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Save Now, Pay Later: The Unfortunate Reality of *PLIVA v. Mensing*

INTRODUCTION

In 2001 and 2002, Gladys Mensing and Julie Demahy were prescribed Reglan,¹ a drug often utilized for treating acid reflux.² Their pharmacists gave them generic metoclopramide, which they took, as prescribed, for several years.³ Both women developed tardive dyskinesia, a severe neurological disorder characterized by involuntary movements of the face, torso, and extremities.⁴ Demahy experienced violent shaking, blinked excessively, and often struggled to speak and write.⁵ The disorder was so damaging that Demahy was forced to stay at home due to her inability to work effectively or drive safely.⁶ Mensing's situation was not any better. Extremely limited in control of her movement, Gladys Mensing was forced to rely on her granddaughter to help her bathe.⁷ Also plagued with an inability to control the movement of her tongue and facial muscles,⁸ Gladys struggled to be understood by others.⁹

In separate lawsuits, both Mensing and Demahy alleged that the generic drug manufacturers of metoclopramide were liable under state tort law for failure to provide adequate warning labels.¹⁰ At the

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1. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2573 (2011).

2. *Gastroesophageal reflux disease* is the medical term for *acid reflux*. *Demahy v. Wyeth Inc.*, 586 F. Supp. 2d 642, 643 (E.D. La. 2008), *aff'd sub nom. Demahy v. Actavis, Inc.*, 593 F.3d 428 (5th Cir. 2010), *rev'd sub nom. PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011).

3. *PLIVA*, 131 S. Ct. at 2573.

4. *Demahy*, 586 F. Supp. 2d at 644.

5. Ramon Antonio Vargas, *Slidell Woman's Case Against Generic Drug Manufacturer Has Attention of U.S. Supreme Court*, THE TIMES-PICAYUNE (Mar. 28, 2011, 4:15 PM), http://www.nola.com/health/index.ssf/2011/03/slidell_womans_case_against_ge.html.

6. *Id.*

7. Am. Ass'n for Justice, *The Story of PLIVA v. Mensing*, <http://vimeo.com/20439521> (last visited Apr. 8, 2013).

8. Brad Allen, *Important Generic-drug Case Has Minnesota Roots*, MINNPOST (Mar. 25, 2011), <http://www.minnpost.com/business/2011/03/important-generic-drug-case-has-minnesota-roots>.

9. Am. Ass'n for Justice, *supra* note 7.

10. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2573 (2011). Although Mensing asserted a number of claims, inherent in each claim was the allegation that the generic companies "failed to adequately warn about the association between long-term ingestion of [metoclopramide] and movement disorders." *Mensing v. Wyeth, Inc.*, 562 F. Supp. 2d 1056, 1058 (D. Minn. 2008), *rev'd*, 588 F.3d 603 (8th Cir. 2009), *rev'd sub nom. PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011). Mensing had also initially sued the brand-name drug manufacturer for

district court level, Mensing's failure-to-warn claims were held to conflict with and to be preempted by federal law.¹¹ The Eighth Circuit Court of Appeals reversed, stating that the Food, Drug, and Cosmetic Act (FDCA) did not preempt Mensing's failure-to-warn claims against the generic manufacturers.¹² Demahy's failure-to-warn claims were not held at either the district court level or at the Fifth Circuit Court of Appeals to be preempted.¹³ Mensing's and Demahy's cases were eventually consolidated and brought before the Supreme Court, which rejected the failure-to-warn claims that each plaintiff asserted due to preemption by federal law.¹⁴

The Court stated that even assuming that the failure-to-warn allegations were valid, the claims were preempted due to the impossibility of the manufacturers being able to comply with both federal and state drug law.¹⁵ Specifically, the Court relied on the Food and Drug Administration's (FDA) belief that the generic drug manufacturers, unlike their brand-name counterparts, could not unilaterally have utilized the Changes-Being-Effectuated (CBE) process that allows a drug manufacturer to enhance a warning label without prior FDA approval.¹⁶ The *PLIVA* decision came just two years after the Court reached the opposite conclusion regarding brand name drugs in *Wyeth v. Levine*.¹⁷ In *Wyeth*, the Supreme Court held that failure-to-warn claims against *brand-name* drug manufacturers were *not* preempted by federal law. Noting the "unfortunate hand that federal drug regulation ha[d] dealt"¹⁸ Mensing and Demahy, the *PLIVA* Court admitted that

finding pre-emption here but not in *Wyeth* makes little sense. Had Mensing and Demahy taken Reglan, the brand-name drug prescribed by their doctors, *Wyeth* would control and

fraud and negligent misrepresentation, but that issue was not brought before the Supreme Court. *Mensing v. Wyeth, Inc.* 588 F.3d 603, 605 (8th Cir. 2009), *rev'd sub nom.* *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011). Demahy sued specifically under the Louisiana Products Liability Act for "failure to warn of the risks of neurological disorder after long-term use of metoclopramide." *Demahy v. Actavis, Inc.*, 593 F.3d 428, 431 (5th Cir. 2010) (citation omitted), *rev'd sub nom.* *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011).

11. *Mensing*, 562 F. Supp. 2d at 1056.

12. *Mensing*, 588 F.3d at 614.

13. *Demahy*, 593 F.3d at 428; *Demahy v. Wyeth Inc.*, 586 F. Supp. 2d 642, 642 (E.D. La. 2008), *aff'd sub nom.* *Demahy v. Actavis, Inc.*, 593 F.3d 428 (5th Cir. 2010), *rev'd sub nom.* *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011).

14. *PLIVA*, 131 S. Ct. at 2572.

15. *Id.* at 2578.

16. *Id.* at 2575. See *infra* Part I.B.1 (regarding the CBE process).

17. *Wyeth v. Levine*, 555 U.S. 555, 581 (2009).

18. *PLIVA*, 131 S. Ct. at 2581.

their lawsuits would not be pre-empted. But because pharmacists, acting in full accord with state law, substituted generic metoclopramide instead, federal law pre-empts these lawsuits.¹⁹

In *PLIVA*, the majority attempted to escape accountability for such an unjust result by pointing out that its duties did not extend to determining whether a statutory scheme was “unusual or even bizarre.”²⁰ With this statement, the majority pretended that drug labeling laws were undeniably clear and consequently not open to multiple interpretations. Rather than take an in-depth look into the purpose of the FDA and the regulations at issue, the majority instead sought to shift the burden to Congress and the FDA, noting that they possess the ability to change the law and regulations, respectively.²¹

The Supreme Court’s decision in *PLIVA*, which held that state failure-to-warn claims are preempted by federal law, is problematic because it applies a lower standard for “impossibility preemption” than required by precedent.²² In *Wyeth*, the Court emphasized that a defense of impossibility preemption is held to a *demanding* standard. In rejecting the plaintiffs’ various arguments, the *PLIVA* Court was too shortsighted in its application of the relevant FDA regulations. The future effect of the *PLIVA* Court’s decision will likely be twofold: (1) Consumers of generic drugs will be without proper remedies in failure-to-warn suits, and (2) Brand-name drug manufacturers will be forced to shoulder the responsibility of generic drug manufacturers. To properly fix the current situation, the FDA must either modify the CBE rules or create a separate, yet similar avenue allowing generic drug manufacturers to “unilaterally” modify their drugs’ labels.

This Comment discusses the *PLIVA* Court’s problematic analysis in reaching its decision, the harms that this decision creates, and

19. *Id.* (citations omitted).

20. *Id.* at 2582 (quoting *Cuomo v. Clearing House Ass’n, L.L.C.*, 129 S. Ct. 2710, 2733 (2009) (Thomas, J., concurring in part and dissenting in part)).

21. *Id.*

22. *Wyeth*, 555 U.S. at 573 (emphasis added). *Wyeth* sets out various impossibility preemption examples, none to which the current standard would apply. *PLIVA* regards neither a situation in which “state law penalizes what federal law requires,” *id.* at 589 (quoting *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 873 (2000)), nor a case in which state law claims “‘directly conflict’ with federal law,” *id.* (citing *Am. Tel. & Tel. Co. v. Central Office Tel., Inc.*, 524 U.S. 214, 227 (1998)), nor a case “‘where compliance with both federal and state regulations is a physical impossibility,’” *id.* at 589–90 (quoting *Fla. Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142–43 (1963)). As stated in *Wyeth*, the Supreme Court has generally instituted a very narrow impossibility standard. *Id.* at 590.

lastly, the options available to correct the current situation. Part I provides the necessary background, first touching upon the FDA with a focus on the drug approval process. Subsections of Part I present relevant information on federal drug labeling regulations, state duties regarding drug labeling, and pertinent information on federal preemption of state laws. Part II presents and then critiques the Court's analysis in *PLIVA*. It then compares the *PLIVA* analysis with the Court's analysis in *Wyeth*, showing why the two decisions are incompatible. Part III discusses the effect this decision is likely to have on consumers and drug manufacturers. Finally, Part IV suggests possibilities for fixing the drug labeling problems that the *PLIVA* decision has created.

I. BACKGROUND

A. *The FDA and the Drug Approval Process*

A brief exploration of the FDA, as well as the drug approval process, helps explain why *PLIVA* is so problematic. The FDCA was passed in 1938 as part of a transformative renovation of the public health system.²³ The FDCA authorized the FDA to require evidence of the safety of new drugs from their manufacturers.²⁴ The FDCA's scope has since been expanded through statutory amendments, which has led to increased FDA power regarding regulation of pharmaceutical drugs.²⁵

There are two sets of regulations concerning the drug approval process: one for brand-name drugs, which are the first to enter the market, and one for generic drugs, which apply after patent protection for the brand-name drugs has expired.²⁶ According to the FDA, a *generic drug* is defined as a drug that is equivalent in both quality and performance to a brand-name drug.²⁷

Among its duties relating to the purpose of promoting public health, the FDA is required to ensure that all drugs for human consumption are safe and effective.²⁸ To accomplish this goal, the FDCA mandates that no drug be introduced into interstate commerce

23. *Legislation*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/RegulatoryInformation/Legislation/default.htm> (last updated July 9, 2012).

24. *Id.*

25. Lesley A. Stout, *Making Changes: Generic Drug Labeling and the Case Against Federal Preemption*, 98 KY. L.J. 623, 628 (2010).

26. See 21 U.S.C. § 355(b) (2006 & Supp. V 2011); *id.* § 355(j).

27. *FAQs About CDER*, U.S. FOOD AND DRUG ADMINISTRATION, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/FAQsaboutCDER/> (last updated Oct. 20, 2010).

28. 21 U.S.C. § 355(b).

without prior approval.²⁹ There are two different standards for approval depending on whether the drug is “new” (brand name) or “generic.”³⁰

1. Brand-Name Drug Approval

To introduce a new drug into the market, a drug manufacturer must submit a New Drug Application (NDA) for approval.³¹ The NDA ensures that the FDA has enough information to determine whether the drug is safe and effective, whether its benefits outweigh its risks, whether the proposed labeling is appropriate, and what the labeling should contain.³² In order to have the necessary information to make these determinations, the NDA requires full reports of investigations relating to the drug’s safety and effectiveness, as well as the drug’s proposed labeling.³³

2. Generic Drug Approval and Hatch–Waxman

Prior to 1984, generic and brand-name drugs had to abide by the same rules.³⁴ Generic drugs sought to be introduced into the market were required to go through the same NDA process as their brand-name counterparts.³⁵ Such a system kept generic drug costs high, not allowing consumers to benefit from the lower costs of generics as they do today. In an effort to “make available more low cost generic drugs by establishing a generic drug approval procedure,”³⁶ Congress passed the Drug Price Competition and Patent Term Restoration Act

29. *Id.* § 355(a).

30. Compare *id.* § 355(b) (dealing with approval of applications for *new* (brand name) drugs), with *id.* § 355(j) (2004) (dealing with approval of applications for *generic* drugs).

31. *New Drug Application (NDA)*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm> (last updated Aug. 20, 2010).

32. *Id.* The NDA’s goals also allow for a determination of whether the drug’s “identity, strength, quality, and purity” will be adequately preserved, but that goal is not relevant to the issue at hand. *Id.*

33. 21 U.S.C. § 355(b). Although the NDA requires more information, such as a statement regarding the drug’s composition, for the purposes of discussing failure-to-warn claims, the rest of the requirements are beyond the scope of this Comment.

34. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2574 (2011).

35. *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998).

36. H.R. REP. NO. 98–857(I), at 14 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647.

of 1984,³⁷ commonly referred to as the Hatch–Waxman Amendments.³⁸

With the passing of these amendments, generic drugs no longer needed to submit their own NDA. Instead, to gain FDA approval, generic drugs need only prove that they are essentially the same in all respects as an already approved drug.³⁹ They do this by submitting an Abbreviated New Drug Application (ANDA).⁴⁰ In an ANDA, a generic drug manufacturer must supply information to the FDA that proves, among other things, that their drug (1) has the same active ingredient(s) as the approved brand-name drug; (2) has the same route of administration, dosage form, and strength as the approved brand-name drug; and (3) is the bioequivalent to the approved brand-name drug.⁴¹ In addition to demonstrating that the nature of each drug is essentially identical, the generic drug manufacturer must show that the labeling proposed for its drug is the same as that of the previously approved brand-name drug.⁴²

The Hatch–Waxman Amendments have been instrumental in the creation of low-cost generic drugs. Because generics no longer need to independently prove their own safety and efficacy, generic manufacturers are able to introduce their drugs into the market at a much lower cost than that of the brand-name manufacturers.⁴³ The costs of bringing a generic drug into the market are estimated to be only 1 to 2 million dollars, a massive drop from the billion or more dollars required for a brand-name drug.⁴⁴ With the ability to bring drugs into the market at lower costs, generic drugs can be sold at a lower cost. This ultimately benefits the consumer. In fact, in 2009,

37. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

38. *PLIVA*, 131 S. Ct. at 2574. The amendments are commonly called the Hatch–Waxman Amendments because Senator Hatch and Congressman Waxman sponsored the amendments.

39. *Id.* at 2583 (Sotomayor, J., dissenting).

40. 21 U.S.C. § 355(j) (2006 & Supp. V 2011).

41. *Id.* § 355(j)(2)(A) (2006). Bioequivalent drug products are pharmaceutical equivalents. They are deemed to be interchangeable with the brand-name drug because they are regarded as therapeutically equivalent. *Orange Book Preface*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm079068.htm> (last updated Feb. 3, 2012).

42. 21 U.S.C. § 355(j)(2)(A)(v). There are two exceptions in which the labeling need not be identical. They deal with “changes required because of differences approved under a petition . . . or because the new drug and the listed drug are produced or distributed by different manufacturers.” *Id.* However, these exceptions are beyond the scope of this Comment.

43. *PLIVA*, 131 S. Ct. at 2583 (Sotomayor, J., dissenting).

44. OFFICE OF SCI. & DATA POLICY, U.S. DEP’T OF HEALTH & HUMAN SERVS., EXPANDING THE USE OF GENERIC DRUGS 5 (2010), *available at* <http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib.pdf>.

the average retail prescription price for a generic drug was 76% less than that of its brand-name counterpart.⁴⁵

3. State Laws Regarding Substitution

Congress was not alone in its desire to expand the use of generic drugs.⁴⁶ Over the years leading up to the Hatch–Waxman Amendments, states enacted legislation allowing pharmacists to substitute generic drugs for brand-name drugs when filling a prescription.⁴⁷ While the FDA regulates overall labeling standards, the laws regulating the practice of pharmacy exist at the state level.⁴⁸ These laws vary from state to state.⁴⁹ Regardless of the variation among their laws, at a minimum, each state allows some type of generic substitution.⁵⁰ In every state, however, substitution can only occur when the physician has not indicated that the brand-name drug must be given.⁵¹ When such notice has not been provided, some states require substitution of the generic drug for the brand-name drug.⁵² Other states allow it but do not mandate it.⁵³ Additionally, some states require that for substitution to occur, the pharmacist must obtain the patient’s consent.⁵⁴ In Louisiana, where Demahy brought suit, the pharmacist is allowed, but not required, to substitute as long as the physician does not mandate using the brand-name drug.⁵⁵ In Minnesota, where Mensing’s failure-to-warn claims were first heard, the pharmacist is required to substitute as long as the physician does not prescribe the brand-name drug and include the words *dispense as written* or letters *DAW* on the prescription.⁵⁶

The impact on generic drugs from the Hatch–Waxman Amendments as well as state substitution laws has been astonishing. In 1984, the first year after the enactment of the Hatch–Waxman Amendments, only 19% of those drugs sold in the United States

45. *Id.*

46. It is also worthwhile to note that encouragement of generic drug substitution does not stop with the FDA or states; even many insurance companies structure their plans in such a way as to promote generics. *PLIVA*, 131 S. Ct. at 2584 n.2 (Sotomayor, J., dissenting).

47. *Id.* at 2583.

48. OFFICE OF SCI. & DATA POLICY, *supra* note 44, at 7.

49. *Id.*

50. *Id.* at 14–19.

51. *See id.*

52. *Id.*

53. *Id.*

54. *Id.*

55. *Id.* at 15.

56. *Id.* at 16.

were generic.⁵⁷ In contrast, in 2009, generic drugs constituted 75% of all prescription drugs distributed.⁵⁸ Currently, 90% of prescriptions that have a generic version available are filled with the generic.⁵⁹ Before brand-name drugs, and consequently their generic and less expensive counterparts, can enter the market, the FDA must approve them.

B. Federal Drug Labeling Requirements

Federal preemption of failure-to-warn claims depends on whether generic drug manufacturers can unilaterally change their labels. To properly compare the decisions of *Wyeth* and *PLIVA*, a background of labeling requirements, both in general, as well as those specific to generic manufacturers, is necessary.

For FDA approval, a NDA must include the proposed labeling of the drug.⁶⁰ The purpose of labeling is to provide information that will allow for the safe and effective use of the drug.⁶¹ A drug manufacturer's labeling duties do not stop after initial approval, however. In fact, the FDA can rescind approval of a drug found to be mislabeled.⁶² A drug is misbranded if its label is false or misleading or if it lacks "adequate warnings against . . . unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users."⁶³ To avoid rescission for misbranding, regulations establish that "labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved."⁶⁴

These labeling requirements are not exclusive to brand-name drugs. According to the FDA, these same regulations apply to generic drugs.⁶⁵ Throughout the amendments to the FDCA and FDA regulations, it has always "remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times."⁶⁶ This duty includes not only

57. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2584 (2011) (Sotomayor, J., dissenting).

58. *Id.*

59. *Id.*

60. 21 U.S.C. § 355(b)(1)(F) (2006).

61. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3922 (Jan. 24, 2006).

62. 21 U.S.C. § 355(e) (Supp. V 2011).

63. *Id.* § 352(a), (f) (2006).

64. 21 C.F.R. § 201.80(e) (2012).

65. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2576 (2011).

66. *Wyeth v. Levine*, 555 U.S. 555, 570–71 (2009).

creating an adequate label but also making sure that its drugs' warnings are adequate for the entire time that the drug is on the market.⁶⁷ While a potential contradiction may exist between the duty to have adequate labeling at all times and the generic's duty to have identical labeling to the brand-name drug, the FDA resolves this conflict by stating that generic drug manufacturers must ask the agency to strengthen the label applying to both the generic and the brand-name equivalent as soon as they become aware of safety problems.⁶⁸

1. The Changes-Being-Effectuated Process

The CBE process is one method available for brand-name drug manufacturers to make label changes. The CBE process has its origins in a 1965 FDA policy attempting to allow certain changes in the labeling and manufacturing of drugs to be implemented as soon as possible.⁶⁹ To accomplish this, the agency decided it would not take action against particular changes implemented prior to FDA approval.⁷⁰ The CBE process allows manufacturers "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction" or "[t]o add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product"⁷¹ without first waiting for FDA approval.⁷² According to the FDA, however, any change should be regarded as temporary⁷³ because the ultimate authority over drug labeling "continues to rest with FDA."⁷⁴ With respect to generic drug manufacturers, the FDA interprets the CBE process to allow generic drug manufacturers to change their labels *only* when their brand-name counterpart has already done so.⁷⁵

2. Generic Drug Labeling Changes

Even though generic drug manufacturers possess the same ultimate responsibility as brand-name drug manufacturers to ensure

67. *Id.* at 571.

68. *PLIVA*, 131 S. Ct. at 2576.

69. Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2849 (Jan. 16, 2008).

70. *Id.*

71. 21 C.F.R. § 314.70(c)(6) (2012).

72. *Id.*

73. Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2850 (Jan. 16, 2008).

74. *Id.* at 2849.

75. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2575 (2011).

the adequacy of their labels,⁷⁶ they must initially rely upon the brand-name manufacturer's labeling. To get FDA approval, a generic drug manufacturer must submit its ANDA with information showing that the proposed labeling of the new drug is identical to that of an already approved brand-name drug.⁷⁷ Although the generic manufacturer merely copies an already existing label,⁷⁸ it is not powerless regarding label content. According to the FDA, if, during the application phase, an ANDA applicant believes that certain safety information should be added to a drug's label, then it should contact the FDA.⁷⁹ The FDA will then decide whether to revise the labeling for both the generic and the brand-name drug.⁸⁰ The FDA should also be contacted if, after approval, the ANDA holder believes that the labels are inadequate regarding safety.⁸¹ In either case, the FDA determines whether the labels of both the generic drug and the brand-name drug should be changed.⁸²

C. State Duties

Products liability developed to increase consumer protection from dangerous products.⁸³ State tort law mandates that all drug manufacturers ensure that their products have safe and adequate labeling.⁸⁴ In *PLIVA*, the state laws applied were from Minnesota and Louisiana.⁸⁵ Tort law from Minnesota and Louisiana requires drug manufacturers who know or should know of their product's danger to label their products in a manner that renders them reasonably safe.⁸⁶ Under Minnesota law, when a manufacturer "of a product has actual or constructive knowledge of danger to users, the . . . manufacturer has a duty to give warning of such dangers."⁸⁷ In Louisiana, the law states that "a manufacturer's duty to warn

76. *Id.* at 2576.

77. 21 U.S.C. § 355(j)(2)(A)(v) (2006). Although there are some exceptions to this rule, they are not the norm, they do not apply in the instant case, and they are not within the scope of this Comment.

78. *Id.* § 355(b)(1), (j)(2)(A)(v).

79. Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17,950, 17,961 (Apr. 28, 1992).

80. *Id.*

81. *Id.*

82. *Id.*

83. *E. River S.S. Corp. v. Transamerica Delaval, Inc.*, 476 U.S. 858, 866 (1986).

84. *PLIVA*, 131 S. Ct. at 2577.

85. *Id.* at 2573.

86. *Id.*

87. *Id.* (alteration in original) (quoting *Frey v. Montgomery Ward & Co.*, 258 N.W.2d 782, 788 (Minn. 1977)).

includes a duty to provide adequate instructions for safe use of a product.”⁸⁸ Thus, state tort law requires that labels contain adequate warnings regarding their products’ danger. The failure to do so allows an injured consumer to bring a failure-to-warn claim.⁸⁹ However, if preempted by federal law, then failure-to-warn claims cannot provide a remedy for injured consumers.

D. Preemption

The basis of federal preemption is the Supremacy Clause which states:

This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.⁹⁰

Although powerful, the framers did not intend for this clause to grant the federal government unlimited power.⁹¹ Federal law has been found to preempt state law in three ways: (1) express preemption, (2) field preemption, and (3) conflict preemption.⁹² Express preemption exists where Congress has provided “explicit preemptive language.”⁹³ Field preemption occurs “where the scheme of federal regulation is so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it.”⁹⁴ Lastly, conflict preemption occurs in two instances: “where ‘compliance with both federal and state regulations is a physical impossibility,’ or where state law ‘stands as an obstacle to the

88. *Stahl v. Novartis Pharm. Corp.*, 283 F.3d 254, 269–70 (5th Cir. 2002).

89. See Hannah B. Murray, Note, *Generic Preemption: Applying Conflict Preemption After Wyeth v. Levine*, 16 MICH. TELECOMM. & TECH. L. REV. 255, 258 (2009).

90. U.S. CONST. art. VI, cl. 2.

91. See Joseph F. Petros III, *The Other War On Drugs: Federal Preemption, The FDA, and Prescription Drugs After Wyeth v. Levine*, 25 NOTRE DAME J.L. ETHICS & PUB. POL’Y 637, 644 (2011).

92. *Gade v. Nat’l Solid Wastes Mgmt. Ass’n*, 505 U.S. 88, 98 (1992).

93. *Pac. Gas & Elec. Co. v. State Energy Res. Conservation & Dev. Comm’n*, 461 U.S. 190, 203 (1983).

94. *Gade*, 505 U.S. at 98 (quoting *Fidelity Fed. Sav. & Loan Ass’n v. de la Cuesta*, 458 U.S. 141, 152–53 (1982)) (internal quotation marks omitted).

accomplishment and execution of the full purposes and objectives of Congress.”⁹⁵

Physical impossibility preemption was at issue in *PLIVA*. Physical impossibility preemption does not require that the laws at issue conflict in all aspects.⁹⁶ As with all preemption cases, analysis should be guided by two jurisprudential cornerstones.⁹⁷ First, the intent of Congress is the most important factor in every preemption case.⁹⁸ Second, when dealing with preemption in a field that states have traditionally occupied, there is a presumption against preemption.⁹⁹ In *PLIVA*, however, the majority considered no such presumption.

II. *PLIVA v. MENSING*

In *PLIVA v. Mensing*, the two plaintiffs, Gladys Mensing and Julie Demahy, alleged that their long-term use of metoclopramide caused them to develop tardive dyskinesia and that the manufacturers were therefore liable under state laws for failure to provide adequate warning labels.¹⁰⁰ The plaintiffs “claimed that ‘despite mounting evidence that long term metoclopramide use carries a risk of tardive dyskinesia far greater than that indicated on the label,’ none of the Manufacturers had changed their labels to adequately warn of that danger.”¹⁰¹ The manufacturers countered the plaintiffs’ allegations by stating that federal law preempted such state law claims.¹⁰² Specifically, the manufacturers alleged preemption due to impossibility.¹⁰³ They stated that due to the federal statutes and FDA regulations requiring generic drugs to have the same safety and efficacy labels as their brand-name counterparts, it would have been impossible to follow a state law that required a different label.¹⁰⁴ The

95. *Gade*, 505 U.S. 88 at 98 (quoting *Florida Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142–43 (1963)); *id.* (quoting *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941)).

96. As endorsed by the Court in the instant case, partial impossibility will lead to partial preemption: state law is “naturally preempted to the extent of any conflict with a federal statute.” *PLIVA v. Mensing*, 131 S. Ct. 2567, 2577 (2011) (quoting *Crosby v. Nat’l Foreign Trade Council*, 530 U.S. 363, 372 (2000)).

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

98. *Id.*

99. See *id.* (imposing a “clear and manifest” standard with regard to the purpose of Congress in order to supersede the State’s historic police powers (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996))).

100. *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2573 (2011).

101. *Id.* (quoting *Mensing v. Wyeth*, 588 F.3d 603, 605 (8th Cir. 2009)) (citing *Demahy v. Actavis, Inc.*, 593 F.3d 428, 430 (5th Cir. 2010)).

102. *Id.*

103. *Id.*

104. *Id.*

Court agreed, holding that the failure-to-warn claims were preempted by federal law.¹⁰⁵

A. The Majority's Analysis

The Court stated that if the plaintiffs' allegations were true, then the manufacturers were required under state law to use a different, safer label.¹⁰⁶ The Court outlined the relevant federal and state requirements concerning drug labeling requirements.¹⁰⁷ According to the majority, the relevant inquiry was "whether, and to what extent, generic manufacturers may change their labels *after* initial FDA approval."¹⁰⁸

While Mensing and Demahy claimed that there were several ways in which the manufacturers could have altered their warning labels, the Court disagreed, relying on the FDA's interpretation of its own regulations as evidence to the contrary.¹⁰⁹ According to the FDA, generic drug manufacturers must always use the same warning labels as their brand-name counterparts.¹¹⁰

The plaintiffs first argued that the manufacturers could have changed their warning labels with the CBE process.¹¹¹ The Court rejected such a notion, again deferring to the FDA's opposing viewpoint.¹¹² The Court presented the FDA's interpretation of the CBE regulation, which allows changes on generic labels only when its brand-name counterpart has already made a change, unless the FDA indicates otherwise.¹¹³ Unilaterally changing the generic drug's warning label, according to the FDA, would violate the statutes and regulations that require the generic's label to match that of its brand-name counterpart.¹¹⁴ The Court deferred to the FDA's interpretation because the agency's interpretation was not found to

105. *Id.*

106. *Id.* at 2574. The plaintiffs alleged that the manufacturers knew or should have known of the high risk of tardive dyskinesia with respect to long-term use of metoclopramide and, as a result, knew or should have known that their labels were inadequate with regard to warning of that risk. *Id.*

107. *Id.* at 2573–74.

108. *Id.* at 2574.

109. *Id.* at 2574–75. The FDA's interpretations of its own regulations are "controlling unless plainly erroneous or inconsistent with the regulation[s]" or there is any other reason to doubt that they reflect the FDA's fair and considered judgment." *Id.* at 2575 (alteration in original) (citing *Auer v. Robbins*, 519 U.S. 452, 461, 462 (1997)).

110. *Id.* at 2574–75.

111. *Id.* at 2575.

112. *Id.* at 2574–75.

113. *Id.* at 2575.

114. *Id.*

be “plainly erroneous or inconsistent with the regulation.”¹¹⁵ The Court added that neither of the plaintiffs provided any reason why the agency’s interpretation should be doubted.¹¹⁶ Adopting the FDA interpretation, the Court essentially dismissed the CBE process as an available option for the generic manufacturers to make the state-required changes.¹¹⁷

The plaintiffs then argued that the manufacturers could have provided so-called Dear Doctor letters “to send additional warnings to prescribing physicians and other healthcare professionals.”¹¹⁸ Such letters can be sent by manufacturers and are used to relay important information about their drugs, including significant health hazards and important labeling changes.¹¹⁹ Addressing the Dear Doctor argument, the Court once again deferred to the FDA’s interpretation.¹²⁰ The FDA stated that Dear Doctor letters qualify as labeling.¹²¹ As such, they pose two particular problems: First, a Dear Doctor letter with “substantial new warning information would not be consistent with the drug’s approved labeling,” and second, the sending of Dear Doctor letters by a generic manufacturer but not its brand-name counterpart would suggest a therapeutic difference between the two drugs and therefore could be misleading.¹²² Thus, the Court determined that Dear Doctor letters were not available as an option for the generic manufacturers to provide the additional warnings required by state law.¹²³

Although the FDA dismissed the CBE process and Dear Doctor letters as possible methods by which the generic drug manufacturers could change their warning labels, it did believe that the manufacturers possessed an option for updating their labels. The FDA stated that manufacturers not only could have but were required to have proposed stronger warning labels to the FDA if they believed that such labels were necessary.¹²⁴ The FDA based this duty on its interpretation of 21 U.S.C. § 352(f)(2), which provides that a drug is misbranded unless its labeling has sufficiently adequate warnings that protect its users.¹²⁵ The FDA’s interpretation of this statute states that a drug’s labeling should be

115. *Id.* (quoting *Auer v. Robbins*, 519 U.S. 452, 461 (1997)).

116. *Id.*

117. *Id.* at 2575–76.

118. *Id.* at 2576 (citations omitted).

119. 21 C.F.R. § 200.5 (2012).

120. *PLIVA*, 131 S. Ct. at 2576.

121. *Id.*

122. *Id.*

123. *Id.*

124. *Id.*

125. *Id.*

revised “as soon as there is reasonable evidence of an association of a serious hazard with a drug.”¹²⁶ The FDA reconciled the manufacturer’s duty to maintain adequate labels and its duty of maintaining an identical label to that of its brand-name counterpart by stating that generic drugs, in instances requiring an updated label, are required to ask the FDA to strengthen the label for both it and its brand-name counterpart.¹²⁷

While the defendants disagreed with the FDA’s determination that such a duty existed, the majority did not address this argument, rather stating that preemption would be found even if such a duty existed.¹²⁸ The majority addressed the question of preemption under the assumption that the federal law did in fact require the manufacturers to ask the FDA to initiate a label change.¹²⁹

The Court found preemption based on its view that it was impossible for the generic manufacturers to comply with both the federal and state laws.¹³⁰ The Court dismissed the FDA’s suggested avenue of change whereby a generic manufacturer would ask for help, finding that state law “*demand*ed a safer label” and was not concerned about the “*possibility* of a safer label.”¹³¹ Thus, whether such action might have worked was, in the Court’s opinion, irrelevant.¹³² Ultimately, the Court determined that the question of impossibility is determined by “whether the private party could *independently* do under federal law what state law requires of it.”¹³³ The Court went on to define this *independent* standard: “[W]hen a party cannot satisfy its state duties without the Federal Government’s special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes.”¹³⁴

A lesser standard, according to the Court, would essentially eliminate any preemption except for express preemption.¹³⁵ Further, the Court found support for its decision through its belief that the phrase of the Supremacy Clause “any [state law] to the Contrary notwithstanding,” is a *non obstante* provision.¹³⁶ This provision,

126. *Id.* (quoting 21 C.F.R. § 201.57(e) (2006)) (internal quotation marks omitted).

127. *Id.*

128. *Id.* at 2576–77.

129. *Id.* at 2576. Such help by the FDA would require the brand name to first update its label, thus allowing the generics to do so as well.

130. *Id.* at 2577.

131. *Id.* at 2578 (emphasis added).

132. *Id.* at 2579.

133. *Id.* (emphasis added).

134. *Id.* at 2581.

135. *Id.* at 2579.

136. *Id.* at 2580 (alteration in original) (citation omitted).

according to the Court, “indicates that a court need look no further than ‘the ordinary meanin[g]’ of federal law, and should not distort federal law to accommodate conflicting state law.”¹³⁷

The Court briefly touched on *Wyeth* and its view of why the two rulings are not contrary to one another.¹³⁸ Specifically, the Court pointed out that the CBE regulation¹³⁹ gave Wyeth, the brand-name drug manufacturer in that case, the ability “‘to unilaterally strengthen its warning’ without prior FDA approval.”¹⁴⁰ The Court admitted, however, that the FDA retained the power to rescind any unilateral change that Wyeth should make.¹⁴¹ Nevertheless, the Court read *Wyeth* as only “ask[ing] what the drug manufacturer could independently do under federal law, and in the absence of clear evidence that Wyeth could not have accomplished what state law required of it, found no pre-emption [and held that] ‘the possibility of impossibility’ was ‘not enough.’”¹⁴² The Court then distinguished *PLIVA* from *Wyeth* by stating that “here, ‘existing’ federal law directly conflicts with state law.”¹⁴³ According to the Court, the question in *PLIVA* was not one of a possibility of *impossibility* as it had been in *Wyeth* but rather “whether the possibility of *possibility* defeats pre-emption.”¹⁴⁴

Lastly, the *PLIVA* Court admitted that “finding pre-emption here but not in *Wyeth* makes little sense.”¹⁴⁵ However, the Court attempted to shed responsibility for its reasoning simply because it is not the Court’s duty to determine if laws are “‘unusual or even bizarre.’”¹⁴⁶

B. Lack of Compatibility with Wyeth v. Levine

The *PLIVA* decision is troubling due to its apparent discrepancy with *Wyeth*, which was decided just two years prior. Even the

137. *Id.* (alteration in original) (quoting *Wyeth v. Levine*, 555 U.S. 555, 588 (2009) (Thomas, J., concurring)). Kennedy did not join in this part, and as such, there were only four justices who endorsed it. This statement directly conflicts with the presumption against preemption. *Id.* at 2591 (Sotomayor, J., dissenting).

138. *Id.* at 2581 (majority opinion).

139. 21 C.F.R. § 314.70(c)(6)(iii) (2006).

140. *PLIVA*, 131 S. Ct. at 2581 (quoting *Wyeth v. Levine*, 555 U.S. 555, 573 (2009)) (citation omitted).

141. *Id.* at 2581 n.8.

142. *Id.* (citations omitted).

143. *Id.* (citation omitted).

144. *Id.* (citation omitted).

145. *Id.* at 2581.

146. *Id.* at 2582 (quoting *Cuomo v. Clearing House Assn., L.L.C.*, 129 S. Ct. 2710, 2733 (2009) (Thomas, J., concurring in part and dissenting in part)).

majority in *PLIVA* pointed out this inconsistency.¹⁴⁷ Although it attempted to reconcile the two decisions, an in-depth analysis of *Wyeth* shows why they are incompatible.

I. *Wyeth v. Levine*

In *Wyeth*, the suit, like in *PLIVA*, was based on a failure to warn.¹⁴⁸ However, the defendant in *Wyeth* was a brand name, not a generic drug manufacturer.¹⁴⁹ In its defense, the brand-name drug manufacturer in *Wyeth* argued that preemption existed in both the physical impossibility sense, as well as the “purposes and objectives” sense.¹⁵⁰

The Court began its preemption analysis by noting two aspects of preemption that have been set out by federal jurisprudence.¹⁵¹ First, in every preemption case, Congress’ intent is the most important factor.¹⁵² Second, there is a presumption against preemption, especially in those fields that states have traditionally occupied.¹⁵³ In order to rise to the level of preemption, Congress’ intent for federal law to supersede state law must be clear and manifest.¹⁵⁴ The Court then touched upon the FDCA’s history, giving examples of various times throughout its history in which Congress made sure not to invalidate state law.¹⁵⁵ In its rejection of *Wyeth*’s arguments that the manufacturer was not allowed to update its labeling, the Court noted that a drug manufacturer “bears responsibility for the content of its label at all times,” and with the CBE regulation, the manufacturer could provide an updated warning before receiving FDA approval.¹⁵⁶ The FDA could have rejected the labeling changes, but without “clear evidence” that the FDA would have rejected such a change, the Court could not have come to the conclusion that impossibility preemption applied.¹⁵⁷ In closing, the Court emphasized the FDA’s traditional belief that state law served as a “complementary form of drug

147. The majority stated that “finding pre-emption here but not in *Wyeth* makes little sense.” *Id.* at 2581.

148. *Wyeth v. Levine*, 555 U.S. 555, 558 (2009).

149. *Id.* at 559.

150. *Id.* at 563–64.

151. *Id.* at 565.

152. *Id.*

153. *Id.*

154. *Id.*

155. *Id.* at 567.

156. *Id.* at 570–71.

157. *Id.* at 571.

regulation,”¹⁵⁸ thus providing further support for why a finding against preemption was logical.

2. *PLIVA's Lack of Conformity with Wyeth*

The *PLIVA* and *Wyeth* decisions are not compatible. Although complete focus on the CBE regulation would suggest a legitimate reason for the distinction between these two cases, such a narrow approach is not proper. The Court in *PLIVA* addressed generic, not brand name, manufacturers' ability to change their warning labels. Thus, the rules and regulations applicable in *PLIVA* were slightly different from *Wyeth*. It is true, as the *PLIVA* Court pointed out, that the CBE regulation did not grant the generic manufacturers the ability to unilaterally change their labels.¹⁵⁹ Nevertheless, the variation in the regulations should not have led to different results because the generic manufacturers in *PLIVA* still retained the ability to institute change.¹⁶⁰

The dissent in *PLIVA* characterized the majority's decision as one which disturbs the landscape of impossibility preemption.¹⁶¹ According to the dissent, the “possibility of impossibility” had never, until this decision, been enough to warrant preemption.¹⁶² However, the majority countered such an assertion, characterizing *PLIVA* as a question, not of “possibility of impossibility” but rather one of “possibility of possibility.”¹⁶³ Although they appear distinct, there is no meaningful difference in the two standards.

According to the majority, the *possibility of impossibility* standard applied in *Wyeth* because the labels could be changed by manufacturers unilaterally, even though the FDA could later

158. *Id.* at 578. In doing so, the Court rejected the 2006 preamble, which expresses the FDA's newly formulated opinion “that state law ‘frustrate[s] the agency's implementation of its statutory mandate,’” stating that such a view does not “merit deference” based on “the ‘complex and extensive’ regulatory history and background relevant to this case” that provides otherwise. *Id.* at 580 (alteration in original) (footnote omitted) (citations omitted).

159. *PLIVA v. Mensing*, 131 S. Ct. 2567, 2575 (2011). Here one can give deference, as the Court did, to the FDA's interpretation of the CBE process. It is, however, beyond the scope of this Comment to delve into whether such a reading was correct. This Comment assumes that the Court and the FDA were correct regarding this determination.

160. Although rejected by the Court in *PLIVA*, the FDA noted that the generic manufacturers could have asked for FDA assistance, which may have eventually resulted in updated labels for both the generic and the brand-name drugs. *Id.* at 2576–77.

161. *See id.* at 2582 (Sotomayor, J., dissenting).

162. *Id.*

163. *Id.* at 2581 n.8 (majority opinion).

disapprove and rescind the changes.¹⁶⁴ Yet, this is essentially what occurred in *PLIVA*. In *PLIVA*, the majority acknowledged that had the generic manufacturers reached out to the FDA, they might have eventually complied with both federal and state law labeling requirements.¹⁶⁵

To summarize: In *Wyeth*, brand-name manufacturers could make changes, but those changes could later be rescinded. In *PLIVA*, generic manufacturers could make changes only after FDA approval. The majority determined that such a distinction was enough for different rulings.¹⁶⁶ However, such reasoning is illogical. In both instances, ultimate compliance was dependent on the FDA. Finding preemption in one situation but not the other, merely based on the timing of the FDA's participation in the label change, is unsound.

If the brand-name manufacturers in *Wyeth* had unilaterally changed their label, only to have that revision rescinded, they no longer would have been in compliance with state law. Similarly, if the generic manufacturers in *PLIVA* had requested a label change but were denied, then they would have never complied with state law. Different conclusions should not be reached regarding impossibility preemption simply because a brand-name manufacturer has the ability to comply with state laws *temporarily* while the a generic manufacturer lacks such an ability. Ultimate compliance is dependent on the FDA. A slight timing difference should not dictate a different result regarding preemption.

There would also be no substantial difference in compliance with state and federal law if each manufacturer's requested or implemented change would have been approved (as in the case of the generic) or not revoked (as in the case of the brand name). Again, the only difference would be a slight one and only with regard to timing. For example, if the brand-name manufacturer in *Wyeth* had instituted a change under the CBE process and had not had that change later revoked when the FDA reviewed that change, it would have complied with both state and federal laws from the moment the change was instituted. If the generic manufacturer in *PLIVA* had submitted a proposed change to the FDA and had that change approved, then the manufacturer would have fulfilled its federal duties throughout the entire process and its state duties from the moment it was able to implement the approved change. In these two examples, ultimate compliance with state law again depends on the FDA. The only

164. *Id.* at 2581.

165. *Id.* at 2578. By reaching out to the FDA, the generic manufacturers might have been able to have the corresponding brand-name label changed, ultimately leading to their compliance with both state and federal law. *Id.*

166. *See id.* at 2581.

difference between the generic and the brand-name manufacturer in such situations is that the brand name will have been in compliance with its state duty for a longer period of time. However, a slight distinction in time, simply because the generic must wait a bit longer to institute a certain change does not merit a difference in preemption determinations.

As shown by these two examples, the only logical finding of preemption would occur in the first example in which the generic or brand-name drug manufacturer had attempted to comply with both state and federal duties, only to find that the FDA prevented it from doing so. As such, the only real difference between the two avenues available for change, because they applied to brand-name and generic manufacturers, was that in the case where the FDA ultimately agrees with the need for a change, the generic manufacturer's compliance with state law would be at a slight delay. Such a delay does not merit a different conclusion regarding preemption.

As evidenced by the previous examples, the FDA plays a strong role in ultimately determining whether a labeling change is admitted. Thus, the *PLIVA* majority's focus on the brand-name manufacturer "unilaterally" being able to strengthen its label is simply misplaced. Just as the generic manufacturers in *PLIVA* might have been unable to comply, so might have the brand-name manufacturers in *Wyeth*. While the majority sought to distinguish between a "possibility of possibility" and a "possibility of impossibility,"¹⁶⁷ no such distinction was justified. A brand-name manufacturer *may* later have its update rescinded, as could have been the case in *Wyeth*; such a situation could be interpreted as a possibility that compliance with state law may eventually be impossible or as a possibility that compliance may be possible. The two only differ depending on the phrasing of the question raised.

A central premise of federal labeling requirements is the belief that manufacturers are responsible for their label's content at all times.¹⁶⁸ Ultimately, this is even more reason to support the *clear evidence* standard endorsed by the *Wyeth* dissent, whereby a

167. *Id.* at 2581 n.8. Here, the majority stated that the "Court in *Wyeth* asked what the drug manufacturer could independently do under federal law, and in the absence of clear evidence that *Wyeth* could not have accomplished what state law required of it, found no pre-emption." *Id.* It then distinguished this with the current situation in which the manufacturer could not have changed his label without the FDA's prior approval. Why the Court ignored the latter part of the above-quoted line, *absence of clear evidence*, is beyond reason. If the manufacturers were held to such a standard in the instant case, then surely, without showing that they at least attempted to initiate the required changes, preemption would not have been found.

168. *Id.* at 2576.

manufacturer does not escape liability (because preemption is not found) without first showing such clear evidence that it would not have been able to comply with both federal and state law.¹⁶⁹

The *PLIVA* dissent correctly highlighted many of the problems regarding the *PLIVA* majority's preemption analysis. In particular, the dissent noted aspects of impossibility preemption that were ignored in its analysis.¹⁷⁰ Additionally, the majority invents a new preemption rule, stating that the impossibility question is determined by whether "the private party could *independently* do under federal law what state law requires of it."¹⁷¹

In support of this *independent* standard, the majority cites *Wyeth*, where preemption was not found, in which the defendant could have *unilaterally* done what was necessary to comply with both state and federal law.¹⁷² Clearly, the majority misinterpreted the meaning of *unilaterally* in the *Wyeth* decision. Yes, the manufacturer in *Wyeth* was able to make changes by following the CBE process, and yes, the manufacturer could update its label without first seeking FDA permission. However, as the *Wyeth* majority recognized, the ultimate decision of whether the updated label could remain was in the hands of the FDA.¹⁷³ Dependence on the FDA concerning a later judgment is not independence. The *PLIVA* majority took the notion of unilaterally making a change dependent on subsequent approval and extended it to unilaterally making a completely independent change. Further, as the dissent pointed out, *Wyeth* provided no evidence that unilateral action is a necessary requirement to defeating preemption, just that it is sufficient.¹⁷⁴

Like the manufacturer's ability in *Wyeth* to initiate change, the manufacturer in *PLIVA* could also have initiated the required change simply by petitioning the FDA. And like *Wyeth*, without subsequent FDA approval or assistance, there would have been no ultimate compliance with state law. However, the *PLIVA* decision did not account for whether the generic manufacturers had even attempted to

169. *Id.* at 2588 (Sotomayor, J., dissenting).

170. See *id.* at 2582–83, for the dissent's statement that the majority invents new principles of pre-emption law out of thin air to justify its dilution of the impossibility standard. It effectively rewrites our decision in *Wyeth* And a plurality of the Court tosses aside our repeated admonition that courts should hesitate to conclude that Congress intended to pre-empt state laws governing health and safety.

Id.

171. *Id.* at 2579 (emphasis added). The dissent made this point in its critique of the majority's analysis. *Id.* at 2589 (Sotomayor, J., dissenting).

172. *Id.* at 2579 (majority opinion).

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

174. *PLIVA*, 131 S. Ct. at 2590 (Sotomayor, J., dissenting).

initiate a change.¹⁷⁵ Therefore, the ruling of impossibility preemption was improperly reached. The Court should have instituted the *clear evidence* standard that was required in *Wyeth*, especially in light of the burden of proving impossibility falling on the defendant.¹⁷⁶ This is the proper approach because courts must hold defendants claiming impossibility preemption to a “demanding” standard.¹⁷⁷ The dissent advocated the correct approach when it stated that “defendants will usually be unable to sustain their burden of showing impossibility if they have not even attempted to employ that mechanism” made available by the Federal Government, which would allow for complying with state law, even in those instances in which “that mechanism requires federal agency action.”¹⁷⁸

III. EFFECTS OF FINDING IMPOSSIBILITY

The Court’s decision in *PLIVA* not only affects the doctrine of impossibility preemption but will also have a strong impact on consumers and brand-name drug manufacturers. Regarding preemption, *PLIVA* significantly broadens what is deemed impossible, thus extending preemption’s reach. Additionally, as noted in the *PLIVA* dissent, the presumption against preemption, especially regarding state laws concerning health and safety, is seemingly forgotten.¹⁷⁹

A. Impact on Preemption

An unfortunate consequence of the new impossibility standard established in *PLIVA* is that much state law that is complementary to federal law will be undermined. Not requiring defendants to show that they made an attempt to comply with both state and federal law will make self-regulation no longer a priority for the manufacturers, thus removing a much-needed complement to FDA regulation.¹⁸⁰

175. *Id.* at 2589. Note that the dissent explained that the manufacturers made the argument that “the FDA had itself considered whether to request enhanced warnings in light of the evidence on which a plaintiff’s claim rests but had decided to leave the warnings as is.” *Id.*

176. *See Wyeth*, 555 U.S. at 573.

177. *PLIVA*, 131 S. Ct. at 2589 (Sotomayor, J., dissenting) (citing *Wyeth*, 555 U.S. at 573).

178. *Id.*

179. *Id.* at 2583. Along with this notion, it is worthwhile to note that prior to the instant case, “a ‘strong’ showing of conflict ‘to overcome the presumption that state and local regulation . . . can constitutionally coexist with federal regulation’” was necessary to find implied preemption. *Id.* at 2591 (alteration in original) (quoting *Hillsborough Cnty. v. Automated Med. Labs., Inc.*, 471 U.S. 707, 716 (1985)).

Without fear of state failure-to-warn claims, manufacturers of generic drugs will no longer possess the necessary incentive to initiate updating their warning labels. As previously mentioned, the FDA possesses limited resources¹⁸¹ and will therefore lose much-needed assistance. Thus, the *PLIVA* preemption decision directly conflicts with the FDA's long-established goal of consumer protection.¹⁸² The effects will be especially problematic in those instances in which the generic drug manufacturer is the sole vendor of a drug in the market. In these instances, without a brand-name manufacturer to turn to, either consumers will be left without a failure-to-warn remedy altogether, or a brand-name manufacturer will unfittingly be faced with extended liability.

B. Consumers Without a Remedy or Drug Manufacturers with Newfound Liability?

The most important aspect of *PLIVA* is the effect that it will have on similar scenarios in the future. Unless the Supreme Court decides to overrule *PLIVA* in the near future, which is unlikely, then there are really only two possibilities of what may result in future instances when a consumer is injured due to a generic drug's failure to warn. Either these consumers will be left without a remedy, or brand-name manufacturers will become liable for generic drug manufacturer's failure to warn. Neither result is just.

If consumers are left without a remedy, then the entire purpose behind drug warning labels is defeated.¹⁸³ Although consumers could still bring other types of suits against generic manufacturers, those types of suits are not as straightforward or as easy to prove as those regarding a failure to warn.¹⁸⁴ Alleging design defect, contaminated drug, or manufacturing glitch subjects consumers to "murkier and more perilous waters."¹⁸⁵

180. *Wyeth*, 555 U.S. at 578.

181. *Id.*

182. *See History*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/default.htm> (last updated Mar. 1, 2013). The FDA is the "oldest comprehensive consumer protection agency in the U.S. federal government." *Id.*

183. *See Wyeth*, 555 U.S. at 578.

184. *Generic Drug Manufacturers Shielded From State-Law Failure-to-Warn Claims*, MCGUIRE WOODS (Jun. 28, 2011), <http://www.mcguirewoods.com/Client-Resources/Alerts/2011/6/Generic-Drug-Manufacturers-Shielded-From-State-Law-Failure-to-Warn-Claims.aspx>.

185. *Id.*

The consequence of not being able to bring failure-to-warn suits against generic manufacturers is that injured parties may turn to the brand-name manufacturer. This result would be highly unjust. Brand-name drug manufacturers already bear the huge initial costs of drug approval and should not be forced to worry about liability for all labeling defects, regardless of whether they are in a position to know that a change is necessary.¹⁸⁶ As previously mentioned, generics dominate the market in overall presence.¹⁸⁷ It is not fair to hold brand-name manufacturers liable for an entire market in which they have only a small share and, consequently, a minor share of the profits.¹⁸⁸ Further, once generic versions of a drug become available, brand-name manufacturers often exit the market.¹⁸⁹ In these instances, regardless of how the question of liability plays out, injured consumers will essentially be left without an adequate remedy.

Furthermore, greater liability for brand-name manufacturers will burden the entire market for drugs. Already faced with incredibly high entry costs, brand-name drug manufacturers' fear of indefinite liability would strike at their primary incentive for serving as drug innovators—profit.¹⁹⁰ This in turn could lead to less innovation for brand-name drug manufacturers and, as a result, a more stagnant evolution of medicine. Ultimately, consumers would be hurt most by such a result.

186. This is by no means a suggestion that brand-name drug manufacturers should never be found liable regarding a generic drug's label. If the generic reasonably relied on a brand name's label, and the generic did not have any reason to update that label, but it is found that the brand name neglected its duty to make the necessary changes, then clearly the just result would be for the brand name to be accountable. However, that is beyond the scope of this Comment. In the instant case, focus is placed on the generic drug's liability, assuming that it failed to make a change that it had a duty to make based on information it either knew or should have known.

187. See *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2584 (2011) (Sotomayor, J., dissenting) (noting that 75% of all drugs in 2009 were generics and 90% of all prescriptions for which there was a generic were filled with a generic).

188. While a brand-name manufacturer does get the exclusive right to market a drug while the drug is under patent protection, *id.* at 2581–82 n.9 (majority opinion), that does not mean that the manufacturer should be subject to indefinite liability for their drug, regardless of whether the manufacturer profited handsomely due to such exclusivity.

189. *Id.* at 2593 (Sotomayor, J., dissenting).

190. Although it is true that brand-name manufacturers often reap the benefits of market exclusivity during the period of a drug's patent protection, such a period is necessary to recoup the initial entry costs. The possibility of further liability would disrupt such a balance.

C. FDA Losing Necessary Assistance?

Perhaps the most serious cries for change should come from the FDA. As the *Wyeth* Court noted, “[T]he FDA [has] traditionally regarded state law as a complementary form of drug regulation. The FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about the drugs, especially in the postmarketing phase as new risks emerge.”¹⁹¹ With *PLIVA*, the safety of consumers is further compromised.

IV. FIXING THE CURRENT SITUATION

To fix this problematic labeling state of affairs, Congress should amend the FDA laws, which would be the most logical thing to do. Congress can either extend the CBE regulations to generics, or it could create a separate and distinct, yet similar option for generic manufacturers.¹⁹²

A. Extending the CBE Process to Generics

As previously discussed, origins of the CBE process can be traced to when the Commissioner of Food and Drugs “concluded that in the interest of drug safety certain kinds of changes in the labeling and manufacturing of new drugs . . . should be placed into effect at the earliest possible time.”¹⁹³ Thus, the CBE process was born out of the notion that certain changes were extremely important

191. *Wyeth v. Levine*, 555 U.S. 555, 578–79 (2009).

192. There has also been speculation that a fund akin to that provided for by the National Vaccine Injury Compensation Program will be implemented for pharmaceutical drugs. See *Congressional Action Awaited Post High Court’s Generic Preemption Ruling*, 17 FDA WEEK, no. 26 (2011). However, this fund is unnecessary. This may seem like a good option regarding the effect it may have on helping to free brand-name manufacturers from the fear that they will assume all liability in failure-to-warn suits. However, a detrimental result of it would be to free all drug manufacturers from a fear of failure-to-warn suits, which will in turn lead to less consumer protection. (One of the objectives by Congress with respect to the fund was to protect industry and the medical profession from liability regarding vaccine-related injuries. National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-11 (2006). In the current situation, one could expect one of the results to be the same. This would go contrary to and take away from the benefit that self-regulation provides.) Diminishing the manufacturer’s incentive to continuously regulate its drug labels, this approach would serve more as an after-the-fact remedy, rather than the more beneficial preventative approach, which the current standards require.

193. Supplemental New-Drug Applications, 30 Fed. Reg. 993, 993 (Jan. 30, 1965).

and should be instituted as soon as possible. In extending the CBE process to generics, the FDA would reinforce the purpose behind the CBE process. With generics often in control of a certain market, and brand-name drug manufacturers exiting the market after generic versions of their drugs are approved, logically the CBE process should extend to generics.

The FDA argues that the CBE process does not extend to generics because allowing such an option would disrupt the *sameness* requirement between the generic drug and its brand-name counterpart.¹⁹⁴ Such a problem is easily fixed. If the CBE process were to extend to generics, then the “sameness” duty that is imposed on generics would need to extend to brand-name drugs. That way, whenever a generic drug manufacturer initiates a change under the CBE process, then the brand-name manufacturer would need to do the same. A discrepancy might occur only if the two manufacturers were attempting to make a change at the same time. However, as noted in *PLIVA*, situations in which generic manufacturers uncover new information requiring a label change are very rare.¹⁹⁵ Nonetheless, that does not excuse the FDA from creating an avenue available to generic manufacturers. A consumer should not suffer injury simply because situations like this do not occur very often. If the FDA is correct that these situations are not at all common, then the extension of the CBE process to generic drug manufacturers should not disrupt the rules and regulations as they exist.

Further, if uncovering new information for a label update occurs once a generic drug is on the market, the manufacturer that is more likely to uncover such information is the one with the greater market share, whether it is the generic manufacturer or the brand-name manufacturer.¹⁹⁶ This is logical because that manufacturer would be exposed to more information that may evidence the need to change the labeling.¹⁹⁷ Such a system would incentivize generic drug

194. *PLIVA*, 131 S. Ct. at 2575. “The FDA argues that 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.” *Id.* (citations omitted).

195. *Id.* at 2581 n.9.

196. This is logical because both generic drug manufacturers and brand-name drug manufacturers would presumably receive reports of adverse effects of their drugs. The greater its share of the market, then presumably the more likely one of its drugs will have an adverse reaction.

197. However, it should be noted that because brand-name drug manufacturers are required to provide extensive clinical trials before obtaining approval, certain situations may arise in which a label change is necessary based on *both* new data that has been collected since the generic equivalent has entered the market, as well as prior data that came about during the brand-name drug’s exclusivity period. In this situation, the brand-name manufacturer would clearly be the one with the

manufacturers to ensure their products' safety, thus ensuring the safety of consumers and therefore fulfilling the purpose of the CBE process.

B. The CBE As Merely a Starting Point?

The CBE process could also be extended to only those manufacturers whose generic drugs have a certain percentage of the market or have been on the market for a certain period of time. Although such a determination may be difficult, the benefits are twofold. First, generics would not be prematurely liable for such inadequacies. Second, brand-name manufacturers who have benefited from exclusivity of the market for years and may have profited handsomely will retain the incentive to update their warning labels until their generic counterparts are in a position to do so. A potential conflict might arise if a generic manufacturer were to discover grounds for new warning labels quickly after entering the market because the generic manufacturer would not yet possess a requisite market amount and thus would be unable to initiate the change. However, such an occurrence is unlikely. Because failure-to-warn claims arise when manufacturers are aware or should be aware of a danger, and such new information is rarely discovered,¹⁹⁸ it is unlikely that such an occurrence would exist prior to the generic at least being in the market for a substantial period of time and also having a substantial market share.

If the FDA prefers to initiate a separate process for generics, one based on the CBE process, then that may work as well. One option would be a process that requires the generic manufacturer to submit its findings not only to the FDA but also to the brand-name manufacturer once it initiates a change. That way, should the brand-name manufacturer object for any reason, it will be able to share its thoughts with the generic manufacturer as well as the FDA. In allowing the brand-name manufacturer to do so, it would be unnecessary to amend the sameness requirement so that labels do not have to be copied until the ultimate FDA approval is received for such a change. Critics may argue that this would enable the labeling of generic drugs to be different from brand-name drugs,

better chance of uncovering such information requiring a label change. These situations do not affect the CBE extension proposal because it would merely extend that ability to generic drugs, thus leaving untouched the liability, and therefore incentive, for brand-name manufacturers to continuously monitor and update their labeling.

¹⁹⁸. *PLIVA*, 131 S. Ct. at 2581 n.9.

thus defeating the purpose of the sameness requirement. However, this process could be relatively short; if the FDA did not agree with such a change, then the period of time in which there is a discrepancy between the two labels would be brief.

CONCLUSION

The ultimate responsibility for labeling resides with manufacturers, as it should. Manufacturers are the most knowledgeable parties when it comes to their own products. It is only logical that they should be allowed to have some control over their labeling. The Court's unfortunate ruling in *PLIVA* that federal law preempts state failure-to-warn claims regarding generic drugs presents several problems. Of these, the biggest problem will ultimately be felt by the consumers, who will most likely be left without a meaningful remedy. If the burden shifts to brand-name manufacturers, consumers will still be at a loss because they will be poorly protected, as generic manufacturers will no longer be incentivized to maintain safe and adequate warning labels. This is especially disheartening considering that the FDA's ultimate purpose in drug regulation is to protect consumers.¹⁹⁹

However, not all hope is lost. The FDA could either extend the CBE process to generic manufacturers or create a separate avenue for generic manufacturers that is based on the CBE process. With anywhere from one-third to one-half of generics no longer having a brand-name counterpart marketed²⁰⁰ and with the prevalence of generics continuing to increase, the time to act is now.

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199. See *History*, *supra* note 182.

200. *PLIVA*, 131 S. Ct. at 2584 (Sotomayor, J., dissenting).

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