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Making Changes: Generic Drug Labeling and the Case Against Federal Preemption

Lesley A. Stout

INTRODUCTION

In April of 2007, Diana Levine visited her local clinic to receive treatment for a migraine headache. She received an initial injection of Phenergan for nausea and Demerol for her headache. After her symptoms failed to subside, Levine returned for a second visit, where she received Phenergan by a method referred to as “the IV-push method,” by which the drug is administered into a vein. Injection of the drug through an intravenous drip or intramuscular injection has been found to be safe; however, injection into a vein carries serious risks. In Levine’s case, the effort to inject the drug into her vein punctured an artery, and the drug traveled into her arterial blood resulting in the spread of gangrene and the amputation of her arm. Levine subsequently filed suit against Wyeth, the brand-name manufacturer of Phenergan, based on common-law negligence and strict liability theories. While the Phenergan label warned of the complications associated with inadvertent intra-arterial injection, she alleged that the

1 J.D. expected May 2010, University of Kentucky College of Law; M.Phil. in International Relations, May 2006, University of Cambridge; B.A. in International Relations, May 2002, Centre College. The author would like to thank Lou Bogard for his assistance.
3 Id.
4 Id.
7 Wyeth, 129 S. Ct. at 1191.
8 Id. at 1192 n.1 (reproducing the label as it appeared at the time of Levine’s injury, as follows: “The warning for ‘Inadvertent Intra-arterial Injection’ stated: ‘Due to the close proximity of arteries and veins in the areas most commonly used for intravenous injection, extreme care should be exercised to avoid perivascular extravasation or inadvertent intra-arterial injection. Reports compatible with inadvertent intra-arterial injection of Phenergan Injection, usually in conjunction with other drugs intended for intravenous use, suggest that pain, severe chemical irritation, severe spasm of distal vessels, and resultant gangrene requiring amputation are likely under such circumstances. Intravenous injection was intended in all the cases reported but perivascular extravasation or arterial placement of the needle is now suspect. There is no proven successful management of this condition after it occurs. . . . Aspiration of dark blood does not preclude intra-arterial needle placement, because blood is
labeling was defective nevertheless "because it failed to instruct clinicians to use the IV–drip method of intravenous administration instead of the higher risk IV–push method." In response, Wyeth argued "Levine’s failure–to–warn claims were preempted by federal law," relying on theories of implied field and conflict preemption. Wyeth maintained it could not comply with both federal and state law and therefore state law must yield to federal law.

Ms. Levine’s case and the issue of federal preemption made its way to the United States Supreme Court in November of 2008, with the Court handing down its decision on March 4, 2009. The Supreme Court agreed with Levine and held that Wyeth failed to show that it was impossible to comply with both federal and state requirements or that complying with state law would frustrate federal objectives. The regulations in place permitted the company to “unilaterally strengthen its warning” and Levine’s state common–law actions were not preempted by federal law.

The fact that Wyeth had previously received Food and Drug Administration (FDA) approval for the warning label did not excuse the company’s failure to maintain an adequate warning label.

The Supreme Court’s decision in Wyeth v. Levine provides critical guidance to brand–name drug manufacturers in evaluating their responsibilities and potential liabilities under federal and state laws. It also ensures that consumers injured by brand–name drugs may pursue causes of action under state common law. However, the case leaves unanswered the preemption question with respect to generic drug manufacturers. While the statutory rules and regulations governing the labeling of generic and brand–name drugs are similar, they are not identical. The differences between the two processes have led to sharp disagreements over the ability of generic drug manufacturers to update and strengthen their warning labels independently of brand–name manufacturers.

discharged upon contact with Phenergan Injection. Use of syringes with rigid plungers or of small bore needles might obscure typical arterial backflow if this is relied upon alone. When used intravenously, Phenergan Injection should be given in a concentration no greater than 25 mg per mL and at a rate not to exceed 25 mg per minute. When administering any irritant drug intravenously, it is usually preferable to inject it through the tubing of an intravenous infusion set that is known to be functioning satisfactorily. In the event that a patient complains of pain during intended intravenous injection of Phenergan Injection, the injection should be stopped immediately to provide for evaluation of possible arterial placement or perivascular extravasation.”

9 Id. at 1192.
10 Id.
11 Id. at 1196.
12 Id. at 1187.
13 Id. at 1199.
14 Id.
15 See infra text accompanying notes 78–88.
Courts across the country are addressing questions presented by the constitutional issue of federal preemption. When, and to what extent, do federal laws supersede and prevent the application of state laws on a given issue? The central question with respect to preemption in the case of generic drugs is as follows: should state common-law tort claims based on a failure to warn be permitted when generic drug manufacturers’ labels have been approved by the FDA and yet are shown to be inadequate? This Note will show that state common-law tort claims should not be barred based on federal preemption.

The FDA’s Center for Drug Evaluation and Research generally defines a generic drug as "a drug product that is equivalent to brand name products in terms of quality and performance." The D.C. Circuit Court in Mova Pharmaceutical Corp. v. Shalala described generic drugs as “versions of brand-name prescription drugs that are often sold without a brand name and that contain the same active ingredients, but not necessarily the same inactive ingredients, as the original.” When seeking FDA approval, generic drugs use the same warning labels as those borne by the brand-name drugs they replicate without performing additional testing or studies. Because of the unique process by which generic drug labels are approved and modified, questions arise with regard to how far generic drug manufacturers may go in altering their labels.

Since the Supreme Court handed down its decision in Wyeth v. Levine pertaining to the federal preemption of brand-name pharmaceuticals, a number of courts have relied on it in deciding cases involving the preemption of generic drug claims. In Kellogg v. Wyeth, the United States District Court for the District of Vermont looked to Wyeth v. Levine in denying the defendant generic drug manufacturer’s motion for immediate appeal based on the court’s prior decision denying preemption. In Schrock v. Wyeth, Inc., the United States District Court for the Western District of Oklahoma relied on Levine when it found that the plaintiff’s state law


17 FDA, FAQs about CDER, http://www.fda.gov/AboutFDA/CentersOffices (follow “About the Center for Drug Evaluation and Research” hyperlink; then follow “FAQs about CDER” hyperlink) (last visited Jan. 6, 2010).


failure-to-warn claim was not preempted by federal drug labeling law and
denied the defendant's motion to dismiss on preemption grounds. In
addition, the federal court for the Northern District of Illinois in Stacel v.
Teva Pharmaceuticals, USA, also looked to Levine in holding that the plaintiff's
state law causes of action against a generic drug manufacturer were not
preempted by the Federal Food, Drug, and Cosmetic Act (FDCA).
In yet another turn of events following Levine, the Third Circuit Court of
Appeals in the case Colacicco v. Apotex, Inc., relied on Levine when it vacated
a judgment in which it had previously found preemption and dismissed
claims against both brand-name and generic drug manufacturers.

Despite the proliferation of scholarly articles addressing questions of
preemption and brand-name drugs, little to no attention has been paid
to questions involving generic drugs. This Note attempts to fill that void
and addresses the following issues: Assuming the brand-name drug's label
meets FDA specifications, is the defense of "implied conflict preemption"
strengthened for generic manufacturers because of the FDA regulations
requiring generics to maintain identical labeling to those of the brand-
name drugs they replicate? Are regulations that require a brand-name
manufacturer to update a label also available to generic drug manufacturers?
Must the labels of the brand-name drug and generic drug be identical at all
times, or is even a temporary discrepancy grounds for a drug being deemed
misbranded? Finally, what are the policy considerations associated with
permitting generic manufacturers to maintain the preemption defense?

When a drug injures a person as a result of an inadequate warning label,
the manufacturer of that drug should be held liable irrespective of whether
the manufacturer is the original brand-name company or a generic company
replicating both the chemical structure and the warning label of the
brand-name drug. The duty to update a drug's warning label following the
acquisition of new evidence pertaining to a drug's side effects or potential
for adverse health reactions should not rest solely with the brand-name
drug manufacturer, especially when FDA procedures exist for generic
manufacturers to update their warning labels. A drug's beneficial purposes
are compromised when doctors and patients are not fully informed as to
the dangers associated with prescribing it. Moreover, what benefit does an
inexpensive drug with an inadequate warning provide when the effects of
its use could be more harmful than not using it in the first place?

23 Stacel v. Teva Pharms., USA, 620 F. Supp. 2d 899, 907 (N.D. Ill. 2009); see also Bartlett
24 Colacicco v. Apotex, Inc., No. o6–3107 (3d Cir. Apr. 28, 2009) [not yet available on
LexisNexis or Westlaw].
25 See generally Mary J. Davis, The Battle Over Implied Preemption: Products Liability and
the FDA, 48 B.C. L. Rev. 1089 (2007); Richard A. Epstein, The Case for Field Preemption of State
Part I of this Note will detail the generic drug approval history and process. Part II will examine the principles of preemption and recent questions presented by the generic drug labeling debate. Part III will set forth the case against federal preemption and explain why generic drug manufacturers should not escape liability for failure to update their labels and warn consumers of the risks associated with the use of their drugs. Part IV will explain the arguments in favor of preemption and why courts should ultimately reject these arguments. Finally, Part V will discuss the policy implications of preventing generic manufacturers from claiming the defense of federal preemption when faced with state common-law tort claims.

The importance of the preemption debate will only increase as the number of generic drug manufacturers seeking approval for new drugs continues to rise, with more than two hundred brand-name medications coming off-patent over the next few years. According to the Generic Pharmaceutical Association, generic drugs account for sixty-nine percent of all prescriptions dispensed in the United States. Moreover, the generic industry is growing at a rate of more than seven percent, outstripping the growth rate for the world pharmaceutical market. With such high growth numbers, it follows that the number of injuries associated with generic drugs will also rise. Thus, an increased need exists for consumers to be able to hold the correct manufacturer responsible for the failure to warn of dangers and to ensure manufacturers are aware of their responsibilities and potential liabilities.

I. THE DRUG APPROVAL PROCESS

To understand the current debate over preemption and generic drugs, one must first examine a brief history of the drug approval process and how that process incorporates the approval of generic drugs. While efforts to protect consumers against misbranded or fraudulent food and drug products began in the states even before the twentieth century, federal efforts to create a national system for regulating food and drugs moving in interstate commerce only came to pass in 1906 with the passage of the Pure Food and Drug Act. In 1938, Congress enacted the Federal Food, Drug, and Cosmetic Act (FDCA). Since its initial

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26 See Mark B. McClellan, Remarks of the Commissioner of Food and Drugs, 58 Food & Drug L.J. 191, 198 (2003).
28 Id.
29 See Davis, supra note 25, at 1099–1100 (citing 1 James T. O'Reilly, Food and Drug Administration §§ 3:1–4 (2d ed. 2005)).
30 Federal Food, Drug, and Cosmetic Act, Pub. L. No. 78-717, 52 Stat. 1040 (1938) (codi-
passage, changing industry practices and standards led Congress to broaden the scope of the legislation, resulting in the federal regulation of all aspects of pharmaceutical drug manufacturing and marketing.\(^{31}\)

In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch–Waxman Amendments, which amended the FDCA.\(^{32}\) Congress undertook these changes in order to slow rising drugs costs and increase the availability of low–cost generic drugs.\(^{33}\) The Hatch–Waxman Amendments resulted in an expedited approval process for generic drugs, while lengthening patent terms for innovator drugs.\(^{34}\)

According to the Congressional Budget Office, in 1994 alone, purchasers saved roughly $8 to $10 billion by substituting generic for brand–name drugs.\(^{35}\) These reductions in cost are directly attributable to the expedited approval process for generic drugs.\(^{36}\) Under the FDCA, brand–name drug manufacturers must complete a New Drug Application (NDA) with the FDA.\(^{37}\) Prior to passage of the Hatch–Waxman Amendments, manufacturers of generic versions of FDA–approved brand–name drugs were likewise required to file new NDAs, including new studies documenting a drug’s safety and effectiveness.\(^{38}\)

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\(^{31}\) Jodie M. Gross & Judi Abbott Cutty, *The Federal Preemption Debate in Pharmaceutical Labeling Product Liability Actions*, 43 *Tort Trial & Ins. Prac.* L.J. 35, 43 (2008) (arguing in favor of finding federal preemption in cases involving brand–name drugs); see also Drug Amendments of 1962, Pub. L. No. 87–781, 76 Stat. 780 (1962); Michelle Meadows, *Promoting Safe and Effective Drugs for 100 Years*, FDA CONSUMER, Jan.–Feb. 2006, http://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/CentennialEditionofFDAConsumer/ucm093787.htm (noting with respect to the 1962 Kefauver–Harris Amendments that “before marketing a drug, firms now had to prove not only safety, but also provide substantial evidence of effectiveness for the product’s intended use” and “the 1962 amendments required that the FDA specifically approve the marketing application before the drug could be marketed”).


\(^{35}\) Id. at ix (these figures represent retail prices).

\(^{36}\) Id. at 43.


This process changed under the Hatch–Waxman Amendments. Original, or pioneer, applicants for FDA approval must still file full NDAs; however, manufacturers of generic versions of the original drug may instead file an Abbreviated New Drug Application (ANDA). This abbreviated application relies on the FDA's previous approval of the original drug without requiring a new set of studies. It mandates that the generic drug manufacturer establish the following:

1. the generic drug is “bioequivalent” to the pioneer drug;
2. its active ingredients, route of administration, strength and dosage form are “the same as” those of the pioneer drug;
3. the inactive ingredients are not “unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug.”

Generic manufacturers must also show that “the labeling proposed for the new [generic] drug is the same as the labeling approved for the listed drug . . . except for changes required . . . because the new drug and the listed drug are produced or distributed by different manufacturers.”

While FDA regulations require that generic manufacturers use the same labeling as that of the reference drug as part of the application process, FDA regulations nevertheless do permit labeling differences with respect to “expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(4)(D) of the act.”

As a result of the above regulations, generic drug manufacturers argue that both during and after their initial application process their labels must be the same as that of their brand–name counterparts. This Note will show that the applicable statutes and regulations do not support this contention, and generic drug manufacturers have a continuing duty, independent of brand–name manufacturers, to ensure that their labels reflect new information in an accurate and timely manner.

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39 See 21 U.S.C. § 355(j); see also Mova Pharm. Corp., 140 F.3d at 1063.
40 Mova Pharm. Corp., 140 F.3d at 1063.
42 Id. (citing 21 U.S.C. § 355(j)(2)(A)(v)).
44 Id.
II. PREEMPTION PRINCIPLES

As the Supreme Court originally set forth in *Gade v. National Solid Wastes Management Association*, federal law has been found to preempt state law in three situations: "(1) express preemption, where a federal statute contains 'explicit preemptive language'; (2) field preemption, in which the federal regulatory scheme is 'so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it'; and (3) implied conflict preemption."46

Under principles of implied field preemption, "federal law so thoroughly occupies a legislative field 'as to make reasonable the inference that Congress left no room for the States to supplement it.'"47 Under implied conflict preemption, "state law is pre-empted if that law actually conflicts with federal law."48 Conflict preemption exists in two situations: when "it is impossible for a private party to comply with both state and federal requirements, or where state law stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress."49

Impossibility and obstacle preemption arose as issues in *Wyeth v. Levine*.50 Wyeth, the brand-name drug manufacturer, argued that if it had strengthened its warning to be in compliance with state law, it would have found itself in violation of federal law based on the unauthorized distribution of the drug and claims of misbranding. Thus, it argued it was impossible for it to comply with both state and federal law.51 Wyeth also attempted to argue obstacle preemption, stating that compliance with state law would obstruct federal labeling requirements.52 Wyeth maintained that Levine's state tort claims interfered with congressional intent, which it argued gave expert agency officials the duty of making drug labeling decisions.53 The Court saw this as an "untenable interpretation of congressional intent and an overbroad view of an agency's power to pre-empt state law."54 The Court ultimately rejected both preemption arguments.

With respect to express preemption, the FDCA does not contain a generally applicable express preemption provision dealing with

48 Id.
51 Id. at 1196.
52 Id. at 1199.
53 Id.
54 Id.
prescription drugs, thereby preventing both brand-name and generic drug manufacturers from claiming express preemption and leaving the debate to claims centered on implied preemption. The FDCA does include, however, an express preemption provision for medical devices. When Congress enacted this provision in 1976, it elected against inserting a similar provision for prescription drugs. The omission of an express preemption provision for drugs and the inclusion of a provision for medical devices serve as important evidence of the congressional intent not to preempt state common-law tort claims.

In the case of brand-name drugs, the FDA under the Bush Administration publicly supported the implied preemption of state law claims. As for generic drugs, the FDA took steps that suggested it supported preemption. On January 16, 2008, the FDA issued a proposed rule, entitled “Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices.” The FDA proposed this rule to amend regulations regarding changes to an approved new drug application (NDA) in order to codify its position that a supplemental application to amend the labeling for an approved product is only necessary “to reflect newly

55 Davis, supra note 25, at 1092 (citing Caraker v. Sandoz Pharms. Corp., 172 F. Supp. 2d 1018, 1035 (S.D. Ill. 2001) (showing that the FDCA pharmaceutical provisions do not contain preemption provisions)).

56 21 U.S.C. § 360k(a) (2006) (noting that “[e]xcept as provided in subsection (b) . . . , no State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement— (1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and (2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter”).

57 Wyeth, 129 S. Ct. at 1200.

58 Id. (stating that “if Congress thought state-law suits posed an obstacle to its objectives, it surely would have enacted an express pre-emption provision at some point during the FDCA’s 70-year history. But despite its 1976 enactment of an express pre-emption provision for medical devices, see § 521, 90 Stat. 574 (codified at 21 U.S.C. § 360k(a)), Congress has not enacted such a provision for prescription drugs”).

59 See Amicus Brief for the United States in Support of the Defendant–Appellee and Cross–Appellant, and in Favor of Reversal of the District Court’s Order Denying Partial Summary Judgment to Defendant–Appellee and Cross–Appellant at 1–2, Motus v. Pfizer, Inc., 358 F.3d 659 (9th Cir. 2004) (Nos. 02–55372, 02–55498), 2002 WL 3203084 (“The FDA . . . has a clear interest to ensure that state tort law does not undermine the agency’s authority to protect the public health through enforcement of the FDCA’s prohibition against false or misleading labeling of drug products. To require a warning of a supposed danger that FDA concludes has no actual scientific basis, no matter the warning’s language, would be to require a statement that would be false or misleading, and thus contrary to federal law. In such a case, federal law must prevail. The United States files this amicus curiae brief . . . to make clear the basis for federal preemption and the error in the district court’s opinion.”).

acquired information” or “to add or strengthen a contraindication, warning, precaution, or adverse reaction.” The 2008 Proposed Rule specifically included the statement in a footnote that generic drug manufacturers cannot utilize a procedure known as the Changes Being Effected (CBE) mechanism. This procedure allows drug manufacturers to make unilateral, post-approval labeling changes, subject to FDA notice and approval. Thus, a brand-name manufacturer who discovered evidence that suggested a drug had an inadequate warning could, prior to FDA approval, utilize the CBE procedure and change the label to indicate the new information. Although only in a footnote, the FDA inserted the following statement: “CBE [Changes Being Effected] changes are not available for generic drugs approved under an abbreviated new drug application under 21 U.S.C. 355(j). To the contrary, a generic drug manufacturer is required to conform to the approved labeling for the listed drug.”

The proposed rule specifically excluded generic drugs from the CBE requirement, thereby requiring that generic labels conform to the approved label for the listed drug. The FDA, however, issued the final rule on September 22, 2008, omitting the above reference to generic drugs. In fact, the final rule does not mention generics or the ANDA approval process for generic drugs.

The recent change in White House administration has brought about a new position with respect to preemption. On April 28, 2009, the U.S. Department of Justice, Civil Division, Appellate Staff, sent a letter to the Clerk for the U.S. Court of Appeals for the Third Circuit notifying the court that, contrary to the previous administration’s decision to participate as amicus curiae in the generic drug case of Joseph C. Colacicco v. Apotex, Inc., the new administration would not take a position on the case in light of the Supreme Court’s decision in Wyeth v. Levine. The Justice Department stated: “The [FDA] has not yet conducted the sort of reexamination of various preemption issues following the Supreme Court’s decision in [Wyeth] that would be necessary to inform a position of the United States in this case.”

Moreover, on May 20, 2009, President Obama released a memorandum to the heads of all executive departments and agencies noting that

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61 Id. The rule also dealt with changes to the biologics license application (BLA) and medical device premarket approval application (PMA).
62 Id. at 2849 n.1.
63 Id. at 2849.
64 Id. at 2849 n.1 (emphasis added).
67 Id.
“preemption of State law by executive departments and agencies should be undertaken only with full consideration of the legitimate prerogatives of the States and with a sufficient legal basis for preemption.”

The president then proceeded to clarify that preemption provisions should not be included in preambles alone without also being included in the corresponding regulation, preemption provisions should only be included where legally justified, and heads of departments and agencies should review regulations from the past ten years to determine whether preemption provisions were justified.

This statement reflects a move away from the previous administration’s public support for preemption. In addition, the Supreme Court in *Wyeth v. Levine* noted that the FDA’s position on preemption, at least under the previous administration, was not entitled to deference.

### III. The Case Against Preemption

#### A. Statutory Arguments Opposing Preemption

An examination of the statutory and regulatory provisions governing the generic drug approval process and labeling requirements reveals why arguments supporting preemption must fail. The FDCA sets forth the basic

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69 Id. at 24,693–94 (“To ensure that executive departments and agencies include statements of preemption in regulations only when such statements have a sufficient legal basis: 1. Heads of departments and agencies should not include in regulatory preambles statements that the department or agency intends to preempt State law through the regulation except where preemption provisions are also included in the codified regulation. 2. Heads of departments and agencies should not include preemption provisions in codified regulations except where such provisions would be justified under legal principles governing preemption, including the principles outlined in [Clinton] Executive Order 13132. 3. Heads of departments and agencies should review regulations issued within the past 10 years that contain statements in regulatory preambles or codified provisions intended by the department or agency to preempt State law, in order to decide whether such statements or provisions are justified under applicable legal principles governing preemption. Where the head of a department or agency determines that a regulatory statement of preemption or codified regulatory provision cannot be so justified, the head of that department or agency should initiate appropriate action, which may include amendment of the relevant regulation.”).


70 *Wyeth v. Levine*, 129 S. Ct. 1187, 1204 (2009) (noting that “Congress has repeatedly declined to pre-empt state law, and the FDA’s recently adopted position that state tort suits interfere with its statutory mandate is entitled to no weight”).
requirement in 21 U.S.C. § 352 that all drugs and devices have adequate warning labels. This provision describes the labeling requirements that prevent a drug from being misbranded. Section 352(f) states that a drug is misbranded unless it includes

(1) adequate directions for use; and (2) such adequate warnings against use in those pathological conditions or by children where its use may be dangerous to health, or against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users . . . .71

Section 352 makes no distinction between generics and brand-name drugs. It applies to both types of drugs. As a result, both generics and brand names have a statutory obligation to maintain adequate warning labels or risk being deemed misbranded and subject to removal from the market.72

FDA regulations further affirm the need to maintain adequate warning labels. The specific requirements on the content and the format of drug labeling are provided in 21 C.F.R. § 201.57. The warning must “describe clinically significant adverse reactions” and “the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established.”73

Again, the FDA makes no distinction in § 201.57 with respect to prescription generic drugs and brand-name drugs. Moreover, the language that a “causal relationship need not have been definitely established” makes clear that the FDA places importance on ensuring labels are updated to reflect new hazards as soon as “reasonable evidence” becomes known.74

B. The Statutory and Regulatory Requirements of the Approval Process for Generic and Brand-Name Drugs

As previously explained,75 the manufacturer of a generic drug submitting an application under the ANDA approval process must show that the label on the generic drug is the same as that on the reference-listed drug.76

72 21 U.S.C. § 355(e). See also Morris v. Wyeth, Inc., 642 F. Supp. 2d 677, 682 (W.D. Ky. 2009) (stating that “[f]ederal regulation simply provides that if a drug manufacturer’s label is unsubstantiated, then the FDA can remove the drug from the market”).
74 21 C.F.R. § 201.57(c)(6)(i).
75 See supra notes 39–42.
76 See 21 U.S.C. § 355(j)(2)(A)(v) (requiring “information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug”).
While the FDA may withdraw its ANDA approval should the labeling no longer conform with that of the reference-listed drug, there appear to be no instances in which the FDA has done so as a result of a generic manufacturer strengthening or adding a warning. In addition, the CBE regulations found in 21 C.F.R. § 314.70 provide a means by which drug manufacturers can make post-approval labeling changes, subject to FDA notice and approval. The question then becomes: can generic manufacturers take advantage of this provision to propose their own changes? The actual language of the regulation indicates the answer to this question is yes.

Manufacturers who submit abbreviated applications, referring to generic manufacturers who follow the ANDA process, are addressed in 21 C.F.R. § 314.97. Section 314.97 requires generic manufacturers to comply with 21 C.F.R. § 314.70 and § 314.71. Turning to § 314.70(c), this section allows a manufacturer to supplement and make other changes to an approved application. At no point does this section exclude or limit its application to only brand-name or only generic drugs. Therefore, any argument that generic manufacturers cannot take advantage of the CBE process as defined in § 314.70 to enhance their warning labels is plainly refuted by the actual language of the regulations.

During such time when the generic manufacturer implements an enhanced or new warning and the brand-name manufacturer awaits FDA approval, the labels on the generic drug and on the reference-listed drug will inevitably be different. While 21 U.S.C. § 355(j)(2)(A)(v) requires that the labels of generics and the reference-listed drugs be identical in the approval process, this later lapse in conformity has been acknowledged by the FDA. Although referring to labeling changes proposed by brand-name manufacturers instead of generic manufacturers, the FDA noted in its guidance to the drug industry that “[b]ecause the regulations state that the labeling of the generic must be the same as the innovator [brand-name drug], the revision should be made at the very earliest time possible.”

79 21 C.F.R. § 314.97.
80 Id.
81 21 C.F.R. § 314.70(c).
85 Id. at 5 (emphasis added).
The FDA knew there would be some lapse in conformity while updating the labels. Again, the FDA was referencing changes proposed by brand names. Nevertheless, it is worth recognizing that the FDA knew there would be times when the labels were not the same. To make the argument that the labels must always be identical runs counter to the FDA's own acknowledgment that sometimes, under the regulations, that will not be the case.

C. Conflict Preemption and Generic Drugs

As previously noted, under principles of conflict preemption, “state law is pre-empted if that law actually conflicts with federal law.”\(^8\) In light of the requirement that generic drug manufacturers conform the labels on their products to the labels on the approved brand-name drugs at the time they submit an application for FDA approval,\(^8\) the argument may be made that the defense of implied conflict preemption in particular, based on state-law claims for failure to warn, is strengthened for generic manufacturers. As the following cases will show, however, such arguments may be refuted by looking to the language of the applicable statutes, regulations, and case law.

1. The Timing of the Labeling Change.—Proponents of preemption insist that federal law mandates generic drug manufacturers use the same label as the brand-name manufacturer at all times.\(^8\) As already discussed, labeling differences at certain times will be inevitable.\(^8\) Moreover, courts addressing this question have focused their attention on updating labels as soon as information is available as opposed to insisting on the need to maintain identical labels.\(^8\)

This issue was raised in the case *Kellogg v. Wyeth*.\(^9\) In the years from 2000 to 2004, Ethel Kellogg took the generic drug metoclopramide, the generic form of the brand-name drug Reglan, for the treatment of gastroesophageal reflux disease.\(^9\) As a result of her prolonged use of this drug, Kellogg eventually developed a condition known as tardive dyskinesia syndrome.\(^9\) Her symptoms included oral dystonic facial grimacing, lip twisting, tongue thrusting, difficulty swallowing, and difficulty controlling her hands and

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\(^8\) See *supra* text accompanying notes 83–85.

\(^9\) *Kellogg*, 612 F. Supp. 2d at 436.

\(^9\) *Id.* at 424.

\(^9\) *Id.*
arms. Unfortunately for Kellogg, it was not until July 2004, after she had ceased taking the generic drug metoclopramide, that the FDA approved a labeling change to the brand-name drug label. The new label warned that therapy should not exceed twelve weeks. Meanwhile, Kellogg had been taking the generic form of the drug for four years. She sued, alleging that the drug’s generic and brand-name manufacturers were both liable for failing to warn her about the dangers of overexposure to the drug. The generic manufacturer countered by arguing that “because federal law require[d] them to label their product with exactly the same label as the one approved by the [FDA] for the name brand manufacturer, federal law preempt[ed] any state court tort claim based on failure-to-warn.”

The United States District Court for the District of Vermont was not persuaded by this argument and held that FDA approval of a generic drug label does not preempt state failure-to-warn claims. The court stated that “[t]he obligation to revise a label to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug applies to both generic and listed drug manufacturers.” The court refused to accept the argument made by the generic manufacturer that it was “prohibited from strengthening [its] drug labels without prior agency approval.” Rather, the generic manufacturer had an obligation to update the label as soon as information of a potential hazard surfaced. Indeed, the regulations governing these procedures “make[] clear that a generic manufacturer must take steps to warn its customers when it learns it may be marketing an unsafe drug.” Simply maintaining a label that matches the brand-name label is not sufficient for compliance. According to the court in Mensing v. Wyeth, “[21 C.F.R.] § 201.57(e) does not permit generic manufacturers passively to accept the inadequacy of their drug’s

94 Id.
95 Id. at 427. In 2009, pursuant to the Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 901, 121 Stat. 823, 922 (2007), the Food and Drug Administration ordered manufacturers of metoclopramide to add a “Boxed Warning” to their labels, warning of the potential for developing tardive dyskinesia in patients who take the drug for at least three months.
96 Kellogg, 612 F. Supp. 2d at 427.
97 Id. at 424.
98 Id. at 423–24.
99 Id. at 424.
100 Id. at 436.
101 Id. at 426 (emphasis added).
103 Mensing v. Wyeth, Inc., 588 F.3d 603, 608 (8th Cir. 2009).
104 Id. at 609.
So while it is correct to say the generic label must be the same as the brand-name label at the time of approval, it does not follow that the two must always remain identical for the sake of being the same.

In Laisure–Radke v. Par Pharmaceutical, Inc.,106 the United States District Court for the Western District of Washington held that the plaintiff’s state products liability claims, which were based on a generic manufacturer’s duty to provide adequate warnings on its labels, were not preempted by federal law.107 The defendants argued that “under federal regulations, a generic pharmaceutical manufacturer has no ability to alter the labeling of its drug product and is prohibited from providing warnings different from or in addition to those contained on the label of the reference listed drug.”108 The Laisure–Radke court rejected this contention.109 It based its reasoning in part on the fact that while generic manufacturers must submit the same label as the brand-name counterparts when seeking approval under the ANDA process, the generic manufacturer, nevertheless, has “the same power and duty to add or strengthen [its] warnings, as do the manufacturers of pioneer drugs, and therefore, the same liability.”110 The regulations governing the process for requesting changes to approved labels do not distinguish between NDAs and ANDAs.111 Thus, drugs approved through the original process and those approved through the expedited ANDA process may be held to the same standards in terms of subsequent changes to their labels based on new information.

The court in Laisure–Radke looked to the Fourth Circuit case Foster v. American Home Products Corp.112 for guidance regarding federal preemption.113 Foster specifically dealt with the question of whether a brand-name manufacturer may be held liable for negligent misrepresentation based on an injury actually caused by a generic drug. The Foster plaintiffs sued Wyeth following the death of their daughter after she took the generic form of one of the brand-name drugs Wyeth manufactured.114 While the court held that, under Maryland law, no cause of action for negligent

105 Id.
107 Id. at *18.
108 Id. at *2.
109 Id. at *10.
110 Id.
111 See 21 C.F.R. §§ 314.70, 314.71 (2009). The court in Laisure–Radke noted that the statutes on which it relied had been updated but the updates were not effective at the time the case was heard. Laisure–Radke, 2006 U.S. Dist. LEXIS 78804, at *12 n.1.
114 Foster, 29 F.3d at 166.
misrepresentation existed against one manufacturer for injuries caused by another,^{115} it also found that "manufacturers of generic drugs approved pursuant to [ANDAs] may alter a drug's labeling '[t]o add or strengthen a contraindication, warning, precaution or adverse reaction' or '[t]o delete false, misleading or unsupported indications for use or claims for effectiveness' without prior FDA approval."^{116} The court went on to note that "[w]hen a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed."^{117} Again, the specific question before the court involved brand-name manufacturers. Nevertheless, subsequent rulings by courts across the country found this reasoning persuasive.^{118}

2. CBE Provisions and Generic Drugs.—Generic manufacturers also maintain that the Changes Being Effected (CBE) process in 21 C.F.R. § 314.70 does not apply to them; therefore, they are prevented from adding or strengthening the warning labels on their products without prior FDA approval.^{119} This argument was rejected by the Kellogg v. Wyeth court upon reconsideration following the Supreme Court's decision in Wyeth v. Levine.^{120} Relying on Levine, the United States District Court for the District of Vermont noted that the Supreme Court's holding was not so narrowly drawn as to say the CBE provision applied only to

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^{115} Id. at 172.

^{116} Id. at 169 (citing 21 C.F.R. §§ 314.70(c)(2), 314.97 (1993)) (emphasis added).

^{117} Id.


^{119} See 21 C.F.R. § 314.70 (2009); see also Kelly v. Wyeth, No. 2003–3314F, 2007 Mass. Super. LEXIS 136, at *9 (Mass. Super. Ct. Apr. 12, 2007). In May of 2000, Kelly was treated for gastrointestinal problems and was prescribed a brand-name drug for which the pharmacist dispensed the generic version metoclopramide. Id. at *1–2. Kelly subsequently developed a movement disorder known as akathisia as a result of taking the generic drug. Id. at *2. The generic manufacturer, Teva, argued for summary judgment based on federal conflict preemption. Id. at *1. Teva maintained that it was impossible to comply with both FDA regulations and Massachusetts state tort law. Id. at *8–9. The court looked to the Foster v. Am. Home Prods. Corp., 29 F.3d 165 (4th Cir. 1994), decision, as well as Laisure–Raide, No.C03–3654RSM, 2006 U.S. Dist. LEXIS 78804 (W.D. Wash. Apr. 3, 2006), in deciding that even if Teva was not in a position to unilaterally change its label through the moderate changes procedure, it nevertheless had a duty to apply for a labeling change through the CBE procedures in 21 C.F.R. § 314.70(c). Id. at *13–15. The Kelly court distinguished this case from that of Dowhal v. SmithKline Beecham Consumer Healthcare, in which the defendant drug manufacturer first petitioned the FDA for permission to change the label and was later denied. Id. at *16; see Dowhal v. SmithKline Beecham Consumer Healthcare, 88 P.3d 1, 5 (Cal. 2004). By contrast, in the Kelly case, Teva had made no proposals to the FDA for a labeling change to reflect the newly discovered dangers. Kelly, 2007 Mass. Super. LEXIS 136, at *16.

brand-name drug manufacturers. The district court then undertook an analysis of Levine and the implications of its holding. It noted that the Supreme Court relied on two guiding principles in reaching its decision. The two principles on which the Court relied are as follows:

one, that "the purpose of Congress is the ultimate touchstone in every preemption case," and, two, that "in all pre-emption cases, and particularly in those in which Congress has legislated in a field which the States have traditionally occupied,' we start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress."

The Supreme Court "noted that as recently as 2007, when Congress granted the FDA the statutory authority to require a manufacturer to change its drug label," it declined to include a provision mandating FDA preapproval of all drug labeling changes, and the FDCA continues to place responsibility for updating a label on the manufacturers.

Finally, based on the above analysis, the Supreme Court held that the CBE provision allows a manufacturer to strengthen a warning without prior FDA approval. The Kellogg court expressly noted that the Supreme Court decision did not include a caveat exempting generic manufacturers from responsibility for updating labels. The Kellogg court went on to deny the defendant's motion for an immediate appeal of the court's previous decision. Thus, in the view of the Kellogg court, the CBE provision could have been used by generic and brand-name manufacturers alike. Of course, Levine did not directly involve generic drugs, so the issue has not been settled definitively.

Other courts have also taken on the issue of whether or not the CBE provision applies to generics and held in the affirmative. As the Fifth Circuit Court of Appeals noted in Demahy v. Actavis, "[T]he CBE regulation ... does not, on its face, distinguish between generic and name brand drug manufacturers; that is, it does not forbid a generic manufacturer from using the CBE process to unilaterally change a label." The court next examined the defendant Actavis's argument that, despite the plain language of

121 Id.
122 See id.
123 Id. (citing Wyeth v. Levine, 129 S. Ct. 1187, 1194 (2009)).
124 Id. (citing Levine, 129 S. Ct. at 1194-95) (ellipses omitted).
125 Id. at 440.
126 Id.
127 Id. at 441.
128 Id. at 442.
§ 314.70, the CBE provision was not available to generic manufacturers based on FDA commentary which said that “the labeling for an ANDA product must, with few exceptions, correspond to that for the reference listed drug.” However, a closer reading of the commentary, in the court’s opinion, revealed that the commentary pertained only to the pre-approval label, not the post-approval label. Furthermore, 21 C.F.R. § 314.97, entitled “Supplements and other changes to an approved abbreviated application,” instructed ANDA applicants to comply with § 314.70, which is the CBE provision. Ultimately, as the court acknowledged, “[h]ad the FDA intended to deny generic manufacturers access to CBE procedures, notwithstanding § 314.97’s plain language, we [the court] might expect the FDA to say so, either in § 314.97 or the CBE provision itself.”

At least one court has held that reaching the question of the availability of the CBE provision to generic manufacturers was not necessary to a finding that state common-law tort law claims were not preempted by federal law. In *Mensing v. Wyeth*, the Eighth Circuit Court of Appeals found it did not even need to reach the issue of CBE applicability. It held that the generic manufacturer defendants “could have at least proposed a label change that the FDA could receive and impose uniformly on all metoclopramide manufacturers if approved.” The court went on to say, “If they realized their label was insufficient but did not believe they could even propose a label change, they could have simply stopped selling the product.”

3. The Role of FDA Approval.—The court’s decision in *Kellogg v. Wyeth* also provides an illustration of why preemption should not be available to generic drug manufacturers as a defense against failure-to-warn claims. Once again, the generic company argued that its label must always be the same as the brand-name manufacturer’s and “a state common law damages action could result in requiring a warning that was not approved by the FDA.” This action, they argued, could in turn subject the manufacturer to penalties under the FDCA or the withdrawal of FDA approval.

First, the court noted that a judgment for damages does not require

130 Id. at *7 (citing 57 Fed. Reg. 17950-01(1992)).
131 Id.
132 Id. at *8.
133 Id.
134 Mensing v. Wyeth, Inc., 588 F.3d 603, 608 (8th Cir. 2009).
135 Id.
136 Id. at 611.
138 Id. at 430.
139 Id.
a drug manufacturer to alter anything on its label. The FDA would have to initiate an action in federal court to address a misbranding violation. The court was quick to note that no evidence existed to show that the FDA had ever proposed the withdrawal of approval for a generic drug because its manufacturer sought to strengthen a label warning. The court went on to state that at any time in the process

a generic manufacturer having new information about the hazards of a drug could have availed itself of the CBE process, could have sought FDA approval for a change in the drug labeling, could have provided health care professionals with stronger warnings, or could have elected not to act and to accept the risk of tort liability should an injured plaintiff prevail on her suit. It was thus not physically impossible to comply with state and federal law.

In terms of obstacle preemption, the Kellogg court was also unable to find preemption on these grounds. First, looking to the history of the FDCA, the court could find “[n]othing in the statute indicat[ing] that tort actions would henceforth stand as an obstacle to these Congressional objectives” of providing lower cost generic drugs.

The defendants instead argued that jury verdicts would, in fact, be “an obstacle to the FDA’s regulations.” In support of their position pertaining to preemption, the defendants cited to a 2006 final rule amending drug labeling regulations, in which the FDA maintained that its regulations with respect to the ANDA and NDA labeling requirements “actually impose a federal ceiling as well as a floor, and that it ‘believes that . . . FDA approval of labeling under the [FDCA] . . . preempts conflicting or contrary State law.” Observing that although the FDA has the authority to engage in rulemaking regarding drug safety, the court did not find that “the agency’s opinion on preemption of State law [was] ‘promulgated in the exercise of that authority.’” Instead, the statement was made in the preamble where

141 Id. (citing Rice v. Norman Williams Co., 458 U.S. 654, 659 (1982)) (noting that “[a] hypothetical or potential conflict is insufficient to warrant preemption”); see also Witczak v. Pfizer, Inc., 377 F. Supp. 2d 726, 731 (D. Minn. 2005) (declining to find an irreconcilable conflict based on “assumptions of what the FDA would have done if defendant had unilaterally strengthened its warning label.
142 Kellogg, 612 F. Supp. 2d at 431.
143 Id. at 432.
144 Id.
145 Id. (citing Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006) (to be codified at 21 C.F.R. pts. 201, 314, & 601)).
146 Id. at 433.
it was not subject to the notice and comment process, thereby entitling it only to Skidmore deference and thus without the authority to preempt.

In further support of this argument against preemption, the court in Mensing v. Wyeth refused the defendant Wyeth's argument that compliance with state and federal law would "obstruct the purposes and objectives of federal law." The generic defendants maintained that proposing a labeling change would result in expensive clinical studies, thereby obstructing the primary purpose of the Hatch-Waxman Amendments, which was to provide low-cost generic drugs more quickly. The court was not persuaded. Generic manufacturers already have a duty to collect and report adverse drug reactions. Moreover, state tort law claims such as the plaintiff's "lend force to the FDCA's premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times."

It should also be noted that a finding of preemption would leave plaintiffs with no avenue in which to seek redress. A finding of preemption of "state failure-to-warn claims would foreclose a remedy that was traditionally available and for which federal law provides no substitute."

To completely take away such state remedies is to leave plaintiffs without a cause of action.

4. Field Preemption and Generic Drugs.—Generic manufacturers have also attempted to rely on principles of field preemption, arguing that only the FDA may determine whether a generic drug label should be revised and arguing against a role for state tort litigation. However, the court in Kellogg v. Wyeth directly countered this contention in saying "the Hatch–Waxman Amendments to the FDCA were enacted in 1984, against the backdrop of decades of federal drug labeling regulation coexisting with state tort litigation." Schrock v. Wyeth, Inc. expressed this same sentiment, noting the "longstanding coexistence of state and federal law in the regulatory history and background" in federal drug labeling regulations.

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147 Id. (citing 21 C.F.R § 10.85(d)(1) ("a statement of policy or interpretation other than the text of a proposed or final regulation constitutes an advisory opinion").
148 Id.; see Skidmore v. Swift & Co., 323 U.S. 134, 140 (1944) (considering the deference to be given an agency administrator's decision by looking to the "thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade").
149 Mensing v. Wyeth, Inc., 588 F.3d 603, 608 (8th Cir. 2009).
150 Id. at 611.
151 Id. at 612.
152 Id. (quoting Wyeth v. Levine, 129 S. Ct. 1187, 1202 (2009)).
155 Id. at 441.
Congress is adept at including preemption provisions when it so chooses, and it clearly chose not to do so in the case of state common-law failure-to-warn claims involving generic drug manufacturers. Moreover, as previously explained, Congress included a preemption provision for medical devices in the FDCA.\textsuperscript{157} It did not, however, include a preemption provision for either brand-name or generic drugs.\textsuperscript{158} It thus seems clear that Congress expected federal and state law to coexist in this field.

5. Conclusion.—Ultimately, generic drug manufacturers may use CBE procedures to update their labels following ANDA approval and, therefore, they should be held liable for failure to warn under state tort law when they fail to update their warning labels to reflect new information. The FDCA includes no express preemption provisions, and support for implied preemption is lacking. Allowing generic drug manufacturers to argue that state tort claims are barred by federal preemption principles ignores the fact that the existing statutes and regulations provide mechanisms by which generic manufacturers may unilaterally update their labels. Thus, the defense of "federal preemption" should not be available to generic manufacturers.

IV. The Case for Preemption

Despite the number of courts declining to find that state tort law claims against generic manufacturers are preempted,\textsuperscript{159} those manufacturers are not without case law supporting their position in favor of preemption.\textsuperscript{160}

\textsuperscript{158} Stacei v. Teva Pharms., USA, 620 F. Supp. 2d 899, 904 (N.D. Ill. 2009).
\textsuperscript{159} See supra Part III.C.
\textsuperscript{160} See Colacicco v. Apotex, Inc., 432 F. Supp. 2d 514, 538 (E.D. Pa. 2006). Colacicco dealt with yet another products liability suit against both the brand-name and generic drug manufacturers based on the labeling deficiencies of a generic drug that allegedly contributed to the plaintiff's wife's suicide. Id. at 518. Similar to the ruling in Foster v. American Home Products Corp., 29 F.3d 165, 166 (4th Cir. 1994), the district court in Colacicco dismissed the complaint against the brand-name manufacturer, finding that the manufacturer did not owe the plaintiff a duty of care when the plaintiff was actually injured by a drug produced by a generic company. Colacicco, 432 F. Supp. 2d at 538-39. The court then ruled that claims against the generic manufacturer were preempted, and the company could not be held liable as a result of FDA regulations which precluded them from strengthening their labels. Id. at 537-38. Finally, the court ruled that preemption was appropriate because the FDA had considered and rejected the particular warning the plaintiff claimed should have been given. Id. at 538.

While the FDA under the previous administration submitted an amicus brief in this case affirming its view that the plaintiff's claims were preempted as a result of the FDA's rejection of the proposed warning at issue, the current administration has since withdrawn its support for the preemption position in light of the Supreme Court decision in Wyeth v. Levine. See supra notes 59, 66-67 and accompanying text. Moreover, the Colacicco decision has since been reversed and remanded based on Levine. Colacicco v. Apotex, Inc., 129 S. Ct. 1578 (2009).
Even in light of the *Wyeth v. Levine* decision, at least one federal district court was willing to still find that state tort law claims against a generic manufacturer for inadequate labeling were preempted based on impossibility conflict preemption.\(^\text{161}\) In *Gaeta v. Perrigo Pharmaceuticals Co.*, the defendant Perrigo was initially granted summary judgment in a case involving a child who sustained liver damage as a result of taking generic over-the-counter ibuprofen.\(^\text{162}\) Following the Supreme Court's decision in *Levine*, the plaintiffs filed a motion for reconsideration.\(^\text{163}\) Nevertheless, the district court declined to change its position, placing strong emphasis on the fact that "[u]nlike in *Levine*... the drug at issue here is a generic rather than a brand-name product."\(^\text{164}\) The court did not read the *Levine* decision as affecting its holding in *Gaeta*.

One of the primary differences in courts finding preemption of state tort law claims against generic manufacturers and those declining to find preemption is the availability of the CBE provision. The *Gaeta* court held that the CBE provision was not available to generic manufacturers and, therefore, a generic manufacturer could not change its label without prior FDA approval.\(^\text{165}\) It did, however, acknowledge the split of opinion among district courts on this very issue.\(^\text{166}\)

In *Conte v. Wyeth, Inc.*, decided prior to *Wyeth v. Levine*, the court held that the brand-name manufacturer Wyeth had a common-law duty to use due care in formulating its warning and that its duty extended to patients and doctors who foreseeably relied on that information, whether it be a


\[^{164}\] Id. at *3.

\[^{165}\] Id. The court based its decision in part on 21 C.F.R. § 314.93, which reads:

A person who wants to submit an abbreviated new drug application for a drug product which is not identical to a listed drug in route of administration, dosage form, and strength, or in which one active ingredient is substituted for one of the active ingredients in a listed combination drug, must first obtain permission from FDA to submit such an abbreviated application.


\[^{166}\] *Gaeta*, 2009 WL 4250690, at *4. The *Gaeta* court also reconsidered the issue of field preemption and the scope of FDA's authority in drug labeling. Id. at *5. The court agreed that the *Levine* case addressed questions concerning the deference to be given to the Preamble and did not use this theory of preemption as a basis for its decision in reconsidering its decision to grant summary judgment to Perrigo. Id.
brand-name drug or its generic equivalent. As a further demonstration of the differences among courts over liability for generic and brand-name manufacturers, the court declined to follow the reasoning of the Foster court and instead held that a brand-name manufacturer could in fact be held liable for inadequate product warnings despite the fact that the plaintiff took a generic form of the drug. The court affirmed summary judgment in favor of the generic manufacturers without discussing issues of preemption. The plaintiff could not prove that her doctor read and relied on the warnings for the generic drug, thereby failing to establish proximate cause. This case only confirms the need for the issue to be definitively resolved by either Congress or the Supreme Court.

In Morris v. Wyeth, also decided prior to the Supreme Court's decision in Wyeth v. Levine, the United States District Court for the Western District of Kentucky denied a plaintiff's motion for reconsideration of the court's dismissal of his strict liability and negligence failure-to-warn claims against the generic manufacturers of the drug metoclopramide. The plaintiff maintained that he was injured as a result of the generic manufacturers' failure to warn of the long-term effects of taking the drug. The district court initially dismissed his claims based on federal preemption. In its reconsideration of his claims, the court first turned to questions involving conflict preemption, rejecting the reasoning of the court in McKenney v. Purepac Pharmaceutical Co., which held that an actual conflict arises only where the generic manufacturer sought a heightened warning that the FDA expressly precluded.

In McKenney, the court concluded that "the FDA's ability to withdraw both brand and generic drugs bearing labels with unsubstantiated claims from the market [is] evidence that regulation of brand and generic drug labeling is indistinguishable for preemption purposes." But the Morris court disagreed. The ability of the FDA to withdraw both types of drugs from the market did not, in its opinion, mean they could both unilaterally change their labels. The two were separate considerations. The court

168 See supra note 112 and accompanying text.
169 Conte, 85 Cal. Rptr. 3d at 304-05.
170 Id. at 320.
171 Id. at 318-19.
173 Id.
174 Id. at 680.
175 Id. at 681-83 (citing McKenney v. Purepac Pharm. Co., 83 Cal. Rptr. 3d 810 (Cal. Ct. App. 2008)).
176 McKenney, 83 Cal. Rptr. 3d at 820.
177 Morris, 642 F. Supp. 2d at 682 (citing McKenney, 83 Cal. Rptr. 3d at 818).
178 Id.
ultimately declined to follow the McKenney finding that the federal regulation of brand-name and generic drugs is indistinguishable for federal preemption purposes.\textsuperscript{179} It considered the two to be different, and while brand names had the ability to change their labels unilaterally, generics could not.

The court considered the questions concerning when a manufacturer “should” as opposed to “must” notify the FDA about a change in safety information for an approved drug application.\textsuperscript{180} The applicable regulations for the ANDA approval process, which apply to generic drug manufacturers, state that an ANDA holder “should” notify the FDA when new safety information comes to light that should be added to a label.\textsuperscript{181} However, an NDA holder which has gone through the process that applies to brand-name drugs “must” notify the FDA about a change in safety information.\textsuperscript{182} Thus, the requirements imposed on generic versus brand-name drugs are different. The court then stated that whether or not an NDA holder is able to unilaterally change its label is an open question to be resolved by the Supreme Court in Wyeth v. Levine, which was pending at the time.\textsuperscript{183}

The Supreme Court later answered this question in the affirmative. In Wyeth v. Levine, the Court stated that “[t]he CBE regulation permitted Wyeth to unilaterally strengthen its warning, and the mere fact that the FDA approved Phenergan’s label does not establish that it would have prohibited such a change.”\textsuperscript{184} While this holding does not definitively settle the question for generic manufacturers, it does not close the door on state failure-to-warn claims against generic manufacturers as a ruling to the contrary would have done. Had the Court held brand-name manufacturers could not unilaterally change their labels without prior FDA approval, it would be arguably more difficult to claim generic manufacturers could do so.

The fact remains that Congress has not spoken directly to the preemption issue, nor has the Supreme Court had an opportunity to address the specific question pertaining to generics. That being said, the Supreme Court has stated that “[i]n all pre-emption cases, and particularly in those in which Congress has ‘legislated . . . in a field which the States have traditionally occupied,’ we ‘start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was

\textsuperscript{179} Id. at 683.
\textsuperscript{180} Id. at 682.
\textsuperscript{181} Id. (citing Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17950, 17961 (Apr. 28, 1992) (to be codified at 21 C.F.R. pts. 2, 5, 10, 310, 314, 320, & 433)).
\textsuperscript{182} Id. (citing Applications for FDA Approval to Market a New Drug, 21 C.F.R. § 314.70(a) (2009)).
\textsuperscript{183} Id.
the clear and manifest purpose of Congress." In addition, as noted by the court in Kellogg v. Wyeth, "It is precisely where Congress has not included an express statement concerning the preemptive effect of its enactment that courts must be mindful that they do not lightly tread on the historic powers of states to protect the health and welfare of their citizens, and apply the presumption." This presumption against preemption has particular force in implied preemption cases where congressional intent is not clear.

Questions involving the presumption against preemption were also raised in Wyeth v. Levine, in which Wyeth argued the presumption should not apply "because the Federal Government has regulated drug labeling for more than a century." The Court disagreed with Wyeth's reasoning, instead noting that the presumption was meant to respect "States as 'independent sovereigns in our federal system,'" which in turn led the Court to note that "Congress does not cavalierly pre-empt state-law causes of action." In his dissent, Justice Alito questioned the application of the presumption against preemption to conflict preemption cases in general. The majority, however, disagreed with this assertion, instead citing a number of cases to the contrary in which the presumption had been upheld.

While Levine dealt with the presumption in the context of brand-name drugs, Barnhill v. Teva Pharmaceuticals USA, Inc., addressed this issue with regard to generic drugs. The district court acknowledged the traditional domain of public health and safety issues as within the states' powers and presumed that "Congress did not intend to supersede the states' powers to regulate." A generic manufacturer would have to show a conflict between state tort law on health and safety matters and federal labeling requirements sufficient to overcome the presumption that the two can coexist. The defendant in Barnhill was unable to establish this conflict. The fact remains that it is possible to comply with federal labeling requirements.

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187 Levine, 129 S. Ct. at 1195 n.3.
188 Id.
189 Id. (citing Medtronic, Inc., 518 U.S. at 485).
190 Id. at 1228–29 (Alito, J., dissenting).
193 Id. at *6 (citing Hillsborough County, 471 U.S. at 715).
194 Id. at *7.
195 Id. at *10–14.
and state warning laws.196

V. POLICY CONSIDERATIONS

Two critical points must be kept in mind: the number of generic drugs on the market being prescribed is only continuing to rise,197 and doctors and pharmacists need to be aware of any dangers associated with the use of such drugs. Relying on the brand-name drug manufacturer alone to maintain an adequate warning label when that label could in fact be deficient is risky at best and outright dangerous at worst. As the market share for generic drugs increases and the share for brand-name drugs decreases,198 the incentive for brand-names to maintain adequate labels may be lessened.

The Morris v. Wyeth, Inc., case also draws attention to the policy considerations underlying the issue of generic drugs and preemption. Morris argued that "the economic burden placed on generic manufacturers to comply with heightened state failure-to-warn liability does not outweigh the life-saving benefit of clearly informing consumers about the risks associated with taking metoclopramide."199 Morris noted that (1) generic manufacturers dominate the market for metoclopramide sales, and (2) the defendants "were aware of the safety concerns associated with [the drug]."200 The defendants, in turn, looked to the initial passage of the Hatch-Waxman Amendments, which were passed with the purpose of making lower-cost generic drugs available to the public "at the risk that not all drugs would be safe for every consumer."201 The court acknowledged these competing interests, yet ultimately sided with the defendants.202

While passage of the Hatch-Waxman Amendments was undoubtedly meant to lower the cost of drugs available to consumers,203 to say that Congress did not equally value the health and safety of the consumers who would ultimately be benefited or harmed by taking the drugs stretches all reasoning. What purpose does an inexpensive drug serve if its side effects lead to dangerous and severe consequences of which the prescribing doctor is unaware?

Equally noteworthy in terms of public policy were the attorneys general of forty-seven states who joined an amicus brief opposing federal conflict preemption for brand-name manufacturers in the Supreme Court

196 Id. at *11.
197 See Facts at a Glance, supra note 27.
198 See id.
200 Id.
201 Id.
202 Id. at 689.
203 See supra note 33.
case, *Wyeth v. Levine.*\(^{204}\) The court in *Morris* noted that while the attorneys general argued that state tort liability does not conflict with federal labeling regulations or interfere with the FDCA, it did not find the brief persuasive.\(^{205}\) Nor was it persuaded by the views of the congressman who originally co-sponsored the Hatch–Waxman Amendments and opposed preemption—U.S. Representative Henry A. Waxman.\(^{206}\) In an amicus brief submitted on behalf of the respondent Levine, eighteen members of Congress joined in opposing preemption of state-law claims, stating that

> [a]ltering the construction of the FDCA at this late date would also frustrate congressional intent and impair the statutory system of federal prescription drug regulation. Far from standing "as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress," state-law claims against pharmaceutical manufacturers "necessarily perform an important remedial role in compensating" injured individuals and in encouraging drug safety.\(^{207}\)

If the amicus brief may stand as an indication of congressional intent, it is quite clear that Congress did not intend to bar state-law claims and saw the importance in allowing such claims.

Despite the fact that the Supreme Court has yet to definitely rule on this issue, it is clear that states and public officials are paying attention to it. Public officials certainly have an interest in ensuring the availability of low-cost drugs. Nevertheless, they also bear a duty to ensure the drugs on the market contain adequate precautions designed to warn consumers of the adverse effects associated with taking such drugs.

**CONCLUSION**

As the number of generic drugs on the market continues to rise,\(^{208}\) issues involving generics and preemption will only continue to confront courts. In *Morris v. Wyeth, Inc.*, the court even acknowledged that the cases cited by the plaintiff were "evidence [of] an emerging split of authority among lower courts over whether FDA regulation of generic drug

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205 *Morris, 642 F. Supp. 2d* at 688.
208 See *Facts at a Glance, supra* note 27.
labeling preempts state failure-to-warn claims." That being said, the decision handed down in *Wyeth v. Levine* goes a long way toward answering preemption questions about prescription drugs in general. The *Kellogg* court noted, in reference to preemption and generic drugs, that "the recent *Levine* decision reduces substantially the grounds for difference of opinion concerning whether federal law preempts state law failure-to-warn cases against drug manufacturers."210

Ultimately, when a drug injures a person as a result of an inadequate warning label, the manufacturer of that drug should be held liable. FDA procedures exist for generic manufacturers to alter or update a warning label. The protection of consumers necessitates that doctors receive the information they need to prescribe safely a drug. This requirement, in turn, means that warning labels must be as accurate as possible and warnings must be updated as soon as new information becomes known. Even if the brand-name manufacturer updates its warning without undue delay, it may take some time before the change is actually indicated on the generic label.211 Permitting generic drug manufacturers to hide behind brand-name manufacturers and the cloak of federal preemption will only lead to further delays and complications in getting safety information to the doctors who rely on the warnings when prescribing drugs. Generic manufacturers therefore should not be permitted to use the defense of federal preemption in defeating state failure-to-warn claims by patients injured as a result of taking those drugs.

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211 Julie Schmit, *Updating Generic–Drug Labels Can Take Months*, USA Today, Apr. 21, 2005, at 3B.