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WHERE'S THE BEEF?: A GUIDE TO JUDGES ON PREEMPTION OF STATE TORT LITIGATION INVOLVING BRANDED DRUGS*

Victor E. Schwartz** and Christopher E. Appel***

The U.S. Supreme Court has issued several decisions since 2009 that clarify the landscape for when a state tort claim against a pharmaceutical manufacturer is preempted.¹ Generally speaking, claimants are permitted to bring lawsuits under state law alleging a defect in the design or warnings associated with a branded drug approved by the Food and Drug Administration (FDA), but are barred from bringing such claims with respect to an FDA-approved generic drug.² The Supreme Court has recognized exceptions in the case of branded drugs where a claim may be impliedly preempted, including where a pharmaceutical manufacturer shows “clear evidence” that the FDA would not have approved a proffered change to the branded drug’s warning label.³

In 2019, the Court in *Merck Sharp & Dohme Corp. v. Albrecht*⁴ added to its preemption jurisprudence by examining what constitutes “clear evidence” and how that decision must be made. The Court responded to lower federal and state courts struggling over how to apply this language and rendered new, significant guidelines with respect to when preemption is an available defense for branded drug manufacturers.⁵ Critically, the Court made explicit that the question of whether clear evidence exists that the FDA would not have approved a warning change “is a legal one for the judge, not a jury.”⁶

* This Article is dedicated to the memory of University of Cincinnati College of Law Professor John Murphy. Professor Murphy’s teachings inspired generations of students and his lessons will continue with them always.

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1. See *Wyeth v. Levine*, 555 U.S. 555 (2009); *Pliva, Inc. v. Mensing*, 564 U.S. 604 (2011); *Bruesewitz v. Wyeth, LLC*, 562 U.S. 223 (2011); *Mutual Pharm. Co. v. Bartlett*, 570 U.S. 472 (2013); see also *infra* Part I.A.

2. See *Wyeth*, 555 U.S. at 555; *Mensing*, 564 U.S. at 604.

3. *Wyeth*, 555 U.S. at 571.

4. 139 S. Ct. 1668 (2019).

5. See, e.g., *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 282 (3d. Cir. 2017) (stating that “clear evidence” exception created a “cryptic and open-ended” standard for which “lower courts have struggled to make it readily administrable”), *vacated*, 139 S. Ct. 1168 (2019).

6. *Albrecht*, 139 S. Ct. at 1679.

The Court further clarified the legal requirements for a branded drug manufacturer to successfully assert such a preemption defense, namely that “it fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug’s label to include that warning.”⁷

This Article examines the Court’s decision in *Albrecht* and new issues expected to arise as lower courts interpret it. The Article’s goal is to assist judges and others as to whether a branded drug manufacturer has made a sufficient showing, for preemption purposes, that the FDA’s action or inaction provides clear evidence that the agency would not approve a warning change. Part I discusses the Supreme Court’s preemption jurisprudence regarding pharmaceutical products to provide an overview of the legal environment in which *Albrecht* was decided. It then examines the *Albrecht* decision. Part II analyzes outstanding issues in the wake of *Albrecht* and suggests how they should be resolved. It further discusses judges’ required branded drug preemption analysis. Part III examines the role of preemption regarding FDA-approved drugs now and in the future.

The Article concludes that the Supreme Court opened the door in *Albrecht* to potentially broader availability of branded drug preemption. The Court’s decision to vest the authority to make preemption determinations in the pharmaceutical context exclusively with judges, as well as other statements, reflect the notion that preemption should be available where the FDA has directly or indirectly rejected a proposed warning change after receiving all of the material drug information. In that regard, and to give full effect to the Court’s decision, judges should avoid an overly rigid or inflexible approach to preemption determinations regarding branded drugs.

I. U.S. SUPREME COURT’S KEY PHARMACEUTICAL PREEMPTION DECISIONS

A. Overview of Preemption Landscape

The U.S. Supreme Court began to clarify the circumstances in which tort claims against a pharmaceutical manufacturer are preempted in its landmark 2009 ruling in *Wyeth v. Levine*.⁸ *Wyeth* addressed a major threshold issue in pharmaceutical litigation of whether a patient’s claim that a branded drug contained an inadequate warning under state

7. *Id.* at 1678.

8. 555 U.S. 555 (2009).

law was preempted where the FDA specifically approved the warning. The precise issues involved whether the branded drug manufacturer could comply with both the FDA's labeling requirements and state common law warning requirements as determined by a jury, or whether these competing requirements presented an "unacceptable obstacle" or "impossibility" that impliedly preempted the state claim.⁹

The Court held that these types of "conflict preemption" do not categorically bar a state failure-to-warn claim because a branded drug manufacturer may "unilaterally strengthen its warning," and therefore (at least theoretically) comply with competing federal and state requirements, pursuant to an FDA regulation.¹⁰ That regulation, called the "changes being effected" (CBE) regulation, permits a branded drug manufacturer to "add or strengthen" its warning by filing a supplemental application with the FDA.¹¹ The Court explained that because the branded drug manufacturer "need not wait for FDA approval" to proceed in changing its warning pursuant to the CBE regulation, it is not impossible for the manufacturer to comply with federal law and the potential state law warning requirements as determined by juries across fifty states.¹² The Court recognized that "some state-law claims might well frustrate the achievement of congressional objectives," but maintained that "Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness."¹³

In reaching this decision, the Court appreciated that "the FDA retains authority to reject labeling changes made pursuant to the CBE regulation in its review of the manufacturer's supplemental application."¹⁴ The Court explained that a branded drug manufacturer could successfully claim it could not comply with both federal and state warning requirements in a situation in which there was "clear evidence that the FDA would not have approved a change" in warning.¹⁵ As discussed in the introduction, this exception is the predicate for the Court's decision in *Albrecht*.

In 2011, the Court, in *Pliva, Inc. v. Mensing*,¹⁶ examined preemption in the context of FDA-approved generic drugs. Here, the Court reached the opposite conclusion with respect to preemption of a state

9. *Id.* at 563, 573 (internal quotation omitted).

10. *Id.* at 560, 573.

11. *Id.* at 568 (quoting 21 C.F.R. §§ 314.70(c)(6)(iii)(A), (C) (2008)).

12. *Id.*

13. *Id.* at 575, 581.

14. *Id.* at 571.

15. *Id.*

16. 564 U.S. 604 (2011).

failure-to-warn claim, finding federal law created “impossibility” for a generic drug manufacturer to unilaterally change its warning to comply with potentially different state law requirements.¹⁷ Specifically, the Court stated that pursuant to Congress’s 1984 enactment of the Drug Price Competition and Patent Term Restoration Act, commonly called the Hatch-Waxman Amendments, a generic drug’s FDA approval is contingent upon “showing equivalence” with an FDA-approved branded drug; a legal requirement for which the generic drug manufacturer “is responsible for ensuring that its warning label is the same as the brand name’s.”¹⁸

The Court found that this “sameness” requirement applies to any warning label changes *after* the FDA’s initial approval.¹⁹ Therefore, unlike in *Wyeth* where the Court determined that the CBE regulation enabled a branded drug manufacturer to unilaterally change an FDA-approved warning, a generic drug manufacturer could not do so under the CBE process. The Court explained that the FDA had likewise interpreted its regulations “to require that the warning labels of a brand-name drug and its generic copy *must always be the same*,” and that this agency interpretation should be controlling.²⁰

As the Court further recognized, “generic drug manufacturers have different federal drug labeling duties” to promote the separate public policy of allowing “manufacturers to develop generic drugs inexpensively.”²¹ The “special, and different, regulation of generic drugs” has also proven successful in “bringing more drugs more quickly and cheaply to the public” and expanding the generic drug market²²—a market that in 2018 accounted for around 85% of U.S. drug prescriptions.²³

Nevertheless, the Court remained mindful that, from plaintiffs’ perspective, a regime generally allowing state failure-to-warn claims against branded drug manufacturers and barring state failure-to-warn claims against generic drug manufacturers “makes little sense.”²⁴ It declined, however, to “distort the Supremacy Clause in order to create

17. *Id.* at 618.

18. *Id.* at 612-13.

19. *Id.* at 613.

20. *Id.* (emphasis added).

21. *Id.* at 612-13.

22. *Id.* at 626.

23. See Matej Mikulic, *Branded vs. Generic U.S. Drug Prescriptions Dispensed 2005-2018*, STATISTA (Aug. 18, 2020), <https://www.statista.com/statistics/205042/proportion-of-brand-to-generic-prescriptions-dispensed/>; see also *Generic Drug Facts*, FOOD & DRUG ADMIN. (June 1, 2018), <https://www.fda.gov/drugs/generic-drugs/generic-drug-facts> (reporting findings of IMS Health Institute study that “generic drugs saved the U.S. health care system \$1.67 trillion from 2007 to 2016”).

24. *Pliva, Inc. v. Mensing*, 564 U.S. 604, 625 (2011).

similar pre-emption across a dissimilar statutory scheme[.]" and acknowledged that "Congress and the FDA retain the authority to change the law and regulations if they so desire."²⁵

The Court further illuminated the pharmaceutical preemption landscape in 2011 in *Bruesewitz v. Wyeth, LLC*.²⁶ Here, the Court determined that the National Childhood Vaccine Injury Act of 1986, which created a no-fault compensation program "to stabilize the vaccine market and facilitate compensation" for legitimate vaccine injury claims, expressly preempted all design defect claims against vaccine manufacturers.²⁷ In doing so, the Court recognized that the Act's vaccine design improvement and compensation provisions "reflect[] a sensible choice to leave complex epidemiological judgments about vaccine design to the FDA and the National Vaccine Program rather than juries."²⁸

In 2013, the Court, in *Mutual Pharmaceutical Co. Inc. v. Bartlett*,²⁹ addressed preemption for generic drug manufacturers with respect to design defect claims. It determined that the same "impossibility" at issue in *PLIVA* preventing generic drug manufacturers from unilaterally changing the FDA-approved warning copied from the equivalent branded drug applied to changing the design of an FDA-approved generic drug.³⁰ The Court explained that the Food, Drug and Cosmetics Act (FDCA) "requires a generic drug to have the same active ingredients, route of administration, dosage form, strength, and labeling as the brand-name drug on which it is based," and that redesigning the composition of a generic drug would necessarily result in a new drug compound that would require a New Drug Application (NDA) to be marketed and sold.³¹ Accordingly, the Court determined that a "straightforward application of pre-emption law" bars any design defect claim against a generic drug manufacturer.³²

The Court's precedents establish multiple areas in which state tort claims against a pharmaceutical manufacturer are preempted by

25. *Id.* at 626.

26. 562 U.S. 223 (2011).

27. *Id.* at 228.

28. *Id.* at 239.

29. 570 U.S. 472 (2013).

30. *See id.* at 484-86.

31. *Id.* at 483-84. The Court additionally rejected the notion, advanced in a dissenting opinion by Justice Sotomayor and in the decision below by the U.S. Court of Appeals for the First Circuit, that a generic drug manufacturer could escape the impossibility of complying with both its federal- and state-law duties by choosing not to make the drug at all. *See id.* at 488-89. As the Court explained, "if the option of ceasing to act defeated a claim of impossibility, impossibility pre-emption would be 'all but meaningless,'" and it would also mean that *PLIVA* and "the vast majority—if not all—of the cases in which the Court has found impossibility pre-emption, were wrongly decided." *Id.*

32. *Id.* at 493.

federal law. Specifically, claims alleging either a design or warning defect in an FDA-approved generic drug are preempted, as are any product liability claims alleging injury from a vaccine. Relatedly, the Court, in *Riegel v. Medtronic, Inc.*, which was decided in 2008 a year before *Wyeth*, found that claims related to medical devices given premarket approval by the FDA are expressly preempted pursuant to the Medical Device Amendments of 1976.³³ Only with respect to branded drugs that comprise around 10% of U.S. drug prescriptions is a preemption defense generally not available to the manufacturer.³⁴ It is against this backdrop that the Court decided *Albrecht*.

B. The U.S. Supreme Court Clarifies the Law Regarding Branded Drug Preemption

Albrecht involved claims by more than 500 individuals who took the branded drug Fosamax, which is approved by the FDA to treat and prevent osteoporosis in postmenopausal women.³⁵ They alleged Fosamax's FDA-approved warning label before 2011 was defective in failing to adequately warn of the drug's risk of injury from "atypical femoral fractures" (i.e. fractures of the femur bone).³⁶ Fosamax's manufacturer, Merck Sharpe & Dohme Corp. (Merck), defended the failure-to-warn claims, which were brought under the law of multiple states and consolidated in a multi-district litigation (MDL) action, on the basis that the FDA considered and rejected efforts by Merck to add a specific warning about Fosamax's risk of causing bone "stress fractures."³⁷ This rejection, Merck argued, provided "clear evidence" the FDA would not approve a warning change, entitling the company to a preemption defense under the exception set forth in *Wyeth*.

Fosamax was approved by the FDA in 1995 without a warning referencing a risk of bone fractures.³⁸ As far back as 1990, when Fosamax was undergoing preapproval clinical trials, Merck's scientists expressed concern that Fosamax could at least theoretically inhibit bone remodeling, which is the process through which bones are continuously broken down and built back up again, to a degree that would cause bone fractures.³⁹ Merck brought these concerns to the FDA's attention when the company applied for approval of Fosamax,

33. *Riegel v. Medtronic, Inc.*, 552 U.S. 312 (2008).

34. See Mikulic, *supra* note 23.

35. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1673-75 (2019).

36. *Id.* at 1674.

37. *Id.* at 1668, 1675.

38. *Id.* at 1674.

39. *Id.*

but the FDA, “perhaps because the concerns were only theoretical,” approved Fosamax’s warning label without requiring any mention of this risk.⁴⁰

In the decade following Fosamax’s approval, Merck began receiving adverse event reports from the medical community indicating that individuals who had taken Fosamax for more than five years were suffering atypical femoral fractures.⁴¹ Merck and others in the medical community began analyzing this adverse event data and additional case studies and scholarship examining possible connections between long-term Fosamax use and bone fractures.⁴² By 2008, Merck believed there was sufficient evidence to support additional warnings for prescribing physicians, and applied to the FDA for preapproval to change Fosamax’s label.⁴³ Merck did so by submitting Prior Approval Supplement (PAS) applications to the agency which presented data, analyses and other information to support proposed labeling changes.⁴⁴

Specifically, Merck proposed including in the “Precautions” section of Fosamax’s label, under the heading “Low-Energy Femoral Shaft Fracture,” a discussion of reported bone stress fractures occurring in the absence of trauma.⁴⁵ Merck additionally proposed referencing the potential for “low-energy femoral shaft fracture” in the “Adverse Reactions” section of Fosamax’s label.⁴⁶ The FDA approved the addition to the Adverse Reactions section, but rejected Merck’s proposed change to the Precautions section.⁴⁷ The agency explained that the proposed change to the Precautions section lacked adequate justification in the relevant medical literature.⁴⁸

Merck subsequently resolved in 2008 to effectuate changes to Fosamax’s label through the CBE process. It adopted the proposed changes to the Adverse Reactions section with which the FDA expressed agreement, but did not adopt the proposed changes to the Precautions section with which the FDA expressed disagreement.⁴⁹ Such agency disagreement also continued for several additional years.

40. *Id.*

41. *Id.*

42. *See id.*

43. *See id.*

44. *Id.*; *see also* 21 C.F.R. § 314.70(b) (discussing Prior Approval Supplement (PAS) criteria).

45. *In re Fosamax (Alendronate Sodium): Prods. Liab. Litig.*, No. 08-08(JAP)(LHG), 2014 WL 1266994, at *3 (D.N.J. Mar. 26, 2014), *vacated*, 852 F.3d 268 (3d Cir. 2017), *vacated*, 139 S. Ct. 1668 (2019).

46. *Id.*; *Albrecht*, 139 S. Ct. at 1674.

47. *Albrecht*, 139 S. Ct. at 1674.

48. *Id.*; *see also In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d at 277.

49. *See Albrecht*, 139 S. Ct. at 1674.

For instance, in 2010, the FDA issued a Drug Safety Communication in which it stated that “[a]t this point, the data that FDA has reviewed have not shown a clear connection between bisphosphonate [Fosamax] use and a risk of atypical subtrochanteric femur fractures.”⁵⁰ The FDA stated, however, that it was “working closely with outside experts, including members of the . . . American Society of Bone and Mineral Research Subtrochanteric Femoral Fracture Task Force, to gather additional information that may provide more insight.”⁵¹

In 2011, the FDA ordered a change to Fosamax’s label based on its own analysis, notwithstanding the agency’s continued doubts about the existence of a causal relationship between the drug and potential injury.⁵² Merck again proposed warning language referencing bone “stress fractures,” but the FDA decided to expressly reference “[a]typical”, “low-energy”, or low trauma fractures of the femoral shaft to communicate the “seriousness” of the type of injury that could result.⁵³ Merck and the FDA ultimately agreed to add a brief, approximately 200-word discussion of atypical femoral fractures to the Warnings and Precautions section of Fosamax’s more than 12,000-word label (totaling 23 pages of physician prescribing and warning information).⁵⁴

Individuals who took Fosamax between 1999 and 2010 sued Merck for failing to warn about a risk of atypical femoral fractures. The MDL court rejected this argument, finding the claims preempted.⁵⁵ It explained that the “evidence surrounding whether the FDA felt that a label change was necessary . . . provides clear evidence that the FDA *would have* rejected a stronger Precautions warning because the FDA

50. *In re Fosamax (Alendronate Sodium): Prods. Liab. Litig.*, 2014 WL 1266994, at *4 (internal citation omitted).

51. *Id.*

52. *See Albrecht*, 139 S. Ct. at 1675; *In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 278 (3d Cir. 2017), *vacated*, 139 S. Ct. 1668 (2019) (stating that FDA “reiterated that it was still ‘not clear if bisphosphonates are the cause’” of atypical unusual femur fractures in the agency’s October 2010 announcement of a pending warning label change).

53. *Albrecht*, 139 S. Ct. at 1674-75 (internal citations omitted).

54. *Id.*; FOOD & DRUG ADMIN., REF. ID 3083184, FOSAMAX FULL PROSCRIBING INFORMATION (Feb. 2012), *available at* https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021575s017lbl.pdf. As the Court explained in *Albrecht*:

Although we commonly understand a drug’s “label” to refer to the sticker affixed to a prescription bottle, in this context the term refers more broadly to the written material that is sent to the physician who prescribes the drug and the written material that comes with the prescription bottle when the drug is handed to the patient at the pharmacy These (often lengthy) package inserts contain detailed information about the drug’s medical uses and health risks.

139 S. Ct. at 1672-73 (internal citations omitted).

55. *In re Fosamax (Alendronate Sodium): Prods. Liab. Litig.*, 2014 WL 1266994, at *16.

did reject a stronger Precautions warning.”⁵⁶ The court further determined that had Merck used the CBE process to unilaterally adopt its proposed warning about bones stress fractures—again in a proposed section titled “Low-Energy Femoral Shaft Fracture”—the company would have been subject to liability for misbranding.⁵⁷

The U.S. Court of Appeals for the Third Circuit reversed the preemption ruling of the MDL court, making several, ultimately incorrect interpretations of *Wyeth*’s “clear evidence” exception along the way.⁵⁸ First, the court determined that “the term ‘clear evidence’ refers solely to the applicable standard of proof,” which requires the branded drug manufacturer to “prove that it is *highly probable* that the FDA would not have approved a change to the drug’s label.”⁵⁹ Second, the court determined that “the ultimate question of whether the FDA would have rejected a label change is a question of fact for the jury rather than for the court.”⁶⁰ Therefore, the court concluded it could only affirm the decision of the MDL court upon a finding that “no reasonable juror could conclude that it is anything less than highly probable that the FDA would have rejected Plaintiff’s proposed atypical-fracture warning had Merck proposed it to the FDA.”⁶¹

In articulating this “demanding and fact-sensitive” standard, the court acknowledged that juries would need to perform a preemption “assessment [that] is certainly complex.”⁶² It argued, however, that requiring a jury to evaluate and make inferences regarding “correspondence, agency statements, contemporaneous medical literature, the requirements of the CBE regulation, and whatever intuitions the factfinder may have about administrative inertia and agency decision-making processes” involves an assessment “little different from the type of fact questions that are routinely given to a jury.”⁶³ The court also asserted that this complex assessment “does not require any special legal competence or training.”⁶⁴ It further opined that having juries determine whether a branded drug manufacturer satisfies such a standard in light of the FDA’s regulatory framework “will not drastically change how defendants will litigate

56. *Id.* (emphasis in original).

57. *Id.* at *3-4, *16.

58. *See In re Fosamax (Alendronate Sodium) Prods. Liab. Litig.*, 852 F.3d 268, 268 (3d Cir. 2017), *vacated*, 139 S. Ct. 1168 (2019).

59. *Id.* at 282, 295 (emphasis added).

60. *Id.* at 282.

61. *Id.* at 295.

62. *Id.* at 271, 293.

63. *Id.* at 293, 289.

64. *Id.* 293.

the preemption defense.”⁶⁵

The U.S. Supreme Court took the opportunity in accepting review in *Albrecht* to clear up some misconceptions, by the Third Circuit and other lower courts, about the “clear evidence” exception. First, the Court, in a unanimous decision authored by Justice Breyer, explained that the exception was never intended to set forth a heightened evidentiary standard, or any evidentiary standard, for pharmaceutical preemption determinations.⁶⁶ Rather, the Court’s reference to “clear evidence” in *Wyeth* simply described a need for clarity regarding “whatever the means the FDA uses to exercise its authority” in communicating disapproval of a proposed change to a drug’s warning.⁶⁷ Second, and relatedly, the Court stated that the “complexity” inherent to the “nature and scope” of the FDA’s determinations, including the alleged disapproval of a proposed warning change, means “the question is a legal one for the judge, not a jury.”⁶⁸

As the Court explained, “judges are better suited than are juries to understand and to interpret agency decisions in light of the governing statutory and regulatory context.”⁶⁹ “Judges,” the Court continued, “are experienced in ‘[t]he construction of written instruments,’ such as those normally produced by a federal agency to memorialize its considered judgments,” and “are normally familiar with principles of administrative law.”⁷⁰ The Court also reasoned that placing pharmaceutical preemption determinations exclusively with judges “should produce greater uniformity among courts; and greater uniformity is normally a virtue when a question requires a determination concerning the scope and effect of federal agency action.”⁷¹ Accordingly, the Court concluded that the “‘better positioned’ decisionmaker is the judge” with respect to whether the “clear evidence” exception is satisfied.⁷²

The Court additionally clarified judges’ required preemption analysis regarding the existence of “clear evidence.” The Court stated that “‘clear evidence’ is evidence that shows the court that the drug manufacturer fully informed the FDA of the justifications for the warning required by state law and that the FDA, in turn, informed the

65. *Id.* at 294.

66. *See* Merck Sharp & Dohme Corp. v. *Albrecht*, 139 S. Ct. 1668, 1679 (2019).

67. *Id.*

68. *Id.* at 1679-80.

69. *Id.* at 1680.

70. *Id.* (quoting *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388 (1996)).

71. *Id.*

72. *Id.*

drug manufacturer that the FDA would not approve a change to the drug's label to include that warning."⁷³ The Court recognized that federal law permits the FDA to communicate its disapproval of a warning in a variety of ways, including notice-and-comment rulemaking setting forth labeling standards, formally rejecting a warning label that would have been adequate under state law, or other agency action carrying the force of law.⁷⁴ The Court also made clear that the question of the FDA's "disapproval 'method'" was not before the Court, stating only that the "means must lie within the scope of the authority Congress has lawfully delegated."⁷⁵ It explained further that "the judge must simply ask himself or herself whether the relevant federal and state laws 'irreconcilably conflic[t]'" in reviewing whatever "method" the FDA expressed disapproval.⁷⁶

Two concurring opinions offered widely divergent views on how lower courts might apply the "clear evidence" exception. Justice Thomas authored a concurring opinion endorsing a narrow view of what expressions of FDA disapproval of a warning change would be sufficient to demonstrate impossibility and preempt a state failure-to-warn claim against the branded drug manufacturer.⁷⁷ He dismissed the basic notion that the "FDA would have rejected a hypothetical labeling change submitted via the CBE process" because "neither agency musings nor hypothetical future rejections constitute pre-emptive 'Laws' under the Supremacy Clause."⁷⁸ In his view, preemption could only be obtainable where the FDA has issued a final ruling rejecting a manufacturer's application to change a warning or has issued a supplemental ruling formally rejecting a warning change made unilaterally by the manufacturer pursuant to the CBE process.⁷⁹ Because Merck withdrew its preapproval applications to implement a warning change via the CBE process—a responsive action to the FDA's expressed disapproval—and did not include in the CBE application the proposed changes to Fosamax's "Precautions" section for which the FDA expressed disapproval, Justice Thomas concluded there had been no final agency action precluding Merck's compliance with federal and state law requirements.⁸⁰

Justice Alito, in a concurring opinion joined by Chief Justice

73. *Id.* at 1672.

74. *Id.* at 1679.

75. *Id.*

76. *Id.* (quoting *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982)).

77. *See id.* at 1681-83 (Thomas, J., concurring).

78. *Id.* at 1682.

79. *See id.* at 1682-83.

80. *See id.*

Roberts and Justice Kavanaugh, advanced a more pragmatic approach to whether a branded drug manufacturer can successfully claim preemption under the “clear evidence” exception.⁸¹ He emphasized the “real world” nature of a branded drug manufacturer’s dealings with the FDA, whereby “if the FDA declines to require a label change despite having received and considered information regarding a new risk, the logical conclusion is that the FDA determined that a label change was unjustified.”⁸² Justice Alito was especially troubled by what he felt was a “one-sided account” by the majority of the Court of the case facts which downplayed the “extensive communication between Merck and the FDA during the relevant period.”⁸³

In particular, Justice Alito detailed multiple communications between the FDA and Merck in which the agency expressed its disapproval of a proposed change to Fosamax’s warning. These communications included a phone conversation in 2008, while Merck’s application to change Fosamax’s label was pending, in which an FDA official purportedly told Merck that “[t]he conflicting nature of the literature does not provide a clear path forward, and more time will be need[ed] for FDA to formulate a formal opinion on the issue of a precaution around these data.”⁸⁴ They also included an email from another FDA official about a week later stating “the FDA would ‘close out’ Merck’s applications if Merck ‘agree[d] to hold off on the [Precautions] language at this time.’”⁸⁵ That communication further indicated that the FDA “would then work with . . . Merck to decide on language for a [Precautions] atypical fracture language, if it is warranted.”⁸⁶

Such communications, combined with the FDA’s Safety Announcement issued months later stating that the agency reviewed the data and found no “clear connection” to a risk of atypical femoral fractures, supported the “logical conclusion” that the FDA would not have approved a change in warning.⁸⁷ Justice Alito also found it telling that “the Safety Announcement concluded by admonishing healthcare professionals to ‘continue to follow the recommendations in the drug label when prescribing oral bisphosphonates’ [e.g., Fosamax] and patients to ‘not stop taking their medication unless told to do so by

81. *See id.* at 1684-86 (Alito, J., concurring).

82. *Id.* at 1684.

83. *Id.* at 1685.

84. *Id.* (quoting internal Merck memorandum describing call provided as part of case record).

85. *Id.* at 1685-86 (quoting case record).

86. *Id.* at 1686 (quoting case record).

87. *Id.* (quoting FDA Safety Announcement).

their healthcare professional.”⁸⁸ He additionally noted that “the FDA itself, speaking through the Solicitor General, takes the position that the FDA’s decision not to require a label change prior to October 2010 reflected the FDA’s ‘determin[ation]’ that a new warning ‘should [not] be included in the labeling of the drug.’”⁸⁹

Justices Alito, Kavanaugh, and Chief Justice Roberts concluded that failure-to-warn claims against Merck should be preempted because “for years the FDA was: aware of this [warning] issue, communicating with drug manufacturers, studying all relevant information, and instructing healthcare professionals and patients alike to continue to use Fosamax as directed.”⁹⁰ These “extensive” communications by the FDA provided “clear evidence” that the FDA would not approve a change in Fosamax’s warning; an agency determination that warranted preemptive effect under *Wyeth*.⁹¹

II. NAVIGATING THE CONTOURS OF BRANDED DRUG PREEMPTION TODAY

Although the Supreme Court’s primary holding in *Albrecht*—that judges, not juries, must make pharmaceutical preemption determinations—is fairly straightforward, there are a number of outstanding issues that will likely play out in lower courts in the wake of the decision. The Court even acknowledged that it accepted review of *Albrecht* in light of “differences and uncertainties among the courts of appeals and state supreme courts in respect to the application of *Wyeth*” and the “clear evidence” exception, and that the Court’s decision to remand the case centered on the “determinative question” of the required decisionmaker without articulating precisely what will, and will not, satisfy the “clear evidence” exception.⁹² Nevertheless, the Court did “elaborate *Wyeth*’s requirements along the way” to help guide judges in their preemption analysis.⁹³

A. Pragmatism Should Govern Whether the “Clear Evidence” Exception Is Satisfied

The most important outstanding issue following *Albrecht* is what communication, action, or inaction by the FDA is sufficient to satisfy the “clear evidence” exception. As indicated in Part I, members of the Court

88. *Id.* (quoting FDA Safety Announcement).

89. *Id.* (quoting Brief of United States as Amicus Curiae).

90. *Id.*

91. *Id.* at 1685.

92. *Id.* at 1676, 1679 (majority opinion).

93. *Id.* at 1676.

had differing opinions on this issue. Justice Thomas supported the requirement of a formal FDA ruling explicitly rejecting a proposed warning change, leaving no doubts whatsoever, while Justices Alito, Kavanaugh, and Chief Justice Roberts supported a more flexible approach that considers the full scope of the branded drug manufacturer's interactions and communications with the FDA.⁹⁴

The majority of the Court expressed the “clear evidence” exception as requiring “evidence that shows the court that the drug manufacturer *fully informed* the FDA of the justifications for the warning required by state law and that the FDA, in turn, *informed* the drug manufacturer that the FDA would not approve a change to the drug's label to include that warning.”⁹⁵ This formulation, similar to that of Justices Alito, Kavanaugh, and Chief Justice Roberts, focuses on the exchange of information between the FDA and branded drug manufacturer. It omits an express requirement of a formal agency ruling rejecting a manufacturer's preapproval application to change a warning or subsequent rejection of a manufacturer's unilateral warning change made pursuant to the CBE process. In this regard, the Court appeared to adopt a more practical or functional approach to whether the FDA's communications signal disapproval of a proposed warning change.

Such a practical approach is also more consistent with the Court's primary holding to vest the preemption analysis exclusively with judges who “are better equipped to evaluate the nature and scope of an agency's *determination*.”⁹⁶ Indeed, if the Court intended that the FDA needed to make a formal ruling rejecting a proposed warning change or a warning change effectuated by the manufacturer pursuant to the CBE process in every circumstance, there would be little need for a preemption analysis. Rather, by adopting the “fully informed” and “informed” terminology that underscores the information exchange between the branded drug manufacturer and the FDA as the standard for the “clear evidence” exception, the Court appeared to envision a broader set of circumstances in which the FDA's communications would carry a preemptive effect.⁹⁷ The Court appeared to task judges with the preemption analysis precisely because the answer may not always be “clear cut,” and “judges are better suited than are juries to understand and to interpret agency decisions.”⁹⁸

This practical approach additionally makes greater sense from a public policy standpoint. If a branded drug manufacturer believes a change in a drug's warning is warranted, it has two options: 1) seek the FDA's

94. See *supra* notes 81-91 and accompanying text.

95. *Albrecht*, 139 S. Ct. at 1672 (emphasis added).

96. *Id.* at 1680 (emphasis added).

97. *Id.* at 1672.

98. *Id.* at 1680.

preapproval of a change to the drug's existing approved warning by submitting a PAS application; or 2) effectuate the change through the CBE process.⁹⁹ As discussed, Merck utilized both paths by first submitting PAS applications, which resulted in the FDA communicating its approval of a proposed change to Fosamax's "Adverse Reactions" section (but not to the drug's "Precautions" section), before using the CBE process to ultimately effectuate the change to the "Adverse Reactions" section.¹⁰⁰ If Merck, to obtain preemption, was required to have included in its CBE application the changes to Fosamax's "Precautions" section for which the FDA consistently communicated its disapproval and then await a formal, subsequent rejection by the FDA of that warning change, the result would have been a series of inconsistent warnings to prescribing physicians.

It is not difficult to imagine how problematic and disruptive such a requirement would be. Risk-adverse branded drug manufacturers unsure about a potential need for an added warning would have an incentive to pursue warning changes more readily through the CBE process just so the FDA formally repudiates the warning change *after* it has been made, which would establish a clear basis to preempt failure-to-warn claims. As a result, branded drug warnings could experience increased volatility through back-and-forth labeling changes introduced by the manufacturer and rejected by the FDA, creating confusion for prescribing physicians and impeding patient safety.¹⁰¹

The FDA also appears to share this concern. In its brief in *Albrecht*, the agency, speaking through the Solicitor General, indicated that the FDA has historically "accepted PAS applications instead of CBE supplements . . . particularly where significant questions exist on whether to revise or how to modify existing drug labeling."¹⁰² The agency's "Guidance for Industry" on safety labeling changes also states that warning changes based on new safety information made pursuant to the CBE process should be reserved for situations in which the manufacturer's proposed changes are "identical" to those for which the FDA has communicated approval.¹⁰³ "In *all* other situations," the FDA

99. See 21 C.F.R. § 314.70(b), (c) (2020); see also *Gayle v. Pfizer Inc.*, 452 F. Supp. 3d 78, 85 (S.D.N.Y. Apr. 7, 2020) ("Two avenues exist for manufacturers to update their drug labels.").

100. See *supra* notes 42-49 and accompanying text.

101. See *Albrecht*, 139 S. Ct. at 1673 (stating objective of FDA regulations to "exclude '[e]xaggeration of risk, or inclusion of speculative or hypothetical risks,' that 'could discourage appropriate use of a beneficial drug'" (quoting Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, & Med. Devices, 73 Fed. Reg. 2848, 2851 (Jan. 16, 2008))); see also *infra* notes 143-150 and accompanying text.

102. *Albrecht*, 139 S. Ct. at 1685 (Alito, J., concurring) (quoting Brief of United States as Amicus Curiae).

103. U.S. FOOD & DRUG ASS'N, CONTROL NO. 0910-0734, GUIDANCE FOR INDUSTRY: SAFETY

has explained, the branded drug manufacturer should submit a PAS application to “propose alternative labeling changes that reflect the new safety information.”¹⁰⁴ The public policy objective here is to promote collaboration between the FDA and the branded drug manufacturer to build “consensus on wording of the labeling change,” not encourage the manufacturer to rely on the CBE process as a tool to force the FDA’s hand into removing all doubts about the agency’s position for the purpose of a “clear evidence” preemption analysis.¹⁰⁵

Requiring a formal FDA rejection of a branded drug manufacturer’s warning change effectuated through the CBE process would also prove needlessly inefficient and wasteful where the FDA has made its position known in its response to a manufacturer’s PAS application (which was the case with Merck in *Albrecht*). The CBE process involves a significant, costly undertaking for a branded drug manufacturer that additionally stretches the FDA’s limited resources. It is intended to be used “sparingly.”¹⁰⁶ Pursuant to the CBE process, a branded drug manufacturer endeavoring to “add or strengthen” a drug’s labeling must prepare “a full explanation of the basis for the change” to reflect “newly acquired information.”¹⁰⁷ The newly acquired information must include data, analyses, or other information that provide “reasonable evidence of a causal association” of a “clinically significant adverse reaction[]” to a drug;¹⁰⁸ onerous requirements designed to protect against misuse or overuse of the CBE process.¹⁰⁹ At the very least, such an undertaking may be needlessly duplicative of a PAS application, which among other

LABELING CHANGES – IMPLEMENTATION OF SECTION 505(O)(4) OF THE FD&C ACT, 7 (2013), available at <https://www.fda.gov/media/116594/download>.

104. *Id.* (emphasis added).

105. *Id.* at 11.

106. *McGrath v. Bayer HealthCare Pharm., Inc.*, 393 F. Supp. 3d 161, 170 (E.D.N.Y. 2019) (“[T]he FDA contemplated that the CBE regulation would be used sparingly, noting it ‘would not allow a change to labeling to add a warning in the absence of reasonable evidence of an association between the product and an adverse event.’”) (quoting Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, & Med. Devices, 73 Fed. Reg. at 2851)).

107. 21 C.F.R. § 314.70(c)(3), (6)(iii). “Newly acquired information is data, analyses, or other information not previously submitted to the Agency, which may include (but is not limited to) data derived from clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events, or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to the FDA.” 21 C.F.R. § 314.3.

108. 21 C.F.R. § 201.57(c)(6)(i); see also *Utts v. Bristol-Myers Squibb Co.*, 251 F. Supp. 3d 644, 659 (S.D.N.Y. 2017), *aff’d sub nom. Gibbons v. Bristol-Myers Squibb Co.*, 919 F.3d 699 (2d Cir. 2019) (“[T]he CBE regulation requires that there be sufficient evidence of a causal association between the drug and the information sought to be added.”).

109. See *Merck Sharpe & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1673 (2019) (stating these requirements are meant to “exclude [e]xaggeration of risk, or inclusion of speculative or hypothetical risks,” that “could discourage appropriate use of a beneficial drug”) (quoting Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, & Med. Devices, 73 Fed. Reg. at 2851)); see also *infra* Part II.B (discussing CBE regulation).

things similarly requires the branded drug manufacturer to package a “detailed description of the proposed change,” a “description of the methods used and studies performed to assess the effects of the change” and the “data derived from such studies.”¹¹⁰

Even before *Albrecht* was decided, courts recognized that the “plain language” of *Wyeth* does not support the “contention that manufacturer submission and express rejection of a proposed warning is required to satisfy the clear evidence standard.”¹¹¹ Rather, the “relevant inquiry in each conflict preemption case since [*Wyeth v. Levine*] is stated as whether the FDA *would have* rejected a proposed labeling change, not whether the FDA did in fact issue an explicit rejection.”¹¹² *Wyeth*’s clear evidence exception, therefore, “necessarily considers instances where a manufacturer has not submitted a labeling change to the FDA.”¹¹³

Early judicial interpretations of *Albrecht* suggest a pragmatic approach that examines the totality of the communications between the FDA and branded drug manufacturer, and does not require a formal or explicit FDA rejection, is becoming more deeply entrenched. For example, in 2020, a federal district court in Missouri determined that failure-to-warn claims against the manufacturer of the branded blood thinner Pradaxa, which was approved by the FDA in 2010 to reduce the risk of stroke and blood clots in patients with atrial fibrillation, were preempted pursuant to the “clear evidence” exception.¹¹⁴ Here, plaintiffs sued the manufacturer for allegedly failing to add stronger warnings about the risk of bleeding.¹¹⁵ The court found the claims preempted not based on any specific action by the FDA, but rather “in light of the known issues and the ongoing give-and-take between [the branded drug manufacturer] and the FDA on these issues.”¹¹⁶

Specifically, the plaintiffs alleged that several studies of Pradaxa after it obtained FDA approval and a more detailed label for the drug’s sale in the European Union constituted “newly acquired information” requiring

110. 21 C.F.R. § 314.70(b)(3).

111. See *Seufert v. Merck Sharp & Dohme Corp.*, 187 F. Supp. 3d 1163, 1169 (S.D. Cal. 2016); see also *Cerveney v. Aventis, Inc.*, 155 F. Supp. 3d 1203, 1213-16 (D. Utah 2016) (“Courts have universally rejected the notion that *Levine* requires a showing that the manufacturer attempted to apply the warning suggested by the plaintiff but that the labeling was ultimately rejected by the FDA.”), *rev’d on other grounds*, 855 F.3d 1091 (10th Cir. 2017).

112. *Seufert*, 187 F. Supp. 3d at 1169 (emphasis added).

113. *Id.* at 1170; see also *id.* (“Courts in this Circuit and others have considered several factors in assessing conflict preemption, including the regulatory history of the drug or drug class at issue, temporal gaps between FDA action and accrual of a plaintiff’s claims, citizen petition submissions and rejections, available scientific data, and whether the FDA has reviewed the particular harm at issue and the consistency of any resulting conclusions.”).

114. *Ridings v. Maurice*, 444 F. Supp. 3d 973, 981-83, 998 (W.D. Mo. 2020).

115. See *id.* at 988.

116. *Id.*

the manufacturer to add stronger U.S. warnings pursuant to the CBE process.¹¹⁷ The court determined that this information, while helpful, did not provide conclusive new safety information because the FDA had always “understood that the use of Pradaxa presented a trade-off between an increased risk of stroke and an increased risk of major bleeding” based on different dosages.¹¹⁸ The court went further, though, in stating that even if the information cited by the plaintiffs constituted “newly acquired information,” the branded drug manufacturer “offered sufficient ‘clear evidence’ that the FDA . . . nonetheless would have rejected the warning(s).”¹¹⁹

The court explained that the FDA had contemporaneously reviewed the studies cited by the plaintiff, as well as other information provided to the agency by the branded drug manufacturer, and consistently declined to pursue additional warnings.¹²⁰ In light of this ongoing study and cooperation with the branded drug manufacturer, the court held that “the FDA’s *continued inaction* does represent clear evidence.”¹²¹

A federal district court in Louisiana reached a similar conclusion in another case decided within a year of *Albrecht*.¹²² The plaintiff alleged various tort claims, including failure-to-warn, against the manufacturer of the branded drug MultiHance, a Gadolinium-Based Contrast Agent (GBCA) approved by the FDA in 2004 for intravenous injection to create clearer, sharper images in MRI and MRA scans.¹²³ The plaintiff, who experienced an adverse reaction after being injected with the drug, argued that a specific warning about potential health risks of “gadolinium retention” was required by the manufacturer.¹²⁴ The court rejected this argument based on the absence of purported new safety risk information requiring the branded drug manufacturer to change the warning, and “more importantly” because there was “clear evidence that the FDA would not have approved a warning about the alleged adverse health consequences of a GBCA injection.”¹²⁵

The court reached this conclusion not based on any FDA rejection of a PAS application or CBE supplement by the branded drug manufacturer,

117. *See id.* at 993-94.

118. *Id.* at 993.

119. *Id.* at 998.

120. *See id.* at 993-98.

121. *Id.* at 998 (emphasis added). The court cautioned, however, that “it should not always be the case that simple inaction by the FDA in light of submitted data will always be ‘clear evidence’ that the FDA would reject a particular warning.” *Id.*

122. *See Thomas v. Bracco Diagnostics Inc.*, No. 3:19-CV-00493, 2020 WL 1016273 (W.D. La. Feb. 27, 2020).

123. *See id.* at *1.

124. *See id.* at *1, *6-8.

125. *Id.* at *10.

but rather based on independent action by the agency. The FDA approved a revised warning in 2018, about a month before the plaintiff's injection, which specifically addressed the presence of gadolinium retention in the body.¹²⁶ The added warning, however, stated that "clinical consequences" of gadolinium retention had not been established.¹²⁷ Because the "FDA had actually issued a revised warning informing the medical community that retention occurred but specifically adding that no causal relationship . . . has been established," the court determined that there was "clear evidence" the FDA would not have approved a proffered labeling change specifying health risks of gadolinium retention.¹²⁸

Courts have also found that the FDA's denial of a citizen petition to change a branded drug's warning may be sufficient to establish "clear evidence" that the agency would not approve a labeling change. As the U.S. Court of Appeals for the Tenth Circuit explained, there is "nothing in *Wyeth* or *Albrecht* excluding [a branded drug manufacturer] from justifying preemption" where the FDA has rejected a petition by an entity that is not the manufacturer.¹²⁹ Similarly, a North Dakota trial court stated that it would be "nonsensical" to interpret *Albrecht* "so narrowly" as to ignore the FDA's denial of a citizen petition in applying the "clear evidence" exception because "[r]egardless of who submitted the proposed warning or labeling change, the FDA has already decided that the relevant evidence and policies do not meet the standard to justify a change."¹³⁰

Such applications of the "clear evidence" exception following *Albrecht* underscore the importance of an approach with flexibility to account for the many ways modifications of branded drug warning labels occur in practice. "Clear evidence," as the Supreme Court explained, must not be confused in this context with a heightened evidentiary burden or an explicit showing that removes all doubt about whether a branded drug manufacturer can comply with federal and state requirements.¹³¹ The Court's refined standard avoided rigid or formalistic requirements to focus the analysis on the information exchange with the FDA, namely whether the agency was "fully informed" and in turn "informed" the branded drug manufacturer of agency determinations.¹³² This

126. *See id.* at *6, *10.

127. *Id.* at *6.

128. *Id.* at *10; *see also* *Drescher v. Bracco Diagnostics Inc.*, No. CV-19-00096-TUC-RM (LCK), 2020 WL 699878, at *5 (D. Ariz. Jan. 31, 2020) (stating that although the FDA ultimately required a label change for GBCAs in 2018, "that label explicitly refutes a causal association").

129. *Cerveney v. Aventis, Inc.*, 783 Fed. Appx. 804, 808 n.9 (10th Cir. 2019) (affirming dismissal of plaintiffs' state law failure-to-warn, fraud and negligent misrepresentation claims).

130. *State v. Purdue Pharma L.P.*, No. 08-2018-CV-01300, 2019 WL 3776653, at *2 (N.D. Dist. Ct. July 22, 2019).

131. *See Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1679 (2019).

132. *Id.* at 1678.

information contemplates “extensive communication” and an “ongoing give-and-take” between the branded drug manufacturer and the agency regardless of whether a warning change is ultimately effectuated by the FDA approving a manufacturer’s PAS application, approving or rejecting a manufacturer’s change made pursuant to the CBE process, or by the agency acting on its own to adopt a warning change.¹³³ It may also include a negative inference in approved warning information as seen with the GBCA MultiHance or the FDA’s denial of a third party’s citizen petition to effectuate a warning change. Courts applying the “clear evidence” exception should approach the preemption analysis with the understanding that the exception is designed for function over form, and that in the complex area of pharmaceutical regulation, FDA communications, action, and inaction can demonstrate “clear evidence” that the agency would not adopt a proffered warning change.

B. Conducting a Branded Drug Preemption Analysis

The Supreme Court’s effort in *Albrecht* to “elaborate” the “clear evidence” exception raises the issue of how judges charged with a branded drug preemption analysis are meant to fulfill that responsibility. As discussed in the previous section, approaching this responsibility with a sense of pragmatism and willingness to consider the totality of the circumstances and information exchange between the FDA and branded drug manufacturer is a key first step. But what are each of the steps in a branded drug preemption analysis today?

Courts deciding whether a failure-to-warn claim against a branded drug manufacturer is preempted often break down the analysis into two parts.¹³⁴ The first part examines whether the path identified in *Wyeth* in which the branded drug manufacturer may unilaterally change an FDA-approved warning—i.e. the CBE process—is even available to the manufacturer.¹³⁵ If the CBE process is not available, the rationale set forth in *Wyeth* for allowing a claim against a branded drug manufacturer fails, meaning the claim should be preempted because the manufacturer cannot legally change a warning without FDA approval.

Although the Court in *Wyeth* may have created an impression that a

133. *Id.* at 1685 (Alito, J., concurring); *Ridings v. Maurice*, 444 F. Supp. 3d 973, 998 (W.D. Mo. 2020).

134. See, e.g., *Adkins v. Boehringer Ingelheim Pharms., Inc.*, No. X03HHDCV1606065131S, 2020 WL 1890681, at *4 (Conn. Super. Ct. Mar. 13, 2020) (discussing “two-pronged” nature of preemption analysis); *Gayle v. Pfizer Inc.*, 452 F. Supp. 3d 78, 87 (S.D. N.Y. 2020) (discussing plaintiffs’ failure to satisfy “first step” of preemption analysis).

135. *Adkins*, 2020 WL 1890681, at *4 (stating that *Albrecht* maintained “the first, CBE prong of the preemption test”).

branded drug manufacturer is generally free to unilaterally change a warning if and when it sees fit, FDA regulations make plain that the circumstances are limited.¹³⁶ As mentioned previously with respect to the burdens associated with the CBE process, a branded drug manufacturer can only pursue a warning change through the CBE process in light of “newly acquired information.”¹³⁷ Newly acquired information is defined as “data, analyses, or other information not previously submitted to the [FDA],” which means a branded drug manufacturer’s unilateral warning change cannot be predicated on information the manufacturer has already supplied the agency in obtaining initial approval of a branded drug’s warning or a subsequent approval or rejection of a revised warning.¹³⁸ Newly acquired information may include “data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) *if the studies, events, or analyses reveal risks of a different type or greater severity or frequency* than previously included in submissions to FDA.”¹³⁹

In addition, the newly acquired information must provide “reasonable evidence of a causal association” of a “clinically significant adverse reaction[]” to a drug.¹⁴⁰ A clinically significant adverse reaction includes reactions that have a “significant impact on therapeutic decision-making,” such as a risk that is “potentially fatal” or “serious even if infrequent.”¹⁴¹ Therefore, new data or analyses that evaluate adverse events or other impacts of a branded drug, but do not

136. See *MacMurray v. Boehringer Ingelheim Pharms., Inc.*, No. 2:17-CV-00195, 2017 WL 11496825, at *2 (D. Utah Dec. 17, 2017) (“The CBE regulation is restrictive Labeling changes pursuant to the CBE regulation may only be made on the basis of ‘newly acquired information.’”).

137. 21 C.F.R. § 314.70(c)(3), (6)(iii) (2016).

138. 21 C.F.R. § 314.3(b) (2016); see also *Roberto v. Boehringer Ingelheim Pharms., Inc.*, No. CPLHHDCV166068484S, 2019 WL 5068452, at *13 (Conn. Super. Ct. Sept. 11, 2019) (“[A]ny claim that a drug label should be changed based solely on ‘information previously submitted to the FDA is preempted because the CBE regulation cannot be used to make a label change based on such information.’”) (quoting *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Pracs. & Prod. Liab. Litig.*, 185 F. Supp. 3d 761, 769 (D.S.C. 2016)).

139. 21 C.F.R. § 314.3(b) (2016) (emphasis added). The newly acquired information must also accomplish one of five statutory objectives, including a change to: 1) “add or strengthen a contraindication, warning, precaution, or adverse reaction”; 2) “add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage”; 3) “add or strengthen an instruction about dosage and administration”; 4) “delete false, misleading, or unsupported indications for use or claims for effectiveness”; and 5) “Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.” 21 C.F.R. § 314.70(c)(6)(iii) (2016).

140. 21 C.F.R. § 201.57(c)(6)(i) (2015); see also *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 392 (7th Cir. 2010) (“It is technically a violation of federal law to propose a CBE that is not based on reasonable evidence.”) (citing 18 U.S.C. § 1001).

141. Requirements on Content and Format of Labeling for Human Prescription Drugs and Biological Products, 71 Fed. Reg. 3922-01, 3946 (Jan. 24, 2006); 21 C.F.R. § 201.57(c)(6)(i) (2015).

expressly identify a causal association to a clinically significant adverse reaction, are irrelevant to a preemption analysis because they offer no actionable intelligence that would enable the manufacturer to pursue a warning change pursuant to the CBE process.¹⁴²

As the Supreme Court recognized in *Albrecht*, the limitations set forth in the CBE process serve to “exclude ‘[e]xaggeration of risk, or inclusion of speculative or hypothetical risks,’ that ‘could discourage appropriate use of a beneficial drug.’”¹⁴³ A plaintiff pursuing a failure-to-warn claim against a branded drug manufacturer thus bears the initial burden of demonstrating the existence of newly acquired information for which the manufacturer failed to act upon by pursuing a unilateral warning change through the CBE process.¹⁴⁴

A number of branded drug preemption cases decided in the wake of *Albrecht* have turned on the sufficiency of purported newly acquired information. For example, in 2020, the U.S. District Court for the Southern District of New York rejected failure-to-warn claims involving the FDA-approved cholesterol-lowering drug Lipitor.¹⁴⁵ Plaintiffs’ alleged that Lipitor’s manufacturer needed to include specific warnings about the risk of type-2 diabetes, citing some 6,000 adverse event reports.¹⁴⁶ The court determined that adverse event reports that merely “describe instances where patients taking Lipitor were diagnosed with type 2 diabetes but do not reach any conclusions regarding a causal association . . . cannot constitute ‘newly acquired information’” under a “plain reading” of the FDA’s regulations.¹⁴⁷

In finding the claims preempted, the court recognized that the CBE requirement that newly acquired information show “a basis to believe there is a causal relationship between the drug and the occurrence of the adverse event” provides a “backstop to prevent manufacturers from

142. See, e.g., *In re Celexa & Lexapro Mktg. & Sales Pracs. Litig.*, 779 F.3d 34, 42 (1st Cir. 2015) (finding claim preempted because label change not allowed under CBE regulation absent “newly acquired information”).

143. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1673 (2019) (quoting 73 Fed. Reg. 2848, 2851 (2008)).

144. See *Adkins v. Boehringer Ingelheim Pharms., Inc.*, No. X03HHDCV1606065131S, 2020 WL 1890681, at *5 (Conn. Super. Ct. Mar. 13, 2020) (“[T]he burden of going forward and identifying the purported newly acquired information must fall on the plaintiff because ‘it would be virtually impossible for the defendants to prove a negative and negate the existence of newly acquired information without knowing exactly what newly acquired information the plaintiff relies upon.’”) (quoting *Roberto v. Boehringer Ingelheim Pharms., Inc.*, No. CPLHHDCV166068484S, 2019 WL 5068452, at *11 n.9 (Conn. Super. Ct. Sept. 11, 2019)).

145. See *Gayle v. Pfizer Inc.*, 452 F. Supp. 3d 78, 87-89 (S.D.N.Y. 2020).

146. See *id.* at 88.

147. *Id.* The court additionally rejected the plaintiffs’ argument that adverse event reports which “offer no analysis” could be sufficient to shift the burden onto the manufacturer to demonstrate “clear evidence” that the FDA would have rejected plaintiffs’ proffered warning change without satisfying the first part of the preemption analysis. *Id.*

warning of every possible adverse reaction in an effort to insulate themselves from any conceivable liability.”¹⁴⁸ “Over-disclosure,” the court cautioned, “dilutes warnings of more significant adverse reactions both by likelihood and severity of the reaction and can unjustifiably deter patients from a helpful drug or therapy.”¹⁴⁹ Consequently, new information “without any analysis indicating causality” is inadequate and “misses the mark.”¹⁵⁰

The U.S. District Court for the Eastern District of New York reached a similar conclusion shortly after *Albrecht* was decided in a case involving another GBCA branded as Magnevist.¹⁵¹ Here, a plaintiff argued that Magnevist, which was approved by the FDA in 1988, required a specific warning about gadolinium retention resulting in fibrosis in light of several medical studies.¹⁵² The court found that the plaintiff’s failure-to-warn “allegations focus on gadolinium retention, which is not, by itself, [a] ‘clinically significant adverse reaction,’” were unaccompanied by data establishing “the requisite causal connection” to an actual risk of harm.¹⁵³ “Studies concluding it ‘remains unknown whether GBCAs induce toxic effects’ and that ‘further studies are required to address possible clinical consequences of gadolinium deposition,’” the court explained, “do not constitute reasonable or well-grounded scientific evidence of ‘clinically significant adverse effects’ under the CBE regulation.”¹⁵⁴ For instance, in dismissing one of the studies proffered by plaintiff as “newly acquired information,” the court reasoned that a “single study performed on mice does not make a risk ‘apparent’ or otherwise constitute ‘reasonable evidence of an association’ between Magnevist and fibrosis.”¹⁵⁵ As the court appreciated, “to ensure that only ‘scientifically accurate information appears in the approved labeling’ the FDA prefers a more cautious approach, and finds that because ‘labeling that includes theoretical hazards not *well-grounded* in scientific evidence can cause meaningful risk information to lose its significance,’ there must be ‘*sufficient* evidence of a causal association between the drug and the information sought to be added.”¹⁵⁶

148. *Id.* at 85 (quoting 21 C.F.R. § 201.57(c)(7)).

149. *Id.*

150. *Id.* at 88.

151. *See* McGrath v. Bayer HealthCare Pharms. Inc., 393 F. Supp. 3d 161 (E.D.N.Y. 2019).

152. *See id.* at 165.

153. *Id.* at 168.

154. *Id.* at 169-70.

155. *Id.* at 170.

156. *Id.* at 169 (quoting *Utts v. Bristol-Meyers Squibb Co.*, 251 F. Supp. 3d 644, 659 (S.D.N.Y. 2017)) (emphasis in original); *see also* *Klein v. Bayer Healthcare Pharms. Inc.*, No. 2:18-cv-01424-APG-EJY, 2019 WL 3945652, at *5 (D. Nev. Aug. 21, 2019) (“[Plaintiff] does not plead facts showing that Bayer had or should have had newly acquired information permitting it to unilaterally add her desired

If a plaintiff can demonstrate the existence of “newly acquired information” with the requisite evidence of a causal association to support a labeling change under the CBE regulation, the second part of the preemption analysis shifts the burden to the branded drug manufacturer to show “clear evidence” that the FDA would not have approved the proffered labeling change based on that information.¹⁵⁷ As discussed, the branded manufacturer at this stage should be permitted to rely on the information the FDA had at its disposal and the totality of the communications between the agency and manufacturer to establish that the agency was “fully informed” of justifications supporting a different warning to comply with state law.¹⁵⁸ A similar pragmatic approach to the information exchange should also apply to the FDA’s communications that “inform” the branded drug manufacturer that the agency will not approve an altered warning.¹⁵⁹ Subsequent action to reject a potential warning change or continued inaction by the FDA should additionally serve as sufficient evidence that the “fully informed” agency has made a determination not to alter a warning, which “informed” the manufacturer for the purposes of satisfying “clear evidence” under *Albrecht*.¹⁶⁰

The Court in *Albrecht* charged judges with making these determinations because they are “better suited than are juries to understand and to interpret agency decisions” and the import of the FDA’s communications that “memorialize its considered judgments.”¹⁶¹ Judges are well-suited to discern whether the FDA’s communications with a branded drug manufacturer are intended to foreclose further deliberation about a potential warning change (and carry a preemptive effect), or accomplish some other objective such as seeking greater information about a potential drug risk or continuing a dialogue about potential labeling changes.¹⁶² Judges should not be limited in their analysis to only formal FDA decisions and forced to turn a blind eye to what might be repeated, glaring indications by the agency to a manufacturer that a drug’s warnings should not be changed. Such an approach would undermine the purpose of having a judge perform a branded drug preemption analysis.

Judges should also appreciate that a pragmatic approach to deciding whether clear evidence exists that the FDA would not approve a warning change promotes the development of safer drugs. It avoids the creation

warning under the CBE regulation.”).

157. See *Utts*, 251 F. Supp. 3d at 661.

158. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1678 (2019).

159. See *supra* Part II.A.

160. See *supra* Part II.A.

161. *Albrecht*, 139 S. Ct. at 1680.

162. See, e.g., *In re Avandia Mfg., Sales & Prods. Liab. Litig.*, 945 F.3d 749, 759 (3d Cir. 2019) (finding that the FDA’s response letter to a proposed change sought additional information from manufacturer such that the agency was not “fully informed” and had not rejected the proposal).

of unsound incentives for branded drug manufacturers to pursue unnecessary FDA rulings that formally reject every conceivable warning change simply to obtain a surefire preemption defense where the agency has made its position clear by telling the manufacturer to “hold off” or that the science “does not provide a clear path forward” for a labeling change.¹⁶³ This concern becomes more pronounced and antithetical to drug safety where a branded drug manufacturer is placed in the position of having to use the CBE process to unilaterally implement a warning change to protect itself from potentially massive liability exposure, and the FDA subsequently reverses that decision. The result may be needless inconsistency in the warnings provided to prescribing physicians that can cause confusion, or possibly excessive warnings that dilute more significant warnings or cause physicians to disregard other warnings. The FDA, meanwhile, is forced to exhaust its limited resources to respond; resources that could otherwise be devoted to evaluating the risks of other drugs and advancing drug safety.¹⁶⁴

III. THE ROLE OF PREEMPTION FOR FDA-APPROVED DRUGS

The Supreme Court’s decision in *Albrecht* supplements a legal environment in which failure-to-warn claims related to the vast majority of U.S. drug prescriptions are preempted under federal law.¹⁶⁵ Congress has established such a regime to further various public policy objectives, perhaps most notably the inexpensive development of generic drugs that comprise the vast majority of drug prescriptions.¹⁶⁶ Congress has appreciated that having lay juries across fifty states “second guess” the labeling cost-benefit analysis of the expert agency responsible for ensuring drug safety and efficacy may not necessarily improve drug safety. Nevertheless, with respect to branded drugs that are typically newer products, Congress has determined that the value of having juries provide a separate means of ensuring drug safety and effectiveness is a worthwhile “layer of consumer protection that complements FDA regulation.”¹⁶⁷ Of course, as the Supreme Court has recognized, “Congress and the FDA retain the authority to change the law and regulations if they so desire.”¹⁶⁸

Doctrines such as the “clear evidence” exception fit within this

163. *Albrecht*, 139 S. Ct. at 1685-86 (quoting case record).

164. See *Wyeth v. Levine*, 555 U.S. 555, 578 (2009) (stating that the “FDA has limited resources to monitor the 11,000 drugs on the market”).

165. See *supra* Part I.A.

166. See *supra* notes 21-23 and accompanying text.

167. See *Wyeth*, 555 U.S. at 579.

168. *Pliva, Inc. v. Mensing*, 564 U.S. 604, 626 (2011).

framework to remove any second guessing of the FDA's determinations where the agency has made its position known not to approve a warning change and has effectively placed the branded drug manufacturer in a box. It follows that the manufacturer that has been informed of the FDA's position not to approve a warning change should not be required to engage in a fruitless pursuit to unilaterally change a warning only to have the FDA override that change.

A significant public policy reason for this approach is that the cost of developing a branded drug and bringing it to market is already an enormously expensive undertaking. Some studies estimate the average research and development investment for a new drug at around \$1.3 billion, with other studies suggesting total costs closer to \$3 billion.¹⁶⁹ These costs reflect the fact that most drug treatments fail to obtain FDA approval and represent a sunk cost for the manufacturer.¹⁷⁰ The full research, development and approval process can also take 12 to 15 years, creating a relatively narrow window for the branded drug manufacturer to recoup its investment where drug patents generally end after 20 years.¹⁷¹

Allowing failure-to-warn claims against branded drug manufacturers can impose substantial additional costs after a drug obtains FDA approval and is marketed for sale. Every year, branded drug manufacturers face thousands of lawsuits related to their products. In 2020, pending product liability MDLs alone involved at least twenty different drug products, consolidating tens of thousands of cases in federal courts.¹⁷² Pharmaceutical product liability is estimated to result in billions of dollars of added costs each year.¹⁷³

The substantial front-end investments and unpredictable back-end liability costs create a challenging environment for new drug innovation. Although competition from generic drug companies can

169. See Olivier J. Wouters, et al., *Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018*, 323 J. AM. MED. ASSN. 844 (Mar. 3, 2020), available at <https://jamanetwork.com/journals/jama/article-abstract/2762311> (estimating a \$1.3 billion mean research and development investment to bring a new drug to market and referencing other studies that estimate a \$2.8 billion expense).

170. See *id.*

171. See Leigh Ann Anderson, *FDA Drug Approval Process*, DRUGS.COM (Apr. 13, 2020), <https://www.drugs.com/fda-approval-process.html> (explaining the 12-to-15-year new drug development process).

172. See *Pending MDLs*, U.S. JUD. PANEL ON MULTIDISTRICT LITIG. (May 15, 2020), <https://www.jpml.uscourts.gov/pending-mdls-0> (providing links to lists of MDLs organized under different categories).

173. See Erin Bosman et al., *\$4 Billion Price Tag for Pleasing Plaintiffs' Bar? New Study Estimates Costs of FDA's Proposed Rule on Generic Drug Labeling*, JD SUPRA (Feb. 26, 2014), <https://www.jdsupra.com/legalnews/4-billion-price-tag-for-pleasing-plaint-15927/> (discussing analysis of proposed rule change to subject generic drug companies to failure-to-warn liability and estimating the increased product liability cost at \$4 billion annually).

prove beneficial in enabling consumers to obtain life-saving medications more cheaply, it can also result in an uneven playing field where the branded drug company must absorb all product liability (even after its drug patent expires) and the generic drug company is generally free of that concern. In addition, the branded drug manufacturer bears responsibility and costs related to post-sale monitoring of its drug and ensuring the FDA has updated information about adverse drug reactions or potential newly discovered drug risks.¹⁷⁴ Therefore, for a branded drug manufacturer, the availability of a preemption defense is critical to mitigating the least predictable burdens and costs associated with the development of a drug innovation.

This unpredictability has also increased in recent years. A few courts have expanded state tort law to subject a branded drug manufacturer to liability for injury to a person who consumed a generic drug manufacturer's product. These "innovator liability" theories argue that because a branded drug manufacturer (i.e. innovator) created the branded version of a drug and obtained FDA approval of the warning that generic drug manufacturers are required by law to copy, the branded drug manufacturer should be subject to warning liability for any harm resulting from a generic version of that drug.¹⁷⁵

In 2014, the Alabama Supreme Court became the first state high court to adopt an innovator liability theory, but the decision was short-lived and effectively overturned by the Alabama Legislature the following year.¹⁷⁶ Since that time, several other courts have accepted innovator liability theories. For example, in 2017, the California Supreme Court held that a branded drug manufacturer may be subject to liability where the plaintiff consumed a generic version of the drug, even where the branded drug manufacturer had completely divested its interests in the branded drug six years before the plaintiff's injury.¹⁷⁷ In 2018, Massachusetts' high court similarly embraced innovator liability where a branded drug manufacturer acts recklessly with respect to its duty to update labeling that a generic drug competitor

174. See *Step 5: FDA Post-Market Drug Safety Monitoring*, U.S. FOOD & DRUG ADMIN. (Jan. 4, 2018), https://www.fda.gov/patients/drug-development-process/step-5-fda-post-market-drug-safety-monitoring#Active_Surveillance (discussing drug manufacturer post-sale monitoring duty).

175. See Victor E. Schwartz, et al., *Warning: Shifting Liability to Manufacturers of Brand-Name Medicines When the Harm was Allegedly Caused by Generic Drugs has Severe Side Effects*, 81 FORDHAM L. REV. 1835 (2013).

176. See ALA. CODE ANN. § 6-5-530(a) (2020) (superseding *Wyeth, Inc. v. Weeks*, 159 So. 3d 649 (Ala. 2014), effectively reversing the Alabama Supreme Court's adoption of the innovator liability theory).

177. See *T.H. v. Novartis Pharm. Corp.*, 407 P.3d 18 (Cal. 2017).

copies.¹⁷⁸

The vast majority of courts, however, have rejected innovator liability theories, recognizing they are antithetical to a basic principle of product liability that an entity is not liable for injuries caused by a competitor's product.¹⁷⁹ For example, in rejecting such a theory, the Iowa Supreme Court referred to innovator liability as "Deep pocket jurisprudence" that is "law without principle."¹⁸⁰ The court also expressed concerns about the potential for subjecting branded drug manufacturers to limitless liability, stating it would instead continue to adhere to "bedrock principles" and not "contort Iowa's tort law in order to create liability"¹⁸¹

Nevertheless, the threat of further judicial adoption of innovator liability theories places greater pressure and uncertainty on the branded drug manufacturers that develop society's drug innovations. The critical importance of these innovations, and threats posed by excessive liability, are also amplified in times of health crisis, for example the coronavirus (COVID-19) pandemic. Doctrines such as the "clear evidence" exception provide an avenue of relief to innovating drug manufacturers to at least curb their liability exposure where the FDA has indicated the manufacturer has acted responsibly with respect to its warning obligation. A pragmatic approach to judicial applications of the "clear evidence" exception following *Albrecht* represents sound public policy because it provides liability protection in a fair manner that does not effectively disregard what might be years of "extensive communication" and collaboration

178. See *Rafferty v. Merck & Co., Inc.*, 92 N.E.3d 1205, 1219 (Mass. 2018) ("[A] brand-name manufacturer that controls the contents of the label on a generic drug owes a duty to consumers of that generic drug not to act in reckless disregard of an unreasonable risk of death or grave bodily injury.").

179. See, e.g., *McNair v. Johnson & Johnson*, 818 S.E.2d 852, 867 (W. Va. 2018) ("[T]here is no cause of action in West Virginia for failure to warn and negligent misrepresentation against a brand-name drug manufacturer when the drug ingested was produced by a generic drug manufacturer."), *aff'd per curiam*, 773 F.App'x 681 (4th Cir. 2019) (affirming dismissal after remand from West Virginia Supreme Court of Appeals); *Johnson v. Teva Pharms. USA, Inc.*, 758 F.3d 605, 614-16 (5th Cir. 2014) (finding plaintiff's innovator liability claims against branded drug manufacturer foreclosed under Louisiana Products Liability Act (LPLA)); *Foster v. Am. Home Prods. Corp.*, 29 F.3d 165, 168 (4th Cir. 1994) ("Maryland law requires a plaintiff seeking to recover for an injury by a product to demonstrate that the defendant manufactured the product at issue."); In *Re: Zantac (Ranitidine) Prods. Liab. Litig.*, MDL No. 2924, 2020 WL 7866660 (S.D. Fla. Dec. 31, 2020) (concluding that "none of the 35 jurisdictions that the Court analyzed would recognize Plaintiffs' theory of liability under which Defendants may be held liable for injuries sustained by Plaintiffs' ingestion of a product that Defendants did not manufacture, sell, or distributed").

180. See *Huck v. Wyeth, Inc.*, 850 N.W.2d 353, 380 (Iowa 2014) (quoting Schwartz et al., *supra* note 175, at 1871); see also Victor E. Schwartz & Phil Goldberg, *Iowa High Court Exposes Pharma 'Innovator Liability' for What it Is: Deep-Pocket Jurisprudence*, LEGAL OP. LETTERS (Wash. Legal Found., D.C.), Sept. 12, 2014, at 1, available at <https://www.wlf.org/2014/09/12/publishing/iowa-high-court-exposes-pharma-innovator-liability-for-what-it-is-deep-pocket-jurisprudence/> (discussing cases).

181. *Huck*, 850 N.W.2d at 380.

between a branded drug manufacturer and the FDA.¹⁸²

The availability of preemption for warning claims involving generic drugs, vaccines, and branded drugs where the “clear evidence” exception is satisfied raises an issue that drives all pharmaceutical litigation: how should the law deal with individuals who have suffered injury from taking a drug, but may be left uncompensated? Again, failure-to-warn claims related to generic drugs that comprise the vast majority of U.S. prescriptions are preempted, meaning that most individuals injured by an FDA-approved drug cannot recover from the manufacturer.¹⁸³ This situation is why plaintiffs’ attorneys have resorted to asserting innovator liability theories that try to shift blame to a branded drug manufacturer that not only did not make the product that allegedly caused injury, but is often competing directly with the generic drug manufacturer that did.¹⁸⁴ If a tortured expansion of product liability law offers an unjust and unprincipled way to address the problem of uncompensated plaintiffs, what might be a solution?

The National Vaccine Injury Compensation Program (VICP) provides an example of a system that strikes a balance between promoting the broad use of vaccines and accounting for injuries that may result where claims against the drug manufacturer are preempted.¹⁸⁵ Pursuant to this system, an individual injured by an FDA-approved vaccine can file a claim with a no-fault victim compensation fund.¹⁸⁶ As the Supreme Court has recognized, the VICP is “designed to work faster and with greater ease than the civil tort system” by providing for informal adjudication of injury claims and reducing the legal requirements for a claimant to obtain a recovery.¹⁸⁷

The VICP, which is funded by an excise tax on each purchased dose of a covered vaccine, was adopted precisely because lawsuits against vaccine manufacturers and health care providers “threatened to cause vaccine shortages and reduce U.S. vaccination rates, which could have caused a resurgence of vaccine preventable diseases.”¹⁸⁸ By generally preempting all design and warning claims and channeling injury

182. *Merck Sharp & Dohme Corp. v. Albrecht*, 139 S. Ct. 1668, 1684-86 (2019) (Alito, J., concurring).

183. See STATISTA.COM, *supra* note 23.

184. See Schwartz et al., *supra* note 175.

185. See *National Vaccine Injury Compensation Program*, HEALTH RES. & SERVS. ADMIN., <https://www.hrsa.gov/vaccine-compensation/index.html> (last updated Nov. 2020) (outlining vaccine injury compensation program).

186. See *id.*

187. *Bruesewitz v. Wyeth LLC*, 562 U.S. 223, 228 (2011) (quoting *Shalala v. Whitecotton*, 514 U.S. 268, 269 (1995)).

188. See *National Vaccine Injury Compensation Program*, *supra* note 185.

claims into a no fault compensation system, the VICP has played a vital role in stabilizing the production and broad use of vaccines.¹⁸⁹

A similar approach might provide a balanced solution with respect to the development of drugs other than vaccines. Such an approach would require legislation, and would surely involve greater scope and complexity, but would get to the heart of the compensation issue. It could do so without undermining the benefits federal law provides through preemption; benefits that include having an expert federal agency set forth labeling requirements in a manner uninhibited by potentially inconsistent lay jury determinations, promoting the continued development of inexpensive generic drugs, and advancing drug innovations through more predictable costs and liability exposure.

Although the specifics of a compensation fund model are beyond the scope of this Article, policymakers searching for an optimal balance of competing public policies may find value in it. Judges tasked with preemption determinations, on the other hand, must apply the law as it exists and leave any future regime change to Congress. With respect to the “clear evidence” exception, the Supreme Court has articulated an approach for judges that fairly balances the competing policy interests under the current liability system.

IV. CONCLUSION

The Supreme Court’s decision in *Albrecht* resolved several important outstanding issues regarding the application of the “clear evidence” exception, but also left open precisely what evidence will suffice to show that the FDA would not have approved a labeling change to a branded drug. The Court held that such determinations must be made by judges, not juries, and provided guidance to judges on how to conduct a modern branded drug preemption analysis. This analysis focuses on the exchange of information between the FDA and the branded drug manufacturer to assess whether the manufacturer “fully informed” the agency of the justifications for a warning change and whether the FDA “informed” the manufacturer that the agency would not approve a warning change. Judges applying this standard should adopt a pragmatic and flexible approach that looks at the totality of the FDA’s communications, action or inaction to determine whether the agency has made its position clear, and avoid any rigid approach that considers only formal agency rulings. An overly narrow approach would ignore circumstances in which the

189. See Emily Levine & Andrea Davey, *The National Vaccine Injury Compensation Program and Maternal Immunizations*, 11 J. HEALTH & LIFE SCI. L. 32, 39 (2017) (“Very few cases have been filed and pursued against vaccine manufacturers or administrators in post-VICP civil litigation.”).

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FDA has made plain its position not to change a drug's labeling, and invite adverse consequences that can impair physicians' ability to properly prescribe drug treatments and impede safety improvements. A pragmatic approach also strikes a fairer balance in reducing unpredictable liability costs for branded drug manufacturers that can hinder new drug innovations. *Albrecht* provides judges with a sound path forward for making reasonable preemption determinations and is up to them to implement it.