Status of the Preemption Defense in Pharmaceutical Products Liability Cases

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1. What is Impossibility Preemption?

Under the Supremacy Clause of the Constitution, state law is preempted in three circumstances. First, "Congress can define explicitly the extent to which its enactments pre-empt state law."[1] Second, "state law is pre-empted where it regulates conduct in a field that Congress intended the Federal Government to occupy exclusively."[2] Third, state law is preempted "to the extent that it actually conflicts with federal law . . . where it is impossible for a private party to comply with both state and federal requirements, or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."[3] The third type of preemption is often described as "impossibility" preemption.

This paper discusses how the impossibility preemption defense is applied in pharmaceutical products liability cases. First, we discuss the United States Food and Drug Administration ("FDA") processes underlying the impossibility preemption defense. We then turn to its application in several seminal Supreme Court cases in the pharmaceutical context and how those holdings have been applied by various federal courts of appeals: (1) *Wyeth v. Levine*,[4] (2) *PLIVA, Inc. v. Mensing*,[5] *Mutual Pharmaceutical Co. v Bartlett*;[6] and (4) *Merck Sharp & Dohme Corp. v. Albrecht*.[7] We conclude with a discussion of examples of pending products liability lawsuits arguing the impossibility preemption defense and how those arguments may continue to be made in the future.

A. The FDA Standards Underlying Impossibility Preemption

1. *Federal Regulation of Generic Drugs — Duty of Sameness*

In 1984, Congress amended the Food, Drug, and Cosmetic Act ("FDCA") under the Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Amendments.[8] While"[d]rug companies that bring a new product to market are required to file a New Drug Application ('NDA')," involving "costly and time intensive clinical trials," generic pharmaceuticals "receive accelerated approval by the FDA through the

1 *English v. Gen. Elec. Co.*, 496 U.S. 72, 78 (1990).

2 *Id.* at 79.

3 *Id.* (internal marks and citation omitted).

4 555 U.S. 555, (2009);

5 564 U.S. 604 (2011);

6 570 U.S. 472 (2013).

7 139 S. Ct. 1668, 1672, 203 L. Ed. 2d 822 (2019)

8 Pub. L. No. 98-417, 98 Stat. 1585 (1984).

submission of an Abbreviated New Drug Application ('ANDA')."[9] An ANDA "only requires the generic manufacturers to provide proof that their product is identical in both composition and labeling to a previously approved brand name product and to maintain the labeling pursuant to the requirements imposed on the brand name drug by the FDA."[10] Generic medications must have the same active ingredients, route of administration, dosage form, strength, and labeling as their branded counterparts.[11] Under this framework, generic drug companies are permitted to "gain FDA approval simply by showing equivalence to a reference listed drug that has already been approved by the FDA."[12]

This "duty of sameness" extends beyond the physical label on the generic medication and applies to any promotional and marketing materials.[13] Labeling includes "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."[14] The FDA has explained that "labeling" encompasses:

> [b]rochures, booklets, mailing pieces, detailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug and references published . . . for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug and which are disseminated by or on behalf of its manufacturer, packer, or distributor.[15]

1. *The Changes Being Effected Process for Brand Name Manufacturers*

Prospective drug manufacturers are required to work with the FDA to develop appropriate labels when they apply for FDA approval of a new drug.[16] While drug manufacturers generally seek advance permission from the FDA to make substantive changes to their drug

9 *Moore v. Zydus Pharm. (USA), Inc.*, 277 F.Supp.3d 873, 878-79 (E.D. Ky. 2017).

10 *Id.*; *see also McMurray v. Boehringer Ingelheim Pharms., Inc.*, No. 17-cv-00195, 2017 WL 11496825, at *5-6 (D. Utah Dec. 6, 2017) (recognizing FDA requirement that generic products are identical to approved branded products).

11 U.S.C. § 355(j)(2)(A); *see also* 21 C.F.R. § 314.150(b)(10).

12 *Mensing*, 564 U.S. at 612.

13 *See* 21 U.S.C. § 321(m); 21 C.F.R. § 202.1(*l*)(2).

14 21 U.S.C. § 321(m).

15 21 C.F.R. § 202.1(*l*)(2).

16 *Albrecht*, 139 S. Ct. at 1672; 21 U.S.C. §§ 355(a), 355(b), 355(d)(7); 21 C.F.R. § 314.125(b)(6).

labels, drug makers also can use an alternative process to make further label changes through an FDA regulation allowing "changes being effected" or "CBE."[17] CBE allows a drug manufacturer to bypass the FDA when a drug manufacturer adds or strengthens a warning label when there is "newly acquired information" about the "evidence of casual association" between the drug and a risk of harm.[18]

While a brand manufacturer may use the CBE process, when appropriate, to modify labeling and add or strengthen a warning without prior FDA approval, a generic manufacturer may only use the CBE procedure "to match an updated brand-name label or to follow the FDA's instructions." [19] In all other situations, "CBE changes unilaterally made to strengthen a generic drug's warning label would violate the statutes and regulations requiring a generic drug's label to match its brand-name counterpart's."[20] In other words, federal law requires that "generic drug labels be the same at all times as the corresponding brand-name drug labels."[21]

2. The Seminal Supreme Court Cases Applying Impossibility Preemption in Pharmaceutical Products Liability Cases

A. *Wyeth v. Levine*

In *Wyeth v. Levine*, the Supreme Court held that a state law failure to warn claim was not preempted against a brand-name manufacturer, Wyeth, because it had the ability to unilaterally make changes to the drug's label.[22] In that case, the plaintiff received an antihistamine to treat nausea via an IV-push, i.e. injection directly into the plaintiff's vein.[23] The plaintiff filed suit against Wyeth after developing gangrene, which led to amputation of the plaintiff's forearm.[24] Though the drug's label warned of risks related to gangrene and amputation, it did not recommend that physicians administer the drug via intravenous drip.[25] The plaintiff argued that had the product had an adequate label warning about the risks of intravenous delivery, the injuries would not have occurred. In response, Wyeth argued that it could not have changed the

17 *Albrecht*, 139 S. Ct. at 1672.

18 *Id.*

19 *Mensing*, 564 U.S. at 614.

20 *Id*.

21 *Id*. at 618.

22 *Wyeth*, 555 U.S. at 558-59.

23 *Id.*

24 *Id*.

25 *Id*. at 560.

label to include risks about receiving the product via an IV-push because it was previously approved by the FDA, and would have needed supplemental FDA approval to change the label.[26]

The Supreme Court disagreed and determined that under the FDCA,[27] a brand-name manufacturer has ultimate responsibility for a drug's label, including warnings.[28] The Court relied on the CBE provision which permits the manufacturer to make certain changes to a drug's label without waiting for FDA approval, including to "add or strengthen a contraindication, warning, precaution, or adverse reaction" or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product."[29] The Court concluded: "Failure-to-warn actions, in particular, lend force to the FDCA's premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times . . . FDA long [has] maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation."[30]

In finding that the failure to warn claim was not preempted, the Court summarized its analysis of impossibility preemption:

> Impossibility pre-emption is a demanding defense. On the record before us, Wyeth has failed to demonstrate that it was impossible for it to comply with both federal and state requirements. The CBE regulation permitted Wyeth to unilaterally strengthen its warning, and the mere fact that the FDA approved Phenergan's label does not establish that it would have prohibited such a change.[31]

B. *PLIVA v. Mensing*

Only two years after the Court's decision in *Wyeth*, the Supreme Court again addressed impossibility preemption in *PLIVA v. Mensing*. In *Mensing*, two consumers sued manufacturers of generic metoclopramide under Louisiana and Minnesota tort law claiming that the long-term use of the product caused tardive dyskinesia.[32] The plaintiffs argued that the generic drug manufacturers had an obligation to change the product's label to adequately warn consumers about the risk of developing tardive dyskinesia. In response, the generic drug manufacturers

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26 *Id*. at 568.

27 21 U.S.C. § 301 *et seq.*

28 *Wyeth*, 555 U.S. at 570-71 ("Yet through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.").

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

30 *Id.* at 578.

31 *Id*. at 573.

32 *Mensing*, 564 U.S. at 610.

argued that the state tort laws were preempted by federal law because it was impossible for the manufacturers to comply with the federal and state requirements.[33] Specifically, the manufacturers argued that because the FDCA requires a generic product label to be identical to the name-brand version (i.e., to maintain the duty of sameness), generic drug manufacturers do not have the ability to change a drug's label.[34]

The Court agreed with the generic manufacturers. According to the Court, because it would have been unlawful under federal law for the generic manufacturers to do what state law required of them, the state law was preempted.[35] The Court reasoned:

> If the Manufacturers had independently changed their labels to satisfy their state-law duty, they would have violated federal law. Taking [plaintiffs'] allegations as true, state law imposed on the Manufacturers a duty to attach a safer label to their generic metoclopramide. Federal law, however, demanded that generic drug labels be the same at all times as the corresponding brand-name drug labels. *See*, *e.g.*, 21 CFR § 314.150(b)(10). Thus, it was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal-law duty to keep the label the same.[36]

The majority emphasized the fact that the generic manufacturers could not have undertaken to change the product label without prior "special effort" from the FDA permitting them to do so.[37] Accordingly, because "state law imposed a duty on the Manufacturers to take a certain action, and federal law barred them from taking that action," the state law was preempted.[38]

The majority also rejected an argument by the plaintiffs and the federal government as an amicus that the generic manufacturers' ability to ask the FDA for approvals to change the labels defeated preemption.[39] Ultimately, the Court focused on whether the generic manufacturers could *independently* make changes to the product label, including through the FDCA's CBE

33 *Id*.

34 *Id*. at 613.

35 *Id*. at 618.

36 *Id*.

37 *Id*. at 623.

38 *Id* at 624.

39 *Id*. at 620-21.

process as a brand-name manufacturer would have been able to do. In determining that they could not, the Court held that the state law claims were preempted.[40]

C. *Mutual Pharmaceutical Company v. Bartlett*

Similarly, *in Mutual Pharmaceutical Co. v. Bartlett*, the Court addressed the question of impossibility preemption and generic drug manufacturers. In *Bartlett*, the plaintiff was prescribed brand-name Clinoril, a non-steroidal anti-inflammatory drug for shoulder pain and was dispensed a generic version of the drug.[41] After taking the drug, the plaintiff developed acute case of toxic epidermal necrolysis.[42] The drug's label did not warn of toxic epidermal necrolysis as a potential side effect and the plaintiff sued the generic manufacturer under New Hampshire state law for failure to warn and design defect claims.[43] Following the *Mensing* decision, the plaintiff argued, and appellate court agreed, that a generic manufacturer could choose to stop selling the product if it were unable to comply with both federal and state law.[44]

Again, the Supreme Court disagreed with the plaintiff and appellate court, and concluded that based upon a straightforward application of preemption law, the state law was preempted because it was impossible for the generic manufacturer to comply with its federal requirements and the New Hampshire state law duties.[45] The Court also stated that the "stop selling" argument was "no solution" because adopting this "stop-selling rationale would render impossibility pre-emption a dead letter and work a revolution in th[e] Court's pre-emption case law."[46]

However, the *Bartlett* decision left open one question of whether state law would be preempted with a theoretical design defect claim that does not involve warnings and which is parallel to the federal misbranding statute.[47] According to the Court, "The misbranding statute requires a manufacturer to pull even an FDA-approved drug from the market when it is 'dangerous to health' even if 'used in the dosage or manner, or with the frequency or duration prescribed, recommended, or suggested in the labeling thereof.'"[48] The Court did not reach a

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40 *Id*.

41 *Bartlett*, 570 U.S. at 477-78.

42 *Id*. at 478.

43 *Id*. at 479.

44 *Id*.

45 *Id*. at 482-85.

46 *Id.* at 475, 488-90 (rejecting the stop-selling rationale as "incompatible" with pre-emption jurisprudence because, in "every instance in which the Court has found impossibility pre-emption, the 'direct conflict' between federal- and state-law duties could easily have been avoided if the regulated actor had simply ceased acting").

47 *Id*. at 487 n.4.

48 *Id*. (quoting 21 U.S.C. § 352(j)).

decision as to whether such a claim would have been preempted in *Bartlett* because neither party raised it at the lower court levels.[49]

1. *The Aftermath of Mensing and Bartlett*

Following the *Mensing* and *Bartlett* decisions, there was a "tsunami of cases" analyzing the impossibility preemption defense.[50] In those cases, appellate and district courts throughout the country applied the holdings to conclude that state laws are preempted by federal law when it is impossible for the defendant to comply with both duties and where the defendant could not take independent action to comply.[51] Those decisions have applied the impossibility preemption analysis to generic drug manufacturers,[52] wholesale distributors,[53] and direct retailers.[54] However, those decisions have not stopped plaintiffs from attempting to plead "creatively" around impossibility preemption.

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49 *Id*.

50 *See, e.g.*, *Watson v. Mylan Pharm., Inc.*, 701 Fed. App'x 729, 731-32 (10th Cir. 2017); *Schrock*, 727 F.3d at 1290; *Watson*, 701 Fed. App'x at 731-32. *See also McDaniel v. Upshur-Smith Labs., Inc.*, 893 F.3d 941, 945-47 (6th Cir. 2018); *Brinkley v. Pfizer, Inc.*, 772 F.3d 1133, 1139-40 (8th Cir. 2014); *In re Darvocet, Darvon, and Propoxyphene Prods. Liab. Litig.*, 756 F.3d 917, 932-36 (6th Cir. 2014); *Drager v. PLIVA USA, Inc.*, 741 F.3d 470, 475-76 (4th Cir. 2014); *Johnson v. Teva Pharm. USA*, 758 F.3d 605, 612-14 (5th Cir. 2014); *Lashley v. Pfizer, Inc.*, 750 F.3d 470, 473-76 (5th Cir. 2014) (per curiam); *Strayhorn v. Wyeth Pharm.*, 737 F.3d 378, 393-98 (6th Cir. 2013); *Morris v. PLIVA, Inc.*, 713 F.3d 774, 777 (5th Cir. 2013); *Guarino v. Wyeth, LLC*, 719 F.3d 1245, 1249 (11th Cir. 2013); *McNair v. Johnson & Johnson*, 694 Fed. App'x. 115, 118 (4th Cir. 2017). The United States District Court for the District of Utah has similarly noted *Mensing's* holding. *See, e.g.*, *McMurray*, 2017 WL 11496825, at *5-6; *Elkins v. Mylan Labs., Inc.*, No. 12-cv-255, 2013 WL 3224599, at *2-3 (D. Utah June 25, 2013).

51 *See, e.g.*, *In re Darvocet*, 756 F.3d 917, 932-33 (6th Cir. 2014) (finding preemption because, "if generic drug manufacturers, but not the brand-name manufacturer, sent such letters, that would inaccurately imply a therapeutic difference between the brand and generic drugs and thus could be impermissibly misleading"); *Lashley v. Pfizer, Inc.*, 750 F.3d 470, 474-75 (5th Cir. 2014) (concluding that a claim was preempted because "the duty of sameness prohibits the generic manufacturers from taking such action unilaterally, they are dependent on brand-names taking the lead" (quotation omitted)); *Morris v. PLIVA, Inc.*, 713 F.3d 774, 777 (5th Cir. 2013) (stating that a claim against generic manufacturers was preempted because the manufacturers "were not at liberty" to communicate warnings where "no brand-name manufacturer sent a warning based on the . . . label change"); *Schrock v. Wyeth, Inc.*, 727 F.3d 1273, 1288 (10th Cir. 2013) (concluding that an express-warranty claim against a generic drug manufacturer was preempted because there was no argument that the manufacturer "could have modified or supplemented the warranties allegedly breached without running afoul of the duty of sameness"); *Smith v. Teva Pharm. USA, Inc.*, 437 F.Supp.3d 1159, 1165-67 (S.D. Fla. 2020) (determining that federal law prohibited wholesale distributors from changing labels and, accordingly, failure to warn claims against them were preempted); *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Practices & Prods. Liab. Litig.*, MDL No. 2:14-mn-02502-RMG, 2016 WL 7368203, at *2 (D.S.C. Nov. 1, 2016) ("a pharmacy also has no authority to unilaterally change a drug's label" and thus, any claims against the pharmacy based on the label are preempted); *Greager v. McNeil-PPC, Inc.*, 414 F.Supp.3d 1137 (N.D. Ill. 2019) (dismissing as preempted claims against retailer of a generic OTC medication because the retailer does not hold the New Drug Application).

52 *E.g.*, *In re Darvocet*, 756 F.3d at 932-33; *Schrock v. Wyeth*, 727 F.3d at 1288.

53 *E.g.*, *Smith*, 437 F.Supp.3d at 1165-67.

54 *E.g.*, *Greager v. McNeil-PPC, Inc.*, 414 F.Supp.3d at 1141.

D. *Merck Sharp & Dohme Corp. v. Albrecht*

Six years after the *Bartlett* decision, in 2019, the Supreme Court provided further context of how to apply the "clear evidence" standard for a brand name pharmaceutical preemption case. In *Albrecht,* the Supreme Court looked at whether state law failure to warn claims for a prescription drug for osteoporosis were preempted by federal law.[55] The plaintiffs alleged that the drug's label failed to warn that it may cause "atypical femoral fractures."[56] The opinion contains three key rulings that have instructed courts to determine if a preemption defense is appropriate for branded pharmaceutical warning labels.

First, the Court held that a preemption defense for failure to warn is "one for a judge to decide, not a jury."[57] Second, the Court enumerated what constitutes "clear evidence" for a preemption defense.[58] 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 drug manufacturer that the FDA would not approve a change to the drug's label to include that warning."[59] Third, and finally, the Supreme Court explained that the FDA's actions can be the premise for a preemption defense if they are taken "pursuant to the FDA's congressionally delegated authority."[60]

E. Circuit Courts Interpretation of "Clear Evidence" Standard under *Albrecht*

1. *The Third Circuit Applied a Two Prong Test Based on the Albrecht Opinion to Determine Preemption Should Not be Applied to State Law Failure to Warn Claims*

In *In re Avandia Marketing, Sales & Products Labiality Litigation,* the Third Circuit reversed a decision that preempted state law claims for failure to warn against GlaxoSmithKline ("GSK") brought by two health benefit plans ("Plans").[61] The Plans alleged that GSK failed to warn users that its type-2 diabetes treatment drug, Avandia, may increase certain cardiac risks prior to 2014.[62] At specific issue was a 2011, pre-approval phase letter that GSK had written to the FDA requesting to include a warning regarding cardiac risks from Avandia.[63] The FDA

55 *Albrecht*, 139 S. Ct. at 1672.

56 *Id*.

57 *Albrecht*, 139 S. Ct. at 1672.

58 *Id.*

59 *Id*.

60 *Id*. at 1679.

61 *In re Avandia Mktg., Sales & Prod. Liab. Litig.*, 945 F.3d 749, 752 (3d Cir. 2019).

62 *Id*. at 753.

63 *Id*. at 754.

stated it needed more information before it would conclude that the warning label must include information regarding cardiac risks.[64] In 2014, the FDA approved including a cardiac risk warning to Avandia's label after further trials and research was completed for the drug.[65] Applying *Albrecht*, the Third Circuit found that the claims against GSK were not preempted.

The Third Circuit explained that demonstrating that federal law prohibited a drug manufacturer from adding a warning that would satisfy state law required the drug manufacturer to meet a two part test under *Albrecht*: (1) the manufacturer fully informed the FDA of the justifications for the warning required by state law and (2) the FDA, in turn, informed the drug manufacturer that the FDA would not approve changing the drug's label to include that warning.[66] GSK argued it met this standard based on its 2011 letter and the FDA's response to the letter prohibiting them from including the warning in the Avandia label.

The Third Circuit disagreed and explained the neither prong of the test was met. Regarding whether the FDA was fully informed, the court determined FDA was not "fully informed" in 2011 because it had requested more information and continued to review testing of the drug for three more years.[67] The court concluded that the further testing and additional information the FDA learned was necessary for the FDA to be fully informed.[68] In its analysis of the second prong, the court again focused on the FDA's response to the 2011 letter. The Third Circuit noted that the FDA's response, at best, served as evidence that the FDA was prohibiting a label change.[69] The court determined, however, that the letter was not a complete confirmation of the FDA's disapproval of the label change and for GSK to prove this point it must provide more evidence.[70] The Third Circuit concluded neither prong of the test was met.[71]

2. *The Seventh Circuit Held that a Preemption Defense is Allowed if an Agency's Actions Would Prohibit a Label Change*

In *Dolin v. GlaxoSmithKline LLC*, prior to the Supreme Court's ruling in *Albrecht*, the Seventh Circuit had ruled that a plaintiff's state law claims based on labeling deficiencies for a plaintiff who was suing for the suicidal effects of the drug *Paxil* were preempted.[72] After

64 *Id*.

65 *Id*.

66 *Id*. at 758

67 *Id*.

68 *Id*.

69 *Id*. at 760.

70 *Id*.

71 *Id*.

72 *Dolin v. GlaxoSmithKline LLC*, 951 F.3d 882, 886 (7th Cir. 2020).

Albrecht, the plaintiff appealed arguing that the defendant GSK did not meet the "clear evidence" standard as set out in *Albrecht* to have been granted a preemption defense.

The Seventh Circuit recognized that *Albrecht* appeared to create a shift in how the "clear evidence" standard applied and seemed to require that a manufacturer "actually requested a change [to the label] that the FDA rejected."[73] The Seventh Circuit explained however, that in its view, the Supreme Court did not adopt a new standard but rather focused and clarified the older standard.[74] The Seventh Circuit stated that in *Dolin*, the record was clear that GSK had disclosed "relevant data" of Paxil's connection to potential underlying adult-suicidality in 2006 to the FDA.[75] And the record also showed that the FDA rejected a "Paxil-Specific" warning in 2007 when it formally mandated that all SSRIs (Selective Serotonin Reuptake Inhibitors (commonly prescribed as antidepressants)) carry a uniform, class-wide warning label.[76] The Court then stated that the 2007 formal requirements that all SSRIs carry the same warning label would qualify as agency action pursuant to the FDA's congressional authority, and therefore the agency's actions for this case decided the preemption issue and preemption was appropriate and affirmed.[77]

3. *The Southern District of New York Stated that Albrecht Still Requires Plaintiffs to Show a Casual Connection Between an Injury and the Alleged Deficient Warning Label*

In *McGrath v. Bayer HealthCare Pharmaceuticals, Inc.*, the plaintiffs suing Bayer Healthcare Pharmaceuticals Inc. and other defendants (together "Bayer") brought a failure to warn strict liability claim for failure to alert consumers of a potential injury resulting from exposure to Magnevist, which can cause retained gadolinium in patients with normal renal function.[78] The plaintiffs alleged that retained gadolinium led to "fibrosis."[79] Bayer moved to dismiss the failure to warn claims stating they were preempted by the FDA's regulatory scheme.[80] The plaintiffs argued that Bayer had received "newly acquired information" that its drug would cause fibrosis that required it to modify its warning label.[81] The plaintiffs relied on

73 *Id*. at 890.

74 *Id*. at 891.

75 *Id*.

76 *Id*.

77 *Id*.

78 *McGrath v. Bayer HealthCare Pharms. Inc.*, 393 F. Supp. 3d 161, 164 (E.D.N.Y. 2019).

79 *Id*.

80 *Id*.

81 *Id*. at 167-168.

Albrecht, arguing that the defendants could not show "clear evidence" that FDA would not have approved a label change.[82]

The Southern District of New York rejected the plaintiffs' arguments finding that the studies they relied on in their complaint only showed a hypothetical risk and not a "casual connection" of possible fibrosis, and a manufacturer is only required to warn consumers of an actual risk under the CBE regulation.[83] Further, the district court noted there were studies that showed the alleged side effects plaintiff was stating were not reasonable grounds to modify a label under the CBE regulation.[84]

3. The Current Landscape of Impossibility Preemption in Pharmaceutical Litigation

A. Impossibility Preemption and Pending Lawsuits

1. *The Zantac MDL Case Study*

Following the Supreme Court's decisions in *Wyeth*, *Mensing*, *Bartlett*, and *Albrecht*, plaintiffs' lawyers have become more inventive in their attempts to argue around impossibility preemption in large pharmaceutical litigations. One such example is *In Re Zantac (Ranitidine) Products Liability Litigation*, 20-md-2924 (S.D. Fla.) (the "Zantac MDL").[85] The Zantac MDL plaintiffs alleged claims against all levels of the pharmaceutical supply chain from brand-name and generic manufacturers to wholesale distributors, repackagers, retailers, and pharmacies.[86] According to the plaintiffs, Zantac and generic ranitidine-containing products contain dangerous amounts of a carcinogenic compound, N-Nitrosodimethylamine ("NDMA"), and that their consumption of Zantac and ranitidine-containing products led to injuries in the form of various types of cancers.[87] Plaintiffs' claims in the Master Personal Injury Complaint against the non-brand-name manufacturer defendants included counts alleging strict products liability and negligence based on failures to warn, design defects, and negligent product design and manufacturing.[88]

82 *Id*.

83 *Id*.

84 *Id.* at 170.

85 *See* ECF Nos. 1-2, No. 20-md-2924 (Feb. 6, 2020).

86 *E.g.*, Master Personal Injury Compl., ECF No. 887, No. 20-md-2924 (June 22, 2020); Am. Master Personal Injury Compl., ECF No. 2759, No. 20-md-2924 (Feb. 8, 2021).

87 *See, e.g.*, Master Personal Injury Compl., at ¶¶ 1, 19, 272-73.

88 Master Personal Injury Compl., at ¶¶453-541, ECF No. 887, No. 20-md-2924 (June 22, 2020).

Relying on the impossibility preemption holdings in *Mensing* and *Bartlett*, defendants at each level of the supply chain filed motions to dismiss the Master Personal Injury Complaint.[89] The non-brand-name manufacturer defendants argued that each of the plaintiffs' claims were in fact failure to warn and design defect claims at their cores, even though they may have been creatively called negligence claims. Accordingly, they argued such claims were preempted because generic manufacturers, wholesale distributors, repackagers, and retailers and pharmacies do not have the ability to take independent action to change a drug's label.[90] In response to defendants' arguments on impossibility preemption, the plaintiffs argued that their design defect and failure to warn claims were parallel to the federal misbranding statute, and therefore, were not preempted because the federal misbranding statute and state law prohibit the same thing: selling dangerous drugs.[91] The Zantac plaintiffs cited to *Bartlett*'s footnote 4[92] and argued, "Yet *Bartlett* could not have been clearer that its [impossibility preemption] holding *did not apply* to allegations of misbranding."[93] The plaintiffs further argued that, at bottom, their allegations were misbranding claims, and that as the FDA had never analyzed the allegedly new information that Zantac and ranitidine contained NDMA, and therefore led to plaintiffs' injuries, their claims were not preempted.[94]

The district court disagreed with the plaintiffs and granted defendants' motions to dismiss in full.[95] In its analysis of impossibility preemption under *Mensing* and *Bartlett*, the district court held: "Plaintiffs' claims based on alleged product and labeling defects that Defendants could not independently change while remaining in compliance with federal law are dismissed with prejudice as pre-empted. Because all of Plaintiffs' counts against Defendants in the Master Complaints incorporate such allegations, all counts against Defendants are dismissed."[96]

The district court also addressed the plaintiffs' arguments that parallel misbranding claims are not preempted under *Bartlett* footnote 4.[97] The court analyzed the requirements of the

89 *See* ECF Nos. 1580 (Brand-Name Manufacturer Defendants' Motion to Dismiss), 1582 (Generic Manufacturer Defendants' Motion to Dismiss), 1583 (Distributor Defendants' Motion to Dismiss), 1584 (Retailer and Pharmacy Defendants' Motion to Dismiss), No. 20-md-2924 (Aug. 24, 2020).

90 ECF Nos. 1582-84.

91 *See, e.g.*, Plaintiffs' Opp'n to Brand-Name Defendants' Mot. to Dismiss, ECF No. 1976 at 15-20 (Oct. 1, 2020).

92 *Bartlett*, 570 U.S. at 487 n.4

93 Plaintiffs' Opp'n to Brand-Name Defendants' Mot. to Dismiss, ECF No. 1976 at 18 (emphasis in original).

94 *Id*. at 21-22 ("The key question concerns *when* the relevant information should have come to light, at which point Defendants' products were both misbranded under federal law—whether Defendants subjectively knew or not—and actionable under state design-defect law.").

95 ECF Nos. 2512 (Order Granting Generic Manufacturer and Repackager Defendants Motion to Dismiss) (Dec. 31, 2020), 2513 (Order Granting Distributor, Retailer, and Pharmacy Defendants Motion to Dismiss) (Dec. 31, 2020).

96 *In re Zantac (Ranitidine) Prods. Liab. Litig.*, 510 F.Supp.3d 1141, 1162 (2020).

97 *Id*. at 1159-61.

federal misbranding statute and its interaction with impossibility preemption, and noted that no court has adopted plaintiffs' misbranding arguments.[98] The court reasoned, "*Mensing* and *Bartlett* dictate that Plaintiffs' claims are pre-empted if they are based on alleged product defects that Defendants could not independently change while remaining in compliance with federal law, even if those defects rendered the products misbranded."[99] The court therefore held that the misbranding arguments did not overcome impossibility preemption, and stated:

> A finding that Plaintiffs can avoid pre-emption by alleging that defects in ranitidine products made the products misbranded under 21 U.S.C. § 352 would render the vast body of pre-emption caselaw in the drug context, including binding Supreme Court decisions, meaningless. If Plaintiffs' position were accepted, a plaintiff could avoid pre-emption simply by asserting, for example, that a drug's labeling was "false or misleading in any particular" or that the drug was "dangerous to health when used" as prescribed. *See* 21 U.S.C. § 352(a)(1), (j). The Court cannot adopt a position that would render pre-emption caselaw meaningless.[100]

The Zantac MDL plaintiffs appealed the district court's orders granting the motions to dismiss, and have teed up the question of whether impossibility preemption bars a claim under state law when plaintiffs allege a parallel violation of federal law.[101] That question remains pending at the Eleventh Circuit.

2. *Other Attempts to Side-Step Impossibility Preemption*

Plaintiffs have also attempted to avoid impossibility preemption arguments in other ongoing litigations with more success than in the Zantac MDL.

For example, *in In Re Valsartan, Losartan, and Irbesartan Products Liability Litigation*, 16-md-2875 (D.N.J.) (the "Sartan MDL"), the plaintiffs made many of the same arguments as did the plaintiffs in the Zantac MDL and succeeded in defeating defendants' motions to dismiss. There, the plaintiffs alleged that generic valsartan drugs contained nitrosamines, including NDMA, and that those "known carcinogens" caused injuries to the plaintiffs.[102] Like in the

98 *Id*. at 1161.

99 *Id*.

100 *Id*. at 1160-61.

101 Civil Appeal Statement, No. 21-10306 (Feb. 11, 2021); Civil Appeal Statement, No. 21-12618 (Oct. 27, 2021) ("1. Preemption: Where a plaintiff pleads a defect in a drug or its warnings based on post-approval scientific evidence the FDA never considered, is that state-law claim preempted even though both state and federal law required drug sellers to remove the unsafe product from the market? 2. Preemption: Where a defendant can perform some, but not all, of the requirements imposed by state common law, does impossibility preemption bar liability for the actions the defendant could have taken?").

102 *In re Valsartan, Losartan, & Irbesartan Prod. Liab. Litig.*, No. MDL 2875 (RBK-JS), 2020 WL 7418006, *slip. op.*at *2 (D.N.J. Dec. 18, 2020).

Zantac MDL, defendants at different levels of the supply chain submitted motions to dismiss based on numerous arguments, including preemption.[103] With regard to impossibility preemption, the Sartan MDL defendants argued that the FDCA preempted the plaintiffs' negligence *per se*, strict liability-defective design, breach of express warranty, fraud misstatement and negligent misstatement, and state consumer-protection law claims.[104]

Relying on *Wyeth*, the district court disagreed and denied the defendants' motion to dismiss, and noted, "As for the 'impossibility defense', the Court found it nearly impossible for a drug manufacturer to succeed there, because a drug manufacturer never relinquishes its responsibility to present accurate labelling."[105] The court did not differentiate between brand-name and generic manufacturers, did not address how *Wyeth* affected the non-manufacturer defendants, and did not apply the *Mensing* and *Bartlett* holdings.

Similarly, in *In Re Metformin Marketing and Sales Practices Litigation*, 20-cv-2324 (D.N.J.) (the "Metformin Action"), the question of impossibility preemption is ripe for decision. In the Metformin Action, the plaintiffs alleged that metformin products prescribed for the treatment of type-2 diabetes contained NMDA, and that the NDMA caused injuries to the plaintiffs.[106] As in the Zantac and Sartan MDLs, the defendants moved to dismiss based on numerous arguments, including lack of standing and preemption. In response, the plaintiffs argued that impossibility preemption does not apply because the defendants could have complied with both the federal and state requirements at the same time because the NDMA impurity rendered the generic version of the metformin drugs non-equivalent to the brand-name version, and thus, misbranded.[107] As of the date of this paper, the motions have been fully briefed, but there has been no decision by the district court.

B. **What's Next?**

The issues surrounding impossibility preemption are not going anywhere anytime soon. As is clear from the examples of the currently-pending arguments in the Eleventh Circuit in the Zantac MDL and the motions to dismiss in the Metformin Action, there are numerous opportunities for courts to address the question of impossibility preemption, and how misbranding claims fit into the *Mensing* and *Bartlett* jurisprudence. Indeed, the question of *Bartlett* footnote 4 and Plaintiffs' strategies to use it as an end-around for preemption likely will be addressed by the Eleventh Circuit in this calendar year. And, as the question continues to make its way through various district courts, it is also likely that it will percolate to other appellate courts in the not-too-distant future, until, and unless, the question is put before the Supreme Court. Ultimately, plaintiffs in large products liability lawsuits are going to continue to

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103 *Id*. at *5-*6.

104 *Id*. at *7.

105 *Id*.at *8.

106 *E.g.*, Am. Compl., ECF No. 128, at ¶¶ 8-10, 126-27, 367, 376, No. 2:20-cv-02324-MCA-MAH (June 21, 2021).

107 ECF No. 135, at 27-29, No. 2:20-cv-02324-MCA-MAH (Sept. 28, 2021).

argue that the allegations include parallel misbranding claims in a transparent attempt to keep all levels of the pharmaceutical supply chain in those litigations.