Marquette Law Review

Volume 100
Issue 4 *Summer 2017*

Article 6

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12 ANGRY MEN V. THE AGENCY: WHY PREEMPTION SHOULD RESOLVE THIS CONFLICT IN DRUG LABELING LITIGATION

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The Supreme Court has found in favor of preemption in tort liability cases involving matters of heavy federal regulation in which Congress has delegated implementation of a statute involving technical subject matter to the agency. It has not been the case, however, in matters concerning the labeling of prescription drugs, despite the fact that the FDA has exclusively regulated drug labeling for more than a century. In fact, the current state of affairs now allows a jury to substitute the judgment of the FDA in approving a label on a name-brand drug for their own in state law failure to warn claims, allows for preemption on the same question when a generic drug manufacturer is involved, and a proposed rule by the FDA set to be released in April of 2017 could remove the protection of preemption for generic manufacturers, in contravention of the purpose and goals of the Hatch–Waxman Amendments to the FDCA. To support the delegation of power given to FDA to regulate drug labeling, prevent juries from second-guessing the propriety of an FDA-approved drug label, and encourage generic manufacturers to remain in the market and provide consumers access to drugs at a lower cost, Congress should provide for express preemption to both name-brand and generic manufacturers in failure to warn cases.

* Assistant Professor of Law, Detroit Mercy School of Law. I wish to thank my colleagues at Detroit Mercy Law for their support and encouragement during the writing of this article. I also wish to thank the many students who have contributed to the research for the article including Sharon Rangi, Javon David, & Tiffany Mausolf, as well as Sara McNamara, Editor In Chief, and the entire staff at Marquette Law Review for their diligence in editing and thoughtful suggestions. Finally, to my husband & family for everything.

I. INTRODUCTION

Despite the fact that the regulation of the labeling of prescription drugs has rested exclusively with the FDA since 1932, state courts continue to be clogged with lawsuits filed by plaintiffs who claim a defect in the labeling. These lawsuits ask state court juries to question the propriety of the content of the FDA-approved, drug warning label and substitute their judgment for the FDA's. Both name-brand or "pioneer" drug manufacturers, as well as generic manufacturers—who produce approximately 80% of the drugs dispensed in the marketplace—routinely raise the issue of implied preemption as a defense because the FDA exclusively controls the content of drug labeling. Inconsistent holdings across the country finally forced the issue to the Supreme Court beginning in 2009.

However, the Supreme Court has exacerbated this situation by handing down conflicting rulings that offer generic drug manufacturers the protection of preemption, but allow state tort claims to proceed against name-brand manufacturers. As a result of these holdings, a plaintiff who has been given the name brand drug may seek redress in state court against the manufacturer for a claim of failure to warn, but a plaintiff who has been dispensed a generic form of that same drug will be unable to sue

the generic manufacturer as such claims are preempted.[1] Though the Court admitted that application of preemption in one instance and not the other "makes little sense,"[2] the Court attributed the discord to the different federal statutes and regulations that govern each instance. Namely, the Court found that a name brand drug manufacturer has, in some cases, a window in which it may issue a new drug warning label before seeking approval by the FDA, but a generic manufacture cannot make any change to the label at any time as its label must always be "the same as" the FDA-approved label of the name brand drug.[3]

In response to the apparent discord between the holdings in these cases, the FDA issued a Notice of Proposed Rulemaking in July 2013, entitled, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products."[4] The FDA now proposes that the generic manufacturer has the same "opportunity" as name-brand manufacturers to update their label to reflect necessary warnings before the FDA approves the proposed changes to the label. In other words, the federal duty of "sameness" imposed by the FDCA and the current regulations for both name-brand and generic drug labeling would be gone.

This Article argues for the application of federal preemption in tort liability cases that question the propriety of the drug warning label as approved by the FDA. The Article will also demonstrate that the new proposed regulation set to be enacted by the FDA in the summer of 2017 does NOT properly answer the call to provide the Court with an "occasion . . . to consider the pre-emptive effect of a specific agency regulation bearing the force of law."[5] The Court wanted the FDA to promulgate rules and regulations explaining the federal labeling requirements and the impact of state law tort claims on the regulatory scheme. As Justice Breyer put it, the Court can sustain a finding of preemption when the FDA determines "whether and when state tort law acts as a help or a hindrance to achieving the safe drug-related medical care that Congress sought" and embodies "those determinations in **lawful** specific regulations describing . . . when labeling requirements serve as a ceiling as well as a floor."[6] Simply put, the proposed regulation is not

1. *See* PLIVA, Inc. v. Mensing, 564 U.S. 604 (2011); Wyeth v. Levine, 555 U.S. 555 (2009).

2. *PLIVA,* 564 U.S. at 625.

3. *Id*. at 613.

4. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985-02 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pt. 314, 601).

5. *Wyeth,* 555 U.S. at 580.

6. *Id*. at 582 (Breyer, J., concurring) (emphasis added).

lawful, and it is time for Congress to step in and provide an express preemption clause within the FDCA.

Part I of this Article will first demonstrate that the historical purpose of the FDA has always been to occupy the field of drug regulation. Part II will explain the enactment of the FDCA and its relative amendments, including the Hatch–Waxman Amendment, and the issue of preemptive force and effect. Part III of this Article will track some of the major federal regulatory cases that have come out of the Court over the last twenty-five years to demonstrate the Court's willingness to expressly preempt state law tort claims in instances where the agency expresses its intent to preempt state law claims, state law tort claims would stand as an obstacle purpose and accomplishment of the regulatory scheme, or where the regulatory scheme is so pervasive as to "occupy the field" in that area of law. In Part IV, this Article will present the most recent drug labeling cases that have come out of the Court to demonstrate the inconsistency in its holdings with prior cases in which preemption was applied in the face of stringent federal regulations.

Part V of this Article will discuss the effects of the proposed new regulation on the federal regulatory scheme and the economic dangers to the industry. Finally, Part VI of this Article will advocate that, in order to avoid any future confusion as to the purpose and intent of the FDCA and the regulatory discretion given to the FDA, Congress should expressly preempt state law tort claims in drug labeling cases as this area has historically been a matter of federal regulation, and there are significant dangers in exposing drug manufacturers to the opinions of state court juries on the propriety of their label.

II. THE HISTORY OF DRUG LABELING REGULATION

Prior to 1906, drug labeling was completely unregulated by the federal government. As John Swann, Ph.D. and historian at the FDA in Rockville, MD noted in a Centennial Edition of the *FDA Consumer* magazine,

> At the turn of the 20th century, there were no regulations to protect the public from dangerous drugs. "It was a menacing marketplace filled with products such as William Radam's Microbe Killer and Benjamin Bye's Soothing Balmy Oils to cure cancer. . . . Products like these were, at a minimum, useless remedies that picked the pocket of the user, but they could also be downright harmful."[7]

7. Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, 40 FDA CONSUMER

As a result, new drugs were introduced to the market by both individuals and companies, and these groups and were free to choose what labeling, if any, would accompany the product.[8] Often times, the labeling was either false or completely misleading, and the use of some of these drugs caused severe injuries and even death.[9]

In response to this problem, on June 30, 1906, the federal government exerted control over the labeling of foods and drugs when President Roosevelt signed the Pure Food and Drugs Act (known as "the Wiley Act") into law.[10] The Act was administered by the Bureau of Chemistry and prohibited the interstate transport of misbranded or adulterated food and drugs.[11] According to the FDA, "[t]he basis of the law rested on the regulation of product labeling rather than pre-market approval."[12] According to the Act, drugs had to comply with the standards of purity, strength, and quality set by the United States Pharmacopoeia or the National Formulary, unless the label stated how the product differed from that standard, and a drug label could not be false or misleading.[13]

From the very beginning, although drug and food manufacturers objected to the federal government's apparent authority and control over the labeling arena, the Supreme Court gave deference to the agency's intent to occupy the field of labeling. For example, in *Hippolite Egg Co. v. United States*, the Court upheld the agency's authority as a proper exercise of Congress's power under the Commerce Clause.[14]

In 1912, in response to a ruling by the Supreme Court that the FDA did

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14, 14 (Jan.–Feb. 2006).

8. *Id*. at 16.

9. *Id*. ("'To establish fraud, the bureau had to show that the manufacturer knew the product was worthless, and this proved difficult in many cases,' Swann says. For example, Lee Barlett, a former shirt salesman from Pittsburgh, promoted a medicine called Banbar as being effective for diabetes. Banbar was an extract of horsetail weed. The government took Barlett to court for selling a misbranded drug and even showed the death certificates of people with diabetes who had taken Banbar. But the jury ruled in Barlett's favor.")

10. Wiley Act, Pure Foods and Drug Act, ch. 3915, 34 Stat. 768 (1906).

11. *Id*.

12. *The 1906 Food and Drugs Act and Its Enforcement*, U.S. FOOD & DRUG ADMIN., (June 18, 2009), https://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm054819.htm [https://perma.cc/QQ7E-UWJX].

13. *See* Wiley Act, ch. 3915, 34 Stat. at 769; John P. Swann, *How Chemists Pushed for Consumer Protection—The Food and Drugs Act of 1906*, U.S. FOOD & DRUG ADMIN., (Oct. 3, 2012), https://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/Chemistsandthe1906Act/ucm126648.htm [https://perma.cc/L94E-QUJ5].

14. 220 U.S. 45 (1911). *See also* Hoke and Economides v. United States, 227 U.S. 308, 322 (1913).

not apply to false therapeutic claims because the nature of uncertainty in the realm of medical knowledge made it difficult to regulate, Congress passed the Sherley Amendment which made it illegal to sell drugs that the manufacturer knew to be worthless.[15] Despite this effort to regulate the actual product itself, the FDA continued to only regulate the warning labels for drugs. Regardless, according to the FDA's records, seizures of misbranded drugs increased in the 1920s and 1930s.[16] In fact, drugs were really the only commodity for which the labeling could be regulated based on established compendia. Because no such standards existed for food, cosmetics, or medical devices, the Agency could not regulate in that area. As one historian has stated, "[t]wo firms might have very different ideas of what peanut butter or jelly or even bread was supposed to be."[17]

Consequently, despite Agency efforts to inspect manufacturing establishments to ensure compliance with the law, the FDA truly did not work to prevent the marketing, manufacturer, or introduction of any unsafe food or drug on the market. For example, in 1937, more than 100 people died after taking Elixir Sulfanilamide, a liquid form of a drug that had been effective in the treatment of streptococcal infections when dispensed in a pill or powder form.[18] However, because the FDA did not require approval or testing of drugs, no one discovered that the chemical used, diethylene glycol, to effect the liquid formulation was poisonous and deadly.[19] Consequently, the only violation with which the agency could charge the manufacturer was selling a misbranded drug in interstate commerce as "elixirs" had to contain alcohol as a drug vehicle and Elixir Sulfanilamide did not contain alcohol.[20]

In June of 1938, in large part because of the Sulfanilamide cases, President Roosevelt signed the Food, Drug, and Cosmetic Act into law.[21] For the first time in history, the FDA was given regulatory authority over the labeling for drugs and biological products. The Act required all new drugs to be approved as safe by the FDA before they can be marketed.[22] Further, the law required that drug labels had to carry adequate directions

15. H.R. Cong. Res. 11877, 62d Cong. (1912) (enacted); *see also* Swann, *supra* note 13.

16. *The 1906 Food and Drugs Act and Its Enforcement*, *supra* note 12.

17. Swann, *supra* note 13.

18. Carol Ballentine, *Taste of Raspberries, Taste of Death: The 1937 Elixir Sulfanilamide Incident*, 15 FDA CONSUMER 18, 18 (June 1981).

19. *Id*.

20. Swann, *supra* note 13.

21. 21 U.S.C. §§ 301–92. (1938).

22. *Id.*

for safe use.[23] However, initially, false advertising of drugs came under the jurisdiction of the Federal Trade Commission. In 1962, Congress passed the Kefauver-Harris Amendments to the Act that continued to strengthen the control of the agency over the labeling of drugs by transferring the regulation of prescription drug advertising from the FTC to FDA.[24] In 1966, Congress passed the Fair Packaging and Labeling Act, legislation that required all consumer products in interstate commerce to be honestly and informatively labeled, with FDA enforcing provisions on foods, drugs, cosmetics, and medical devices.[25]

III. THE FOOD, DRUG, & COSMETICS ACT: A FEDERAL REGULATORY PROCESS FOR APPROVAL OF DRUGS AND DRUG LABELING

A. The Process of Federal Regulatory Approval

Under the Federal Food, Drug, and Cosmetic Act (FDCA),[26] the Food and Drug Administration (FDA) is charged with the regulation of the manufacture, sale, and labeling of prescription drugs. Through the FDCA, Congress charged the FDA with ensuring that drugs are safe and effective under the conditions prescribed, recommended, or suggested in the labeling,[27] and that they are not misbranded.[28] In order for a prescription drug to enter the stream of commerce, the FDA must approve both the listed drug, as well as the labeling of the drug.[29] Such approval means that the drug and its label have been evaluated and is deemed "safe and effective" by the FDA.[30]

After a period of time expires, other manufacturers may seek approval to market a generic version per the Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch–Waxman Amendments.[31] The FDCA requires a generic manufacturer to demonstrate bioequivalence to the listed drug, and that the labeling for the

23. *Id*.

24. Kefauver–Harris Amendments, Drug Amendments of 1962, Pub. L. 87-781, § 131, 76 Stat. 782–84 (1962).

25. 15 U.S.C. §§ 1451–61 (1967).

26. 21 U.S.C. § 301 (2012).

27. 21 U.S.C. §§ 355(d), 393(b)(2)(B) (2012).

28. 21 U.S.C. §§ 321(n), 331(a), (b), (k), 352 (2012).

29. 21 U.S.C. § 355(a) (2012).

30. 21 U.S.C. § 355(b).

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

generic drug "is the same as the labeling approved for" the listed drug.[32] Although the pioneer drug manufacturer may make changes to the label of the listed drug, those changes must be approved by the FDA.[33] Because of the requirement of "sameness" under the FDCA, at no time may the labeling of a generic version of a listed drug be different than that of the approved label for the listed drug. In other words, a generic manufacturer may not make a change to the label of a generic drug unless the change is approved by the FDA and made by the name brand drug manufacturer first.

Under the FDCA, the process for FDA approval of a new drug and its corresponding labeling begins with the filing of a "New Drug Application" (NDA).[34] The NDA **must** contain "the labeling proposed to be used for such drug,"[35] otherwise it would be considered "misbranded" under the Act. The label must provide "a discussion of why the benefits exceed the risks [of the drug] under the conditions stated in the labeling,"[36] in order to allow the FDA to evaluate whether the drug is safe and effective under the conditions of use set forth in the label. In other words, the label provides the FDA the basis for evaluation of the risk of the drug itself.[37] In fact, the agency itself has stated, "[d]rug labeling serves as the standard under which FDA determines whether a product is safe and effective."[38]

The FDA will issue an approval of an NDA based on evaluation of several factors, a majority of which involve an evaluation of the safety and efficacy of the drug based on the conditions of use set forth in the label itself.[39] For example, the FDA considers whether the reports given by the drug manufacturer include "adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling."[40] Further, the FDA evaluates whether the "results of such tests

32. 21 U.S.C. § 355(j)(2)(A)(v). *See also* 21 U.S.C. § 355(j)(4)(G).

33. 21 C.F.R. §§ 314.70(b), (b)(3), (c), (c)(2)(i) (2001).

34. *See* 21 U.S.C. § 355(a); 21 C.F.R. § 314.50(c)(2)(i) (2001).

35. 21 U.S.C. § 355(b)(1)(F); 21 C.F.R. § 314.50(c)(2)(i), (e)(2)(ii) (2010).

36. 21 C.F.R. § 314.50(d)(5)(viii); 21 C.F.R. § 314.50(c)(2)(ix).

37. *See* Christine H. Kim, *The Case for Preemption of Prescription Drug Failure-to-Warn Claims*, 62 FOOD & DRUG L.J. 399, 405 (2007) ("The centerpiece of risk management for prescription drugs is its labeling . . . ." (citation omitted)).

38. Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2848, 2850 (proposed Jan. 16, 2008) (quoting 50 Fed. Reg. 7470 (Feb. 22, 1985)).

39. 21 U.S.C. § 355(d) (2012).

40. 21 U.S.C. § 355(d)(1).

show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions."[41] The FDA also considers whether there is sufficient information to determine whether the drug is safe for use under the conditions set forth in the label OR whether there is "a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof."[42] Finally, the FDA determines whether, "based on a fair evaluation of all material facts, such labeling is false or misleading in any particular."[43]

Once the label is approved, a manufacturer may NOT make any changes to the drug, including the labeling, until it seeks and receives approval from the FDA.[44] This includes instances in which the manufacturer becomes aware of issues, such as a "clinically significant hazard," for which a change in the label would ultimately make the drug and its label safer and more effective.[45] Although there is a mechanism by which a labeling change can be made prior to FDA approval, called a "changes being effected" or "CBE" regulation, the FDA has emphasized that prior approval changes are only to be made in the most exigent of circumstances.[46] In fact, in the preamble to the final rule, the FDA stated:

> Drug labeling serves as the standard under which FDA determines whether a product is safe and effective. Substantive changes in labeling . . . are more likely than other changes to affect the agency's previous conclusions about the safety and effectiveness of the drug. Thus, they are appropriately approved by FDA in advance, unless they relate to important safety information, like a new contraindication or warning, that should be immediately conveyed to the user.[47]

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch–Waxman Amendments to the FDCA or the Hatch–Waxman Act.[48] Under Hatch–

41. 21 U.S.C. § 355(d)(2).
42. 21 U.S.C. § 355(d)(5).
43. 21 U.S.C. § 355(d)(7).
44. *See* 50 Fed. Reg. 7470 (Feb. 22, 1985).
45. 21 CFR § 314.70(b)(4) (2010).
46. *Id*.
47. 50 Fed. Reg. 7470.
48. Pub. L. No. 98-417, 98 Stat. 1585 (1984).

Waxman, Congress achieved two goals: first, they were able to promote the entry of generic drug manufacturers to the market, and second, they were able to provide incentives for pioneer drug manufacturers to continue to research and develop new drugs to bring to the market.[49] In short, this first goal, relevant to this Article, provided generic drug companies an easier and shorter method to bring generic versions of the drugs developed, manufactured, and sold by a pioneer drug company and approved by the FDA without fear of a patent infringement claim by the pioneer drug company. In order to gain FDA approval, the generic drug company need only provide proof of its products' bioequivalence with the pioneer drug, as well as proof that the labeling of the generic drug is "the same as" that of the pioneer drug to comply with the requirements of the FDCA .[50]

Prior to its enactment, only 19% of drugs prescribed in the United States were generic.[51] Today, generic drugs account for approximately 80% of drugs prescribed and dispensed, and there is evidence that the use of generic drugs has saved consumers and the health care industry, including federal and state governments, over $200 billion annually, and over $1.2 trillion between 2003 and 2012.[52]

B. The FDCA and Preemption

As demonstrated above, the FDCA requires FDA to approve both the drug and its label as safe and effective.[53] In other words, Congress, in enacting the FDCA, placed sole control of the regulation of the manufacturing, labeling, and marketing of prescription drugs in the hands of the FDA. Although no express preemption language appears within the Act, it is clear that Congress at least contemplated some discord between state and federal law in this area. To that end, Congress placed a qualified "savings clause" within the 1962 Amendments which provides:

> Section 202. Nothing in the amendments made by this Act to the Federal Food, Drug, and Cosmetic Act shall be construed as invalidating any provision of State law which

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49. *Id.*

50. *Id.*

51. CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY ix (July 1998).

52. *Generic Drug Savings in the U.S.*, IMS HEALTH & GENERIC PHARM. ASS'N (2013), http://www.gphaonline.org/media/cms/Generic_Cost_Fact_Sheet.pdf [https://perma.cc/8N6Y-JP6A].

53. *See* 21 U.S.C. § 355 (2012).

> would be valid in the absence of such amendments **unless there is a direct and positive conflict between such amendments and such provision of State law**.[54]

In short, although recognizing the ability of states to regulate for the health, safety, and welfare of their citizens, Congress intended that State laws that directly conflict with the FDCA are to be preempted.

In 2006, in the preamble to a regulation governing the content and format of prescription drug labels, the FDA declared that the FDCA establishes "both a 'floor' and a 'ceiling,'" so that "FDA approval of labeling . . . preempts conflicting or contrary State law."[55] It further stated that certain state-law actions, such as those involving failure-to-warn claims, "threaten FDA's statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs."[56]

In 2007, Congress passed the Federal Food and Drug Administration Amendments Act (FDAAA), the most extensive revision of the FDCA since 1962.[57] The Act contains multiple provisions, the most relevant to this Article being those that significantly expand the FDA's enforcement and surveillance powers as they relate, in part, to labeling, and establish a program for post-market risk identification.[58]

Although there is no provision for express preemption, Congress incorporated and reinforced the requirements of the applicable FDCA provisions and the regulations promulgated by the FDA:

> (I) Rule of construction
>
> This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under subsection (j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).[59]

Shortly after the legislation was passed, lawyers predicted that the plaintiff's bar would use this provision to undermine any arguments that

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54. Kefauver–Harris Amendments, Drug Amendments of 1962, Pub. L. 87-781, § 202, 76 Stat. 793 (1962) (emphasis added).

55. 72 Fed. Reg. 3922, 3934–35 (2006).

56. *Id*. at 3935.

57. Food and Drug Administration Amendments Act of 2007, Pub. L. 110-85, 121 Stat. 823 (2007).

58. *Id*. §§ 901, 911.

59. 21 U.S.C. § 355(o)(4)(I) (2012).

Congress intended to preempt state law failure to warn or inadequate warning claims when it expanded the FDA's oversight and control over labeling as detailed above.[60] However, on January 16, 2008, the FDA published Notice of Proposed Rules clarifying its position on the preemptive effect of its drug labeling approvals of both new and prior approved drugs.[61] In that Notice, the FDA acknowledges that Congress intended the agency to be the "expert" in the field of drug labeling.

> FDA is the expert public health agency charged by Congress with ensuring that drugs, biologics, and medical devices are safe and effective, and ensuring that the labeling for approved products appropriately informs users of the risks and benefits of the product. Accordingly, the Federal Food, Drug, and Cosmetic Act (the act) requires new drugs, biologics, and certain Class III medical devices to be approved by FDA prior to their distribution in interstate commerce. See 21 U.S.C. 505(a); 42 U.S.C. 262(a)(1); 21 U.S.C. 360e(a). Under these provisions, FDA's review and prior approval of both the product and its proposed labeling is a necessary condition of lawful distribution of the product in interstate commerce.[62]

The FDA also reiterated the fact allowing a manufacturer to utilize the CBE process to change the label on a drug prior to approval by the agency should only be done in the most exigent of circumstances:

> The CBE supplement procedures set forth in

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60. *See* Kristin Hicks, FDA Preemption After the Food and Drug Amendments Act of 2007, at 10 n.48 (May 2008) (J.D. Writing Requirement, Harvard Law School), http://nrs.harvard.edu/urn-3:HUL.InstRepos:8592147 [https://perma.cc/MF63-RZR7] (citing The FDA Amendments Act of 2007, ARNOLD & PORTER LLP, at 9 (2007), http://arnoldporter.com/resources/documents/A&PCA_ExecutiveSummary-TheFDA_Oct107_V2.pdf [https://perma.cc/7BUK-VCQK] (arguing that the rule of construction is "undoubtedly a tool that will be used by plaintiffs seeking to undermine preemption in 'failure to warn' cases); James M. Beck (@Bexis), *The 2007 FDCA Amendments and Preemption,* DRUG AND DEVICE LAW, (Oct. 18, 2007), https://www.druganddevicelawblog.com/2007/10/2007-fdca-amendments-and-preemption.html [https://perma.cc/JC6M-FGRM] ("[T]he ink's hardly dry on the FDAAA before the plaintiffs are at it again, claiming that an obscure 'rule of construction,' facially applicable only to a single section of the new act, somehow undermines preemption as to the FDCA as a whole."); *see also* Susan J. Pannell, *Claim Based on Deceptive Drug Ads is Preempted, Third Circuit Holds*, 43 TRIAL 16, 18 (Nov. 2007) (quoting American Association for Justice regulatory counsel, Gerie Voss, as stating: "With the recent passage of the Food and Drug Administration Amendments Act of 2007, Congress stated its intent that FDA regulation should not preempt the field and that drug companies continue to have an independent obligation to promptly update a label to warn consumers of a drug's risks").

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

62. *Id.* at 2849.

> §§ 314.70(c)(6)(iii), 601.12(f)(2), and 814.39(d) must be understood in light of these statutory requirements (*that drugs, biologics, and certain medical devices are required to be approved by the FDA prior to distribution in interstate commerce)*. Allowing sponsors to unilaterally amend the labeling for approved products without limitation—even if done to add new warnings—would undermine the FDA approval process required by Congress. Indeed, permitting a sponsor to unilaterally rewrite the labeling for a product following FDA's approval of a product and its labeling would disrupt FDA's careful balancing of how the risks and benefits of the product should be communicated. Accordingly, FDA has issued regulations providing that, prior to a sponsor making most labeling changes, it must submit a supplemental application fully explaining the basis for the change and obtain the prior approval by FDA of the supplemental application. See §§ 314.70(b), 601.12(f)(1), 814.39(a)(2).
>
> The CBE supplement procedures are narrow exceptions to this general rule. Although CBE supplements permit sponsors to implement labeling changes before FDA approval of the change, FDA views a CBE supplement as a mechanism primarily designed to provide information to FDA so that the agency can decide when safety information should be included in the labeling for a product.[63]

Finally, the agency further noted that the 2007 Food and Drug Administration Amendments Act (FDAAA) provided streamlined procedures for the FDA to rapidly review and approve safety related drug labels and warnings based on new information.[64] In a footnote, it noted that "[f]ederal law governs not only what information must appear in labeling, but also what information may not appear" and that "FDA interprets the act to establish both a 'floor' and a 'ceiling,' such that additional disclosures of risk information can expose a manufacturer to liability under the act if the additional statement is unsubstantiated or otherwise false or misleading."[65] As such, FDA interpreted the FDAAA as a continued expression of congressional intent that the agency retain exclusive control over the approval process for the labeling of approved drugs.

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63. *Id*.
64. *Id.* at 2849–50.
65. *Id.* at 2850 n.3.

Most importantly, in response to comments filed by states that because the FDAAA lacks an express preemption clause Congress did not intend to foreclose claims by plaintiffs for failure to warn, FDA stated, "FDA does not believe that the absence of an express preemption provision with respect to drugs affects the application of the doctrine of implied preemption."[66]

IV. THE COURT AND PREEMPTION

Under the Supremacy Clause of the Constitution, federal law "shall be the supreme Law of the Land . . . any Thing in the Constitution or Laws of any State to the Contrary notwithstanding."[67] In the absence of a clear expression of preemption within federal law, the "purpose of Congress is the ultimate touchstone of pre-emption analysis."[68] The Supreme Court has acknowledged that it must begin with the assumption that "the historic police powers of the States [a]re not to be superseded . . . unless that was the clear and manifest purpose of Congress."[69] However, as acknowledged by the *PLIVA* court, "[w]here state and federal law 'directly conflict,' state law must give way."[70] As acknowledged by Justice Scalia in his dissent in *Cipollone v. Liggett Group, Inc.*, the Court has indeed historically found that,

> [w]here state law is in actual conflict with federal law, see, e.g. *Pacific Gas & Elec. Co. v. State Energy Resources Conservation and Development Comm'n.,* 461 U.S. 190, 204 (1983), or where it "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941), or even where the nature of Congress's regulation, or its scope, convinces us that "Congress left no room for the States to supplement it," *Rice* [*v. Santa Fe Elevator Corp,* 331 U.S. 218, 230, (1947)], we have had no difficulty declaring that state law must yield.[71]

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66. Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, 49,605 (Aug. 22, 2008) (to be codified at 21 C.F.R. pt. 314, 601, 814).

67. U.S. Const., Art. VI, cl. 2.

68. Cipollone v. Liggett Grp., Inc., 505 U.S. 504, 542 (1992) (internal quotation marks omitted).

69. Riegel v. Medtronic, Inc., 552 U.S. 312, 334 (2008) (Ginsburg, J., dissenting) (quoting Rice v. Santa Fe Elevator Corp., 331 U.S. 218, 230 (1947)).

70. PLIVA, Inc. v. Mensing, 564 U.S 604, 617 (2011) (quoting Wyeth v. Levine*,* 555 U.S. 555, 583 (2009) (Thomas, J., concurring)); *see also* Crosby v. Nat'l Foreign Trade Council, 530 U.S. 363, 372 (2000) ("[S]tate law is naturally preempted to the extent of any conflict with a federal statute.").

71. *Cipollone*, 505 U.S. at 545 (Scalia, J., dissenting).

Express preemption exists when Congress manifests its intention that a particular regulation is to supersede state statutes, regulations, or claims. For example, the Federal Cigarette Labeling and Advertising Act of 1965 contains a provision entitled "Preemption" which prohibited states from enacting any requirement with respect to the labels on cigarettes.[72] Further, the Medical Device Amendments of 1976 (MDA) bars states from imposing "any requirement" with respect to the safety or effectiveness of a medical device which is "different from" or "in addition to" the requirements under federal law.[73] The Court ruled that state tort claims, and not just state regulations, were expressly barred by the text of this preemption provision in the MDA, finding "it is implausible that the MDA was meant to 'grant greater power (to set state standards "different from, or in addition to," federal standards) to a single state jury than to state officials acting through state administrative or legislative lawmaking processes.'"[74]

The application of implied, rather than express, preemption occurs when there is either conflict between the state and federal law such that it is impossible to satisfy the requirements of each,[75] or when the "purposes and objectives of Congress" are frustrated by the requirements of state law.[76] Implied preemption can also be imposed when it can be demonstrated that Congress "so thoroughly occupies a legislative field 'as to make reasonable the inference that Congress left no room for the States to supplement it.'"[77] An examination of the Court's jurisprudence in the area of implied preemption reveals a subcategory of the doctrine in matters involving heavy federal agency regulation. Trending in this area is a concept called "agency preemption," a form of implied preemption in which federal agencies "play the dominant role in statutory interpretation,"[78] in which the "Court's final decisions line up with

72. Federal Cigarette Labeling and Advertising Act, Pub. L. 89–92, 79 Stat. 282 (1965) (codified as amended at 15 U.S.C. §§ 1331–40 (2012)).

73. Medical Device Amendments of 1976, Pub. L. 94-295, § 521, 90 Stat. 539, 574 (1976) (codified as amended at 21 U.S.C. § 360k (2012)).

74. *Riegel,* 552 U.S. at 325 (quoting Medtronic, Inc. v. Lohr, 518 U.S. 470, 504 (1996) (Breyer, J., concurring in part and concurring in judgment)).

75. *See PLIVA*, 564 U.S. at 618.

76. *See* Wyeth v. Levine, 555. U.S. 555, 577 (2009).

77. *Cipollone*, 505 U.S. at 516; Fidelity Fed. Sav. & Loan Ass'n. v. De la Cuesta, 458 U.S. 141, 153 (1982) (quoting Rice v. Santa Fe Elevator Corp., 331 U.S. 218, 230 (1947).

78. Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 523 (2012) ("While Congress, with the stroke of a pen, could definitively resolve preemption questions by specifying the impact of its legislation on state law, in reality it often does not, but rather leaves

positions urged by the agenc[ies]."[79] In these matters, the Court is compelled to give weight to the agency's own interpretation of applicable laws and regulations as the agency "is likely to have a thorough understanding of its own regulation and its objectives and is 'uniquely qualified' to comprehend the likely impact of state requirements."[80] In fact, the Court has found that when Congress has delegated implementation of a statute involving technical subject matter to the agency and "the relevant history and background are complex and extensive," "the agency's own views should make a difference."[81]

Finally, as the dissent in *Wyeth* acknowledged, the Court's conflict preemption jurisprudence prohibits any State from "countermanding" the agency's statutorily-valid determinations.[82]

A. Agency Preemption Outside of Drug Warning Cases

In 2000, in the case of *Geier v. American Honda Motor Co.*, the Court found that a state common law tort action was preempted by a 1984 version of the Federal Motor Vehicle Safety Standard, which required auto manufacturers to equip some, but not all, of their vehicles with passive restraints.[83] One of the plaintiffs in *Geier* was seriously injured in an automobile accident in a vehicle that was not equipped with airbags or other passive devices.[84] Among their claims, the injured plaintiff and her

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open a wide interpretive space for courts to fill. And while courts reiterate that congressional intent is the touchstone of preemption analysis, they increasingly rely on the views propounded by federal agencies either in regulations or else in preambles or litigation briefs.") (footnote omitted).

79. Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449, 477 (2008).

80. Geier v. Am. Honda Motor Co., 529 U.S. 861, 883 (2000) (quoting Medtronic, Inc. v. Lohr, 518 U.S. 470, 496 (1996)).

81. Williamson v. Mazda Motor of Am., 562 U.S. 323, 335–36 (2011) (quoting *Geier,* 529 U.S. at 883).

82. Wyeth v. Levine*,* 555 U.S. 555, 609 (2009) (Alito, J., dissenting) (citing Buckman Co. v. Plaintiffs' Legal Comm., 531 U.S. 341, 348 (2001) (after the FDA has struck "a somewhat delicate balance of statutory objectives" and determined that petitioner submitted a valid application to manufacture a medical device, a State may not use common law to negate it)); Int'l Paper Co. v. Ouellette, 479 U.S. 481, 494 (1987) (after the EPA has struck "the balance of public and private interests so carefully addressed by" the federal permitting regime for water pollution, a State may not use nuisance law to "upse[t]" it); Chicago & N. W. Transp. Co. v. Kalo Brick & Tile Co.*,* 450 U.S. 311, 321 (1981) (after the Interstate Commerce Commission has struck a "balance" between competing interests in permitting the abandonment of a railroad line, a State may not use statutory or common law to negate it).

83. 529 U.S. 861.

84. *Id.* at 865.

parents alleged that the vehicle was negligently designed because it did not have a driver's side airbag.[85]

In order to resolve the case, the Court was faced with interpreting a federal statute which seemed to both provide for express preemption and allowed for the imposition of liability, even if the federal standards were satisfied.[86] In determining that the preemption provision, when read with the savings clause, actually "leav[es] adequate room for state tort law to operate" where federal law creates only a floor or minimum standard, the Court found a way to give life to both parts of the federal act.[87] However, in reasoning that can and should be applied in drug labeling cases, the Court went one step further and held that the savings clause could not permit state tort law claims that actually conflict with federal law.[88] In doing so, the Court looked to congressional intent behind the Act, acknowledging that it has "repeatedly 'decline[d] to give broad effect to saving clauses where doing so would upset the careful regulatory scheme established by federal law.'"[89]

Central to the Court's analysis was its admitted reliance on the amicus brief filed by the Department of Transportation that interpreted the at-issue regulation and took a position that "a tort suit such as this one would 'stan[d] as an obstacle to the accomplishment and execution' of those objections."[90] The Court acknowledged that, "Congress has delegated to DOT authority to implement the statute; the subject matter is technical; and the relevant history and background are complex and extensive. The agency is likely to have a thorough understanding of its own regulation and its objectives and is 'uniquely qualified' to comprehend the likely impact of state requirements."[91] The Court ultimately took the position that "[i]n these circumstances, the agency's own views should make a difference."[92]

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85. *Id*.

86. *Id.* at 869.

87. *Id.* at 868.

88. *Id.*

89. *Id.* at 870 (citing United States v. Locke, 529 U.S. 89, 106–07 (2000) (citations omitted)).

90. *Id.* at 883 (quoting Brief for United States as Amicus Curiae at 25–26, Geier v. Am. Honda Motor Co., 529 U.S. 861 (1999) (No. 98-1811), 1999 WL 1045115 at *26 (quoting Hines v. Davidowitz, 312 U.S. 52, 67 (1941))).

91. *Id*. (quoting Medtronic, Inc. v. Lohr, 518 U.S. 470, 496, 506 (1995)) (Breyer, J., concurring in part and concurring in judgment).

92. *Id.* (citing City of New York v. FCC, 486 U.S. 57, 64 (1988); Hillsborough Cty. v. Automated Med. Labs., Inc., 471 U.S. 707, 714 (1985); Fidelity Fed. Sav. & Loan Ass'n v. De la Cuesta, 458 U.S. 141, 158 (1982); Blum v. Bacon, 457 U.S. 132, 141 (1982); Chicago & N. W. Transp. Co. v. Kalo Brick & Tile Co., 450 U.S. 311, 321 (1981).

Finally, and perhaps most importantly, the dissent in *Geier* written by Justice Stevens, and with which Justice Souter, Justice Thomas, and Justice Ginsburg joined, acknowledged the importance of the agency's articulated position and intention to occupy the field and thus preempt state law when considering matters of implied preemption, including both instances of conflict preemption and field preemption.[93] "Thus, even in cases where implied regulatory pre-emption is at issue, we generally 'expect an administrative regulation to declare any intention to pre-empt state law with some specificity.'"[94]

Similar to *Geier,* in *Buckman Co. v. Plaintiffs' Legal Committee*,[95] the Court relied heavily on the agency's "detailed regulatory regime" when it held that a state law claim for fraud on the FDA was impliedly preempted.[96] In that case, the plaintiffs argued that defendants made fraudulent representation to the FDA in order to obtain approval for their medical device, orthopedic bone screws.[97] The plaintiffs further claimed that their injuries were caused by those representations because "but for" those representations, the FDA would not have approved the device.[98]

In finding that plaintiffs' claims conflicted with and were therefore impliedly preempted by federal law,[99] the Court held that the basis for the conflict was the fact that the federal statutory scheme, which "amply empowers" the FDA to handle fraud claims and allows the FDA to "achieve a somewhat delicate balance of statutory objectives," would be "skewed" by allowing state law tort claims.[100]

In a policy analysis that could just as easily be applied to state failure to warn claims in the context of drug labeling approval by the FDA, the Court spent a great deal of time discussing the challenges faced by medical

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93. *Geier,* 529 U.S. at 908–09 (Stevens, J., dissenting).

94. *Id.* (quoting California Coastal Comm'n v. Granite Rock Co., 480 U.S. 572, 583, (1987); *see Hillsborough Cty.*, 471 U.S. at 717–18 (noting that too easily implying pre-emption "would be inconsistent with the federal-state balance embodied in our Supremacy Clause jurisprudence," and stating that "because agencies normally address problems in a detailed manner and can speak through a variety of means, including regulations, preambles, interpretive statements, and responses to comments, we can expect that they will make their intentions clear if they intend for their regulations to be exclusive"); *Fidelity,* 458 U.S. at 154 (noting that pre-emption inquiry is initiated "[w]hen the administrator promulgates regulations intended to pre-empt state law").

95. 531 U.S. 341 (2001).

96. *Id*. at 350.

97. *Id.* at 343.

98. *Id.*

99. The Court neither considered nor applied the express preemption provision in the Medical Devices Act under 21 U.S.C. § 360k (2012).

100. *Buckman*, 531 U.S. at 348.

device applicants if suits for fraud on the FDA were not preempted:

> As a practical matter, complying with the FDA's detailed regulatory regime in the shadow of 50 States' tort regimes will dramatically increase the burdens facing potential applicants—burdens not contemplated by Congress in enacting the FDCA and the MDA. Would-be applicants may be discouraged from seeking § 510(k) approval of devices with potentially beneficial off-label uses for fear that such use might expose the manufacturer or its associates (such as petitioner) to unpredictable civil liability. In effect, then, fraud-on-the-FDA claims could cause the Administration's reporting requirements to deter off-label use despite the fact that the FDCA expressly disclaims any intent to directly regulate the practice of medicine, see 21 U.S.C. § 396 (1994 ed., Supp. V) and even though off-label use is generally accepted.
>
> Conversely, fraud-on-the-FDA claims would also cause applicants to fear that their disclosures to the FDA, although deemed appropriate by the Administration, will later be judged insufficient in state court. Applicants would then have an incentive to submit a deluge of information that the Administration neither wants nor needs, resulting in additional burdens on the FDA's evaluation of an application. As a result, the comparatively speedy § 510(k) process could encounter delays, which would, in turn, impede competition among predicate devices and delay health care professionals' ability to prescribe appropriate off-label uses.[101]

B. Preemption in Drug Labeling Cases

Despite the trend of moving toward deference to the agency in matters of heavy federal regulation, in the field of prescription drug labeling, the story is much different. Over the last several years, the Supreme Court's application of federal preemption in the heavily regulated field of prescription drugs has been confusing. In matters involving prescription drugs, the Court has held that a pioneer drug manufacturer can be sued in state court under a theory of failure to warn because it would not be impossible for a manufacturer to comply with the requirements imposed by both federal and state regulations.[102] Further, the Court believes that

101. *Id.* at 350–52 (footnotes omitted).

102. Wyeth v. Levine, 555 U.S. 555, 555 (2009).

allowing state law tort claims to proceed in this heavily regulated field does not create an obstacle to the purposes and objectives of Congress.[103] On the other hand, if that manufacturer is a generic drug manufacturer, the Court has, in light of the applicable regulations governing generic drugs, held that state law tort claims for failure to warn are preempted by FDA regulations because it is impossible for the manufacturer to comply with both state law and federal regulations.[104]

Though the Court attributes this disconnect to the fact that the parties are governed by different regulations, the reality is that the regulations that govern prescription drug labeling are, as a whole for BOTH pioneer and generic manufacturers, among the most complex and pervasive in administrative law. Consequently, the Court's unwillingness to find that state law tort claims are impliedly preempted in the area of drug labeling when they have not struggled in areas of similar, and even less stringent regulatory schemes, is baffling.

Simply put, a review of other cases in which preemption is the issue in light of the fact of heavy federal regulation reveals that the Court's discussions often examine and rely almost exclusively upon the agency's own desire to occupy the field and preempt state law.[105] However, when dealing with prescription drug labeling, the Court has specifically held that the FDA's expressed desire and intent to preempt state law does not merit deference.[106] Moreover, as demonstrated above, the Court has refused to acknowledge that the regulatory framework and scheme of prescription drugs as defined by Congress implies preemption.

1. *Wyeth v. Levine*

In 2009, the United States Supreme Court issued its opinion in *Wyeth v. Levine*, a case filed against a brand-name drug manufacturer for an alleged failure to warn against the dangers of injecting its drug through a particular method.[107] In *Wyeth*, the question before the Court was whether the FDA's drug labeling judgments "preempt state law product liability claims premised on the theory that different labeling judgments were necessary to make drugs reasonably safe for use."[108] In an opinion

103. *Id*. at 581.

104. PLIVA, Inc. v. Mensing, 564 U.S. 604, 625 (2011).

105. *See* Geier v. Am. Honda Motor Co., 529 U.S. 861, 909 (2000) (Stevens, J., dissenting); *Buckman*, 531 U.S. at 348.

106. *Wyeth,* 555 U.S. at 556.

107. *Id*. at 555.

108. *Id.* at 563.

authored by Justice Stevens, the Court ultimately held that FDA judgments on the safety of a particular drug do not preempt state law product liability claims.[109]

The facts in *Wyeth* are worth noting as this was not a claim for a lack of warning for use, but one that questioned the adequacy of the existing warning as it related to the proper administration of the drug.[110] In *Wyeth*, the plaintiff had been intravenously injected through an IV-push method with the drug Phenergan, an antihistamine used to treat nausea and manufactured by Wyeth.[111] The Phenergan warning label stated, in part,

> extreme care should be exercised to avoid perivascular extravasation or inadvertent intra-arterial injection. Reports compatible with inadvertent intra-arterial injection of Phenergan Injection . . . suggest that pain, severe chemical irritation, severe spasm of distal vessels, and resultant gangrene requiring amputation are likely under such circumstances.[112]

Trial court proceedings revealed that, despite the warning label, the physician assistant administered a greater dose than the label prescribed, she may have inadvertently injected the drug into an artery rather than a vein, and that she continued to inject the drug after the plaintiff complained of pain.[113] Regardless of these facts, the jury rendered a verdict that Phenergan's label was both a "but-for" and proximate cause of Levine's injury, thereby rejecting Wyeth's argument that the clinician's conduct was an intervening cause that absolved Wyeth of liability.[114] The plaintiff, who had her arm amputated as a result of the administration of the drug through an IV-push method, took the position that Wyeth should have specifically warned against the use of an IV-push method of injection of the medication as studies had shown that the drug was "corrosive and causes irreversible gangrene if it enters a patient's artery."[115]

The Court acknowledged the correspondence between Wyeth and the FDA on the labeling of Phenergan:

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109. *Id*. at 581.

110. *Id.* at 559–60.

111. According to the Court, "[t]he injectable form of Phenergan can be administered intramuscularly or intravenously, and it can be administered intravenously through either the 'IV-push' method, whereby the drug is injected directly into a patient's vein, or the 'IV-drip' method, whereby the drug is introduced into a saline solution in a hanging intravenous bag and slowly descends through a catheter inserted in a patient's vein." *Id.* at 559.

112. *Id*. at 560, n.1.

113. *Id*. at 559.

114. *Id.* at 562.

115. *Id.* at 559.

> The FDA first approved injectable Phenergan in 1955. In 1973 and 1976, Wyeth submitted supplemental new drug applications, which the agency approved after proposing labeling changes. Wyeth submitted a third supplemental application in 1981 in response to a new FDA rule governing drug labels. Over the next 17 years, Wyeth and the FDA intermittently corresponded about Phenergan's label. The most notable activity occurred in 1987, when the FDA suggested different warnings about the risk of arterial exposure, and in 1988, when Wyeth submitted revised labeling incorporating the proposed changes. The FDA did not respond. Instead, in 1996, it requested from Wyeth the labeling then in use and, without addressing Wyeth's 1988 submission, instructed it to "[r]etain verbiage in current label" regarding intra-arterial injection. After a few further changes to the labeling not related to intra-arterial injection, the FDA approved Wyeth's 1981 application in 1998, instructing that Phenergan's final printed label "must be identical" to the approved package insert.[116]

In other words, as noted by the Court, the FDA retained complete control over the labeling content of Phenergan, even proposing language in 1987 that was incorporated by the drug manufacturer in 1988, and then ultimately rejected by the agency in 1996.[117] It is upon this factual scenario that *Wyeth* believed it was entitled to preemption.

It is critical to note that an error of law made by both the *Wyeth* trial court and the Supreme Court may be, in part, to blame for the ultimate rejection of preemption. The error was made by each court in their respective characterization of the significance of FDA approval of a drug label. As noted by the Justice Stevens, the trial court "instructed the jury that it could consider evidence of Wyeth's compliance with FDA requirements but that such compliance did not establish that the warnings were **adequate**."[118] Justice Stevens, in the first paragraph of the majority opinion, states that "[t]he warnings on Phenergan's label had been deemed **sufficient** by the federal Food and Drug Administration (FDA) when it approved Wyeth's new drug application in 1955 and when it later approved changes in the drug's labeling."[119] However, as provided in the

116. *Id.* at 561–62.
117. *Id*.
118. *Id.* at 562 (emphasis added).
119. *Id*. at 558 (emphasis added).

Act as well as the applicable regulations promulgated by the FDA itself, the FDA approves labeling for "**safety and effectiveness**," not "sufficiency" or "adequacy."[120] "Sufficiency" and "adequacy" are synonymous and suggest acceptability.[121] "Safety and effectiveness" implies essentialness or success.[122] The litmus tests the trial court and Supreme Court use are problematic as they relegate the judgment of the FDA to that of a floor, as opposed to a ceiling. It is within this error that both the trial court, and affirmed by the Supreme Court, found room to allow juries to question that judgment.

On the applicability of preemption, the defendants made two arguments, both of which were rejected by the Court, but were clearly successful in prior cases like *Geier* and *Buckman* as described above. First, Wyeth argued that, because the FDA ultimately approved the labeling for the drug and federal regulations prohibited the manufacturer from unilaterally changing that labeling once it was approved, any claim for failure to warn was therefore preempted.[123] Wyeth's second point was that "recognition of Levine's state tort action creates an unacceptable 'obstacle to the accomplishment and execution of the full purposes and objectives of Congress.'"[124] As correctly noted by Wyeth, "the presumption against pre-emption should not apply . . . because the Federal Government has regulated drug labeling for more than a century."[125]

The Court ultimately disagreed with both of Wyeth's arguments, and thereby started on a path to ignore an administrative agency's delegated powers, the effect of its approval of a drug label, and the agency's intent to regulate in a given field. On the first point, the plaintiff argued that the regulations did provide for the ability for a manufacturer to change a drug warning label before the label change was approved by the FDA, the "'Changes Being Effected' (CBE)" process.[126] Although noting that "of course" the FDA had the authority to ultimately reject any changes made to a label through the CBE process, the Court held that, "absent clear evidence that the FDA would not have approved a change to Phenergan's label, we will not conclude that it was impossible for Wyeth to comply with

120. *See* 21 U.S.C. §§ 355(c), (d) (2012).
121. *Adequate*, MERRIAM WEBSTER DICTIONARY 15, 1248 (11th ed. 2011).
122. *Id.* at 397, 1095.
123. *Wyeth*, 555 U.S. at 563–64.
124. *Id*.
125. *Id*. at 565, n.3.
126. *Id.* at 568–71.

both federal and state requirements."[127]

The reality now is that the Court's holding on this first point puts drug manufacturers in a difficult and unnecessary position. To be clear, as the Court noted, the governing federal regulations do provide a small window, in certain limited instances, in which the manufacturer could implement a labeling change while it waited for approval or rejection from the FDA on the propriety of the labeling change.[128] It is within this window that the Court found the manufacturer could feasibly comply with both the applicable federal regulations, as well as the state requirements of a stronger label.[129] However, the Court goes one step further and also indicates that the only way to avoid this window of opportunity it was giving to plaintiffs was for the manufacturer to provide "clear evidence" that the FDA would ultimately reject the labeling change.[130] As a result, manufacturers in a post-*Wyeth* world must now, as a matter of course, make non-meritorious or unnecessary labeling changes in an effort to receive a rejection decision by the FDA so that the manufacturer has "clear evidence" to insulate itself from a future products liability suit for failure to warn.

Wyeth's second point was that requiring it to comply with state-law judgments that compel a stronger warning than approved by the FDA would obstruct the purposes and objectives of federal drug labeling regulation. In rejecting this argument, the Court chose to ignore both the stated position of the FDA and the amicus brief filed on behalf of the United States that such state law judgments are impliedly preempted under the FDCA, and instead relied on the fact that there is no express preemption provision contained within the Act.[131] In addressing the preamble to the FDA's 2006 regulation in which the agency specifically states that "FDA approval of labeling . . . preempts conflicting or contrary state law" and that state-law failure to warn claims "threaten FDA's statutorily prescribed

127. *Id*. at 571.

128. *Id*. ("Indeed, prior to 2007, the FDA lacked the authority to order manufacturers to revise their labels. *See* 121 Stat. 924–926. When Congress granted the FDA this authority, it reaffirmed the manufacturer's obligations and referred specifically to the CBE regulation, which both reflects the manufacturer's ultimate responsibility for its label and provides a mechanism for adding safety information to the label prior to FDA approval. *See id*., at 925–26 (stating that a manufacturer retains the responsibility 'to maintain its label in accordance with existing requirements, including subpart B of part 201 and *sections 314.70* and 601.12 of title 21, Code of Federal Regulations (or any successor regulations)' (emphasis added)"). *Id.*

129. *Id*.

130. *Id*.

131. *Id*. at 574–75.

role as the expert Federal agency responsible for evaluating and regulating drugs," the Court found it did not merit deference.[132] Rather, the Court relied on what it considers the FDA's "longstanding position" that state law tort claims can coexist with the agency's regulations.[133] However, as will be shown, the Court's reliance on this alleged position by FDA was and is misplaced.[134]

In truth, a review of the citations to the regulations upon which the Court relies, reveal that the FDA has **never** relied upon or encouraged the existence of state law tort claims as part of its regulatory scheme. For example, the *Wyeth* Court quotes language from 59 Fed. Reg. 3948 (1994) entitled "Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules," that provides that "[p]roduct liability plays an important role in consumer protection."[135] However, a closer examination of this quote reveals that the Court took it completely out of context. In fact, the acknowledgement by the FDA of products liability claims was actually made in reference to medical malpractice tort claims filed by a plaintiff who suffered an adverse event as a result of a prescribed drug **against a medical professional** who reported the adverse event to the FDA, and was not an expression of acceptance of state law failure to warn claims against the drug manufacturer.[136]

Further, the Court quotes the FDA as saying that, "in establishing 'minimal standards' for drug labels, it did not intend 'to preclude the states from imposing additional labeling requirements.'"[137] However, a review of the regulation reveals that it applies only to patient labeling for prescription drugs used primarily on an outpatient basis,[138] as opposed to professional labeling for all prescription drugs. In fact, the position of the FDA is actually quite the opposite as it clearly expressed its opinion that claims of failure to warn based on the existing FDA-approved warning are impliedly preempted because "[s]tates may authorize additional labeling,

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132. *Id*. at 575–76.

133. *Id*. at 577.

134. *See infra* Part VI.

135. *Wyeth*, 555 U.S. at 578, n.10.

136. 59 Fed. Reg. 3771, 3948 (Jan. 27, 1994).

137. *Wyeth,* 555 U.S. at 578 (quoting 63 Fed. Reg. 66,378, 66,384 (proposed Dec. 1, 1998)).

138. 63 Fed. Reg. at 66,379 (proposed Dec. 1, 1998). The FDA indicated that this particular regulation "establishes a patient medication information program under which Medication Guides will be required for a small number of products that the FDA determines pose[s] a serious and significant health concern requiring distribution of FDA-approved patient information necessary for the product's safe and effective use. FDA anticipates than an average, no more than 5 to 10 products per year would require such information."

but they cannot reduce, alter, or eliminate FDA-required labeling."[139]

In the dissent in *Wyeth*, Justices Alito, Roberts, and Scalia, were concerned with respect to the certified question itself. They asked whether the first question should be who has the authority and responsibility to determine the adequacy of the warning label for Phenergan, the FDA or a state court jury.[140] The dissenters properly stated that,

> [b]y their very nature, juries are ill-equipped to perform the FDA's cost-benefit-balancing function. As we explained in *Reigel,* juries tend to focus on the risk of a particular product's design or warning label that arguably contributed to a particular plaintiff's injury, not on the overall benefits of that design or label; "the patients who reaped those benefits are not represented in court."[141]

In short, the dissent, borrowing from the Brief for the United States as *Amicus Curiae,* characterizes the *Wyeth* case as the use of a "common-law tort suit into a 'frontal assault' on the FDA's regulatory regime for drug labeling" and notes that such use "upsets the well-settled meaning of the Supremacy Clause and our conflict pre-emption jurisprudence."[142] The dissent was not impressed with the fact that there is not an express preemption provision contained within the FDCA, but rather applied the "ordinary principles of conflict pre-emption" which "turn solely on whether a State has upset the regulatory balance struck by the federal agency."[143] Applying this test, the dissenters conclude that "the FDA's 40-year-long effort to regulate the safety and efficacy of Phenergan pre-empts respondent's tort suit."[144]

In addition to the dissent's criticism of the majority's failure to acknowledge the necessity of preemption, the other telling statement of the Court's struggle with the application of conflict preemption to drug labeling claims comes in the majority opinion and is echoed by Justice Breyer in his short concurrence. The point was made in response to Wyeth's argument that the Court should be compelled to find preemption in light of both the FDA's expressed desire to preempt state law claims in

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139. *Id.* at 66,384.

140. *Wyeth*, 555 U.S. at 605 (Alito, J., dissenting).

141. *Id*. at 626 (quoting Riegel v. Medtronic, Inc., 552 U.S. 312, 325 (2008)).

142. *Id*. at 606.

143. *Id*. at 609 (citing Geier v. Am. Honda Motor Co., 529 U.S. 861, 884–85 (2000) (citations omitted)).

144. *Id*. at 610.

the 2006 preamble, as well the Court's analysis in *Geier* (as discussed above), which had a similar regulatory scheme as that of drug labeling under the FDCA.[145] In considering whether the regulatory scheme in *Geier* was truly comparable to that of the drug labeling regulations under the FDCA, the Court rejected Wyeth's argument, stating that the Court's analysis and conclusion in *Geier* was premised, in part, on the "factors the agency had weighed and the balance it had struck," as well as "the agency's explanation of how state law interfered with its regulation."[146] The majority then acknowledged the FDA's similar efforts to justify their position on preemption, yet concluded, "we have no occasion in this case to consider the pre-emptive effect of a specific agency regulation bearing the force of law."[147]

2. *PLIVA v. Mensing*

The Supreme Court's next contribution to the discussion of the propriety of applying the doctrine of federal preemption in state law tort claims involving drug labeling came in 2011 in *PLIVA, Inc. et al. v. Mensing*.[148] In this case, as stated above, the Supreme Court, in a 5–4 decision, held that generic manufacturers of prescription drugs are entitled to federal preemption in state law tort failure to warn claims.[149] More specifically, despite reviewing a similar regulatory scheme for drug labeling for pioneer drug manufacturers in the *Wyeth* case, the *PLIVA* Court found that "federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, these state-law claims."[150]

The facts in *PLIVA* are compelling to note. Each of the plaintiffs in *PLIVA* had been prescribed metoclopramide tablets, a drug that had been approved by the FDA under the brand name of Reglan in 1980.[151] Generic manufacturers were given the ability to produce the drug five years later.[152] In 1985, 2004, and 2009, in response to evidence that had demonstrated that long-term use of metoclopramide caused the severe neurological disorder, tardive dyskinesia, the manufacturer sought and the

145. *Id.* at 580 (majority opinion).
146. *Id*.
147. *Id*.
148. 564 U.S. 604 (2011).
149. *Id.* at 625.
150. *Id*. at 609.
151. *Id*. at 609–10.
152. *Id*. at 609.

FDA approved new warning labels for the drug that strengthened and clarified the warning for this disorder three times.[153]

The plaintiffs in *PLIVA,* Gladys Mensing and Julie Demahy, were prescribed Reglan in 2001 and 2002, respectively, and both received generic metoclopramide from their pharmacists.[154] Both plaintiffs developed tardive dyskinesia after taking the drug for several years as prescribed by their doctors.[155] In separate suits filed in federal courts in Minnesota for the Fifth Circuit and Louisiana for the Eighth Circuit, the plaintiffs claimed that the generic manufacturers were liable under state tort law for failure to adequately warn of the disorder.[156] Each 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 [generic] [m]anufacturers had changed their labels to adequately warn of that danger."[157] In response, the generic manufacturers argued that because "federal statutes and FDA regulations required them to use the same safety and efficacy labeling as their brand-name counterparts," it was impossible for them, as generic manufacturers, to "comply with both federal law and any state tort-law duty that required them to use a different label."[158] Courts in both the Fifth and the Eight Circuits ultimately held that the manufacturers were not entitled to preemption; holdings that have now been overturned by the Supreme Court.[159]

In finding that the Plaintiffs' claims were preempted in *PLIVA*, the Court explicitly acknowledged the problem with reconciling this holding with the one they had rendered in *Wyeth*, which denied the application of preemption in failure to warn claims made against name-brand drug manufacturers.[160] However, in this matter, the majority's analysis focused squarely on the words set forth by Congress in the regulations regarding

153. "[I]n 2009, the FDA ordered a black box warning . . . which states: 'Treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible. . . . Treatment with metoclopramide for longer than 12 weeks should be avoided in all but rare cases.' See Physician's Desk Reference 2902 (65th ed. 2011) [at 2–3]." *PLIVA*, 564 U.S. at 610.

154. *PLIVA*, 564 U.S. at 610.

155. *Id*.

156. *Id.*

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

158. *PLIVA*, 564 U.S. at 610.

159. *Id*. at 610–11.

160. *Id*. at 625.

drug labeling which govern the obligations of generic drug manufacturers.[161] Specifically, the Court relied on the undisputed fact that Congress, in passing the Drug Price Competition and Patent Term Restoration Act, Hatch–Waxman Amendments, had provided that generic drugs would receive FDA approval if they could demonstrate that (1) they are the equivalent to the name-brand or listed drug that has already been approved by the FDA;[162] and (2) that the "[safety and efficacy] labeling proposed . . . is the same as the labeling approved for the [brand-name] drug."[163] In other words, the labeling of a generic drug must match the labeling for the listed drug, in this case Reglan. Though the plaintiffs argued that there were other avenues the manufacturers could have pursued or steps that the manufacturers could have taken in order to satisfy their state-law duty to warn,[164] the Court rejected all of these arguments in light of the "same as" mandate of the federal statute.[165]

The Court took a different position on the "take steps to make labeling changes before FDA approves the new label" argument it had so strongly relied upon in *Wyeth*.[166] In *PLIVA*, the plaintiffs argued that both name-brand and generic manufacturers have a duty to ask for FDA assistance in obtaining a label change once the manufacturer becomes aware of safety problems, and that a failure to satisfy that duty could form the basis for liability in a state law failure to warn claim.[167] However, the Court found that it did not need to resolve the question as to whether such a duty existed because, even if the generic manufacturers had a duty to "take steps" to ask the FDA for help in strengthening the label, it would not have satisfied their state law tort duty to provide adequate labeling.[168] The claim in *PLIVA* was that the defendants should have known that their labels did not adequately warn of the risk of tardive dyskinesia.[169] Assuming that

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161. *Id*. at 612

162. *Id*. at 613 (citing 21 U.S.C. § 355(j)(2)(A) (2012)).

163. *Id*. at 612–13 (citing 21 U.S.C. § 355(j)(2)(A)(v)); *see also* 21 U.S.C. § 355(j)(4)(G); DONALD O. BEERS, GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS §§ 3.01, 3.03(A) (7th ed. 2008).

164. *PLIVA*, 564 U.S. at 614–16. (Plaintiffs argued that the CBE-0 (Changes Being Effected) process and "Dear Doctor" letters were available to the manufacturer. FDA took the position that these were not available to a generic manufacturer as they would cause a generic label to deviate from the "sameness" requirement with respect to the labeling for the listed drug.)

165. *Id*. at 613.

166. *Id*. at 617.

167. *Id*. at 616.

168. *Id*. at 617.

169. *Id*. at 610.

allegation was true, the parties did not dispute that state law would then require the defendants to use a different label.[170] However, a claim that the generic manufacturer should have taken steps to inform FDA that a labeling change was necessary and failed to do so did not equate to a failure to comply with state law.[171]

3. *Bartlett v. Mutual Pharmaceutical Co.*

Most recently, in 2013, in *Mutual Pharmaceutical Co. v. Bartlett*, the Court was again faced with the question as to whether and what extent generic drug manufacturers are entitled to preemption when faced with a labeling and design defect claim.[172] In that case, the plaintiff developed toxic epidermal necrolysis as a result of taking a nonsteroidal, anti-inflammatory drug, and suffered physical disabilities, disfigurement, and near blindness.[173] The plaintiff, in light of the holding in *PLIVA* that failure to warn claims against generic drug manufacturers are preempted, tried a different theory of liability, namely that the manufacturer should "stop-selling" the drug if it believed it to be unsafe.[174] Although the First Circuit held that federal law did not preempt a design defect claim against a generic manufacturer because the generic manufacturer had the option of removing its product from the market and could therefore comply with both federal law labeling and design requirements, as well as state law duties, the Supreme Court disagreed.[175] In a 5–4 decision in which Justices Alito, Roberts, Scalia, Kennedy, and Thomas formed the majority, the Court noted that "adopting the Court of Appeals' stop-selling rationale would render impossibility pre-emption a dead letter and work a revolution in this Court's pre-emption case law."[176]

Interestingly, on the regulatory effect of FDA approval of a drug label, the dissent written by Justice Sotomayor and joined by Justice Ginsburg, takes the position that, "if federal law requires a particular product label to include a complete list of ingredients while state law specifically forbids that labeling practice, there is little question that state law 'must yield.'"[177]

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170. *Id*. at 611.
171. *Id*. at 620–21.
172. 133 S. Ct. 2466 (2013).
173. *Id*. at 2468.
174. *Id*. at 2470.
175. *Id*.
176. *Id*. at 2469–70.
177. *Id*. at 2485 (Sotomayor, J., dissenting) (quoting Felder v. Casey, 487 U.S. 131, 138 (1988)).

In response the majority states, "[w]hat the dissent does not see is that *that is this case* : Federal law requires a very specific label for sulindac, and state law forbids the use of that label."[178] Although this was stated in the context of a generic drug labeling case, it bears noting that this reasoning should apply with equal force in all matters involving drug labeling, both name-brand and generic.

Finally, the Court admits that guidance is needed from Congress on the issue of preemption and prescription drugs:

> Suffice to say, the Court would welcome Congress' "explicit" resolution of the difficult pre-emption questions that arise in the prescription drug context. That issue has repeatedly vexed the Court—and produced widely divergent views—in recent years. See, *e.g., Wyeth v. Levine*, 555 U.S. 555, 129 S. Ct. 1187, 173 L. Ed.2d 51 (2009); *PLIVA*, 564 U.S. —-, 131 S. Ct. 2567. As the dissent concedes, however, the FDCA's treatment of prescription drugs includes neither an express pre-emption clause (as in the vaccine context, 42 U.S.C. § 300aa-22(b)(1)), nor an express non-pre-emption clause (as in the over-the-counter drug context, 21 U.S.C. §§ 379r(e), 379s(d)). In the absence of that sort of "explicit" expression of congressional intent, we are left to divine Congress' will from the duties the statute imposes. That federal law forbids Mutual to take actions required of it by state tort law evinces an intent to pre-empt.[179]

However, the resulting regulation proposed by the FDA in 2013 and discussed below was not the guidance for which the Court was looking.

V. THE 2013 FDA PROPOSED REGULATION

In November of 2013, the FDA issued a proposed rule entitled, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products."[180] The rule was generated as a response to concerns made to the FDA following the *Mensing* decision that created a situation in which state law tort claims for failure to warn are now preempted against generic manufacturers, but not pioneer manufacturers. In this proposed rule, the FDA proposes to "amend its regulations to revise

178. *Id*. at 2479.

179. *Id*. at 2480.

180. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985-02 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pt. 314, 601).

and clarify procedures for application holders of an approved drug or biological product to change the product labeling to reflect certain types of newly acquired information in advance of FDA's review of the change."[181] The proposed rule attempts to "create parity" among pioneer and generic drug manufacturers by allowing generics to make labeling changes of an approved drug to reflect certain types of newly acquired information in advance of the FDA's review of the proposed change through a "changes being effected" (CBE-0) supplement discussed above.[182] In other words, the proposed rule temporarily removes the "sameness" requirement under the Hatch–Waxman Amendments to the FDCA with respect to labeling.

Once publicized in the Federal Register, the proposed rule generated much controversy. In fact, more than 300 comments have been filed with respect to the proposed rule since 2013, and the FDA has held public meetings and reopened the federal docket for more comments, for which the last period closed in April 2016.[183] It should be noted that in May of 2016, the House Appropriations Committee released a new bill that prohibited any of the congressional funding for the FDA to be used to "finalize or implement" the proposed rule.[184] In July of 2016, the FDA delayed its implementation of the proposed rule for the third time since 2013, and deferred the issue to the summer of 2017.[185]

There are several major problems with the proposed rule, each of which will be discussed in turn below. First, the proposed rule directly conflicts with the requirements of federal law under the FDCA and the Hatch–Waxman Amendments, as well as the position the FDA itself has taken for many years. Further, incredibly, the proposed rule will have an adverse impact on safety to consumers of generic drugs. The proposed rule will also have a major detrimental effect on the generic drug industry. Finally, the manner in which the proposed rule was brought to life, as well as the FDA's articulated purpose behind the proposed rule, demonstrate that the FDA is acting out of line in both words and deeds.

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181. *Id*.

182. *Id*.

183. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 81 Fed. Reg. 37.301 § 123 (June 9, 2016).

184. Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, 2017, H.R. 5054, at 91–92, 114th Cong. 2d Sess. (2016).

185. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 81 Fed. Reg. 37.301 § 123 (June 9, 2016).

A. Conflict with Federal Law

First, one of the biggest problems with the proposed rule, in addition to others that are not relevant to this Article, is that that the changes it proposes are contrary to the requirements of the FDCA and the Hatch–Waxman Amendments. In fact, concerns over the legality of the proposed rule have been voiced by members of Congress. For example, in 2014, Republican members of both the House and Senate expressed "grave concerns" that the rule would "conflict directly with the statute, thwart the law's purposes and objectives, and impose significant costs on the drug industry and healthcare consumers."[186]

As mentioned above, the FDCA, through the Hatch–Waxman Amendments, require that generic drugs maintain the same label as their name-brand counterparts at all times.[187] The Supreme Court has agreed with this interpretation, holding as recently as 2013 that, "[a]s *PLIVA* made clear, federal law prevents generic drug manufacturers from changing their labels."[188] In fact, FDA has explained that this "sameness" requirement "reflects the fundamental premise of the [generic drug system] that a generic drug can be relied upon as a therapeutic equivalent of its RLD."[189] This is turn, supports the entire premise and objective of Hatch–Waxman Amendments, which is to "make available more low cost generic drugs."[190] It should come as no surprise, then, that if this proposed rule is enacted, abuse of power challenges will follow.

Congress has vested "authority to promulgate regulations for the efficient enforcement" of the FDCA in the Secretary of Health and Human Services, who in turn delegated that authority to the FDA.[191] The FDA is charged with the regulation and approval of applications to introduce drugs into interstate commerce.[192] However, as is the case with every agency, FDA may not promulgate regulations that conflict with federal

186. Letter from House Energy and Commerce Committee and the Senate Health, Education, Labor and Pensions Committee to Margaret Hamburg, FDA Commissioner (Jan. 22, 2014).

187. 21 U.S.C. § 355(j)(2)(A)(v) (2012).

188. Mut. Pharm. Co. v. Bartlett, 133 S. Ct. 2466, 2476 (citing PLIVA, Inc. v. Mensing, 564 U.S. 604 (2011)).

189. Merits Brief for the United States as Amicus Curiae Supporting Respondents, PLIVA, Inc. v. Mensing 564 U.S. 604 (2011) (Nos. 09-993, 09-1039, 09-1502) (Mar. 2011) at 4.

190. H.R. Rep. No. 98-857, pt. 1, at 14 (1984) *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

191. 21 U.S.C. § 371(a) (2012).

192. 21 U.S.C. § 371.

law.[193] As the proposed rule requires a generic drug company to deviate from the sameness requirement demanded by the FDCA and Hatch–Waxman in certain situations, the rule violates long-standing precedent and is a clear attempt by the FDA to act outside of its permissible authority.

The proposed rule is also contrary to the long-standing position of the FDA that it cannot permit generic manufacturers to deviate from the "sameness" requirements of federal law and utilize the CBE-0 procedures.[194] For example, in 1992, the FDA rejected a proposal that generic drug manufacturers could add other safety warnings to the label of an approved drug.[195] In amicus briefs filed in the Supreme Court in *Mensing*, the FDA stated: "Supplements are subject to substantive standards governing applications, so the CBE regulation must be read in conjunction with regulations pertaining specifically to generic labeling. Those regulations require a generic drug's labeling to be 'the same as the labeling of the [RLD].'"[196]

In that same case, the FDA told the Court that it "consistently [has] taken the position that the ANDA holder may not unilaterally change its approved labeling."[197] Specifically, FDA acknowledged the fact that allowing generic company to utilize CBE-0 procedures would conflict with federal law.[198]

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193. *See* Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837, 844 (1984).

194. 21 U.S.C. § 355 (j)(2)(A)(v) (2012).

195. "Except for labeling differences due to exclusivity or a patent and differences under section 505(j)(2)(v) of the act, the ANDA product's labeling must be the same as the listed drug product's labeling because the listed drug product is the basis for ANDA approval. Consistent labeling will assure physicians, health professionals, and consumers that a generic drug is as safe and effective as its brand-name counterpart. (See [54 Fed. Reg. 28,872, 28,884 (proposed July 10, 1989)]. If an ANDA applicant believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised. After approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised." 57 Fed. Reg. 17950, 17961 (Apr. 28, 1992).

196. Brief for the United States as Amicus Curiae, PLIVA, Inc. v. Mensing 564 U.S. 604, (2011) (Nos. 09-993, 09-1039) (Nov. 2010) at 13; PLIVA, Inc. v. Mensing 564 U.S. 604, 614 (2011) (citing 21 CFR § 314.94(a)(8)(iii)); U.S. Merits Brief, *supra* note 189, at 15).

197. Brief for the United States as Amicus Curiae, *supra* note 196, at 13.

198. *Id.* at 12 ("Supplements are subject to the substantive standards governing applications, so the CBE regulation must be read in conjunction with regulations pertaining specifically to generic labeling. Those requirements require a generic drug's labeling to be "the same as the labeling of the [RLD]." *Id.* at 13.)

B. Concern for Consumer Safety

The requirement of "sameness" under the FDCA and Hatch–Waxman is a product of the concern for consumer safety that formed the basis for the creation of the FDA itself and enactment of the FDCA. Under the FDCA and governing regulations, generic manufacturers do not have access to proprietary information, such as the clinical trial safety research and other drug safety data that is compiled by the pioneer drug manufacturer.[199] Rather, the FDA is the ONLY entity with access to this information, from both the listed drug manufacturer and any generics, and with the expertise to evaluate any proposed label changes in light of this data.[200] To that end, as noted by the FDA in 2008, the FDA's labeling decisions on safety and effectiveness are a reflection of the information to which has access.[201] As noted recently by the president and CEO of the Generic Pharmaceutical Association, "as the gold standard of prescription drug review, the agency is the best, most trusted authority to protect patient safety. That is the FDA's mission and responsibility."[202] Requiring generic manufacturers to make a decision that a labeling change is warranted independent of the name-brand manufacturer and the FDA itself is unfair as such a decision would be made without proper foundation. More importantly, without having access to all of the scientific data submitted to the FDA by the pioneer manufacturer, a change by a generic manufacturer could adversely impact consumer safety.

Additionally, consumer safety would be adversely impacted by the proposed rule because it could have the effect of generating multiple, different labels for a single drug product. As noted by the Generic Pharmaceutical Association (GPhA), a listed, brand drug may have, on average, eight generic equivalents.[203] If each generic manufacturer makes a labeling change, consumers and physicians would be faced with nine different labels for the same drug product, the original label on the listed drug, and the eight generic drugs with different labels. The danger to consumers may be exceedingly high as those eight label changes by generic

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199. *See infra* Part VI.

200. Ralph G. Neas, *The FDA Should Be in Charge of Warning Labels*, U.S. NEWS & WORLD REPORT, Mar. 31, 2014, https://www.usnews.com/opinion/articles/2014/03/27/new-fda-generic-drug-labeling-rule-threatens-patient-safety [https://perma.cc/EDF9-H7TK].

201. 73 Fed. Reg. 2848, 2851 (2008) ("FDA's comprehensive review is embodied in the labeling for the product which reflects thorough FDA review of the pertinent scientific evidence and communicates to health care practitioners the agency's formal, authoritative conclusions regarding the conditions under which the product can be used safely and effectively.").

202. Neas, *supra* note 200.

203. *Id*.

manufacturers would be made without the benefit of the proprietary information necessary to properly determine the necessity for the label change, and would be made prior to FDA approval of the labeling change and a similar label change by the listed drug manufacturer.

Remarkably, the proposed rule ignores the fact that there are multiple manufacturers for virtually every generic drug. Within the proposed rule, the FDA argues that

> [i]n the current marketplace, in which approximately 80 percent of drugs dispensed are generic and, as we have learned, brand name drug manufacturers may discontinue marketing after generic drug entry, FDA believes it is time to provide ANDA holders with the means to update product labeling to reflect data obtained through postmarketing surveillance . . . .[204]

However, this statement presumes that there is only one generic manufacturer for every drug. Rather, multiple generic manufacturers of the same drug may possess only a small percentage of that 80% of the market. Consequently, each generic company would make a decision to change the label of a particular drug based only on its respective market share percentage of anecdotal post-marketing surveillance data.[205]

C. Economic Dangers

The proposed rule has the potential for undermining the entire rationale for Hatch–Waxman as generic drug manufacturers, facing increased litigation risk, may choose to leave the market, thereby increasing drug prices and the potential for shortages.[206] As noted by the Generic Pharmaceutical Association, "[t]he potential flood of products liability litigation against generic pharmaceutical manufacturers ultimately will drive the smaller companies from the market and increase the cost of generic medications, which FDA has not accounted for or addressed in its cost impact analysis."[207]

FDA has admitted that "[a]s a practical matter, genuinely new

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204. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,988 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pt. 314, 601).

205. *See* Ralph Neas, Generic Pharmaceutical Association, Comment Letter on Proposed Rule on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,988 (proposed Nov. 13, 2013), Docket No. FDA-2013-N-0500 at 21 (Mar. 13, 2014).

206. *Id*. at 21–22.

207. *Id*.

information about drugs in long use (as generic drugs typically are) appears infrequently."[208] When such information becomes available, drug labels are changed. However, as noted by the GPhA, a vast majority of lawsuits occur *following* a label change, not as a result of any particular lawsuit itself.[209] For example, according to the GPhA, there were a handful of lawsuits involving the prescription drug, Reglan, in the late 1980s through the 2000s.[210] Once a change to its label was made in 2009, thousands of lawsuits followed.[211] However, "ironically," the 2009 label change did NOT change the part of the label that formed the basis for the lawsuits in the twenty years prior.[212] The GPhA notes a similar flurry of litigation following a labeling change to Paxil and hormone therapy drugs, demonstrating that a change in a label can prompt a flood of products liability litigation.[213] The GPhA's concern that the "real-world effect of a manufacturer's submission of a CBE-0 supplement to update labeling to add what inevitably would be scientifically unsubstantiated safety-related information likely will result in the filing of hundreds, if not thousands, of lawsuits"[214] is thereby legitimized.

FDA has estimated that the annual net social cost of implementation of the proposed rule of between $4237 and $25,852, with the present discounted value over a twenty-year horizon of between $44,890 and $384,616, based primarily on the costs of "submitting and reviewing" paperwork associated with labeling changes.[215] However, many lawmakers and industry groups have called into question the accuracy of the analysis. For example, two Republican legislators wrote a letter to the Office of Information and Regulatory Affairs requesting White House scrutiny of the FDA's cost-benefit analysis because the FDA failed to consider any litigation-associated costs.[216] Further, a 2014 economic analysis by Matrix Global Advisors estimates that annual costs of the

208. U.S. Merits Brief, *supra* note 189, at 34–35.

209. *See* Ralph Neas, Generic Pharmaceutical Association, Comment Letter, *supra* note 205, at 21–22.

210. *Id*. at 21.

211. *Id*.

212. *Id*.

213. *Id.*

214. *Id.*

215. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67985, 67986 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pt. 314, 601).

216. *See* Rep. Bob Goodlatte and Sen. Lamar Alexander, Letter on FDA cost-benefit analysis to Hon. Howard A. Shelanski, Office of Budget and Management (June 25, 2014).

proposed rule would jump to $4 billion if additional costs were considered.[217] On June 4, 2014, a report from the House of Representatives Committee on Appropriations concluded that the proposed rule "fails to provide a net health benefit to consumers and providers" and directed FDA to "complete a new economic analysis of the rule, paying particular attention to the costs of pharmaceutical products."[218]

Although FDA has not proposed any new or revised economic analysis of the impact of the proposed rule, the House Appropriations Committee released a new bill in May of 2016 which prohibited any of the congressional funding for the FDA to be used to "finalize or implement" the proposed rule.[219]

D. Contravention of Agency Purpose

In fact, within the proposed rule, FDA stated that, "[i]f this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs."[220] Moreover, the proposed rule was generated in response to a request by a consumer watchdog group, Public Citizen, and with little to no involvement by relevant industry groups during the drafting process.[221] In fact, FDA has acknowledged that it held meetings with members of the Plaintiffs' bar before the proposed rule was released.[222]

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217. Alex Brill, *FDA's Proposed Generic Labeling Rule: An Economic Assessment*, MATRIX GLOBAL ADVISORS (Feb. 5, 2014), http://www.gphaonline.org/media/cms/Economic_Impact_Study_FDA_Labeling_Rule_-_MGA.pdf [https://perma.cc/8KB3-Z89G].

218. Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2015, H.R. REP. 113-468, at 62 (2014), https://www.congress.gov/congressional-report/113th-congress/house-report/468/1 [https://perma.cc/QB6K-ZNGG].

219. Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Act, 2017, H.R. 5054, at 91–92, 114th Cong. 2d Sess. (2016).

220. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,989 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pt. 314, 601).

221. *Generic Drug Labeling: A Report on Serious Warnings Added to Approved Drugs and on Generic Drugs Marketed Without a Brand-Name Equivalent*, PUBLIC CITIZEN (June 2013), https://www.citizen.org/documents/2138.pdf [https://perma.cc/7SWB-NY84].

222. *See Examining Concerns Regarding FDA's Proposed Changes to Generic Drug Labeling, Hearing Before House Energy and Commerce Committee Subcommittee on Health*, 113th Cong. 2 (Apr. 1, 2014) (statement of Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Admin., Dept of Health and Human Serv.), transcript and video http://democrats.energycommerce.house.gov/index.php?q=hearing/hearing-on-examining-concerns-regarding-fda-s-proposed-changes-to-generic-drug-labeling-subc.

If the clear and inappropriately biased activity by the FDA described above were not enough, it must also be noted that motivation behind the proposed rule is also contrary to the position the FDA has taken in the past that "access to the courts" is not an appropriate basis from which to conduct rulemaking.[223] As noted by the GPhA in its comments to the proposed rule dated March 13, 2014, the premise that tort liability cannot be influenced by the agency has been recognized by the FDA for decades.[224]

In short, the FDA's proposed new regulation is not lawful. It does not achieve those desired ends demanded by the Court and, if enacted by the FDA, will result in challenges to the regulation by generic and pioneer drug pharmaceutical companies as an abuse of power as it directly conflicts with Congress's requirement that the labeling for generics must be the same as is for the listed drug. Most notably, it completely contradicts the purpose for which the FDA was created and the position the Agency has taken that it intends to occupy the field of regulation of drugs and their warning labels.

VI. PREEMPTION, NOT JURIES

Whether the regulation goes into effect or not,[225] Congress should step in and do one of two things. First, Congress could amend or repeal the FDCA and Hatch–Waxman and remove the requirement of "sameness" in order avoid abuse of power challenges against FDA. This Article advocates for the alternative approach—that Congress should remind the FDA of its purpose and reiterate that the agency does and should continue to occupy the entire field of drug labeling, thereby expressly requiring the application of preemption in cases challenging the safety and propriety of a drug warning label.

As demonstrated above, the fact remains that until this proposed

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223. *Id.* at 9.

224. *See* Ralph Neas, Generic Pharmaceutical Association, Comment Letter, *supra* note 205, at 20. *See also* Requirement for Labeling Directed to the Patient, 42 Fed. Reg. 37,636, 37,637 (July 22, 1977) ("[w]hether particular labeling may alter a manufacturer's liability in a given instance cannot be considered as a dispositive factor by the Commissioner in reaching a decision . . ."); Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,437 (June 26, 1979) ("It is not the intent of FDA to influence the civil tort liability of the manufacturer or the physician."); Prescription Drug Patient Labeling; Medication Guide Requirements, 63 Fed. Reg. 66,378-01, 66,383 (Dec. 1, 1998) ("Tort liability can not [sic] be a major consideration for FDA which must be guided by the basic principles and requirements of the . . . regulatory activities.").

225. After several delays, the regulation was set to go into effect in July 2016. However, in May 2016, the FDA announced another delay to the summer 2017.

regulation was released, the FDA has not expected nor has it relied upon state court tort claims to help it regulate and police the drug industry. More importantly, there is absolutely no evidence, other than the lack of an express preemption provision for drug labels within the FDCA, that Congress intends for juries in state law failure to warn claims to set a standard for the content of drug warning labels that MUST ultimately be approved by the FDA. Rather the evidence reveals that both Congress and the FDA believe itself the expert in the area of drug labeling and regulation and was, in fact, created for the purpose of regulating labels on drugs.[226] Therefore, to create parity between name brand and generic drug manufacturers, and to avoid substituting the judgment of the agency on the propriety of drug warning labels for the judgment of a jury, Congress should step in and include an express preemption provision within the FDCA, just as it has done in the past with respect to medical devices.

The danger of allowing state court juries to substitute their judgment for that of the FDA with respect to the content of a drug warning label is substantial for several reasons. First, the evaluative considerations are not the same. When a drug warning label is placed before the FDA for approval, the FDA evaluates the label for safety and effectiveness in light of all individuals that may utilize the drug.[227] The FDA's job is to consider not only the dangers of the drug and how much information to list on the warning label, but also how beneficial the drug will be to individuals who need it.[228] On the other hand, a jury only sees the drug label from an isolated perspective by looking at an injured plaintiff, sometimes with a gross disfigurement, like the plaintiff in *Wyeth* who lost an arm, or compelling story of the adverse effects of a drug, like the plaintiffs in *PLIVA*. From that perspective, the jury is then asked to determine if a "better" or "different" warning label would have prevented the injury from ever occurring.

The dissent in *Wyeth,* acknowledged this danger:

> Indeed, patients like respondent are the only ones whom tort juries ever see, and for a patient like respondent—who has already suffered a tragic accident—Phenergan's risks are no longer a matter of probabilities and potentialities. In contrast, the FDA has the benefit of the long view. Its drug-approval determinations consider the interests of all potential users of a drug, including "those who would

226. *See generally* Wyeth v. Levine, 555 U.S. 555, 575 (2009).

227. *Id.* at 626 (Alito, J., dissenting).

228. *See* 21 U.S.C. § 355(d) (2012).

> suffer without new medical [products]" if juries in all 50 States were free to contradict the FDA's expert determinations. Id., at ——, 128 S.Ct., at 1009. And the FDA conveys its warnings with one voice, rather than whipsawing the medical community with 50 (or more) potentially conflicting ones.[229]

This perspective is not a new one. Rather, in *Reigel, supra*, albeit in the context of medical devices, the Court has found that product liability litigation is "less deserving of preservation" when the FDA conducts the equivalent of a "federal safety review."[230] Further, when discussing whether state court juries should be permitted to adjudicate the safety of a particular design of a medical device, Justice Scalia stated,

> State tort law that requires a manufacturer's catheters to be safer, but hence less effective, than the model the FDA has approved disrupts the federal scheme no less than state regulatory law to the same effect. Indeed, one would think that tort law, applied by juries under a negligence or strict-liability standard, is less deserving of preservation. A state statute, or a regulation adopted by a state agency, could at least be expected to apply cost-benefit analysis similar to that applied by the experts at the FDA: How many more lives will be saved by a device which, along with its greater effectiveness, brings a greater risk of harm? A jury, on the other hand, sees only the cost of a more dangerous design, and is not concerned with its benefits; the patients who reaped those benefits are not represented in court. As Justice Breyer explained in *Lohr*, it is implausible that the MDA was meant to "grant greater power (to set state standards 'different from, or in addition to' federal standards) to a single state jury than to state officials acting through state administrative or legislative lawmaking processes." 518 U.S., at 504. That perverse distinction is not required or even suggested by the broad language Congress chose in the MDA, and we will not turn somersaults to create it.[231]

Further, allowing a jury to question the propriety of the content of a drug warning label to reach a conclusion as to whether an additional warning would have prevented a plaintiff's particular injury flies in the face of long standing precedent that more is not necessarily better. For

229. *Wyeth*, 555 U.S. at 625 (Alito, J., dissenting).

230. Riegel v. Medtronic, Inc., 552 U.S. 312, 323, 325 (2008).

231. *Id*. at 325.

example, although not in the context of products liability, the Court has stated that, "[m]eaningful disclosure does not mean more disclosure. Rather, it describes a balance between 'competing considerations of complete disclosure . . . and the need to avoid . . . [informational overload].'"[232]

In fact, the FDA has acknowledged that too many warnings may be detrimental in that it may discourage physicians and consumers from utilizing an otherwise beneficial drug. In fact, the FDA has repeatedly cautioned against overinclusiveness of warnings in drug labels. For example, the FDA stated that unsubstantiated risk information in labeling "would result in such uncertainty and confusion that the usefulness of [existing] warnings in protecting the public against possible harm would be severely undermined, if not destroyed."[233] Further, in 1979, the FDA noted,

> [p]hysicians are always in a position to pursue additional information through normal educational sources, such as treatises and medical journals . . . [T]he Commissioner does not agree that general statements on good professional practice are appropriate for drug labeling. There are potentially many such statements, which, if all were included in drug labeling, would transform labeling into small textbooks of medicine. As a general policy, therefore, these regulations will not require such statements to be included in labeling.[234]

Recently, in a 2015 article in the *Chicago Tribune* discussing the content of warnings in drug advertisements, the FDA was quoted as stating, "[i]n general, FDA believes that exhaustive lists that include even minor risks distract from, and make it difficult for, consumers to comprehend and retain information about the important risks."[235]

The concern regarding excessive warnings on drug labels is echoed by scholars alike:

> [O]verwarning of prescription drug side effects may adversely affect treatment decisions if other options (which fall outside of the products liability system) do not have to carry equally alarming risk information. The FDA

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232. Ford Motor Credit Co. v. Milhollin, 444 U.S. 555, 568 (1980) (citations omitted).

233 40 Fed. Reg. 28582, 28583 (FDA July 7, 1975).

234. Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,436 (June 26, 1979).

235. John Russell, *Drug Ads Include a Lot of Warnings—Probably Too Many, FDA Says*, CHICAGO TRIBUNE, (Sept. 4, 2015, 1:12 PM), http://www.chicagotribune.com/business/ct-confusing-drug-ads-0906-biz-20150904-story.html [https://perma.cc/4XER-3WDP].

> has an interest in rational prescribing . . . so that a physician can compare them with other available therapies. That goal is not advanced if a drug is made to appear riskier than other drugs and other therapies due to the over-dramatization of risk information. To allow a warning based on inconclusive evidence or scientific hunches results in doctors not prescribing effective drugs to a patient because of the erroneous belief that a side-effect might occur. Alternatively, physicians may tune out if overwhelmed with risk information. In either case, the result may be suboptimal treatment choices.[236]

Conversely, a jury is only asked whether the injury complained of by the plaintiff would have been avoided had the label contained a warning against it. This question may be answered in the affirmative EVEN IF the FDA had already deemed that particular warning unnecessary.

As noted by the Court in *Wyeth,*

> the FDA has the benefit of the long view. Its drug-approval determinations consider the interests of all potential users of a drug, including "those who would suffer without new medical [products]" if juries in all 50 States were free to contradict the FDA's expert determinations. *Id.,* at ––––, 128 S.Ct., at 1009. And the FDA conveys its warnings with one voice, rather than whipsawing the medical community with 50 (or more) potentially conflicting ones. [237]

As predicted, without Congress stepping in to provide the Court with guidance on the issue of preemption, "parochialism" will continue to prevail.[238]

VII. CONCLUSION

As is the case with many products liability cases, there are "dreadful injuries" that "often engender passionate responses."[239] As acknowledged by the dissent in *Wyeth,* however, "tragic facts make bad law."[240] That is the state of affairs in the area of drug labeling litigation.

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236. James M. Beck (@Bexis), *On Overwarning*, DRUG AND DEVICE LAW (Jan. 9, 2014) https://www.druganddevicelawblog.com/2014/01/on-overwarning.html [https://perma.cc/GL7E-EM85] (citing Lars Noah, *Medicine's Epistemology: Mapping The Haphazard Diffusion of Knowledge In The Biomedical Community*, 44 ARIZ, L. REV. 373, 455–56 (2002) (footnotes, citations, and quotation marks omitted).

237. Wyeth v. Levine, 555 U.S. 555, 626 (2009) (Alito, J., dissenting).

238. *Id*.

239. Mut. Pharm. Co. v. Bartlett, 133 S. Ct. 2466, 2478 (2013).

240. *Wyeth*, 555 U.S. at 604 (Alito, J., dissenting).

The impractical effects of *Wyeth, PLIVA, Bartlett*, and the proposed rule are two-fold. First, name-brand drug manufacturers must now make changes to their label without FDA approval through the CBE-0 process, which was always intended by FDA to be a process used in only the most exigent of circumstances, even if they do not believe such a change is necessary to protect the "safety and effectiveness" criteria of FDA initial approval, and receive a subsequent rejection by FDA. Why? Because under *Wyeth,* when faced with a drug labeling tort claim, these manufacturers must demonstrate that FDA would have rejected such a change in order to protect them from liability. Worse yet, consumer safety becomes a significant concern as, when faced with numerous labeling change requests by name-brand manufacturers, not because of necessity but to insulate themselves from liability in future tort claims, the FDA may struggle to determine the propriety of the labeling changes and either not appreciate necessary labeling changes or approve additional, but unnecessary warnings. Further, the same scenario could then play out with generic drugs should the proposed rule go into effect in the summer of 2017, as the rule removes the protection of preemption granted to generic manufacturers in *PLIVA.*

If there was ever a time that preemption was needed in a particular field, it is now. As it is clear that Congress intended to allow the FDA to occupy the field and any attempt to regulate at the state level would stand as an obstacle to the goals and objectives of Congress, Congress needs to be explicit in the delegation of power to the FDA for drug labeling and provide for express preemption within the applicable federal statute.