a class of drugs does not pose a particular risk with its contemporaneous decision to approve a manufacturer's choice to add warnings of that same risk to its drugs' labels? *See Dorsett*, 699 F. Supp. 2d at 1157–58. Should a factfinder consider it more important that the FDA repeatedly rejected efforts to increase required warnings for a particular category of drugs during a certain time period, or that during the same time period the FDA was considering scientific evidence that eventually did lead to

increased warnings? *See Dobbs v. Wyeth Pharm.*, 797 F. Supp. 2d 1264, 1277 (W.D. Okla. 2011) (discussing *Mason*, 596 F.3d at 395). Such "delv[ing]" into speculation about the motives and intentions behind various actions, not to mention the complex facts and standards underlying all of the FDA's decisions, bears little resemblance to the traditional notion that state law will not give way unless it "requires a violation" of federal law. *Exxon Corp.*, 437 U.S. at 131.

Other difficult problems arise with this type of hypothetical-impossibility inquiry. The nature of many failure-to-warn claims means that factfinders will be required to answer not only what the FDA might have done with a given proposed warning, but exactly when the FDA would have done it. It is not uncommon for a failure-to-warn claim to involve a warning that the FDA did eventually adopt after the events giving rise to the particular claim at issue. *See, e.g.*, *In re Actos (Pioglitazone) Prods. Liab. Litig.*, 2014 WL 12776173 (W.D. La. Sept. 5, 2014) (considering argument that defendant should have adopted a warning in 2002 that the FDA began requiring in 2011). If such a claim would be preempted only at the points in time during which the FDA would likely have rejected a given proposed warning, courts could be required to decide exactly when the warning at issue would have been rejected, and when it would have been permitted.

Restricting preemption to cases where the FDA actually rejected a manufacturer's attempt to adopt the warning at issue is not only consistent with settled preemption principles, but it is much simpler to administer. Courts would only have to ask (1) whether the manufacturer attempted to adopt a warning appropriate for the specific injury at issue in the case, (2)

whether the FDA rejected that warning, and (3) whether new material evidence arose after the rejection that would have enabled the company to attempt to add the warning again via the "changes being effected" process. If the answer to either of the first two questions is "no," or if the answer to the third question is "yes," there is no actual impossibility, and therefore no preemption.

This standard would avoid many of the pitfalls that have emerged in the lower courts. The inquiry would not be automatic—courts would still have to examine the language the manufacturer had submitted, and they would have to compare the evidence available at the time of the FDA's rejection to evidence that arose afterward. But those inquiries would be well-defined. A court would not need to consider, for instance, the significance of the FDA's inaction after an important study; its decision to permit or reject a similar warning on a similar drug; or the agency's stated desire to aim for consistent labeling across a specific category of drugs.

The same goes for the need to consider the FDA's rulings on citizen petitions. Although citizen petitions currently constitute a major source of evidence for hypothetical-preemption arguments in the lower courts, they are often unreliable. *See, e.g.*, *Cerveny v. Aventis, Inc.*, 855 F.3d 1091, 1102–03 (10th Cir. 2017) (noting that "brand-name drug manufacturers often file frivolous citizen petitions, asking the FDA to disallow a generic drug's entry into the market," and describing an empirical study suggesting that "citizen petitions are frequently denied because they involve unsupported efforts to stall entry of generic medications into the marketplace"). If preemption turns on the existence of an actual conflict, speculation fueled by resort to this

material would (as it should) be irrelevant to the question of actual impossibility.

What's more, an actual-impossibility standard would deliver little downside. This standard would largely track the same outcomes that have been reached by courts engaging in a more broad-ranging, hypothetical inquiry. Courts have understandably been hesitant to find impossibility-based conflict preemption where the FDA has not actually rejected the specific proposed warning at issue. *See, e.g.*, *Dorsett*, 699 F.Supp.2d at 1157–60; *Forst*, 639 F. Supp. 2d at 952–55; *Lofton*, 682 F. Supp. 2d at 676–78; *Koho*, 17 F. Supp. 3d at 1115–19. And the few cases where courts have found preemption under *Wyeth* have tended to focus on the FDA's actual rejection of the proposed warnings at issue. *See, e.g.*, *In re Depakote*, 87 F. Supp. 3d 916, 922 (S.D. Ill. 2015) ("Abbott tried, on various occasions, to secure approval of a developmental delay warning, and its requests were twice denied by the FDA."); *Dobbs*, 797 F. Supp. 2d at 1276 (finding preemption where the FDA had removed warning language that had been added via the CBE process). An actual-impossibility standard would therefore reinforce what the lower courts already understand—that preemption under *Wyeth* is only appropriate in the face of an actual conflict.

II. In the alternative, if impossibility preemption requires determining the FDA's hypothetical actions, that determination should be made by a jury.

To the extent that this Court holds that an impossibility-preemption defense requires a determination as to what the FDA might have done with a given proposed warning, that determination should be made by a jury. Such a determination could only be made by an inquiry

into complex scientific and case-specific evidence—the kind of inquiry that is firmly within the jury's traditional domain.

Post-*Wyeth* failure-to-warn cases illustrate the point. Because, in these cases, a drug manufacturer did not submit a labeling change to the FDA, it is left to argue that preemption turns on "whether the FDA would have rejected a proposed labeling change, not whether the FDA did in fact issue an explicit rejection." *Seufert v. Merck Sharp & Dohme Corp.*, 187 F. Supp. 3d 1163, 1169 (S.D. Cal. 2016). In the years since *Wyeth*, those courts responding to this hypothetical-impossibility argument have recognized that it is "necessarily fact specific." *Dobbs*, 797 F. Supp. 2d at 1270; *see also In re Depakote*, 87 F. Supp. 3d at 922 (same); *Seufert*, 187 F. Supp. 3d at 1170 (same). The principal inquiry is scientific, not legal, in nature—to determine whether the FDA would permit a given warning to be added, the factfinder must determine whether "reasonable evidence" indicates "an association between a hazard and the drug at issue." *Dobbs*, 797 F. Supp. 2d at 1271 (quoting 21 C.F.R. § 201.57(c)(6)(i)). At bottom, this requires a factfinder "to weigh the evidence submitted by both sides in an attempt to answer the hypothetical question" of what the FDA would have done. *In re: Zofran (Ondansetron) Prods. Liab. Litig.*, 2016 WL 287056, at *3 (D. Mass. Jan. 22, 2016).

Determining what the FDA would have done requires a factfinder to consider the likelihood of various outcomes in a counterfactual scenario. Those counterfactual scenarios involve, at a minimum, the question of what the FDA would have done, based on the available scientific evidence, if a pharmaceutical company had attempted to add a particular warning to its label. *See,*

e.g., *Koho*, 17 F. Supp. 3d at 1115–19; *Lofton*, 682 F. Supp. 2d at 676–78. But counterfactual scenarios can also implicate a host of other key questions—like what the FDA would have done had the manufacturer submitted "information not previously submitted to the FDA indicating the need for a new or strengthened warning." *In re: Zofran*, 2016 WL 287056, at *3.

There is no one-size-fits-all method for resolving this type of inquiry. To answer these questions, a factfinder would need to consider a broad range of relevant facts. This includes "the regulatory history of the drug or drug class at issue," any "temporal gaps between FDA action and accrual of a plaintiff's claims," the existence of relevant "citizen petition submissions and rejections," all "available scientific data," and "whether the FDA has reviewed the particular harm at issue and the consistency of any resulting conclusions." *Seufert*, 187 F. Supp. 3d at 1170.

And these inquiries would often require substantial fact development, including the need to consider expert testimony. *See, e.g.*, *Koho*, 17 F. Supp. 3d at 1117–18. For instance, where a defendant's "preemption argument rests on the premise" that there is no "scientific substantiation" for a "causal link" between a drug and a given risk, expert scientific and/or medical testimony is crucial, if not obligatory. *Id.*; *see also Dobbs*, 797 F. Supp. 2d at 1272 (noting that "[t]he FDA has consistently defined reasonable evidence of a causal association as 'when evidence exists on the basis of which experts qualified by scientific training and experience can reasonably conclude that the hazard is associated with the use of the drug'") (quoting 44 Fed. Reg. 37434, 374634 (June 26, 1979)). The same is true for questions about whether the FDA's statements about that causal

connection in one context necessarily carry over to another. *See Koho*, 17 F. Supp. 3d at 1117–18.

Other fact-specific questions would abound. How might evidence regarding the risks of a drug for a particular demographic group—and the FDA's responses to proposed warnings regarding those risks—imply anything about the suitability for a warning regarding a different demographic group? *See, e.g.*, *Koho*, 17 F. Supp. 3d at 1117–19. And how might the allegedly necessary warnings in a case "compare (or conflict) with . . . label changes and warnings rejected by the FDA" in other cases? *In re: Zofran*, 2016 WL 287056, at *4. And what about "[t]he identity and process by which a labeling change is requested"? *Id.* at *3. That "may be material because the procedural method used could affect the FDA's response to the proposed change." *Id.* at *3.

In some cases, the evidence will point so clearly in one direction that the issue of preemption can be resolved at summary judgment. But in many circumstances, resolving the preemption claim will require the kind of comparative weighing of case-specific scientific evidence that falls comfortably within the jury's traditional role. "In actions at law predominantly factual issues are in most cases allocated to the jury," a principle that "rests on a firm historical foundation." *City of Monterey v. Del Monte Dunes at Monterey, Ltd.*, 526 U.S. 687, 720 (1999). The questions involved in assessing what the FDA would likely have done with a proposed warning are "predominantly factual"—they require the examination of scientific data and testimony, the history of a drug's development, and the context surrounding existing warnings. Analyzing the purposes and effects of the FDA's actions is also properly regarded as a fact-

intensive endeavor; this Court has regarded "complex factual assessments of the purposes and . . . effects of government actions" as core "factual inquiries" that are appropriate for a jury. *Id.* (internal citations omitted).

Indeed, in analogous circumstances, similar fact-finding inquiries are regularly assigned to juries. Take, for instance, the parallel example of drug-fraud tort litigation. In that type of case, an injured plaintiff often claims that a manufacturer's misrepresentation of the safety of a particular drug caused their injury. *See, e.g.*, *In re Neurontin Mktg. & Sales Practices Litig.*, 712 F.3d 21 (1st Cir. 2013); *In re Avandia Mktg., Sales Practices & Prod. Liab. Litig.*, 804 F.3d 633 (3d Cir. 2015). In response, a defendant will frequently raise an affirmative defense that an intervening action of a third party—a doctor who prescribed the drug—breaks the chain of causation. *Id.* at 645 (arguing that "the presence of intermediaries" destroys causation).

Evaluating that defense can involve complicated counterfactual analysis. Juries need to consider and weigh competing evidence regarding how physicians would have seen the drug absent the misrepresentations. *See, e.g.*, *In re Neurontin*, 712 F.3d at 45. Not surprisingly, given the fact-intensive nature of the inquiry, that counterfactual analysis is "a task for the jury." *Id.* at 46; *see also Perez v. Wyeth Labs., Inc.*, 734 A.2d 1245, 1263 (N.J. 1999) ("In each case, a jury must resolve the close question[] of whether a breach of duty has been a proximate cause of harm."). And ultimately, a fact-finder must decide whether the doctor would still have prescribed the drug had she known of the safety problems.

So it is here. When a defendant in a failure-to-warn case raises impossibility preemption as an affirmative

defense, a factfinder must determine what the FDA would have done had it been presented with a particular proposed warning or had it been aware of certain new scientific evidence. The logic is thus no different from that of the intervening-cause affirmative defense: a factfinder must evaluate the likelihood that a third party would have acted in a particular way that would preclude liability the defendant might incur if that same third party were not in the picture. In both contexts, that inquiry often involves a complicated factual analysis of the state of the third party's knowledge of a given drug's risks and benefits at a given point in time.

That the third party in failure-to-warn cases is the FDA rather than a physician or private company is a distinction without a difference. The petitioners in this case raise the fear that a jury would have to "psychoanalyze FDA officials" in an "unbounded inquiry [that] would contravene the presumption that officials exercise their responsibilities faithfully in accordance with the law." Pet. Br. 44. Not so. Because "a presumption of regularity attaches to the actions of Government agencies," *U.S. Postal Serv. v. Gregory*, 534 U.S. 1, 10 (2001), courts can instruct juries that what the FDA would have done can be determined by applying the FDA's standards to the facts at issue in each case. To determine whether the FDA would have rejected a given warning added via the "changes being effected" process, then, a jury could simply evaluate whether there was "reasonable evidence of a causal association" between "a clinically significant hazard" and the drug at issue. 21 C.F.R. § 201.57(c)(6)(i); *see also* 21 C.F.R. § 314.70(c)(6)(iii)(A) (providing that warning labels may be added pursuant to the "changes being effected" process where they "satisf[y] the standard for inclusion in the labeling under § 201.57(c) of this chapter"). That

not only addresses petitioner's fear but demonstrates exactly why it is *unnecessary* for the jury to ask about the mindset of individual FDA officials.

In fact, our drug-safety laws frequently call on juries to examine complex questions regarding drug safety profiles and the state of the FDA's knowledge. For instance, as this Court explained in *Wyeth*, under the FDA's governing statutes, "federal juries will resolve most misbranding claims." 555 U.S. at 570. Finding liability for misbranding, in turn, may require a jury to evaluate whether a company adequately responded to "new and scientifically significant information that was not before the FDA" when it approved the drug at issue. *Bartlett*, 570 U.S. at 487 n.4. None of these tasks requires evaluating the internal psychology of an FDA officer or eschewing the presumption of regularity for federal agency activity. But all, like those here, are appropriate for a jury.

CONCLUSION

The decision below should be affirmed.

Respectfully submitted,

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