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 THE CATO INSTITUTE AS *AMICUS CURIAE* IN SUPPORT OF RESPONDENTS

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QUESTION PRESENTED

More than 500 patients allege that Merck's drug Fosamax caused them to suffer atypical femoral fractures. They claim, among other things, that Merck failed to warn adequately of the risk of such serious fractures. The FDA, in 2009, rejected an inadequate warning proposed by Merck, in part because it underplayed and misidentified the risk involved. Merck did not offer an alternative warning addressing the FDA's concerns, and the FDA eventually ordered a stronger warning for the entire class of drugs at issue. Merck now argues that the plaintiffs' failure-to-warn claim is preempted by the FDA's rejection of its proposed warning and hence the company cannot be held liable for failing to provide a different warning before the FDA itself ordered it.

The question presented is:

Whether the Third Circuit accurately assessed the record evidence in concluding that Merck was not entitled to summary judgment on its preemption defense because the company had not sufficiently shown that the FDA would have rejected a properly worded warning about atypical femoral fractures.

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INTEREST OF *AMICUS CURIAE* [1]

The Cato Institute is a nonpartisan public policy research foundation dedicated to advancing individual liberty, free markets, and limited government. Cato's Robert A. Levy Center for Constitutional Studies helps restore the principles of constitutional government that are the foundation of liberty. To those ends, Cato holds conferences and publishes books, studies, and the annual *Cato Supreme Court Review*.

This case interests Cato because liberty is best preserved by enforcing the Constitution's separation of powers, constraints on legislative and executive action, and respect for the dual sovereignty federalism embodied in the Framer's design. Cato also has an interest in challenging government overreach that interferes with tort law and in protecting doctor and consumer access to information that allows people to make informed choices about medical care.

INTRODUCTION

This case turns on whether agency action rejecting a misleading proposed drug label warning – one that misstated, minimized, and sought to deflect blame for the risk of atypical femoral fractures – preempts state-law claims for failure to provide an accurate and proper warning of the true risk.

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[1] No counsel for a party authored this brief in whole or in part, nor did any person or entity, other than *amicus* or its counsel, make a monetary contribution intended to fund the preparation or submission of this brief. This brief is submitted pursuant to the written blanket consent of all parties, on file with this Court.

The background law for this case is the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S. § 301, *et seq.*, which, since its enactment in 1938, has regulated prescription drugs and their labeling. Despite amendments and expansions of FDA authority, Congress expressly has preserved the "widely available state rights of action * * * for injured consumers" "t[a]k[ing] care to preserve state law." *Wyeth v. Levine*, 555 U.S. 555, 567, 574 (2009). Specifically, the Act preempts state law concerning drug labeling only "upon 'direct and positive conflict' with the FDCA." *Id.* at 567 (quoting Drug Amendments of 1968, Pub. L. No. 87-781, § 202, 76 Stat. 780, 793).

Petitioner Merck manufactures Fosamax, a bisphosphonate, commonly used to treat osteoporosis. JA192. The drug works to inhibit natural bone loss that can lead to osteoporosis, but the drug also slows bone repair, which, over time, can lead to a "debilitating fracture in which the thigh bone, or femur, often breaks in two" without any preceding significant trauma or stress. JA288-89, 292. Such fractures are called atypical femoral fractures ("AFFs").

As reports continued to accumulate linking Fosamax use to AFFs, Merck, after some prodding by the FDA, submitted proposed label changes addressing the risk, albeit in a questionable and misleading manner that downplayed the risk by referring to innocuous sounding "stress fractures" and suggesting alternate causalities other than Fosamax. Pet. App. 14a-16a. The FDA rejected the proposed warning in a Complete Response Letter, stating that "[i]dentification of 'stress fractures' may not be clearly related to the atypical subtrochanteric fractures

that have been reported in the literature. Discussion of the risk factors for stress fractures is not warranted and is not adequately supported by the available literature and post-marketing adverse event reporting." Pet. App. 18a-19a.

Merck did not resubmit revised language for a proposed warning, but the FDA itself eventually announced that it would require all bisphosphonate manufacturers to warn against AFFs. Pet. App. 20a-22a. When petitioner proposed to revise the language drafted by the FDA, adding back references to "stress fractures," the FDA again rejected such revisions, explaining that " 'the term "stress fracture" was considered and not accepted. The Division believes that for most practitioners, the term "stress fracture" represents a minor fracture and this would contradict the seriousness of the atypical femoral fractures associated with bisphosphonate use.' " Pet. App. 22a-23a.

Respondents, a class of individuals who took Fosamax and suffered AFFs between 1999 and 2010, sued Merck claiming petitioner's failure to add an earlier warning of the risk of AFFs caused their injuries. Pet. App. 75a-95a. The district court granted summary judgment to petitioner on the ground that respondents' failure-to-warn claims were preempted because the FDA would not have permitted Merck to add an earlier warning against AFFs. Pet. App.113a-152, 168a-174a.

On appeal to the Third Circuit, the court of appeals quite sensibly held, under current jurisprudence, that it is a factual question whether the FDA's rejection of the misleading proposed warning is predictive of whether the agency *would have* rejected an

accurate warning, thereby preempting any state-law claims. Pet. App. 4a-5a.

Amicus agrees with respondents that, using conventional preemption analysis from *Wyeth v. Levine*, 555 U.S. 555 (2009), and *PLIVA, Inc. v. Mensing*, 564 U.S. 604 (2011), the judgment below was correct in denying summary judgment to petitioner Merck. The FDA's rejection of Merck's defective and misleading proposed warning provides no "clear evidence" that it would also have rejected or rescinded a properly worded warning like the one it ultimately required for the class of drugs at issue in this case. Resp. Br. 25-26, 34-50.

Amicus submits this brief, however, to set forth a more straight-forward alternative ground for affirming the decision below: speculation about what the FDA might have done regarding a warning not presented to it does not constitute properly enacted and directly conflicting "Law[] of the United States" entitled to preemptive effect as the "supreme Law of the Land" under the Supremacy Clause. U.S. CONST., Art. VI, cl. 2.

The only relevant "Law" in this case, the FDCA, 21 U.S.C. § 301, *et seq.*, and its amendments, does not contain an express preemption provision applicable to prescription drug labels or the state-law failure-to-warn claims at issue here. Nor does the statute expressly delegate to the FDA the discretion to decide whether and how much state law to preempt when fulfilling the agency's drug-label-related duties under the Act. Indeed, as Congress periodically amended the Act it took pains to disclaim preemption except in the case of a "direct and positive conflict" between the

amendments and a provision of state law. 76 Stat. 780, 793.

Returning to constitutional provisions and principles regarding federal-law supremacy, the nature of federal "Law," and state sovereignty amply supports respondents in this case. The reserved and preexisting authority of the States should not be trumped by inapt speculation regarding what an agency would have done in different circumstances. If agency action is to be deemed preemptive of state law, it must, at a minimum, have directly addressed the conduct in question and directly and positively conflicted with conduct required by state law. Speculation about what conflicting decision the FDA *might have made* in different circumstances that it did not expressly address generates neither a positive nor a direct conflict with state law and does not constitute constitutionally adequate federal "Law" entitled to preemptive force.

SUMMARY OF ARGUMENT

1. Preemption of state law under the Supremacy Clause first and foremost requires the existence of federal "Law" that is said to supersede state law. As explained by Justice Thomas in *Levine*, such a supreme law must be constitutionally enacted in the manner required of all federal laws – by Congress, through the procedures of bicameralism and presentment. In this case, the relevant congressionally enacted "Law" contains no provision expressly preempting state tort law regarding drug label warnings. And while that law also delegates rulemaking power to the FDA, it does not delegate to the FDA the

authority, in the drug labeling context, to preempt state law on its own initiative.

2. Delegated general rulemaking authority alone is insufficient to claim supremacy over state law. While Congress could pass a statute preempting a field within congressional authority to regulate, mere delegation of rulemaking authority does not by itself result in supreme law that would preempt state law. Agencies may execute federal law with greater or lesser discretion, but it is the underlying law itself that carries (or does not carry) preemptive force via the Supremacy Clause. Insofar as the underlying law fails to make the critical preemptive choice of whether and how far to supersede state law, or even to direct the agency itself to flesh out such preemptive choices pursuant to suitable statutory guidance, subsequent agency action cannot preempt on its own. Even valid agency regulations are not law in the constitutional sense but are merely the fleshing out of congressionally enacted law. To the extent that an agency had authority to *create* "Law" via regulation, that would itself violate the constitutional allocation of power among the executive and legislative branches, an issue with which this Court is now grappling in *Gundy v. United States*, No. 17-6086 (argued Oct. 2, 2018).

Even assuming properly delegated authority to an agency to enact rules having the force and status of "Law" via procedures and legislative standards established by Congress, subsidiary agency actions would not necessarily constitute Law entitled to preemptive supremacy. Agency interpretations, sub-regulatory guidance, or discrete ministerial decisions – such as

rejecting a proposed warning for inaccurate and misleading content – are not themselves law but must be traced back to their original source of authority to determine their preemptive effect. *Levine*, 555 U.S. at 587-88, 600-01 (Thomas, J., concurring in the judgment). Speculation regarding what an agency might have done under different circumstances is yet further removed from anything resembling "supreme Law" entitled to preemptive effect.

The decision below in this case is correct under current or alternative jurisprudence and, if anything, too easily accepts the possibility of preemption. The FDA's rejection of Merck's inaccurate proposed warning was not itself "Law" in direct and positive conflict with an obligation for Merck to provide a different and more accurate warning, and thus could not preempt state law imposing liability for failure to provide such a proper warning. Furthermore, it is not even the FDA's action itself that is argued to preempt the state-law claims here, but rather the dubious inference that rejection of the deficient proposed warning predicted subsequent rejection of any further, properly worded, warning not imposed by the FDA itself. Such flawed speculation that the FDA intended to preempt the field while it pondered its next move, like attempts to read the tea leaves of congressional purposes and objectives, is not "Law" or even in the proximity of "Law" qualifying for supremacy under the Constitution.

3. Finally, allowing the inferential claims of supremacy and preemption proposed by petitioner would inevitably be subject to manipulation and abuse. Here, for example, Merck elected to submit a

proposed warning as a "Prior Approval Supplement" ("PAS") needing pre-approval by the FDA rather than immediately adopting a warning subject to subsequent review, as it could have done under the "changes being effected" or "CBE" process. Resp. Br. 4-5, 11-12. That itself introduced a period of delay during which sales of Fosamax would remain undeterred by a more accurate warning.

Compounding its procedural delay, Merck then misstated and minimized the risk through overinclusion of additional and more minor adverse effects – ordinary stress fractures – thereby making the danger seem less severe and masking the correlation between Fosamax and the more specific, serious, and narrow risk of AFFs. Resp. Br. 12 (setting forth Merck's proposed warning). Merck further sought to minimize and deflect the risk by discussing unsupported alternative causalities to imply that its drug was not a significant cause of the risk in question.

The FDA correctly rejected such inaccurate and misleading efforts, but at the cost of (a) further delay and uncertainty regarding the risk of AFFs and (b) further delay in adoption of the stronger and more specific warning eventually required by the FDA. Resp. Br. 15-18. Had Merck at the outset simply adopted a proper warning through the CBE process, doctors and patients would have had more timely warnings and the ability to monitor or minimize the risk by reducing or eliminating long-term consumption of Fosamax.

Merck now seeks to benefit not merely from the delay it caused by proposing a defective warning, but further by claiming that the FDA's rejection of the

inadequate and misleading warning necessarily implies that the agency would have rejected an accurate warning. That is an abuse of preemption doctrine, pure and simple. Such tactics would serve as a roadmap for future manipulation if Merck's approach to preemption were adopted by this Court.

ARGUMENT

I. Preemption of State Law Depends on Conflict with Federal Law Entitled to Supremacy.

A. Federal Law Entitled to Supremacy Must Be Enacted by the Legislative Branch.

As Justice Thomas, concurring in the judgment, explained in *Levine*, 555 U.S. at 582-88, preemption is a function of the Supremacy Clause, which provides:

> This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any state to the Contrary notwithstanding.

U.S. CONST., Art. VI, cl. 2. Preemption thus depends on the existence of properly enacted federal "Law" prohibiting or irreconcilably conflicting with state law. *Levine*, 555 U.S. at 585-86 (Thomas, J., concur-

ring in the judgment); *Williamson v. Mazda Motor of America, Inc.*, 562 U.S. 323, 340 (2011) (Thomas, J., concurring in the judgment).

This fundamental restraint on preemption – insisting that it be tied to "Law" properly enacted pursuant to the Constitution, recognizes the pre-existing sovereignty of the States, the intentional limits on the powers of the federal government, and the important procedural hurdles of bicameralism and presentment from Article I, § 7, cls.2-3, placed in the path of the exercise of federal power. *INS v. Chadha*, 462 U.S. 919, 945-46, 951, 959 (1983). Accordingly, "in order to protect the delicate balance of power mandated by the Constitution, the Supremacy Clause must operate only in accordance with its terms." *Levine*, 555 U.S. at 585 (Thomas, J., concurring in the judgment).

In this case there is no serious dispute that nothing in the FDCA or its amendments expressly preempts state tort law regarding drug warnings, or that the Act was designed to coexist with such state law. Resp. Br. 3-7. Likewise, there is no dispute that nothing in the Act or the regulations thereunder is in direct and positive conflict with a failure-to-warn claim given that drug companies may unilaterally add a warning to their labels, subject to *post hoc* review by the FDA. 21 C.F.R. § 314.70(c)(6)(iii)(A).

The source of alleged conflict here and in similar cases comes not from a statutory command enacted by Congress or from direct FDA rulemaking, but from a hypothetical future decision by the FDA that supposedly would have prohibited a proper warning as required by state law. The ultimate source of alleged preemption is thus the implausible *inference* that, be-

cause the FDA rejected Merck's initial misleading warning, *any* further warning would have been rejected.

However far the claim of preemption "wander[ed]" from the statutory text in *Levine*, 555 U.S. at 583 (Thomas, J., concurring in the judgment), the claim in this case goes well over the horizon of any statutory connection. It is not Congress's nebulous purposes and objectives we are discussing here, or even the expressly stated, but new and non-binding, agency purpose at issue in *Levine*. 555 U.S. at 575-79 (discussing and rejecting agency preamble claiming that approved labels constitute a ceiling as well as a floor). Rather, preemption here is being inferred from dubious speculation that the agency had the unspoken purpose and objective to preempt *all* future warnings based merely on its rejection of Merck's defective warning. Just as "[c]ongressional and agency musings * * * do not satisfy the Article I, § 7, requirements for enactment of federal law," 555 U.S. at 587 (Thomas, J., concurring in the judgment), surely speculation concerning what the FDA might have done regarding a warning that was not before it does not qualify as federal law capable of preempting state law under the Supremacy Clause. And even if it were factually plausible, such implied agency intent to bar all subsequent warnings related to a class of risks is not "Law" and does not reflect or execute any statutory command adopted by Congress.[2]

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[2] As in *Levine*, this case does not raise any questions concerning an express agency regulation purporting to forbid manufacturers from adding warnings under particular circumstances. 555 U.S. at 576; *id*. at 583 (Breyer, J., concurring). Such a reg-

B. Congress Has Not Delegated to the FDA Authority to Preempt State Law.

A further problem with the purported preemptive effect of speculation regarding future FDA action is that Congress has not delegated to the FDA preemptive discretion in connection with prescription drug labels. Unlike with medical devices or in other statutes, where Congress has included preemption clauses and directed the agency to define the scope of such preemption, here Congress made no such grant of authority.[3] This Court in *Levine* already has rejected the FDA's claim of power to expand the preemptive scope of its drug labelling authority to make it a ceiling as well as a floor, 555 U.S. at 574-75. Absent such express authority in the statute and a guiding principle reconciling state and federal interests, the FDA would have no discernable standards by which to measure any assertion of preemptive supremacy and would essentially be making its own law in an area of constitutional sensitivity.

Not only would such intrusive law be imposed without the protections of bicameralism and presentment, it would likewise violate the separation of

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ulation, if adopted through proper procedures and reviewed for consistency with the underlying statute and other constitutional constraints, might well have enough connection with the FDCA to be entitled to preemptive force. Here, no regulation or any other agency action precluded Merck from curing the defects in its proposed warning identified by the FDA and resubmitting, or even implementing directly through CBE procedures, a warning such as the one ultimately approved.

[3] *See Levine*, 555 U.S. at 576 & n. 9 (giving examples of statutes expressly authorizing agencies to preempt state law).

powers principles underlying the non-delegation doctrine. *See*, *e.g.*, *Department of Transp. v. Association of Am. R.R.,* 135 S. Ct. 1225, 1244 (2015) (Thomas, J., concurring) ("[T]he separation of powers is, in part, what supports our enduring conviction that the Vesting Clauses are exclusive and that the branch in which a power is vested may not give it up or otherwise reallocate it."); *see also Whitman v. American Trucking Ass'ns*, 531 U.S. 457, 486-87 (2001) (Thomas, J., concurring) ("I am not convinced that the intelligible principle doctrine serves to prevent all cessions of legislative power. I believe that there are cases in which the principle is intelligible and yet the significance of the delegated decision is simply too great for the decision to be called anything other than 'legislative.'"). And where the alleged preemption comes from speculative inferences of what the FDA might have done in different circumstances, rather than from an express and specific assertion of preemption of a particular warning required by the State, the delegation concerns multiply even further.

Any suggestion that the FDA has implicitly preempted a state-law claim for failure to warn should be viewed with deep skepticism in order to avoid thorny constitutional problems of delegation of legislative authority. Surely the decision to supersede the authority of sovereign States is fundamentally legislative in nature and, if permissible at all, *Whitman*, 531 U.S. at 487 (Thomas, J., concurring),

requires an express delegation of such authority and significant direction regarding its exercise.[4]

II. A Broad Preemptive Reading Here Would Invite Abuse.

In addition to distorting the constitutional justification for preemption, the preemption theory proposed by Petitioner is subject to manipulation and abuse. If the FDA's rejection of a defective proposed warning can have preemptive force regarding any and all alternative warnings that could have and should have been used, then every drug company would have an incentive to propose warnings that are designed to be rejected and cause delay. This case is the perfect example.

Functionally, petitioner's theory is that any tangential proposed warning relating to a broadly defined risk is enough to preempt failure-to-warn

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[4] At a minimum, a strict test of impossibility should be applied where the only claim of preemption is inconsistency with agency action not even embodied in formal rulemaking. And even then, the supposedly preemptive directive should be explicit in its preemptive intent and well-grounded in the agency's statutory authority. In this case, of course, even if there were unequivocal statements forbidding Merck to adopt any revised warning at all, regardless of content, Merck could still comply with both state and federal law by suspending sales of its drug pending further investigation of the emerging risks. As Justice Thomas has recognized, *Levine*, 555 U.S. at 592-93 (Thomas, J., concurring in the judgment), the FDCA does not create a free-standing right to sell prescription drugs so long as their label is approved by the FDA. That is the inevitable implication of *Levine*'s conclusion that the labelling requirements of the FDCA set a floor, not a ceiling, and its rejection of the FDA's assertion to the contrary.

claims for any related risk until the FDA itself comes up with an adequate warning. Indeed, it is precisely because the FDA found Merck's warning defective that Merck now claims immunity from suit for its failure to propose a better warning. One might suspect – and a jury could certainly find – that Merck sought pre-approval using a defective warning precisely to delay the time when a more effective warning – likely to reduce the use of Fosamax – was put in place.

For example, while Merck had ample information and could have used the CBE process immediately to adopt a warning comparable to the one ultimately drafted by the FDA, it instead chose the slower route of proposing a warning under the PAS process and waiting for the FDA to react. Furthermore, the warning it then proposed was both deficient and self-serving in several ways. First, by repeatedly describing the relevant risk as involving stress fractures, Merck's proposed warning downplayed the severity of the danger and would have reduced the effectiveness of the warning and hence the impact on sales. The FDA recognized the misleading quality of the language Merck proffered when later rejecting its attempts to reincorporate such language into the warning eventually required by the FDA. Pet. App. 22a-23a

Second, the overbroad description of the risk as involving stress fractures allowed Merck to mask the actual correlation between Fosamax and AFFs by including a much larger group of adverse events that had little or nothing to do with Fosamax. By substantially expanding the events to include such more

common types of mild fractures, Merck could pretend that the correlation between all fractures and Fosamax was weak. Of course, when the literature and the studies were reviewed with a narrower focus on the particular and severe AFFs, the data told a more troubling story regarding the risk associated with long-term use of Fosamax. *See* Pet. Br. 14 (discussing task force's reassessment of prior studies focusing on narrowly defined AFFs). The consequence of using an improperly broad category of adverse events is that it made it more difficult for the FDA to evaluate the need for a warning, made it less likely that the FDA would approve the flawed warning, and ensured, at a minimum, further delay. Not surprisingly, all this inured to the commercial benefit of Merck by delaying any loss of sales that would come from adoption of an effective warning.

Third, Merck also included a disingenuous paragraph listing a string of alternate causalities for stress fractures (though not for the more severe AFFs) in a bid to again minimize the risk posed by its drug. Such minimization would again diminish the effectiveness of the proposed warning and, at a minimum, potentially delay a patient going off Fosamax while such other possibilities were investigated. As the FDA noted when rejecting Merck's proposed warning, the misleading discussion of alternate causalities had no basis in the literature.

Each of these factors – using the slower PAS process rather than the immediate CBE process; using misleading language to suggest minor risk, to mask proper analysis of the actual risk, and to distract from the risk of its drug by proposing alternate cau-

salities; failing to correct the identified deficiencies in response to the FDA's Complete Decision Letter; and then attempting to reincorporate its misleading language into the FDA's own proposed warning – raises a disturbing inference of Merck's having gamed the system. Certainly, a jury could find that Merck submitted a defective and misleading warning in order to cause delay, sabotage the likelihood of approval, and undermine any potential warning that might be approved, all while preserving a claim of preemption.

If preemption is found here, then the proliferation of proposed warnings designed to obfuscate or to be rejected and thereby delay adoption of a stronger warning would create a win-win for the drug companies, but unfortunately a lose-lose for state law and the consumers such law seeks to protect.

CONCLUSION

For the foregoing reasons, this Court should affirm the judgment of the court of appeals.

Respectfully submitted,

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