

**ON DRUGS:
RENOVATING IMPOSSIBILITY PREEMPTION**

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ABSTRACT

Preemption issues permeate prescription-drug safety litigation. Despite the volume of precedent and the frequency with which failure-to-warn claims and impossibility preemption defenses arise in individual and mass tort litigation, procedural issues about divining meaning and doctrinal issues about the presumption against preemption’s interpretive role persist. This Essay examines these questions in light of Merck v. Albrecht, currently pending before the Supreme Court, and suggests that this case presents an opportunity to make some minor but salutary renovations to drug preemption doctrine.

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INTRODUCTION

This Essay questions the once and future role of litigation and preemption in the regulation of prescription drugs. It does so by examining the venerable presumption against preemption in light of the Supreme Court’s grant of certiorari in *Merck v. Albrecht*, an appeal from the *Fosamax*® MDL.¹ The impossibility preemption issues in this case present an opportunity to reexamine the jurisprudential presumption against preemption and, I submit here, to refresh it.

The *Fosamax* MDL brings preemption, litigation remedies, and the presumption against preemption squarely before the Supreme Court in a narrow factual context. The case presents the question whether the FDA’s “rejection” of a manufacturer’s proposed warning automatically preempts state-law failure-to-warn claims at summary judgment, or whether it creates a jury issue about the scope and basis of the FDA’s rejection.² The Third Circuit, preserving the issue for the jury, emphasized that *Wyeth v. Levine*’s “clear-evidence test” for impossibility preemption is a “‘demanding defense’ meant to represent a longstanding ‘presumption against pre-emption.’”³ Petitioner, Respondent, amici, and the Court’s own jurisprudence disagree on what role the presumption should play in preemption analysis.⁴

Preemption issues reverberate in prescription drug litigation far beyond the *Fosamax* MDL. But with *Albrecht* as an illustration, this Essay argues that pharmaceutical preemption doctrine would benefit from a more tailored and precise application of the presumption against preemption – a renovation of preemption analysis.⁵ First, I propose that the presumption against preemption buttresses the “clear evidence” standard for impossibility preemption issues in failure-to-warn claims. Next, I argue that the presumption should apply to factual disputes about the circumstances supporting impossibility preemption. And on a broader scale, I propose a presumption that Congress does not intend to

¹ *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 286 (3d Cir. 2017), *cert. granted sub nom. Merck Sharp & Dohme Corp. v. Albrecht*, No. 17-290, 2018 WL 3148288 (U.S. June 28, 2018).

² *Albrecht*, 2017 WL 3701808 (U.S. Aug. 22, 2017) (Petition for writ of certiorari).

³ *In re Fosamax*, 852 F.3d 268, 286 (3d Cir. 2017).

⁴ *See generally*, Elizabeth Y. McCuskey, *Body of Preemption: Health Law Traditions and the Presumption against Preemption*, 89 *TEMPLE L. REV.* 95 (2016).

⁵ *See id.*

displace historic state remedies for drug injury without clearly saying so, focusing on the role of remedy to account for the evolving overlap in federal and state police powers over health and to more precisely calibrate the federalism values inherent in the remedy-regulation relationship.⁶

I. THE HOUSE OF DRUG PREEMPTION JURISPRUDENCE

The Supreme Court has decided so many FDA preemption cases that drug preemption has taken on a life of its own, while also contributing heavily to the general body of preemption jurisprudence. The house that drug preemption built rests on a familiar foundation of preemption doctrine, but expands into a distinct doctrine of its own.

A. Foundations of Preemption

“The pharmaceutical drug industry has been heavily regulated” by federal statute “at least since 1906,” resulting in “a traditional, comprehensive regulatory regime.”⁷ That federal statute – the Federal Food, Drug, & Cosmetic Act (FDCA) – has expanded with numerous amendments and corollaries over the intervening century. State tort historically has supplied the *remedy* for anyone injured by medical products – or any other negligence.⁸ But injury *prevention* through regulation has a long history of federal intervention.

Where state and federal laws overlap, preemption doctrine manages the relationship between the two.⁹ The Constitution’s Supremacy Clause gives duly enacted federal law the “supreme” —or preemptive—power to displace conflicting state laws.¹⁰ Congress’s intent to preempt state laws

⁶ Cf. Elizabeth Y. McCuskey, *On Drugs: Preemption, Presumption, & Remedy*, 38 J. LEGAL. MED. __ (forthcoming 2018).

⁷ *Sorrell v. IMS Health Inc.*, 564 U.S. 552, 586 (2011) (Breyer, J., dissenting).

⁸ Patricia J. Zettler, *Toward Coherent Federal Oversight of Medicine*, 52 SAN DIEGO L. REV. 427, 427 (2015).

⁹ Elizabeth Y. McCuskey, *Body of Preemption: Health Law Traditions and the Presumption against Preemption*, 89 TEMPLE L. REV. 95 (2017).

¹⁰ U.S. CONST. art. VI, cl. 2.; *see generally*, *Preemption*, BLACK’S LAW DICTIONARY (10th ed. 2014) (“The principle (derived from the Supremacy Clause) that a federal law can supersede or supplant any inconsistent state law or regulation.”); *see also* Caleb Nelson, *Preemption*, 86 VA. L. REV. 225, 225 n.3 (2000); Stephen A. Gardbaum, *The Nature of Preemption*, 79 CORNELL L. REV. 767, 768 (1994).

is the ultimate touchstone for preemption analysis.¹¹ Congress may explicitly state its intent to preempt, but in the absence of an explicit statement from Congress, federal law preempts state law if Congress's intent to do so may fairly be implied.¹²

The Court has developed a detailed taxonomy of implied preemptions, including conflict preemption and field preemption.¹³ Conflict preemption arises where state and federal law requirements conflict with each other, forcing one to give way. Conflict preemption itself can arise in two ways: where it is impossible to comply with both federal and state laws,¹⁴ or where state law “stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.”¹⁵ The first form of conflict preemption is known as “impossibility” preemption,¹⁶ and the second as “obstacle” preemption.¹⁷ Within this taxonomy, the allegedly preemptive federal law can come from numerous sources, most frequently federal statutes (which I refer to here as statutory preemption), and administrative agency actions (which I and other scholars refer to as agency preemption).¹⁸

Through these iterations, the Supreme Court has built upon the same “two cornerstones of [] pre-emption jurisprudence.”¹⁹ First, “the purpose of Congress is the ultimate touchstone in every pre-emption case.”²⁰ 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

11 *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996); *Retail Clerks Int’l Ass’n, Local 1625 v. Schermerhorn*, 375 U.S. 96, 103 (1963).

12 *Geier v. Am. Honda Motor Co., Inc.*, 529 U.S. 861, 883–86 (2000).

¹³ See generally *McCuskey*, *supra* note 5, at 96.

14 *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 (1990).

15 *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947); see also *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

16 *Freightliner Corp. v. Myrick*, 514 U.S. 280 (1995).

17 *Hines*, 312 U.S. at 67.

¹⁸ See, e.g., Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 523 (2012); Nina A. Mendelson, *A Presumption Against Agency Preemption*, 102 NW. U. L. REV. 695 (2008); Elizabeth Y. McCuskey, *Agency Imprimatur & Health Reform Preemption*, 78 OHIO ST. L. J. 1099 (2017).

¹⁹ *Wyeth v. Levine*, 555 U.S. 555, 565 (2009).

²⁰ *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996).

unless that was the clear and manifest purpose of Congress.”²¹ Although longstanding, this presumption against preemption has produced some inconsistent applications,²² and recently has been questioned by three sitting Justices²³ and bolstered by four others.²⁴

B. Preemption & Prescription Drug Regulation

A complex body of statutory and administrative laws govern prescription drugs in the United States, reflecting tension among innovation, economy, and safety.²⁵ In building its complex regulatory regimes for brand and generic drugs, Congress has not been a model of legislative clarity when it comes to preemption of state law remedies.²⁶ The frequent contact between this federal regulatory scheme and state products liability tort suits has produced a drug preemption jurisprudence

The Federal Food, Drug, & Cosmetic Act (FDCA) and its many amendments supply the statutory infrastructure.²⁷ The FDCA requires that all new drugs receive FDA approval before being sold,²⁸ and that the FDA’s approval rest on clinical evidence of each drug’s safety and efficacy.²⁹ Before marketing, the manufacturer of a new drug must submit a New Drug Application (NDA), providing both the clinical evidence and proposed language for its labeling on indications, instructions, and warnings.³⁰ If the FDA approves a new drug for sale, the agency must sign off on all label text, too.³¹ The Hatch-Waxman Amendments to the FDCA created an Abbreviated New Drug

²¹ *Id.* at 485, 116 S.Ct. 2240 (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947)); *Levine*, 555 U.S. at 565 (same).

²² See McCuskey, *supra* note 4, at 99-101.

²³ Justice Thomas’s opinion in *PLIVA, Inc. v. Mensing*, specifically rejected the presumption, joined by Chief Justice Roberts and Justices Alito and Scalia. 564 U.S. 604, 621-22 (2011). Justice Kennedy joined all parts of Justice Thomas’s opinion *except* the section rejecting the constitutional preemption.

²⁴ In their *Mensing* dissent, Justices Sotomayor, Ginsburg, Breyer, and Kagan directly supported the constitutional presumption. *Id.* at 626 (Sotomayor, J., dissenting).

²⁵ Patricia Zettler, *Pharmaceutical Federalism*, 92 IND. L. J. 845, 857-60 (2017).

²⁶ McCuskey, *supra* note 18, at 106, 149.

²⁷ 21 U.S.C. § 301 *et seq.*

²⁸ *Id.* § 355(a).

²⁹ *Id.* § 355(d).

³⁰ *Id.* § 355(b)(1)(F); 21 C.F.R. § 201.57(a).

³¹ 21 C.F.R. § 314.105(b).

Application (ANDA) process for approval to market generic forms of already-approved drugs.³² The FDA may approve a generic for sale as long as the manufacturer proves equivalence to its brand-name counterpart,³³ and employs a label identical to the brand's.³⁴

After initial approval, the FDCA authorizes the FDA to approve and mandate changes to a drug's labeling in response to evolving evidence.³⁵ Further, under the 2007 amendments to the FDCA, the FDA must act to initiate label changes once the agency becomes aware of a serious safety risk.³⁶

The FDA's initial and ongoing authority over labeling does not relieve the manufacturer of "responsibility" to "maintain its label" according to "existing requirements."³⁷ The Changes Being Effected (CBE) procedure allows the manufacturer of an approved, brand-name prescription drug to respond to newly-acquired safety information by unilaterally strengthening or adding to its label's safety information.³⁸ With a CBE filing, the manufacturer simultaneously changes its label and notifies the FDA of the change; the FDA may then reject the manufacturer's change.³⁹ Generic drug manufacturers, however, may initiate a CBE for their labels only after the brand makes a label change, and only to the extent that the generics CBE will update the label to match.⁴⁰ Alternatively, a manufacturer may seek the FDA's approval before making significant changes to its label via the Prior Approval Supplement (PAS) process.⁴¹

³² See 21 U.S.C. § 355(j)

³³ *Id.* § 355(j)(2)(A).

³⁴ *Id.*; 21 C.F.R. §§ 314.94 & 314.127.

³⁵ 21 U.S.C. § 355(o)(4); 21 C.F.R. § 315.93. See also *Wyeth v. Levine*, 555 U.S. at 569 (explaining how regulations account for the accumulation of data over the life of an approved drug).

³⁶ 21 U.S.C. § 355(o)(4).

³⁷ 21 U.S.C. § 355(o)(4)(l). See *Wyeth v. Levine*, 555 U.S. at 517, 579.

³⁸ 21 C.F.R. § 314.70(c)(6)(iii).

³⁹ *Id.*

⁴⁰ See 21 C.F.R. § 314.94(a)(8)(iv); *PLIVA v. Mensing*, 564 U.S. at 614-15 (explaining FDA's interpretation of the CBE regulation applied to generics). Congress considered, but did not ultimately pass, a bill that would have permitted generic manufacturers to make the same kind of unilateral CBE changes as brand-name drugs. See Patient Safety and Generic Labeling Improvement Act, S. 2295, 112th Cong. (2012); <https://www.govtrack.us/congress/bills/112/s2295>.

⁴¹ 21 C.F.R. § 314.70(b).

Regulatory pre-approval by the FDA establishes baselines for the safety and efficacy of available drugs, but provides no guarantee, and contributes to the cost of innovation.⁴² Despite the intricate and costly regulatory infrastructure at the FDA, approved drugs still injure or kill many thousands of people per year.⁴³ While the FDA can punish manufacturers and take steps to prevent future injuries,⁴⁴ the agency does not have jurisdiction to directly redress harms that patients suffer and its enabling statute does not grant a federal private remedy.⁴⁵ That is the historic job of state-law litigation remedies, particularly products liability. There are thousands of products liability actions currently pending against drug manufactures, many of which are consolidated into federal Multi-District Litigation (MDL) actions.⁴⁶

Congress over the years has not provided a private right of action for its many drug-related provisions in the FDCA. So FDA-approved drugs are the subjects of products liability litigation pursuant to state-law remedies. State tort theories of liability for prescription drug manufacturers typically focus on defective product design, defective manufacture, defective label design, and failure to warn.⁴⁷

The Supreme Court has addressed preemption issues in most of these theories,⁴⁸ slowly piecing together the preemption puzzle for drug injury

42 Rachel Sachs, *Prizing Insurance: Prescription Drug Insurance as Innovation Incentive*, 165 ANNALS OF INTERNAL MED. 871 (2016); see also Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003).

43 Eric Lindenfeld & Jasper L. Tran, *Beyond Preemption of Generic Drug Claims*, 45 SW. L. REV. 101 (2015).

44 *FDA Requires Strong Warnings for Opioid Analgesics, Prescription Opioid Cough Products, and Benzodiazepine Labeling Related to Serious Risks and Death from Combined Use*, FDA (Aug. 31, 2016), <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm518697.htm> (announcing new warnings for opioids in two therapeutic classes).

45 *Merrell Dow Pharmaceuticals v. Thompson*, 478 U.S. 804, 811 (1986).

46 See, e.g., *In re Abilify (Aripirazole) Prod. Liab. Litig.*, 232 F. Supp. 3d 1342 (J.P.M.L. 2016).

47 Eric Lindenfeld & Jasper L. Tran, *Beyond Preemption of Generic Drug Claims*, 45 SW. L. REV. 101 (2015).

48 See, e.g., *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 350 (2001) (considering claims about medical devices). *Buckman* preemption has been extended to the prescription drug context. See, e.g., *Wyeth v. Levine*, 555 U.S. 555, 609, 129 S. Ct. 1187, 1220, 173 L. Ed. 2d 51 (2009) (Alito, J., dissenting) (citing *Buckman* in a drug-preemption case for the proposition that "Where the FDA determines, in

litigation.⁴⁹ The most prevalent combination of tort theory and preemption doctrine in prescription drug cases continues to be failure-to-warn claims and impossibility conflict preemption defenses. While manufacturing and design defect claims generally have the same preemption analysis for generic and brand drugs,⁵⁰ claims challenging the adequacy of warnings have produced opposite preemption results based on the distinction in brand versus generic.⁵¹

In *Wyeth v. Levine*, the Court held that failure-to-warn claims against a brand drug maker were not preempted by the FDA's approval of its label.⁵² As applied to generic drug manufacturers, the Supreme Court held in *PLIVA v. Mensing* that failure-to-warn claims *were* preempted by the Hatch-Waxman Act and FDA regulations because the generic manufacturer may not change its label without the FDA's prior approval.⁵³ Similarly, the Supreme Court held in *Mutual Pharmaceutical Co. v. Bartlett* that the generic labeling requirements preempt state-law claims alleging design defects in a generic drug's labeling.⁵⁴ Shortly after *PLIVA* and *Bartlett*, the FDA announced a proposal to allow generic manufacturers to unilaterally strengthen their labels in some instances,⁵⁵ but this proposal has not yet been adopted and still faces political resistance.⁵⁶

accordance with its statutory mandate, that a drug is on balance "safe," our conflict pre-emption cases prohibit any State from countermanding that determination.").

⁴⁹ See McCuskey, *supra* note 6. See also McCuskey, *Agency Imprimatur & Health Reform Preemption*, 78 OHIO ST. L. J. 1099 (2017);

⁵⁰ See, e.g., *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466, 2470 (2013); *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 343–44 (2001) (preempting injury claims based on allegations of fraud in the approval process).

⁵¹ Compare *Wyeth v. Levine*, 555 U.S. 555, 581 (2009) (holding failure to warn claims against brand drugs not preempted) with *PLIVA v. Mensing*, 564 U.S. 604, (2011) (preempting failure to warn claims against generic drugs). See also Aaron S. Kesselheim et al., *Risk, Responsibility, and Generic Drugs*, 367 NEW ENG. J. MED. 1679-1681 (2012).

⁵² *Wyeth*, 555 U.S. at 581.

⁵³ *Mensing*, 564 U.S. at 626.

⁵⁴ *Mutual Pharmaceutical Co. v. Bartlett*, 570 U.S. 472, 473 (2013) ("[I]t was impossible for Mutual to comply with both its state-law duty to strengthen the warnings . . . and its federal-law duty not to alter [its] label.").

⁵⁵ See FDA, Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,985 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pts. 314, 601).

⁵⁶ See Eric Lindenfeld & Jasper L. Tran, *Beyond Preemption of Generic Drug Claims*, 45 SW. L. REV. 101, 110-112 (2015).

Even after its many trips to the Supreme Court, conflict preemption continues to play a pivotal role in drug-safety litigation and the nationwide regulatory picture for prescription drugs. Defendant manufacturers raise the preemption question early and often in litigation, and high-stakes multi-district litigation turns on its resolution. The *Fosamax*® MDL discussed at greater length in Part II may resolve thousands of failure-to-warn and products liability claims against Merck based on conflict preemption. The Supreme Court has granted certiorari to consider that resolution.

Throughout this evolution, a special presumption against preemption for state health laws has frequently framed the analysis of preemptive scope, including FDA preemption.⁵⁷ This special presumption applies to regulation under the police power and is based on a “tradition of state regulatory primacy” over citizens’ health, safety, and welfare.⁵⁸ Like other canons of statutory interpretation, courts have not applied the tradition presumption universally or consistently,⁵⁹ but often resort to it in preemption analyses involving FDA regulation.⁶⁰

II. LITIGATION IN THE HOUSE OF DRUG PREEMPTION

The Supreme Court will hear another drug preemption case during its January 2019 sitting. In *Merck, Sharpe, & Dohm v. Albrecht*, the Court granted certiorari to address what effect the FDA’s rejection of a manufacturer’s PAS should have on the analysis of impossibility preemption of state-law failure-to-warn claims.⁶¹ *Albrecht* arises in a relatively narrow factual and procedural context, but potentially brings a host of regulation and preemption issues before the Court, including: whether impossibility is a question of law or fact, whether a manufacturer must establish the FDA’s intent by “clear and convincing

⁵⁷ See McCuskey, *supra* note 18.

⁵⁸ *Id.*; see *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947); see, e.g., Ernest A. Young, “*The Ordinary Diet of the Law*”: *The Presumption Against Preemption in the Roberts Court*, 2011 SUP. CT. REV. 253, 307-08 (2011).

⁵⁹ See McCuskey, *supra* note 18.

⁶⁰ E.g., *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 475 (1996).

⁶¹ *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 286 (3d Cir. 2017), *cert. granted sub nom. Merck Sharp & Dohme Corp. v. Albrecht*, No. 17-290, 2018 WL 3148288 (U.S. June 28, 2018). Obstacle preemption (the other variant of conflict preemption) was not raised in the courts below and is not being pressed by the Merck or amici on certiorari.

evidence” to prove preemption, and, perhaps, what effect to give the longstanding presumption against preemption.

A. Impossibility Preemption through a Litigation Lens: *Merck v. Albrecht*

The *Albrecht* case is both conventional and weird. The preemption theory at its core is familiar: Plaintiffs allege that Merck should have warned them about safety risks omitted from its Fosamax label when plaintiffs took the drug. Merck argues that the FDA would have rejected – and did reject – the warning Plaintiffs wanted it to add. This is classic impossibility preemption under *Wyeth v. Levine* because defendant asserts that federal agency law would have prohibited the change that plaintiffs say state law compels.⁶² But *Albrecht* has some factual wrinkles and peculiar procedural twists.

In March 2008, Merck submitted a periodic safety update to the FDA, with studies and publications on potential links between long-term use of Fosamax and atypical femoral fractures.⁶³ The FDA, “concerned about this developing safety signal,” requested Merck’s investigations and reports about these adverse events, which Merck provided.⁶⁴ While the FDA assessed Merck’s data, Merck also submitted a PAS in September 2008, seeking approval to add warnings to its label.⁶⁵ In its formal Complete Response letter in May 2009, the FDA accepted the PAS for the “Adverse Reactions” section, but rejected it for the “Warnings & Precautions” section.⁶⁶ The parties dispute whether the FDA based its rejection on Merck’s proposed language about “stress fractures” rather than “atypical femoral fractures” (Plaintiffs’ position), or whether the FDA rejected the warning based on insufficient evidence to support a causal link between the drug and the fractures (defendant’s position).⁶⁷

In the courts below, each side mustered bits of circumstantial evidence to support its view of the FDA’s meaning in the Complete Response rejection. Within a year of the rejection, FDA convened a task force to

⁶² 555 U.S. 555 (2009).

⁶³ See *In re Fosamax*, 852 F.3d at 275.

⁶⁴ *Id.*

⁶⁵ *Id.* at 276.

⁶⁶ *Id.* at 276-77.

⁶⁷ *Id.* at 277-78.

study the issue for the whole drug class.⁶⁸ After the task force's report on "evidence of a relationship" between Fosamax use and atypical femoral fractures, the FDA required all manufacturers of bisphosphonates to include a warning in the Warnings & Precautions section.⁶⁹ The FDA asked Merck to include the FDA's specific language about atypical femoral fractures, and Merck counter-proposed its own language about "stress fractures."⁷⁰ The FDA rejected Merck's "stress fracture" language as minimizing the seriousness of the risk, and Merck ultimately implemented the FDA's language in January 2011.⁷¹ Plaintiffs point to these developments after the Complete Response rejection to suggest that the FDA did not reject the PAS on its scientific merits, but rather on its wording.

Merck argued below that its interim correspondence with the FDA, before the Complete Response rejection, suggests the FDA rejected the PAS for Warnings & Precautions because the agency did not believe the evidence at that time supported a warning. The month prior to the Complete Response, a Merck employee's notes state that an FDA representative told her by phone that FDA was working on a class-wide review of the evidence, and needed more time to decide on the Warnings & Precautions issue because "the conflicting nature of the literature does not provide a clear path forward."⁷² A follow-up e-mail from an FDA liaison to Merck stated that the agency would approve the PAS for the Adverse Reactions section, but asked Merck to "hold off on the [Warnings & Precautions] language at this time" so that FDA could decide on "language for a [Warnings & Precautions] atypical femoral fracture language, if it is warranted."⁷³ Merck points to these interim communications as evidence that the FDA based its rejection on concerns about the scientific evidence for the warning.

Factually, the impossibility question thus involves the FDA partially approving and partially rejecting Merck's request to add a proposed warning, then convening a task force and ordering Merck to add a warning proposed by the FDA that was almost the same but not identical to the one it had earlier rejected from Merck.

⁶⁸ *Id.* at 278.

⁶⁹ *Id.*

⁷⁰ *Id.* at 279.

⁷¹ *Id.*

⁷² *Id.* at 277.

⁷³ *Id.*

Procedurally, *Albrecht* comes to the Supreme Court from the Third Circuit’s reversal of summary judgment for Merck. That is not remarkable on its own, but the path to the opinion was unusual. The underlying litigation was consolidated for pre-trial in an MDL with hundreds of other cases alleging atypical femoral fractures caused by Fosamax.⁷⁴ Plaintiffs in the MDL cases all asserted some constellation of similar state-law products liability claims.⁷⁵ Merck asserted the affirmative defense of preemption throughout the litigation.⁷⁶ At summary judgment, the court “reserved decision” on the preemption issue pending development of a trial record.⁷⁷

The MDL district court convened a bellwether trial on a failure-to-warn claim, during which Merck reiterated its preemption defense in motions for judgment as a matter of law.⁷⁸ The district court again reserved decision on preemption and the jury returned a verdict for Merck, finding that the bellwether plaintiff failed to prove she suffered an atypical femoral fracture.⁷⁹ After the verdict, the district court ruled on the preemption issue raised in Merck’s motions for judgment as a matter of law, holding that the bellwether plaintiff’s claims were preempted.⁸⁰

⁷⁴ *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 787 F. Supp. 2d 1355 (J.P.M.L. 2011). MDL consolidation is now commonplace in drug-safety litigation and other mass torts. See PAUL D. RHEINGOLD, LITIGATING MASS TORT CASES, § 15.3 Drug MDLs (May 2018 update) (listing mass tort cases involving prescription drugs active as of May 2018).

⁷⁵ See *id.* Generally, failure-to-warn, defective design, negligence, breach of warranty, unjust enrichment, and violation of state deceptive trade practices statutes. See *In re Fosamax*, 852 F.3d at 280.

⁷⁶ See *In re Fosamax*, 852 F.3d at 280. Generic manufacturers also asserted preemption defenses and succeeded in having some claims against them dismissed. See *In re Fosamax (Alendronate Sodium) Prod. Liab. Litig. (No. II)*, No. CIV. 08-008 GEB-LHG, 2011 WL 5903623, at *6 (D.N.J. Nov. 21, 2011) (granting generic defendants’ motion for judgment on the pleadings because “Plaintiffs’ claims of failure to warn are squarely preempted by *Mensing*”); *In re Fosamax (Alendronate Sodium) Prod. Liab. Litig. (No. II)*, No. MDL 2243 JAP-LHG, 2012 WL 181411, at *4 (D.N.J. Jan. 17, 2012) (same).

⁷⁷ *In re Fosamax (Alendronate Sodium): Prod. Liab. Litig.*, No. 08-08 JAP LHG, 2014 WL 1266994, at *2 (D.N.J. Mar. 26, 2014).

⁷⁸ See *In re Fosamax*, 852 F.3d at 280.

⁷⁹ *Id.*

⁸⁰ *In re Fosamax*, 951 F. Supp. 2d 695, 700 (D.N.J. 2013).

The MDL court then issued an order to show cause – at Merck’s urging – ordering parties to the remaining pre-trial MDL cases to show cause why their claims should not be dismissed on preemption grounds, too.⁸¹ The court assessed responses by Merck and the remaining plaintiffs under the summary judgment standard of Rule 56, which requires the moving party to prove that no genuine issue of material fact exists and that it is entitled to judgment as a matter of law.⁸² The MDL court held that the bellwether trial established the *absence* of a genuine factual issue on preemption and shifted the burden of proving a factual issue to the pre-trial plaintiffs.⁸³ Ultimately, the MDL court found the pre-trial plaintiffs’ failure to warn claims preempted, then extended that preemption to all remaining claims, because it viewed “[t]he entire MDL [as] centered on Merck’s conduct in failing to update Fosamax’s warning label.”⁸⁴

On appeal, the Third Circuit noted these unusual procedures, admonishing the MDL court that “[a] mass tort MDL is not a class action. It is a collection of separate lawsuits that are coordinated for pretrial proceedings – and *only* pretrial proceedings.”⁸⁵ The Third Circuit went on to reverse the MDL court’s grant of summary judgment on preemption in the pre-trial cases, holding that the district court erred in shifting the burden of persuasion to plaintiffs, in holding that no genuine issue of fact existed about the reason for the FDA’s initial rejection, and in prematurely considering preemption of claims other than failure-to-warn.⁸⁶

In reversing, the Third Circuit clarified impossibility preemption doctrine under *Levine* as requiring defendants prove by “clear evidence” that the FDA would have rejected the proposed change,⁸⁷ and that, in cases of conflicting evidence, “the question of whether the FDA would have approved a plaintiff’s proposed warning is a question of fact for the jury.”⁸⁸ Neither doctrinal holding is free from controversy, though there is no circuit split on either.

⁸¹ *In re Fosamax (Alendronate Sodium): Prod. Liab. Litig.*, No. 08-08 JAP LHG, 2014 WL 1266994, at *1 (D.N.J. Mar. 26, 2014).

⁸² *Id.* at *8. See FED. R. CIV. P. 56; *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986).

⁸³ *In re Fosamax*, 2014 WL 1266994, at *8.

⁸⁴ *Id.* at *13.

⁸⁵ *In re Fosamax*, 852 F.3d at 302.

⁸⁶ *Id.*

⁸⁷ *Id.* at 284.

⁸⁸ *Id.* at 293.

The Supreme Court has taken up the preemption question, at the urging of Merck and its supporting amici. In the Supreme Court, the United States participated as amicus supporting the grant of certiorari and has filed a brief in support of Merck on the merits.⁸⁹ In its briefs, the U.S. targets the fact/law question and the ultimate conclusion in the case. The government asserts that interpretations of its administrative decisions declining label changes should be “legal questions for a court to resolve, not factual questions for a jury.”⁹⁰ Weighing in on FDA interpretation for the first time, the United States’ amicus brief states that FDA rejected Merck’s PAS based on insufficient data, not inappropriate terminology, but it introduces no new evidence or affidavits for that conclusion.⁹¹

Merck v. Albrecht encapsulates some structural issues about impossibility preemption that permeate drug-safety litigation: the procedural lens applied to preemption questions in litigation, and the once and future role of the interpretive presumption against preemption.

B. The Procedure of Preemption

1. Standards for predicting FDA decisions

Wyeth v. Levine made plain that the FDA’s CBE process represents the *possibility* that a brand-name drug manufacturer could add a tort plaintiff’s proposed warnings to its label without contradicting the FDA’s judgment.⁹² Indeed, the Court reiterated in *Levine*, it is the “central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times,” though the FDA “retains authority to reject labeling changes.”⁹³ Where a tort plaintiff alleges that a manufacturer should have included a warning that the FDA would have rejected, compliance with both state and federal directives would be an *impossibility*.⁹⁴ The affirmative defense of impossibility preemption in failure-to-warn litigation thus hinges on

⁸⁹ *Merck v. Albrecht*, 17-290, Br. for the United States as Amicus Curiae Supporting Pet’r (Sept. 20, 2018).

⁹⁰ *Merck v. Albrecht*, 17-290, Br. for the United States as Amicus Curiae (May 22, 2018).

⁹¹ *Id.* at p. 19.

⁹² *Wyeth v. Levine*, 555 U.S. 555, 568 (2009).

⁹³ *Id.* at 570-71.

⁹⁴ *Id.*

FDA rejection – either actual or hypothetical – of the additional warning.

The Court in *Levine* explained that impossibility preemption attaches where there exists “clear evidence that the FDA would not have approved a change” to the label that plaintiffs allege necessary to avoid state-law liability.⁹⁵ Because impossibility preemption is an affirmative defense, defendant bears the burdens of production and persuasion on actual impossibility, which is a “demanding” task.⁹⁶ In implementing *Levine*’s “clear evidence” language and the demands of affirmative defenses, lower courts typically have used *Levine*’s facts “as a yardstick” by which to measure each new case’s facts on FDA approval or rejection.⁹⁷ This case-by-case approach has filled in precedent with more opportunities for analogy and distinction, but done little to clarify the applicable standard. The Third Circuit in *Fosamax* explicitly held that *Levine* should be interpreted as announcing a “clear evidence” standard of proof for impossibility preemption defenses in failure-to-warn cases.⁹⁸

Connecting “clear evidence” to its analog “clear and convincing evidence” in standards of proof, the Third Circuit concluded that “for a defendant to establish a preemption defense under [*Levine*], the factfinder must conclude that it is highly probable that the FDA would not have approved a change to the drug’s label.”⁹⁹ In interpreting *Levine*’s “clear evidence” holding, the Third Circuit explained that the subjecting impossibility to an intermediate standard of proof represents the presumption against preemption and the congruously “demanding” standard for the impossibility preemption defense.¹⁰⁰

⁹⁵ *Id.* at 571.

⁹⁶ “Because pre-emption is an affirmative defense, a defendant seeking to set aside state law bears the burden to prove impossibility.” *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 634–35 (2011). See *Silkwood v. Kerr–McGee Corp.*, 464 U.S. 238, 255 (1984). It is a “demanding” defense, *Wyeth*, 555 U.S., at 573, on which a prevailing 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 (1963). The collision between federal and state law must be “inevitable,” *Florida Lime*, 373 U.S., at 143, rather than merely “hypothetical or potential” to support preemption. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982); *Gade v. National Solid Wastes Management Assn.*, 505 U.S. 88, 110, (1992) (KENNEDY, J., concurring in part and concurring in judgment). “In other words, the mere possibility of impossibility is not enough.” *Mensing*, 564 U.S. at 635.

⁹⁷ See *In re Fosamax*, 852 F.3d at 284 & nn.91-93 (surveying cases).

⁹⁸ *Id.*

⁹⁹ *In re Fosamax*, 852 F.3d at 286.

¹⁰⁰ *In re Fosamax*, 852 F.3d at 286 (citing *Levine*, 555 U.S. at 573).

Under the Third Circuit’s formulation, to succeed on a preemption defense, a manufacturer must establish that the FDA’s rejection of an additional warning is “highly probable” and thus satisfying both the plaintiff and the FDA’s demands would have been impossible.¹⁰¹

2. Fact-finding in preemption analysis

Quite a volume of discovery and factual development bear directly on establishing the probability of FDA rejection essential to the impossibility preemption defense.¹⁰² Courts facing drug preemption issues in failure-to-warn claims frequently find their analyses mired in factual disputes about the FDA’s labeling procedures, review of scientific evidence, and communications.¹⁰³ Beneath the interpretive questions about the standards for proving these impossibility facts lie meta-questions about proper allocation of the fact-finding function in preemption analysis.

While most preemption issues present “purely legal questions” about statutory interpretation and Congressional intent, what about impossibility preemption’s core inquiry into the FDA’s probable reaction to specific data? Is resolution of reasonable factual disputes about what the FDA would have decided a question of fact for a jury, or a question of law for a court? *Fosamax* held that it was properly a factual question for a jury, thus potentially bringing this question before the Supreme Court in *Merck v. Albrecht*.¹⁰⁴

¹⁰¹ *E.g.*, In re Testosterone Replacement Therapy Prod. Liab. Litig. (Coordinated Pretrial Proceedings), No. 14 C 1748, 2017 WL 1836435, at *9 (N.D. Ill. May 8, 2017) (finding that summary judgment “evidence indicates a reasonable possibility ‘that the FDA would still have determined that ‘reasonable evidence’ of a link existed—or more precisely, that the possibility of rejection was less than highly probable” and that defendant therefore failed to meet the “clear evidence” standard, quoting *Fosamax*, 852 F.3d at 298).

¹⁰² *See, e.g.*, In re Incretin-Based Therapies Prod. Liab. Litig., 721 F. App’x 580, 584 (9th Cir. 2017) (reversing MDL court’s grant of summary judgment for defendants’ on preemption, explaining “[u]ncertainty about whether the FDA considered the ‘new safety information’ and whether it would have altered the FDA’s conclusion establishes that a disputed issue of material fact should have prevented entry of summary judgment on the defendants’ preemption claim”).

¹⁰³ For example the *Levine* dissenters’ lead reason for dissenting was their disagreement that, “as a factual matter, it is demonstrably untrue that the FDA failed to consider” the risks and benefits of the intravenous administration method plaintiff challenged. *See Wyeth v. Levine*, 555 U.S. 555, 612-21 (2009) (Alito, J., dissenting).

¹⁰⁴ *In re Fosamax*, 852 F.3d at 288-293.

In many impossibility preemption cases, “characterization of the issue” as a question of fact versus law “is nondispositive” because the parties do not dispute the facts material to preemption, allowing the court to proceed on the ultimate question of law.¹⁰⁵ As the Third Circuit in *Fosamax* explained, “when no reasonable jury applying the clear-evidence standard” could “conclude that the FDA would have approved a label change,” then “the manufacturer will be entitled to judgment as a matter of law.”¹⁰⁶ For example, where the parties do not dispute that the FDA rejected a citizen petition on the same drug, same proposed warning, “virtually identical” data, a court may proceed with summary judgment as a matter of law.¹⁰⁷ This factual predicate satisfies preemption doctrine’s “clear evidence” of rejection from which “no reasonable juror” could conclude the FDA would have accepted plaintiff’s proposal, satisfying summary judgment’s standards.¹⁰⁸

In *Fosamax*, Merck and the MDL plaintiffs agreed on the factual predicate for the impossibility issue: Merck’s PAS, the FDA’s May 2009 Complete Response letter approving Merck’s “Adverse Reactions” additions but not approving the “Warnings and Precautions” proposals, the FDA’s 2010 task force report and subsequent requirement of additional “Warnings and Precautions,” Merck’s renewed proposal of “stress fracture” language, and the FDA’s rejection of “stress fracture” as minimizing the severity of risk.¹⁰⁹ But they vigorously disagree about the FDA’s intent in its May 2009 rejection, as well as the reliability of, and inferences drawn from, circumstantial evidence of that intent in the FDA’s interim communications with Merck employees.¹¹⁰

Weighing conflicting evidence and drawing inferences about FDA officials’ motivations, in the Third Circuit’s view, bear the hallmarks of factual questions entrusted to juries.¹¹¹ It emphasized that a “trial by jury” on preemption “would only be necessary in those cases where the

¹⁰⁵ *E.g.*, *Cervený v. Aventis, Inc.*, 855 F.3d 1091, 1099 (10th Cir. 2017).

¹⁰⁶ *In re Fosamax*, 852 F.3d at 282. *Accord* *Dolin v. GlaxoSmithKline LLC*, No. 17-3030, 2018 WL 4001208, at *8-9 (7th Cir. Aug. 22, 2018) (finding plaintiffs’ characterization was an “unreasonable interpretation of the discussions between the FDA and GSK” based on the factual record and granting summary judgment on defendant’s preemption defense).

¹⁰⁷ *See, e.g.*, *Cervený*, 855 F.3d at 1099.

¹⁰⁸ *Cervený*, 855 F.3d at 1099. *See also* *Reckis v. Johnson & Johnson*, 28 N.E.3d 445 (2015).

¹⁰⁹ *See In re Fosamax*, 852 F.3d at 296-98.

¹¹⁰ *Id.*

¹¹¹ *Id.* at 290-92.

evidence presented is more compelling than in [*Levine*], but no ‘smoking gun’ rejection letter from the FDA is available.”¹¹²

This view certainly may be colored by the summary judgment context in which impossibility preemption in failure-to-warn cases frequently ripens for decision. Summary judgment is designed to consider factual evidence, and permits a court to enter judgment as a matter of law only if the evidence reveals no genuine issues of material fact.¹¹³ Because preemption considers the interaction of federal and state law in a federal system, it ultimately depends on a legal judgment about whether and to what extent two sources of law conflict. Some preemption questions, however, are more cleanly questions of law than others, and the Supreme Court has held that resolving at least some questions in preemption cases should be done by juries.¹¹⁴

Impossibility preemption in the FDCA regulatory regime invites factual determinations on several levels. First, *Levine*’s impossibility preemption pits state tort law against a federal *administrative* agency action, rather than a direct conflict with *statutory* text.¹¹⁵ Statutory preemption questions lend themselves more quickly toward resolution as a matter of law in part because the tools of statutory interpretation already guide courts in gleaning meaning from Congress.¹¹⁶ Administrative preemption questions, however, can pit state tort law against a variety of agency activities and discrete circumstances. Second, the counterfactual question at the heart of failure-to-warn preemption asks not whether the FDCA prohibits the warning plaintiff seeks,¹¹⁷ but rather whether a real or hypothetical decision by the FDA

¹¹² *Id.* at 293.

¹¹³ Fed. R. Civ. P. 56.

¹¹⁴ Boyle, 487 U.S. 500, 512-14 (1988).

¹¹⁵ See Sharkey.

¹¹⁶ See generally FRANK B. CROSS, *THE THEORY AND PRACTICE OF STATUTORY INTERPRETATION* 20 (Stanford U. Press 2009); Frank H. Easterbrook, *Judicial Discretion in Statutory Interpretation*, 57 OKLA. L. REV. 1, 12 (2004); William N. Eskridge, Jr. & Philip P. Frickey, *Statutory Interpretation as Practical Reasoning*, 42 STAN. L. REV. 321, 322 (1989); James J. Brudney & Corey Ditslear, *Canons of Construction and the Elusive Quest for Neutral Reasoning*, 58 VAND. L. REV. 1, 12–14 (2005); Abbe R. Gluck & Lisa Schultz Bressman, *Statutory Interpretation from the Inside—An Empirical Study of Congressional Drafting, Delegation, and the Canons: Part I*, 65 STAN. L. REV. 901, 940 (2013).

¹¹⁷ By contrast, most impossibility preemption questions for *generic* drug manufacturers pit the statutory and regulatory “duty of sameness” directly against plaintiff’s proposed deviation, isolating a cleaner question of law. See *PLIVA v. Mensing*.

renders simultaneous compliance with the agency and state tort law *impossible*, inviting multiple layers of factual interpretation.

Yet, where a court must scrutinize the FDA's decision on a CBE, PAS, or petition – as opposed to its lack of action – the conflict arguably pits state tort law against a federal *legal* document representing an agency adjudication.¹¹⁸ The Administrative Procedure Act delegates the task of “determin[ing] the meaning or applicability of the terms of an agency action” to the reviewing court.¹¹⁹ The FDA's May 2009 Complete Response letter fairly can be characterized as an agency adjudication of Merck's PAS and therefore subject to construction by a court.¹²⁰

Even if the Supreme Court adopts this characterization of the Complete Response letter as an administrative document, that should not cut juries out of preemption entirely. Those impossibility cases that have no explicit rejection from the FDA to work against arguably require factual resolution of what the FDA most likely would have decided in a hypothetical case. This speculation, based on circumstantial evidence, reflects the characteristics of fact issues reserved for juries and does not find an analog in the Administrative Procedure Act.¹²¹ The allocation of this core impossibility preemption question as between judge and jury may thus depend on whether the FDA has written a letter, or not.

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These existential, but increasingly situation-specific questions about the procedures and standards for impossibility preemption in prescription drug cases should thus prompt some serious thought about whether this corner of preemption doctrine requires renovation, and, if so, where to start with the refresh.

¹¹⁸ See 5 U.S.C. § 551.

¹¹⁹ See 5 U.S.C. § 706.

¹²⁰ The United States as amicus curiae has advocated for this reading in its merits brief. U.S. Amicus at 18-19.

¹²¹ Cf. *Miller v. Fenton*, 474 U.S. 104, 113 (1985) (describing the difficult delineation between questions of fact for juries and law for judges).

III. RENOVATING IMPOSSIBILITY PREEMPTION

The house that drug preemption jurisprudence has built, stone by stone, is complex and many-chambered. Yet the plodding pace of construction and the labyrinthine design result largely from the messy tasks of interpreting intent and doing so through the lens of litigation.

The myriad federal statutory provisions governing prescription drugs still contain neither a private right of action nor an expression of preemptive intent. This necessarily leaves those people who believe that FDA-approved drugs caused them injury with state-law remedial schemes as their only option for redress, and leaves courts considering those claims' interaction with the FDA's regulatory regime with the notoriously blunt canons of statutory interpretation to determine the federal statute's preemptive intent. Given the indeterminacy and frequency of this task, the federal courts have done some admirable work in parsing the FDCA and filling in precedent on its applications. Any gut-level renovations of drug preemption, at this point, likely would have to come from Congress.¹²²

There are some good reasons to consider renovating drug preemption at this moment. Preemption doctrine draws constant criticism for being opaque, unstable, disingenuously applied, and normatively undesirable.¹²³ As *Albrecht* illustrates, there exist very real disagreements about how to approach even discrete and precedent-heavy corners of the doctrine, like impossibility conflict preemption by prescription drug regulation. Plus, the stakes are high: preemption can be dispositive of thousands of cases involving innovative and complex medicines. Preemption already plays a role in the *National Prescription Opiate* MDL,¹²⁴ where local governments assert fraud, nuisance, and racketeering claims against the makers of prescription opioids for their contributions to the current public health crisis.¹²⁵ Generic defendants in the *Opiate* MDL unsuccessfully sought to avoid consolidation based on

¹²² An example would be the failed Bill to permit generic manufacturers to add warnings to their labels that go beyond the brand counterpart's labeling.

¹²³ See, e.g., McCuskey, *supra* notes 4 & 18.

¹²⁴ See Jan Hoffman, "Can this judge solve the opioid crisis?" N.Y. TIMES (Mar. 5, 2018), <https://nyti.ms/2Fhx7sK>.

¹²⁵ *In re Nat'l Prescription Opiate Litig.*, No. MDL 2804, 2017 WL 6031547 (J.P.M.L. Dec. 5, 2017). See Abbe R. Gluck, et al., *Civil Litigation and the Opioid Epidemic: The Role of Courts in a National Health Crisis*, 46 J. L., MED. & ETHICS __ (forthcoming 2018) (highlighting the "front and center" role of litigation in addressing the opioid crisis, and the preemption defenses that manufacturer defendants have raised).

their distinct preemption analysis, and brand defendants have sought dismissal of the complaints based on impossibility preemption.¹²⁶

This section explores two possible ways to renovate impossibility preemption for the sake of clarity, consistency, and fidelity to the federalism values that animate preemption. The first is to nudge even clearer reason-giving by the FDA in anticipation of preemption. The second is to refresh the presumption against preemption and solidify its role in drug preemption cases. As with any renovation project, however, there lurks the danger that one might not like the finished project. This is particularly inherent in preemption questions, which seem to “inevitably pit your principles against a desired outcome.”¹²⁷

A. Administrative Reason-Giving

The *Albrecht* case, like so many failure-to-warn MDLs of its ilk, raises discrete and dispositive issues about administrative supervision versus manufacturer responsibility. Administrative agencies – particularly the FDA – have long played a pivotal role in preemption.¹²⁸ Crucially, the workings of federal agencies, pursuant to statutory delegations, can themselves preempt state law.¹²⁹

In impossibility preemption of failure-to-warn claims, even the FDA’s *hypothetical* action can displace state tort. A defendant proves

¹²⁶ See Def’s Joint Mot. to Dismiss Pls’ Second Am. Compl, In re National Prescription Opiate Litig. (County of Summit, Ohio, et al. v. Purdue Pharma L.P., et al. Case No. 18-op-45090), 2018 WL 2473919 (N.D. Ohio May 25, 2018).

¹²⁷ Robert R.M. Verchick & Nina A. Mendelson, *Preemption and Theories of Federalism*, in PREEMPTION CHOICE: THE THEORY, LAW, AND REALITY OF FEDERALISM’S CORE QUESTION 32 (WILLIAM W. BUZBEE ED., 2009) (“[Preemption] will inevitably pit your principles against a desired outcome.”). See Scott L. Greer & Peter D. Jacobson, *Health Care Reform and Federalism*, 35 J. HEALTH POL. POL’Y & L. 203, 203–04 (2010);

¹²⁸ See, e.g., Elizabeth Y. McCuskey, *Agency Imprimatur & Health Reform Preemption*, 79 Ohio St. L. J. at 54 (2017); Gillian E. Metzger, *Administrative Law as the New Federalism*, 57 DUKE L. J. 2023 (2008); Nina A. Mendelson, *Chevron and Preemption*, 102 MICH. L. REV. 737 (2004).

¹²⁹ See, e.g., *Geier v. American Honda Motor Co.*, 529 U.S. 861 (2000); *Hillsborough County v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 713 (1985).

See David S. Rubenstein, *Delegating Supremacy?*, 65 VAND. L. REV. 1125, 1136-37 (2012); Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521 (2012); Nina Mendelson, *A Presumption Against Agency Preemption*, 102 NW. U. L. REV. 695 (2008); Brian Galle and Mark Seidenfeld, *Administrative Law’s Federalism: Preemption, Delegation, and Agencies at the Edge of Federal Power*, 57 DUKE L. J. 1933 (2008); William Funk, *Judicial Deference and Regulatory Preemption by Federal Agencies*, 84 TUL. L. REV. 1233 (2010)

impossibility only if it appears highly probable that the FDA would reject the warning that the state tort plaintiff would add. As the doctrine currently stands, construction of the FDA's probable position most likely depends on *what* the FDA says and *in what format* it says it.

Albrecht illustrates that even where the FDA has issued a formal written decision on a proposed warning, its meaning, in light of circumstantial evidence, may be obscured. This inquiry would be streamlined if only the parties could ask the FDA the question in litigation, or the agency could be coaxed to offer additional explanation – a “smoking gun” on the hypothetical rejection question.

The United States' participation as amicus in the Supreme Court in *Albrecht* seems to present such an opportunity. The government asserts on appeal that the FDA rejected the Warnings & Precautions “based on the lack of adequate data to support a warning.”¹³⁰ Merck has seized on these statements from the “FDA's brief” in the Supreme Court as the “smoking gun” of actual rejection, arguing that now “no rational juror could get past this evidence” and that the Court owes deference to the government's explanation on appeal.¹³¹ Yet the government's briefs cite only to the same evidence that was before the trials court and explain why that same evidence supports a conclusion of actual rejection.¹³² And, as the Court explained in *Levine*, the FDA is not authorized to preempt state law directly, and therefore the Court will not defer to its “*conclusion* that state law is pre-empted.”¹³³ Still, many jurists who distrust judicial deference to federal agencies from doctrines like *Chevron*, conversely prioritize deference to the FDA versus state juries.¹³⁴

¹³⁰ U.S. Amicus Br. Supporting Pet'r, at 31.

¹³¹ Pet'r Br., at 25.

¹³² U.S. Amicus Br. Supporting Pet'r, at 30-34 (In short, FDA's 2009 Complete Response Letter ..., when read in the proper context of the governing statutory and regulatory regime – as well as FDA's subsequent regulatory actions regarding Fosamax....”).

¹³³ *Wyeth v. Levine*, 555 U.S. 555, 576 (2009) (emphasis in original).

¹³⁴ See Catherine M. Sharkey, *The Administrative State and the Common Law: Regulatory Substitutes or Complements?*, 65 EMORY L.J. 1705, 1740 (2016) (citing *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 325 (2008) (doubting a jury's ability to assess costs and benefits of a medical device); Richard L. Cupp Jr., *Preemption's Rise (and Bit of a Fall) as Products Liability Reform: Wyeth, Riegel, Altria, and the Restatement (Third) 's Prescription Product Design Defect Standard*, 74 BROOK. L. REV. 727, 753-54 (2009) (exploring the role that mistrust of civil juries has played in recent Supreme Court preemption decisions)).

Invited participation in a Supreme Court appeal will not help clarify the FDA's position in the overwhelming majority of impossibility preemption cases that never make it that far. Participation at the trial stage of litigation would help clarify those cases, and could be achieved through the FDA's intervention,¹³⁵ participation as amicus,¹³⁶ or by creating a new pathway for referring technical questions from the federal courts to the FDA, as Catherine Struve has proposed.¹³⁷ Parties and district courts should consider the existing authority to invite the FDA's input as amicus for those intractable factual questions surrounding warning rejections. But dragging the FDA into litigation to answer factual questions that judges and juries are more than capable of handling would prioritize the FDA's expertise, but also strain its resources, and likely its patience.

Alternatively, statutory or administrative rules and guidance could encourage the FDA to offer further clarifications in its daily activities, rather than in the litigation context. It is, however, hard to imagine a workable, prospective rule that would accomplish this because the FDA already is subject to many reason-giving directives. For example, the FDA *must* notify manufacturers of potentially label-worthy risks,¹³⁸ and *must* initiate discussion with a manufacturer if it disagrees with proposed language.¹³⁹ Further, FDA has committed that its Complete Response Letters *must* describe *all* deficiencies.¹⁴⁰ Additional clarification and explanation directives could threaten to ossify the FDA regulatory process.

The systemic costs of additional reason-giving incentives and procedures likely outweigh any salutary effects on preemption analysis.

¹³⁵ See Fed. R. Civ. P. 24.

¹³⁶ No federal rule or statute addresses amicus curiae at the district court level. See *United States v. Gotti*, 755 F. Supp. 1157, 1158 (E.D.N.Y. 1991). But district courts may invite amicus participation under its inherent authority, e.g., *United States v. Michigan*, 116 F.R.D. 655, 660 (W.D. Mich. 1987), within the purview of its sound discretion, e.g., *Alexander v. Hall*, 64 F.R.D. 152, 155 (D.S.C. 1974).

¹³⁷ See Catherine T. Struve, J.D., *The FDA and the Tort System: Postmarketing Surveillance, Compensation, and the Role of Litigation*, 5 YALE J. HEALTH POL'Y, L. & ETHICS 587, 592 (2005).

¹³⁸ 21 U.S.C. § 355(o)(4)(A).

¹³⁹ *Id.* § 355(o)(4)(C).

¹⁴⁰ 21 C.F.R. § 314.110(a)(1).

B. Refreshing the Presumption against Preemption

Rather than starting renovations with preemption evidence, a more prudent place to start might be with the doctrine itself. The presumption against preemption is one of the canons most frequently applied to preemption questions and offers a promising place to begin.¹⁴¹ The presumption against preemption instructs that courts apply demanding standards to impossibility preemption (as explained in II.B.1, *supra*)¹⁴² and can offer a tie-break principle in truly indeterminate cases.¹⁴³ And, the presumption suggests a higher order preference for preserving state *remedies* that may supplement federal *regulation*.

First, reviving the presumption's utility as a tiebreaker could help break factual impasse in impossibility preemption. As Louise Weinberg has argued, the "presumption in favor of state law" should not automatically "operate[] in cases of identified 'actual' federal-state conflict" because "[i]dentification of a federal-state conflict-in-fact is, precisely, what overcomes the presumption."¹⁴⁴ Impossibility preemption, however, rarely lends itself to cases of direct and actual conflicts. For failure-to-warn claims, the federal laws at issue are procedures by which manufacturers *may* initiate label changes, which the administering agency *may* then modify, accept, or reject. The "actual" impossibility conflict exists when the FDA *has* rejected the warning a state-law plaintiff seeks based on the same or similar data.

In the case of actual rejection, courts would not need to lean on the presumption against preemption because the FDA's rejection

¹⁴¹ See generally McCuskey, *supra* note 4.

¹⁴² See *Wyeth v. Levine*, 555 U.S. at 565. See, e.g., *California v. ARC America Corp.*, 490 U.S. 93, 101–102 (1989); *Hillsborough County v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 716 (1985); *Rush Prudential HMO, Inc. v. Moran*, 536 U.S. 355, 387 (2002); *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, (2001) (all applying the presumption against preemption to conflict preemption questions involving health regulations).

¹⁴³ See McCuskey, *supra* note 4, at 140-41.

144. Louise Weinberg, *The Federal-State Conflict of Laws: "Actual" Conflicts*, 70 TEX. L. REV. 1743, 1756 (1992); accord Young, *The Ordinary Diet of the Law*, at 318 ("One can agree with Nelson that courts should not distort the meaning of federal statutes in order to avoid preemption without accepting that the Framers of the Supremacy Clause meant courts to abandon this basic function."); see also Robert S. Peck, *A Separation-of-Powers Defense of the "Presumption Against Preemption"*, 84 TUL. L. REV. 1185, 1201 (2010) ("The presumption against preemption serves the diffusion of power both vertically and horizontally.").

unambiguously establishes an actual conflict. In all other scenarios, impossibility preemption is a doctrine of speculative conflict, relying on circumstantial evidence and inference – the types of indeterminate questions for which the presumption against preemption functions most effectively.¹⁴⁵ Lingering doubts about propriety of preemption by agency action further suggest that the presumption against preemption may be especially appropriate for drug impossibility preemption cases.¹⁴⁶

On a broader level, the deep traditions underlying drug regulation and state remedies support application of the presumption against preemption to save state remedies in the face of federal regulation. In *Body of Preemption*, I proposed a “scalpel approach” to the presumption, tailoring the presumption to each category of “health” law and examining the regulatory federalism traditions in each category, of “health” laws.¹⁴⁷ I left the categorical tailoring for future research. While this essay does not pick up that gauntlet, it does return to one aspect of the scalpel approach essential to drug-and-device preemption: whether a tailored presumption against preemption should apply with greater force to save state-created *remedies* for injury from preemption by federal *regulation*.¹⁴⁸

“Numerous health law topics have a strong tradition of relying on state *remedies* for injury . . . [but] a varied federal and state tradition regarding *preventive* regulations.”¹⁴⁹ Federal preventive regulation for medical products is normatively desirable on many accounts, including expertise, uniformity, and comprehensiveness¹⁵⁰ that “generalist juries

¹⁴⁵ See McCuskey, *supra* note 4, at 89, 94, 141.

¹⁴⁶ See generally Catherine M. Sharkey, *States vs. FDA*, 18 GEO. WASH. L. REV. 1609 (2015); Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 523 (2012); Nina A. Mendelson, *A Presumption Against Agency Preemption*, 102 NW. U. L. REV. 695 (2008). But see Richard A. Epstein, *The Case for Field Preemption of State Laws in Drugs*, 103 NW. U. L. REV. 54 (2008).

¹⁴⁷ *Id.* at 150-51.

¹⁴⁸ See *id.* at 129-34.

¹⁴⁹ McCuskey, *supra* note 18, at 142 (emphasis in original). Cf. *Bruesewitz v. Wyeth LLC*, 562 U.S. 223, 243 (2011) (holding that the Vaccine Act’s remedial scheme preempted state design defect claims); Catherine M. Sharkey, *Against Categorical Preemption: Vaccines and the Compensation Piece of the Preemption Puzzle*, 61 DEPAUL L. REV. 643, 644-45 (2012) (“[This Act] is the rare example whereby Congress provides for a federally administered compensation fund alongside its newly fashioned regulatory standards”).

¹⁵⁰ See, e.g., Abigail Moncrieff, *The Supreme Court’s Assault on Litigation: Why (and How) It Might Be Good for Health Law*, 90 B.U. L. REV. 2323, 2324-25 (2010); Zettler,

and judges” lack.¹⁵¹ Yet unless Congress decides to fully consolidate regulatory and remedial power in the FDA and infuse the FDA’s jurisdiction with additional rigor,¹⁵² state remedy will continue to play a vital and historic function. State products liability claims have long supplied the remedy for people injured by medical products.¹⁵³ But the prevention of injury through safety, efficacy, and marketing regulations has a substantial history of federal power.¹⁵⁴ Rather than a *regulation-regulation* conflict, drug regulation creates a *regulation-remedy* conflict.¹⁵⁵ A presumption against preemption for state *remedy* of health-related injury would both accurately reflect a legal tradition, and rest on a principled federalism distinction of regulation-remedy.¹⁵⁶

For prescription drug injuries, preemption cuts both ways: it can establish a national floor of protection,¹⁵⁷ but it can leave serious injuries without remedy if it imposes a ceiling of compliance.¹⁵⁸ Preemption, after

Federalism, *supra* note 7; Timothy Stoltzfus Jost, *Health Law and Administrative Law: A Marriage Most Convenient*, 49 ST. LOUIS U. L. J. 1, 16-30 (2004).

¹⁵¹ McCuskey, *supra* note 41.

¹⁵² See Moncrieff, *supra* note 150, at 2362-64, 2376-82 (arguing that it would be desirable to do so).

¹⁵³ See Zettler, *Oversight*, *supra* note 16, at 427 (“The conventional wisdom . . . holds that states regulate medical practice . . . while the federal government regulates medical products.”); *id.* at 452 (“[M]edical malpractice liability—a creature of state law—provides a mechanism for private enforcement of medical practice standards.”); Lawrence O. Gostin, *The FDA, Preemption, and Public Safety: Antiregulatory Effects and Maddening Inconsistency*, 41 HASTINGS CENTER REP. 11, 12 (Sept.-Oct. 2011).

¹⁵⁴ See Zettler, *Federalism*, *supra* note 7, at 890; McCuskey, *supra* note 18, at 122.

¹⁵⁵ Cf. Zettler, *Federalism*, *supra* note 7, at 859-90 (articulating that “state drug regulation has evolved from its historical prominence to largely consist of tort law schemes and state Food, Drug, and Cosmetic Acts that complement or parallel FDA regulation” to new state regulatory efforts); Sharkey, *States*, at 1612 (“[C]ourts should take heed of the degree to which the federal agency considered relevant state interests before acting, placing particular focus on the extent to which states had a meaningful opportunity to articulate their own views of the relationship between state regulations and the federal scheme.”); Sharkey, *Inside*, *supra* note 40 at 523 (“[W]hile courts reiterate that congressional intent is the touchstone of preemption analysis, they increasingly rely on the views propounded by federal agencies either in regulations or else in preambles or litigation briefs.”).

¹⁵⁶ See McCuskey, *supra* note 18, at 152-53.

¹⁵⁷ See *Wyeth v. Levine*, 555 U.S. 555, 555 (2009).

¹⁵⁸ See, e.g., *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 610-11 (2011) (holding that federal law preempts state law that imposes a duty on manufacturers to change a drug label on generic drugs). After *PLIVA*, Congress considered—but did not enact—legislative revisions to restore state remedies. See Patient Safety and Generic Labeling Improvement Act, S. 2295, 112th Cong. (2012).

all, does not determine liability.¹⁵⁹ It merely assigns that task to one authority or another – it is a choice among institutions.¹⁶⁰ In the context of remedy-preemption, the choice is between FDA, as ultimate arbiter of safety, versus judges and juries, as complementary regulators. At a time when the presumption against preemption has come under fire from three Justices, refreshing the doctrine by revealing the deeper principles at work in this interpretive tool could bring some much-needed coherence and consistency to drug preemption.

CONCLUSION

Drug preemption doctrine would benefit from a more tailored and precise application of the presumption against preemption – a renovation of preemption analysis. The presumption against buttresses the “clear evidence” standard for impossibility preemption issues in failure-to-warn claims and presents a valuable tiebreak principle for close fact questions about impossibility. On a broader scale, a renewed reliance on the presumption, focusing on the role of remedy versus regulation, could restore some of preemption’s fidelity to the federalism values animating it. Whether *Merck v. Albrecht* represents an opportunity to accomplish these renovations, or a threat to their foundations will be determined in 2019.

¹⁵⁹ Cf. *Watson v. Mylan Pharm., Inc.*, 701 F. App'x 729, 732 (10th Cir. 2017), *cert. denied*, 138 S. Ct. 679 (2018) (“[A] failure-to-update theory requires more than ‘merely [] the fact of the failure to update.’ It requires ‘that the failure to include th[e] [updated] language proximately caused [the plaintiff’s] injuries.’”) (quoting *Fulgenzi*, 711 F.3d at 588).

¹⁶⁰ See Thomas W. Merrill, *Preemption and Institutional Choice*, 102 NW. U. L. REV. 727 (2008).