

**Generic Drugs and Preemption:
An Analysis of Post-*Levine* Developments,
Trends, and Risk Management Going Forward**

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I. LAYING THE GROUNDWORK: A BRIEF OVERVIEW OF THE PREEMPTION DOCTRINE AND KEY LABELING REGULATIONS FOR NAME BRAND MEDICATIONS

A. Preemption Doctrine

The preemption doctrine is derived from the Supremacy Clause of the United States Constitution, which states, “[t]his Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land” U.S. CONST. art. VI, cl. 2.

As a result of the Supremacy Clause, federal law sometimes preempts state law, either expressly or impliedly. *Bartlett v. Mutual Pharm. Co.*, 2009 WL 3126305, at *9 (D.N.H. Sept. 30, 2009). There are two types of implied preemption: field preemption and conflict preemption. *Id.* “Conflict preemption” exists when “compliance with both federal and state regulations is a physical impossibility,” or state law “stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.” *Pac. Gas & Elec. Co. et al. v. State Energy Res. Conversation & Dev. Comm’n*, 461 U.S. 190, 204 (1983) (citations omitted). Evidence of an actual conflict can include statutory language, regulatory history, or agency commentary. *Geier v. Am. Honda Motor Co., Inc.*, 529 U.S. 861, 885 (2000). Pharmaceutical companies use conflict preemption as a defense against state law failure-to-warn claims.

B. Key Labeling Regulations for Brand-Name Medications

- **New Drug Application (“NDA”)**
 - An NDA is an application submitted prior to FDA approval, demonstrating drug safety and effectiveness. 21 U.S.C. § 355(b)(1) (2008).
 - NDAs must include proposed labeling for a new drug. The FDA can approve or reject NDA labeling. 21 U.S.C. § 355(b), (d); 21 C.F.R. § 314.105 (2008).
 - “The FDA’s premarket approval of a new drug application includes the approval of the *exact text* in the proposed label.” *Wyeth v. Levine*, 129 S. Ct. 1187, 1196 (2009) (emphasis added) (citing 21 U.S.C. § 355; 21 C.F.R. § 314.105(b) (2008)).
- **Changes Being Effected (“CBE”)**
 - “Generally speaking, a manufacturer may only change a drug label after the FDA approves the supplemental application. There is, however, an FDA regulation that permits a manufacturer to make certain changes to its label before receiving the agency’s approval.” *Levine*, 129 S. Ct. at 1196.
 - “Among other things, this ‘changes being effected’ (CBE) regulation provides that if a manufacturer is changing a label to ‘add or strengthen a

contraindication, warning, precaution, or adverse reaction’ or to ‘add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product,’ it may make the labeling change upon filing its supplemental application with the FDA; it need not wait for FDA approval.” *Levine*, 129 S. Ct. at 1196 (citing 21 C.F.R. §§ 314.70(c)(6)(iii)(A), (C)).

- Changes made without prior FDA approval must be based on “newly acquired information” and there must be “sufficient evidence of a causal association with the drug.” 73 Fed. Reg. 49,603, 49,604 (Sept. 22, 2008) (to be codified at 21 C.F.R. pts. 314, 601, 814).
- Newly acquired information is not limited to new data, but also encompasses “new analyses of previously submitted data.” 73 Fed. Reg. at 49,604.

II. WYETH V. LEVINE: A CHANGE IN COURSE FOR FEDERAL PREEMPTION

On March 4, 2009, the Supreme Court decided *Wyeth v. Levine*, 129 S. Ct. 1187 (2009). This long-awaited 6-3 decision marked a change in course for federal preemption. The Court held that FDA name brand drug regulations did not conflict with a state law failure-to-warn claim, and therefore did not preempt such a claim. The Court’s decision, along with its regulatory analysis, opened the door for previously-discouraged state law failure-to-warn claims. However, *Levine* is not a blanket denial of preemption; there are certain limitations to the Court’s holding. As explained in Section VIII, *infra*, these limitations may serve as a framework for drug manufacturers’ risk management and litigation exposure assessments.

A. Summary

The plaintiff (*Levine*) was injected with Phenergan, a name brand drug, by IV-push administration. The drug inadvertently entered *Levine*’s artery and caused gangrene, resulting in amputation of her forearm. IV-push administration is accompanied by a greater risk of intra-arterial exposure. However, “[w]hile Phenergan’s labeling warned against intra-arterial injection,” it did not “contain a specific warning about the risks of IV-push administration.” *Levine*, 129 S. Ct. at 1192. *Levine* brought a state law failure-to-warn claim against the drug manufacturer (*Wyeth*) in state court, arguing the drug’s warning label should specifically disallow IV-push administration or provide more strenuous warnings related to the risks of IV-push administration. *Id.* at 1191-92. *Wyeth* defended based on federal conflict preemption. *Id.* at 1192. The trial court rejected *Wyeth*’s preemption arguments, and the jury found for *Levine*. *Id.* The Vermont Supreme Court affirmed. *Id.* The United States Supreme Court granted certiorari on the issue of conflict preemption, and held that federal name brand drug regulations did not preempt this state law failure-to-warn claim. *Id.* at 1191.

B. Analysis

The Supreme Court held no federal conflict preemption because the state duty to warn did not make compliance with federal regulations impossible, and did not act as an obstacle to congressional objectives.

In its reasoning, the Court noted two factual propositions established by the trial court. First, Levine's injury would not have occurred if Phenergan's label had included an adequate warning about the risks of IV-push administration. *Id.* at 1194. Second, the critical defect in Phenergan's label was the lack of an adequate warning regarding the risks of IV-push administration. *Id.*

Further, the Court allowed its analysis to be guided by "two cornerstones" of "pre-emption jurisprudence." *Id.* First, the "purpose of Congress is the ultimate touchstone in every pre-emption case." *Id.* The Court conducted a historical review of federal drug labeling regulations to help it identify the "purpose of Congress." *Id.* at 1195. In this exercise, the Court identified three events that shaped congressional purpose: in 1962, Congress shifted the burden to show a drug is safe for the public from the FDA to the manufacturers; in 1976 Congress enacted a preemption provision for medical devices but not for drugs; and in 2007, Congress required manufacturers to change a drug's label based on safety information that becomes available after a drug's initial approval. *Id.* at 1195-96. Second, the Court utilized the presumption against preemption: in all preemption cases "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.'" *Id.* at 1194-95 (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996)).

With the two facts, the regulatory framework, and the presumption in mind, the Court first analyzed conflict preemption via impossibility. It noted the FDA's premarket approval of a new drug application includes approving the exact text in the proposed label, and generally a manufacturer may only change a drug's label after the FDA approves a supplemental application. *Id.* at 1196. However, the Court also noted the manufacturer may make certain changes to a drug's approved label without FDA preapproval; the CBE regulation allows a manufacturer to unilaterally add or strengthen a label's warnings. *Id.* It reasoned that these changes are not limited to new data, but encompass "new analyses of previously submitted data." *Id.* at 1196-97. Further, though the FDA can reject label changes made under the CBE, the Court held that Wyeth provided no clear evidence the FDA would have rejected Levine's proposed changes to Phenergan's label. *Id.* at 1198. Without clear evidence that the FDA would have rejected such changes, the Court declined to conclude Wyeth could not comply with both state and federal requirements. *Id.*¹

In response to Wyeth's arguments, the Court held that changing a drug's approved label pursuant to the CBE would not have rendered Phenergan misbranded because misbranding focuses on the substance of the label, not an increased warning. *Id.* at 1197. Additionally, the

¹ Although Wyeth did propose different warning language in 1988, the trial court and the Vermont Supreme Court found that the modification "did not differ in any material respect from the FDA-approved warning." *Id.* at 1199 n.5.

FDA's determination that a drug is misbranded is not conclusive. *Id.* The Court also held that changing the label via the CBE would not have constituted an unauthorized distribution of the drug, because additions to a drug's label do not create a new drug. *Id.*

The Court concluded that when the risk of gangrene from IV-push administration of Phenergan became apparent, Wyeth had a state law duty to provide a warning that adequately described the risk, and the CBE regulation permitted Wyeth to unilaterally provide such a warning. Thus, complying with this state law duty would not make it impossible for Wyeth to comply with FDA regulations.

The Court next analyzed conflict preemption as an obstacle to congressional objectives. In light of the FDA's regulatory framework for drugs, the Court held it is not Congress's purpose to establish both a "floor and a ceiling" for drug regulation. *Id.* at 1199. To support this conclusion, the Court pointed to the fact that the FDCA did not provide a remedy for consumer harm between its enactment in 1906 until 1938 because Congress relied on state tort actions to protect consumers. *Id.* at 1199-1200. Further, the Court emphasized that Congress did not enact an express preemption provision for drug regulation, like it had for medical devices. *Id.* at 1200.

Regarding the FDA's 2006 preamble stating the Act establishes a floor and a ceiling for drug regulation and preempts state law, the Court noted the preamble is not an agency regulation with the force of law. *Id.* A preamble might receive some weight in a preemption analysis, depending on its thoroughness, consistency, and persuasiveness. *Id.* at 1201. Yet, under this standard, the Court held the 2006 preamble receives no deference. *Id.* The Court declined to find the preamble thorough, consistent, or persuasive for several reasons: the FDA previously stated the Act would not preempt state law and then wrote the preamble without giving a notice-and-comment period; the preamble is at odds with the above-established congressional purpose in regulating drugs; and the preamble reverses the FDA's longstanding position that state law provides complimentary drug regulation. *Id.* at 1201-02. The Court then distinguished *Geier v. Am. Honda Motor Co.*, 526 U.S. 861 (2000), where it held that the federal regulatory scheme preempted state tort claims. *Id.* at 1203. The Court noted the difference between the regulatory schemes in *Geier* and this case, and discussed this case's lack of a specific agency regulation claiming federal preemption that bears the force of law. *Id.* As a result, the Court concluded Levine's state law failure-to-warn claim did not present an obstacle to congressional drug regulation objectives, and thus was not conflict preempted.

Justice Breyer concurred, and Justice Thomas concurred in the judgment. Justice Alito, along with Chief Justice Roberts and Justice Scalia, dissented.

C. Limitations and Exceptions

Although *Levine* cuts back on federal conflict preemption, the Court left the door slightly ajar for a different outcome under different facts. The Court's obstacle conflict preemption analysis is broad. Despite the dissent's completely different analysis of congressional objectives in drug regulation, this avenue may be closed. However, litigants may still be able to distinguish their cases under impossibility conflict preemption. In particular, generic drug manufacturers may be able to successfully argue impossibility conflict preemption based on the regulations that

tie generic drug labels to their name brand counterparts. This paper discusses recent federal court decisions regarding generic drugs and federal conflict preemption of state law failure-to-warn claims. Additionally, please see Section VIII(B), *infra*, for a discussion of *Levine*'s limitations and the implications for risk management.

III. PREEMPTION AND GENERIC DRUGS: THE HATCH-WAXMAN AMENDMENTS, KEY REGULATIONS, AND CBE APPLICABILITY

A. The Hatch-Waxman Amendments—Abbreviated New Drug Application (“ANDA”)

- The Hatch-Waxman Amendments codified ANDA procedures.
- According to ANDA requirements, a generic manufacturer must submit “information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug . . . except for changes required because of differences approved under a petition . . . or because the new drug and the listed drug are produced or distributed by different manufacturers” 21 U.S.C. § 355(j)(2)(A)(v).
- “If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition” 21 U.S.C. § 355(j)(2)(C).
- If a generic drug label is different from its name brand counterpart, the abbreviated application must include investigatory evidence that the modified label demonstrates safety and effectiveness. 21 U.S.C. § 355(j)(2)(C).²

B. Changes Being Effected (“CBE”)

- The CBE is located in 21 C.F.R. § 314.70(c)(6)(iii), in Subpart B, which is applicable to “new applications.” *Stacel v. Teva Pharm.*, 620 F. Supp. 2d 899, 905 (N.D. Ill. 2009). It states that drug labels may be changed prior to FDA approval to “add or strengthen a contraindication, warning, precaution, or adverse reaction,” or to “add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product” § 314.70(c)(6)(iii)(A), (C).
- Subpart C, rather than Subpart B, is applicable to generic applications. *Stacel*, 620 F. Supp. 2d at 905.

² Typically, a generic drug’s bioequivalence requirement demonstrates a generic drug’s safety and effectiveness. 21 U.S.C. § 355(j)(2)(A)(v).

- However, 21 C.F.R. § 314.97, in Subpart C, states, “[t]he [generic] applicant shall comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental applications and other changes to an approved abbreviated application.” § 314.97.
- This indicates generic manufacturers are required to comply with the CBE regarding generic labels.

IV. POST-*LEVINE* FEDERAL GENERIC DRUG CASES AGAINST PREEMPTION

A. *Schrock v. Wyeth, Inc.*, 601 F. Supp. 2d 1262 (W.D. Okla. March 11, 2009)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia, a movement disorder. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and tardive dyskinesia. The court denied the generic manufacturer’s motion to dismiss based on federal conflict preemption.

Reasoning

Schrock interpreted *Levine* broadly, holding “the United States Supreme Court has clearly concluded that Congress did not intend [to] preempt state-law failure-to-warn actions.” 601 F. Supp. 2d at 1265. Although *Schrock* involved a generic drug, the court noted defendants’ preemption arguments were “similar, if not identical” to those proffered in *Levine*. *Id.* The court addressed both arguments, holding it is not impossible for drug manufacturers to comply with both federal drug regulations and the state law duty to warn, and the applicable state law regarding drug labeling is not an obstacle to congressional objectives.

(1) Conflict preemption—impossibility:

- *Schrock* quoted *Levine*’s analysis of congressional intent regarding a drug manufacturer’s responsibility to maintain adequate drug labeling: “With respect to a change in drug labels based upon safety information which becomes available after a drug’s initial approval, Congress adopted a rule of construction to make it clear that manufacturers remain responsible for updating their labels. Furthermore, a central premise of federal drug regulation [is] that the manufacturer bears responsibility for the content of its label at all times, and is charged with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.” *Id.* at 1264 (internal quotations omitted). The court then reiterated *Levine*’s statement that unless defendants make a clear evidentiary showing that the FDA would reject a label

change made to comply with a state law duty, making such a change is not impossible. *Id.*

- *Schrock* concluded that when the federal regulations allow a manufacturer to “unilaterally strengthen its warning,” and it is not clear the FDA would reject such a change, “it is not impossible [for a manufacturer] to comply with both federal and state requirements.” *Id.* at 1265.
- This conclusion relies on *Levine*’s understanding of the CBE without independent analysis as to whether that regulation applies to generic drugs.

(2) Conflict preemption—obstacle:

- *Schrock* rejected the argument that the state law duty to provide stronger warnings would be an obstacle to the purposes and objectives of federal drug labeling regulation. *Id.*
- The court quoted *Levine*’s conclusion: “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 [relevant statute’s] 70-year history.” *Id.*
- *Schrock* noted the long-standing coexistence of state and federal law in the regulatory history and background of drug labeling, and consequently concluded a state law failure-to-warn action is not an obstacle to congressional purposes and objectives in regulating drug labeling. *Id.*

Significance

The first written opinion after *Levine*, *Schrock* has the effect of taking a strong stand against preemption for generic drugs. However, *Schrock* did not acknowledge the regulatory differences between name brand labeling and generic labeling when applying *Levine*’s impossibility conflict preemption analysis. *Schrock*’s lack of tailored analysis weakens its persuasiveness and applicability.

B. *Stacel v. Teva Pharm.*, 620 F. Supp. 2d 899 (N.D. Ill. March 16, 2009)

Summary

The plaintiff ingested the generic version of Minocin and subsequently suffered from lupus. She brought claims against the generic manufacturer for failure to warn about the relationship between ingestion of the drug and lupus. The court denied the defendant’s motion to dismiss based on federal conflict preemption.

Reasoning

Unlike *Schrock*, *Stacel* considered the regulatory differences between name brand labeling and generic labeling. However, after acknowledging these differences and conducting its own analysis of the regulations applicable to generic drugs, *Stacel* concluded the plaintiff's state law failure-to-warn claim was not conflict preempted because the CBE applies to generic manufacturers, and congressional objectives for generic drug labeling are the same as those for name brand drug labeling. 620 F. Supp. 2d at 905, 907.

Stacel held defendant's compliance with both the state law duty to warn and the federal labeling regulations for generic drugs is not impossible. *Id.* at 905. Before embarking on its impossibility conflict preemption analysis, the court established that "[i]f generic manufacturers can utilize the CBE, then the logic of *Levine* is directly applicable." *Id.* After reviewing the federal regulations applicable to generic drugs, *Stacel* held "the regulations affecting generic drug applications state explicitly that the CBE provisions apply to generic drug manufacturers just as they do to brand-name manufacturers" and therefore generic drug manufacturers have the same unilateral authority as name brand manufacturers to strengthen labels." *Id.* The court gave no deference to the FDA's statements regarding the CBE's inapplicability to generic manufacturers because they were not subject to notice and comment procedures. *Id.* at 906.

Stacel also held the state law duty to warn was not an obstacle to congressional objectives in regulating generic drugs. *Id.* at 906-07. Reciting the presumption against preemption and considering *Levine*'s observation that Congress utilized state tort actions to help regulate name brand drugs, the court concluded Congress did not feel differently about generic drugs. *Id.* at 907. It noted that though generic drugs must have the same labels as their name brand counterparts during the application process, the Hatch-Waxman Amendments do not require the label to remain the same after approval. *Id.* Therefore, because labeling is the manufacturer's responsibility and the statute does not require identical labels post-approval, state failure-to-warn claims do not conflict with congressional objectives. *Id.*

Significance

Stacel is the first post-*Levine* opinion that interpreted the regulatory scheme and congressional intent with regard to generic drugs. By applying the CBE to generic drugs, the court linked *Levine*'s analysis and ruling to generics.

Combined with the discussion in *Levine*, *Stacel*'s dialogue about deference is telling. Specifically, the court noted "on January 18, 2009, the FDA published a proposed new rule in the federal register, and included a lengthy preamble. Within this preamble, the FDA inserted a footnote which states 'CBE changes are not available for generic drugs approved under an abbreviated new drug application.'"³ *Id.* at 906 (citations omitted). However, despite this explicit statement from the FDA, the court did not alter its analysis on the CBE's applicability.

³ *Stacel* discusses the 2008 preamble, while *Levine* discussed the 2006 preamble.

C. *Kellogg v. Wyeth*, 612 F. Supp. 2d 437 (D. Vt. April 10, 2009)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and the movement disorder. Prior to *Levine*, the court denied the generic manufacturers' motion to dismiss based on federal conflict preemption. In a subsequent order denying defendants' motion to certify for immediate appeal under 28 U.S.C. § 1292(b), the court affirmed.

Reasoning

Kellogg acknowledged that *Levine* did not address preemption for generic drugs. 612 F. Supp. 2d at 439. However, it held that by its plain language, the CBE applies to generic drugs. *Id.* at 441. Further, considering the Hatch-Waxman Amendments were enacted against the backdrop of federal drug labeling regulation coexisting with state tort litigation, and Congress enacted an express preemption provision for medical devices but not drugs, the court concluded the Supreme Court's analysis of congressional objectives for name brand drug regulation also applied to generic drugs. *Id.*

Significance

Kellogg highlights two main points: (1) *Levine*'s reasoning on both impossibility and obstacle conflict preemption applies to generic manufacturers and (2) the Hatch-Waxman Amendments do not authorize preemption with regard to generic drugs. The defendants' argument in this case was unique because it relied on the Hatch-Waxman Amendments rather than the FDA regulations. The decision's rejection of the Hatch-Waxman argument strengthens the argument against preemption for generic drugs.

D. *Pustejovsky v. Wyeth, Inc.*, 2009 WL 3336032 (N.D. Tex. Sept. 4, 2009)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and the movement disorder. The court denied the generic manufacturer's first motion for summary judgment, which was based on federal conflict preemption. For the generic manufacturer's second motion for summary judgment, which was based on the learned-intermediary doctrine, the parties again extensively briefed preemption. The court addressed preemption in a footnote.

Reasoning

In response to the parties' briefing, the court took to a footnote to "reiterate that plaintiff's failure-to-warn claims are not preempted." *Pustejovsky*, 2009 WL 3336032, at *1 n.4. To support this conclusion, the court cited to *Levine* and *Kellogg*. It provided no analysis.

Significance

Pustejovsky's brief address does not seem significant. However, despite the court's lack of analysis and perfunctory statement regarding preemption, this decision stands for another jurisdiction that declines to apply federal conflict preemption to state law failure-to-warn claims involving generic drugs.

Status

The plaintiff appealed to the Fifth Circuit Court of Appeals on October 7, 2009 (#09-10983). The appellant brief is due December 30, 2009.

E. *Bartlett v. Mut. Pharm. Co., Inc.*, 2009 WL 3126305 (D.N.H. Sept. 30, 2009)

Summary

The plaintiff ingested the generic drug Sulindac and subsequently suffered from Stevens-Johnson syndrome and toxic epidermal necrolysis, a condition characterized by large areas of lesions on and necrosis of the skin and mucous membranes. She brought claims against the generic drug manufacturer for failure to warn about the dangers of the drug. The court denied the generic manufacturer's motion to dismiss based on federal conflict preemption.

Reasoning

Bartlett began its analysis like *Levine*, against the backdrop of two preemption principles: (1) congressional intent is the touchstone of every preemption case; and (2) in all preemption cases there is a presumption against preemption unless preemption is the clear and manifest purpose of Congress. The court conducted a detailed, in-depth analysis of the Hatch-Waxman Amendments and the FDA regulations, and concluded it is not physically impossible for generic drug manufacturers to comply with both a state's duty to warn and federal requirements regarding generic drug labels. 2009 WL 3126305, at *11. Further, the court held state law failure-to-warn claims are not an obstacle to Congress's objectives in enacting the Hatch-Waxman Amendments. *Id.* at *24-*25.

(1) Conflict preemption—impossibility:

- The court spends the majority of its opinion discussing the Hatch-Waxman Amendments and the FDA regulations regarding generic drug labeling.

- In analyzing the Hatch-Waxman Amendments, *Bartlett* concluded that a generic drug application cannot be *approved* without the same label as its name brand counterpart, but the Amendments do not prevent a manufacturer from changing the drug's label *post*-approval. *Id.* at *12. The court concluded that this opening precluded impossibility conflict preemption. *Id.*
- In analyzing the FDA regulations governing generic drugs, *Bartlett* noted a similar scenario. The regulations require a generic drug's proposed label to be the same as its name brand counterpart, and the Agency will deny approval if this condition is not met. *Id.* at *13. However, the regulations do not prevent *post*-approval changes to the generic drug's label. *Id.*
- Further, the court held the CBE regulation permits *post*-approval unilateral changes to a generic drug's label. *Id.* It reasoned that nothing in the text of the CBE prevents generic drugs from using it, and the regulations governing generic drugs require they comply with it. *Id.* at *16.
- Regarding the Agency's ability to withdraw a generic drug's approval if the label is no longer consistent with the name brand counterpart's labeling, the court emphasized the difference between the word "consistent" in this regulation and the word "same" in application regulation. *Id.* at *18. Because after approval a generic's label must only stay *consistent* with the name brand counterpart, the generic is not precluded from strengthening its warning via the CBE. *Id.*
- In analyzing the FDA's statements regarding a generic's ability to use the CBE (in the FDA's amicus brief and a footnote in a proposed 2008 revision), *Bartlett* declined to accord them much weight. *Id.* at *19-*20. Ultimately, the FDA withdrew its amicus brief, and the footnote does not accompany an actual change in the regulation. *Id.* Additionally, the court noted that little deference is given to agency statements that are not adjudicatory or subject to notice and comment procedures. *Id.*
- Finally, the court concluded that even if a generic drug could not use the CBE to unilaterally change its label, compliance with state law is still not impossible. *Id.* at *24. If a generic inappropriately utilized the CBE, the FDA would have to enforce the prohibition through proceedings to withdraw its approval of the drug. *Id.* Such proceedings don't turn on a generic label's consistency with its name brand counterpart, but on whether the drug is safe under the conditions of use upon which the application was approved. *Id.* Therefore, the FDA's withdrawal of a generic's application upon it unilaterally changing its label via the CBE is not a foregone conclusion. *Id.* The court noted that a hypothetical conflict is not enough to show impossibility conflict preemption.

(2) Conflict preemption—obstacle:

- *Bartlett* held that state law failure-to-warn claims are not an obstacle to Congress’s purpose in enacting the Hatch-Waxman Amendments. *Id.* at *24. These Amendments were designed to make low-cost generic options more readily available to the public via an abbreviated application procedure. *Id.* The court determined that heightened warnings would not frustrate this purpose. *Id.*
- Additionally, the court held nothing in the Amendments or the regulations indicates Congress sought to relieve generic drug manufacturers of the burden of state products liability law, and there is no evidence the Amendments’ purpose was to displace state law. *Id.* at *24-*25. If Congress intends to preempt state law, such intentions must be expressed more clearly (such as with medical devices). *Id.* at *25. Therefore, the court concluded state law failure-to-warn claims are not an obstacle congressional objectives in regulating generic drugs.

Significance

Bartlett offers an extremely in-depth analysis of impossibility conflict preemption via the Hatch-Waxman Amendments *and* the FDA’s generic drug regulations. Before this case, there was probably more room to argue that the CBE does not apply to generics. Because of this case, that argument is now more difficult to make.

F. *Couick v. Wyeth, Inc.*, No. 3:09 CV 210-RJC-DSC (W.D.N.C. Sept. 30, 2009)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and the movement disorder. The magistrate recommended the court deny the generic manufacturer’s motion to dismiss based on federal conflict preemption.

Reasoning

The magistrate adopted *Kellogg*’s reasoning for preemption and generic drugs. *Couick*, No. 3:09 CV 210-RJC-DSC, slip op. at 6. He focused on the obstacle conflict preemption portion of *Kellogg*’s analysis, highlighting the fact that Congress did not add an express preemption provision to the FDCA when enacting the Hatch-Waxman Amendments, and that the manufacturer bears primary responsibility for adequate labeling. *Id.* The magistrate noted only in passing that a manufacturer may use the CBE to change a generic drug’s label, stating there is “no reason to believe that the FDA would challenge a generic drug company’s decision to use the C.B.E. process to strengthen a label warning” *Id.*

Significance

Though the magistrate professed to adopt *Kellogg*'s reasoning, he did not explain both types of conflict preemption. Instead, he focused solely on obstacle conflict preemption. By leaving out impossibility conflict preemption, the magistrate weakened the analytical force of his opinion. The defendants filed an objection to the magistrate's opinion and recommendation on October 13, 2009.

G. *Munroe v. Barr Labs., Inc.*, 2009 WL 4047949 (N.D. Fla. Oct. 15, 2009)

Summary

The plaintiff ingested the generic form of Adderall and subsequently died. Her mother brought claims against the generic drug manufacturer for failure to provide adequate warnings regarding the drug and cardiac arrhythmia. The manufacturer moved to dismiss based on federal preemption. The court denied the manufacturer's motion.

Reasoning

Munroe noted that several courts have addressed this issue, and opined that the cases coming out against preemption "have the better of the arguments." 2009 WL 4047949, *2. The court declined to rewrite the analysis against preemption, but noted two points: first, the CBE applies to generic drug manufacturers; and second, generic drug manufacturers are subject to the same liability for unsafe products as name brand manufacturers. *Id.*

Significance

Munroe does not add anything new to the analysis against federal preemption. Rather, its primary significance is as yet another decision against preemption for generic drugs. Additionally, *Munroe* makes a fairness argument to support its conclusion, noting that if generic manufacturers are going to reap the benefits of selling drugs without incurring the same cost as name brand manufacturers, then generic manufacturers must also be subject to the same liability as name brand manufacturers.

V. POST-LEVINE FEDERAL GENERIC DRUG CASES FOR PREEMPTION

A. *Morris v. Wyeth, Inc.*, 582 F. Supp. 2d 861 (W.D. Ky. Oct. 24, 2008) (*Morris I*), *aff'd*, No. 1:07-CV-176-R, 2009 WL 424590 (W.D. Ky. Feb. 20, 2009) (*Morris II*), *aff'd*, 2009 WL 736200 (W.D. Ky. March 4, 2009) (*Morris III*)

Wilson v. Pliva, Inc., No. 3:07-CV-00378-R, 2008 WL 4696995 (W.D. Ky. Oct. 24, 2008), *aff'd*, 2009 WL 425027 (W.D. Ky. Feb. 20, 2009)

Smith v. Wyeth, Inc., No. 5:07-CV-18-R, 2008 WL 4697002 (W.D. Ky. Oct. 24, 2008), *aff'd*, 2009 WL 425032 (W.D. Ky. Feb. 20, 2009)

Summary

These three companion cases were decided on October 24, 2008, prior to *Levine*, initially affirmed on February 20, 2009, and reaffirmed by minute order on March 4, 2009, after *Levine*.⁴ The plaintiffs ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia. They brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and the movement disorder. The court granted the generic manufacturers' motions to dismiss based on federal conflict preemption.

Reasoning

The preemption rationale for these cases was articulated prior to *Levine*, and follows *Mensing v. Wyeth, Inc.*, 562 F. Supp. 2d 1056 (D. Minn. 2008). The court held the plaintiffs' state law failure-to-warn claims were conflict preempted via impossibility because generic drug manufacturers cannot unilaterally heighten label warnings under the CBE. *Morris I*, 582 F. Supp. 2d at 867-68. Specifically, the court noted that labeling proposed for generic drugs must be the same as that of their name brand counterparts, and the FDA has the power to withdraw its approval of a generic's application if its label is no longer consistent with its name brand counterpart. *Id.* Because of these regulations, the court held generic drugs were not at liberty to deviate from their name brand counterpart labels via the CBE. *Id.* Additionally, the court found the FDA's statements instructive, because they say the CBE does not apply to generic drugs. *Id.*

On the plaintiffs' motions to reconsider, the court addressed several pre-*Levine* cases against preemption.⁵ *Morris II*, No. 1:07-CV-176-R, 2009 WL 424590, at *3-*8. Yet, the court did not find these cases persuasive, considering two not on point, disagreeing with one regarding its application of the regulatory scheme, and disagreeing with one regarding its understanding of the CBE. *Id.* The court also addressed the anti-preemption views of Representative Waxman and the Attorney General of Kentucky, and held they were not sufficient evidence of congressional intent, emphasizing that neither considered federal preemption or the CBE as they

⁴ *Wilson* and *Smith* are verbatim repetitions of *Morris*, with the appropriate parties' names inserted.

⁵ *Demahy v. Wyeth, Inc.*, 586 F. Supp. 2d 642 (E.D. La. 2008); *Swicegood v. Pliva, Inc.*, 543 F. Supp. 2d 1351 (N.D. Ga. 2008); *McKenney v. Purepac Pharm. Co.*, 83 Cal. Rptr. 3d 810 (Cal. Ct. App. 2008); *Sharp v. Leichus*, No. 2004-CA-0643, 2006 WL 515532 (Fla. Cir. Ct. Feb. 17, 2006).

pertain to generic drug manufacturers. *Id.* at *9-*10. Finally, the court recognized the numerous public policies at issue, but ultimately affirmed its initial holding. *Id.* at *10.

After *Levine*, the court reaffirmed its preemption holding by minute order. *Morris III*, No. 1:07-CV-176-R, 2009 WL 736200, at *1.

Significance

Although there have been several cases ruling against preemption since *Levine*, these companion cases are the only pro-preemption decisions since *Levine*. The reasoning represents a different take on how the generic drug regulations work, and may be a more accurate understanding of how those regulations operate in practice, despite any strict construction of their language. However, the cases' regulatory analysis and subsequent conclusion that generic drugs may not unilaterally change their labels via the CBE is weakened by *Bartlett's* more thorough analysis. Additionally, the cases' reliance on recent FDA statements to interpret the CBE's applicability is weakened by *Levine's* of eschewing that strategy.

Status

The plaintiff in *Smith* appealed to the Sixth Circuit Court of Appeals on April 16, 2009 (#09-5460); the plaintiff in *Wilson* appealed to the Sixth Circuit Court of Appeals on April 20, 2009 (#09-5466); and the plaintiff in *Morris* appealed to the Sixth Circuit Court of Appeals on April 27, 2009 (#09-5509). On June 9, 2009, the court denied the three plaintiffs' motion to consolidate briefing. In all cases, the appellant brief is due December 1, 2009, and the appellee brief is due January 4, 2010.

VI. PRE-LEVINE FEDERAL GENERIC DRUG CASES PENDING ON APPEAL

A. *Demahy v. Wyeth, Inc.*, 586 F. Supp. 2d 642 (E.D. La. Oct. 27, 2008)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and the movement disorder. The court *denied* the generic manufacturer's motion to dismiss based on federal conflict preemption.

Reasoning

Demahy's analysis focused on impossibility conflict preemption and the level of deference accorded to the FDA's interpretation of its regulations. It noted that though a generic drug's label must be the "same as" its name brand counterpart during the application process, after its application has been approved, the FDA will only withdraw that approval if the generic's label is no longer "consistent with" its counterpart. *Demahy*, 586 F. Supp. 2d at 648-49.

Considering this discrepancy, along with the regulations' plain language requirement that generics comply with the CBE, the court held the plaintiff's state law failure-to-warn claims were not conflict preempted. *Id.* at 650, 662. It accorded little deference to FDA statements saying the CBE does not apply to generics. *Id.* at 662.

Status

The defendants appealed to the Fifth Circuit Court of Appeals on December 16, 2008 (#08-31204). The Fifth Circuit heard oral arguments on August 5, 2009, and subsequently requested supplemental briefing. The parties filed supplemental briefs on August 10, 2009.

B. *Mensing v. Wyeth*, 562 F. Supp. 2d 1056 (W.D. Minn. June 17, 2008)

Summary

The plaintiff ingested the generic form of Reglan and subsequently suffered from tardive dyskinesia, a movement disorder. She brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between long-term ingestion of the drug and tardive dyskinesia. The court *granted* the generic manufacturer's motion to dismiss based on federal conflict preemption.

Reasoning

Mensing meshed impossibility and obstacle conflict preemption analyses together, holding it is impossible for a generic drug manufacturer to comply with both a state law duty to warn and the federal drug regulations, which is an obstacle to congressional purposes in enacting the Hatch-Waxman Amendments. 562 F. Supp. 2d at 1065. Further, *Mensing* declined to apply the presumption against preemption, indicating the presumption is not applicable to implied preemption.⁶ *Id.* at 1061. The court emphasized that a generic's proposed labeling must be the same as its name brand counterpart, and the FDA will withdraw the generic's approval if the labeling does not remain consistent. *Id.* at 1062-63. The court also concluded the CBE does not apply to generics: the FDA's own statements say as much, and in light of the regulatory scheme specific to generics, generic manufacturers do not have a duty to increase label warnings. *Id.* at 1064-65. Taking these regulations together, the court held generic labels must always remain the same as their name brand counterparts. *Id.*

Status

The plaintiff appealed to the Eighth Circuit Court of Appeals on December 12, 2008 (#08-3850). The Eighth Circuit heard oral arguments on October 20, 2009.

⁶ This position is overruled by *Levine*, and will probably be addressed by the Eighth Circuit on appeal.

UPDATE

On November 27, 2009 the Eighth Circuit issued a decision in this case, reversing the district court. *Mensing v. Wyeth*, No. 08-3850 (8th Cir. Nov. 27, 2009). It held federal law does not preempt state failure-to-warn claims against generic drug manufacturers. Slip op. at 2. The court began its analysis by noting three main principles utilized by the Supreme Court in *Levine*: congressional intent must be considered; there is a presumption against preemption; and a drug manufacturer bears responsibility for a drug's label at all times. *Id.* at 6-7. In its impossibility analysis, the court held that a generic manufacturer's ability to make label changes under the CBE is immaterial to the preemption analysis. *Id.* at 9. Instead, the court relied changes under other regulations. First, 21 C.F.R. § 201.57(e) allows a generic manufacturer to propose label changes "as soon as there is reasonable evidence of an association of a serious hazard with a drug." *Id.* (quotations omitted). This regulation, combined with a manufacturer's responsibility for a drug's label, make it possible for a generic manufacturer to comply with both state law and FDA labeling requirements. *Id.* at 10. Further, the court determined that defendants' interpretation of the "major changes" portion of 21 C.F.R. § 314.70 is too restrictive; generic manufacturers can change drug labels under this provision as well. *Id.* at 11. Finally, the court held that state law failure-to-warn claims do not obstruct the purposes of the Hatch-Waxman Amendments. *Id.* at 15.

C. *Colacicco v. Apotex, Inc.*, 521 F.3d 253 (3d Cir. Apr. 8, 2008)

Summary

Two adults ingested the generic form of Paxil and Zoloft, and subsequently committed suicide. The relative plaintiffs brought claims against name brand and generic drug manufacturers for failure to warn about the relationship between antidepressants and increased risk of suicide. The court *granted* the generic manufacturer's motion to dismiss based on federal conflict preemption.

Reasoning

Colacicco began its analysis by questioning the applicability of the presumption against preemption in implied preemption cases, and concluded the presumption applied with reduced force. 521 F.3d at 265. It then held it was impossible for generic manufacturers to comply with both the state law duty to warn and the federal regulations in this case because the FDA had on multiple occasions rejected the increased warnings plaintiffs advocated for. *Id.* at 269. Therefore, in these limited circumstances, the court held plaintiffs' state law failure-to-warn claims were preempted. *Id.* at 271-72. However, the court noted the FDA's rejections were expressed via public statements, and had not been subject to notice and comment procedures. *Id.* at 275.

Status

The plaintiffs appealed to the United States Supreme Court (#08-437). On March 9, 2009, after deciding *Levine*, the Court granted certiorari, vacated the judgment, and remanded

the case to the Third Circuit. On April 28, 2009, the Third Circuit remanded the consolidated case (#06-3107, #06-5148) to its respective trial courts in the Eastern District of Pennsylvania and District of New Jersey. That same day, the U.S. Department of Justice withdrew its previously-submitted pro-preemption amicus brief. In the Eastern District of Pennsylvania, (*Colacicco*, #05-5500) the defendants filed a motion for summary judgment based on federal preemption on November 9, 2009. In the District of New Jersey, (*McNellis*, 05-1286) a settlement conference is scheduled for January 5, 2010.

VII. POLITICAL ARENA: DEVELOPMENTS AND TRENDS

On March 5, 2009, Congressman Pallone (D-NJ) and Congressman Waxman (D-CA) introduced the Medical Device Safety Act of 2009. If the bill passes, it will nullify the pro-preemption ruling in *Riegel v. Medtronic, Inc.*, 552 U.S. 312 (2008).⁷ The proposed bill seeks to add language to the Medical Device Amendments specifying that preemption is not permitted. H.R. 1346—111th Congress: Medical Device Safety Act of 2009 (2009) (retrieved July 10, 2009 from GovTrack.us, database of federal legislation; <http://www.govtrack.us/congress/bill.xpd?bill=h111-1346>.) The Medical Device Safety Act of 2009 further demonstrates the current trend against preemption.

Moreover, the FDA is now backing away from its pro-preemption position (as expressed in public statements, interpretation of regulations, amicus briefs, and its preemption preambles of 2006 and 2008), which favored the pharmaceutical industry during the last years of the Bush Administration. For example, on April 28, 2009 (following *Levine*) Appellate Staff Member Sharon Swingle wrote a letter on behalf of the Department of Justice, addressed to the Third Circuit Court of Appeals, withdrawing a previously submitted amicus brief in support of preemption filed in *Colacicco*. The letter stated, “[t]he Food and Drug Administration has not yet conducted the sort of reexamination of various preemption issues following the Supreme Court’s decision in *Levine* that would be necessary to inform a position of the United States in this case.” Letter from Sharon Swingle, Appellate Staff, U.S. Department of Justice, to Ms. Marcia M. Waldron, Clerk for the United States Court of Appeals for the Third Circuit (Apr. 28, 2009).

Further evidence of this political shift came on May 20, 2009, when President Obama issued a memorandum to federal agency heads discussing preemption. (See http://www.whitehouse.gov/the_press_office/Presidential-Memorandum-Regarding-Preemption/). The memorandum cautioned that “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.”

Specifically, President Obama’s memorandum includes three directives:

- Express preemption clauses should only be available if codified.

⁷ *Riegel* involved a catheter that ruptured in a patient’s coronary artery. The catheter received pre-market approval from the FDA. The Supreme Court ruled that plaintiff’s claims against the device manufacturer were preempted due to an express preemption clause in the Medical Device Amendments of 1976 (MDA). 552 U.S. 312 (2008).

- Express preemption clauses should only be codified if justified under legal principles.
- Agency and department heads should review regulations passed in the last 10 years that are designed to preempt state law and determine whether the preemption clauses are consistent with these principles. (Previously, the Bush Administration inserted preemptive language into numerous federal regulations).

Although President Obama’s memorandum does not specifically address conflict preemption, several quotes refer generally to “preemption.” The memorandum demonstrates the abrupt shift of policy from the Bush Administration to the Obama Administration and, together with *Levine*, accentuates the trend away from preemption.

VIII. GOING FORWARD: CONCLUSIONS, RISK MANAGEMENT, AND LITIGATION EXPOSURE IN AN ERA OF UNCERTAINTY

A. What Conclusions Can Be Drawn At This Point in Time?

- Since *Levine*, there has been a political and legal trend away from preemption, including the rejection of preemption in state law failure-to-warn cases involving generic drugs.
- There do not appear to be any post-*Levine* opinions (as opposed to minute orders) in favor of federal conflict preemption of state law failure-to-warn claims.
- However, it is important to recognize the dynamic nature of the case law and the continually changing landscape of the preemption doctrine. Conclusions must not be drawn from a snapshot in time, but analyzed in conjunction with trends and viewed on a continuum.⁸ As each pending case on appeal is decided, *Levine*’s limitations will be clarified and the future of federal conflict preemption for generic drugs will become clearer.

⁸ For examples of pre-*Levine* cases concerning preemption with regard to pharmaceuticals, see

Pro-Preemption: *Gaeta v. Perrigo Pharm. Co.*, 562 F. Supp. 2d 1091 (N.D. Cal. 2008); *Mensing v. Wyeth, Inc.*, 562 F. Supp. 2d 1056 (D. Minn. 2008); *Masterson v. Apotex Corp.*, No. 07-61665-CIV, 2008 WL 3262690 (S.D. Fla., Aug. 7, 2008); *Bolin v. SmithKline Beecham*, No. 08-60523-CIV, 2008 WL 3286973 (S.D. Fla., Aug. 7, 2008); *Valerio v. SmithKline Beechman*, No. 08-60522-CIV, 2008 WL 3286976 (S.D. Fla., Aug. 7, 2008).

Against Preemption: *Foster v. Am. Home Prod. Corp.*, 29 F.3d 165 (4th Cir. 1994); *Demahy v. Wyeth, Inc.*, 586 F. Supp. 2d 642 (E.D. La. 2008); *Barnhill v. Teva Pharm. USA, Inc.*, No. 06-0282-CB-M, 2007 WL 5787186 (S.D. Ala. Apr. 24, 2007); *Laisure-Radke v. Par Pharm., Inc.*, No. C03-365RSM, 2006 WL 901657 (W.D. Wash. Mar. 29, 2006); *Kelly v. Wyeth, Inc.*, 22 Mass. L. Rptr. 384, 2007 WL 1302589 (Mass. Sup. Ct. April 12, 2007); *McKenney v. Purepac Pharm. Co.*, 83 Cal. Rptr. 3d 810 (Cal. Ct. App. 2008).

B. *Levine's* Limitations

As discussed above in Section II, *Levine* leaves the door ajar for future pro-preemption decisions. Understanding *Levine's* exceptions and limitations is critical to managing risk and monitoring litigation exposure going forward:

(1) Conflict preemption—impossibility:

- The Court stated: “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 both federal and state requirements.” *Levine*, 129 S.Ct. at 1198. Thus, “clear evidence” that the FDA would not approve a label change could be sufficient to show impossibility conflict preemption. However, it remains unclear how a manufacturer could satisfy this difficult evidentiary hurdle. *See Forst v. Smithkline Beecham Corp.*, 2009 WL 2256232 (July 29, 2009) (analyzing the FDA’s rejection of a name brand drug’s label).
- The Court suggested what might qualify as “clear evidence,” including: (1) if Wyeth had attempted to give the warning required by state law, but was prohibited from doing so by the FDA; (2) if the FDA had taken affirmative action to preserve the IV-push method of administration or intended to prohibit a stronger label; and (3) if Wyeth had supplied the FDA with an evaluation or analysis concerning the specific dangers posed by the IV-push method. *Id.* at 1198-1199.
- Despite *Bartlett*, *Levine* did not hold the CBE applies to generic drugs. Thus, there may still be room to argue the CBE does not apply to generic drugs based on a thorough analysis of the FDA’s generic drug regulations *and* how those regulations are applied in practice.

(2) Conflict preemption—obstruction:

- The Court concluded the FDA’s 2006 pro-preemption preamble was not “thorough, consistent, and persuasive” enough to support obstacle conflict preemption. *Id.* at 1201. However, there is still the potential to argue that the 2008 preamble, which also supports preemption, is “thorough, consistent, and persuasive” enough to indicate state law failure-to-warn claims pose an obstacle to congressional objectives. Yet, even if this argument can be made successfully, it will still be difficult to overcome *Levine's* holding on obstacle conflict preemption because of the breadth of the analysis.

- The Court concluded its decision by generally recognizing “some state-law claims might well frustrate the achievement of congressional objectives,” which leaves open the possibility of a different outcome under different facts. *Id.* at 1204.⁹

C. Risk Management in an Era of Uncertainty

Regardless of the outcome of cases on appeal and other future decisions, the trend against preemption suggests that generic manufacturers consider conducting labeling evaluation and updates. Generic manufacturers are advised to monitor carefully future decisions as well as new and pending legislation. Moreover, in light of the exceptions in *Levine*, the following risk management practices are recommended:

- In order to utilize a hole in *Levine*’s reasoning, a manufacturer may be required to demonstrate that the FDA has considered and unequivocally rejected a warning against a particular risk. Alternatively, a manufacturer may be required to demonstrate the FDA *would* deny such a change to a drug’s label. Fostering and maintaining a thorough record of FDA correspondence is the best approach to demonstrating the FDA’s actual or hypothetical denial. A manufacturer should not only submit changes to the FDA through appropriate procedures, but should follow up with the FDA and seek explanations regarding rejections or lack of response. The FDA’s non-response following a request for label modification may not be later considered necessarily to shield a manufacturer from liability. In *Levine*, the FDA did not respond to an earlier label change request because it was not substantively different. 129 S. Ct. at 1198, n.5. Even if the FDA rejects a proposed label change, the manufacturer may be well served by following-up regarding the exact reason for the rejection.
- New circumstances involving existing information meet the “newly acquired” information standard and the “new analysis” of old data standard. This suggests more regular reevaluation of labeling and adverse events. A manufacturer is well advised to keep a precise record of what specific risks and information it provides to the FDA. Furthermore, to ascertain the complete set of information the FDA has *considered*, a drug manufacturer could conduct “periodic investigations,” including, for example, FOIA requests to the FDA to learn about information provided to the FDA by other manufacturers. The manufacturer may want to consider erring on the side of modification upon receipt of new “adverse information,” “new analyses” of old data, or “new circumstances.” As the Court explained in *Levine*, “risk information accumulates over time,” and the “same data may take on a different meaning in light of subsequent developments.” *Id.* at 1197.

⁹ For example: if the case involved a design defect as opposed to failure-to-warn claim; if the warning involved a black box or a contraindication; if the alleged injury occurred immediately after the FDA initially approved the label; if the claim involved a “fraud on the FDA claim”; or if the FDA clearly rejected or would reject the proposed warning.

- *Levine* and its progeny have emphasized *the manufacturer remains responsible for the content of the label at all times*. The CBE permits manufacturers to add or strengthen label warnings *without waiting for FDA approval*. The majority of courts currently hold the CBE applies to generic manufacturers. (Note that not all circuits have addressed this question, so generic manufacturers must understand the jurisdictional differences until the Supreme Court decides the issue).
- Generic drug manufacturers should monitor pending legislation seeking to change current regulations or to add a new regulations that specifically addresses the applicability of the CBE to generic manufacturers. Because courts put great emphasis on congressional intent with regard to preemption, future legislation may serve to change the obstacle conflict preemption analysis. (See Section VII above).

D. The Extent of Increased Litigation Exposure

Before *Levine*, anti-preemption trend shifted to a near 50-50 split following the FDA's 2006 and 2008 pro-preemption preambles. As a result, the defense bar's use of preemption increased, and saw increased success.

After *Levine*, that pro-preemption trend has reversed with respect to name brand medications in state law failure-to-warn cases. *Levine* and *Stacel* increased name brand manufacturers' litigation exposure and raised concerns for generic manufacturers. In response, the plaintiffs' bar is forging ahead with state law failure-to-warn claims against generic manufacturers. But there is still an active defense bar aggressively fighting for preemption with regard to generic drugs, believing this issue is far from settled.

Specifically, the generic manufacturer defense bar is anticipating the outcome of legislative efforts as well as court decisions on appeal, particularly decisions that analyze preemption with regard to the Hatch-Waxman Amendments and the FDA's 2008 preamble. However, with the changing political climate and the FDA's rescission of support, courts will need to resolve the discrepancies between past congressional intent in favor of conflict preemption for generics, the deference owed to previous pro-preemption FDA positions, and the deference owed to the FDA's current position statements.

The defense bar may be expected to adopt new strategies to shield drug manufacturers from heightened liability. The Risk Evaluation and Mitigation Strategies ("REMS") portion of 21 U.S.C. § 355-1 may provide an alternative defense for manufacturers. Adopted in 2007, REMS provides the FDA with an optional strategy to "ensure that the benefits of [a] drug outweigh the risks . . ." 21 U.S.C. § 355-1(a)(1). If the Secretary and the reviewing office determine a REMS program is necessary—which can occur either at the time of application or upon receipt of new information—manufacturers will be subjected to a program designed to review the drugs in terms of risk and safety. With respect to generic manufacturers, if a generic drug's name brand counterpart is subjected to a REMS program, the generic manufacturer will also be subject to certain aspects of that program. Case law concerning REMS and preemption is

not yet established. However, the defense bar may use a drug that has gone through the REMS process to argue for preemption. If the drug goes through the REMS process, the FDA evaluates and acts on specific risks. Such actions may provide manufactures with a preemption defense.

Levine and its progeny, despite their impact, have left the door cracked with respect to generic preemption; the next one to two years will dictate the final result. In the meantime, generic manufacturers are well advised to heed the risk management recommendations above and expect increased filings.

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