On March 18, 1925, the deadliest tornado in recorded history struck the United States. Later named the Tri-State Tornado, this merciless twister tore through parts of Missouri, Illinois and Indiana for over three hours. Traveling at speeds in excess of 70 miles per hour, the tornado carved a path of destruction 219 miles long and killed 695 people. In addition to the mass casualties, thousands of structures and entire towns were destroyed by the tornado’s mile-wide path. In the 90 years since, the world has yet to see a tornado match its power and wrath.  

Meteorological experts say the Tri-State Tornado’s extreme devastation was partly attributable to many residents’ mistaken belief that the brooding clouds were nothing more than a thunderstorm. Much like that day in 1925, ominous storm clouds have begun to gather around a new proposal from the Food and Drug Administration (FDA) designed to eliminate federal preemption of state law failure-to-warn claims against generic drug manufacturers. If approved, the proposed rule could have its own devastating consequences by jeopardizing public safety, driving up the cost of generic drugs and increasing product liability litigation for manufacturers. With the public hearing and comment period for the rule now complete, the arguments for and against the proposal are clear. However, one question remains: Is this the end of generic preemption?
If approved, the proposed rule could have its own devastating consequences by jeopardizing public safety, driving up the cost of generic drugs and increasing product liability litigation for manufacturers.

BACKGROUND
The United States Supreme Court has recently considered federal preemption questions involving state law failure-to-warn claims in two landmark cases. In Wyeth v. Levine in 2009, the Supreme Court held that federal law did not preempt a state law tort claim against a brand-name drug manufacturer for inadequate warnings on their product labeling. According to the Court, because the brand-name manufacturer could have unilaterally strengthened the warnings on its product labeling through the “changes being effected” (CBE) process, it was possible for the manufacturer to comply with both federal and state requirements.

Two years later, in Piliva v. Mensing, the Court found that a failure-to-warn claim against a generic manufacturer was preempted. There, the Court reasoned that because the generic manufacturer was not permitted to unilaterally strengthen its warning label through the CBE process or by the use of “Dear Doctor” letters, it was impossible for the generic drug manufacturer to comply with both federal and state requirements.

As a result of the Court’s decisions, a consumer who takes a brand-name drug can sue the manufacturer for inadequate warnings, while one who takes the generic version of the drug cannot. Although all nine justices on the Supreme Court agree that this outcome “makes little sense,” the majority of the Court says it is not the role of the judiciary to “decide whether the statutory scheme established by Congress is unusual or even bizarre,” and that “Congress and the FDA retain the authority to change the law and regulations if they so desire.”

FDA’S PROPOSED RULE
Following the Mensing decision, the consumer rights advocacy group Public Citizen petitioned the FDA to amend its regulations to allow generic drug manufacturers to revise their product labeling through the CBE and prior-approval supplement procedures. In November 2013, the FDA granted that request and proposed a new rule that would allow generic manufacturers to unilaterally update safety labeling to consumers before FDA approval. If finalized, the rule will effectively nullify the Supreme Court’s decision in Mensing and eliminate preemption of failure-to-warn claims against generic drug manufacturers.

Under the FDA’s proposed rule, a generic drug manufacturer would be able to add or strengthen a warning on its product label by submitting to the FDA a CBE supplement – the same process currently used by brand manufacturers. This process would begin when a manufacturer receives certain types of “newly acquired information” related to drug safety. Once in receipt of new information, the generic manufacturer would submit a CBE supplement to the FDA requesting a proposed change to its labeling. At the same time the supplement is submitted to the FDA, the generic manufacturer would also send notice of the proposed labeling change, along with a copy of the information supporting the change, to the new drug application holder of the listed drug, commonly known as the brand-name manufacturer. If approved, the proposed rule could have its own devastating consequences by jeopardizing public safety, driving up the cost of generic drugs and increasing product liability litigation for manufacturers.
As a result of the Court’s decisions, a consumer who takes a brand-name drug can sue the manufacturer for inadequate warnings, while one who takes the generic version of the drug cannot. Once the FDA receives the CBE supplement from the generic manufacturer, the Agency would conduct a review of the proposed labeling changes and determine whether the label update is justified. During this review, the FDA would consider submissions by both the brand-name and generic manufacturers. Any proposed changes during this time would be publicly available via a dedicated webpage, and interested parties could subscribe to a free e-mail service to receive updates.

After reviewing the CBE supplement, the FDA could approve, disapprove, or request modifications to the proposed labeling changes. The FDA would approve the proposed changes only if such changes would also be approved for the brand manufacturer. This process will ensure that the approved labeling for brand-name and generic drugs remains the same. Upon FDA approval, all generic manufacturers would be required to submit a CBE supplement with conforming labeling changes within 30 days. If a generic drug manufacturer fails to update its label, the FDA may take steps to withdraw the product from the market.

CURRENT PRACTICE

The proposed rule is a departure from current practice, which allows only brand-name manufacturers to utilize the CBE supplement process to update their labeling. Because a generic drug is required to have the same labeling as its brand-name counterpart, generic manufacturers must currently wait to make safety-related labeling changes until the brand-name manufacturer has received FDA approval to update its own safety information. The proposed rule would, therefore, “create parity” between brand and generic manufacturers “with respect to submission of CBE supplements for safety-related labeling changes” and facilitate the prompt communication of critical drug safety information to prescribers and the public.

ARGUMENTS FOR AND AGAINST

Supporters of the FDA’s proposal argue that the rule will improve patient safety, hold generic manufacturers legally accountable for inadequate warnings and incentivize robust pharmacovigilance. With generic drugs accounting for an estimated 86% of all dispensed medications, supporters argue that generic manufacturers should be allowed to unilaterally update safety-related product labeling to ensure that patients and prescribers have the most current information. Moreover, by eliminating generic preemption in failure-to-warn claims, the proposed rule would restore the ability of consumers to recover for injuries caused by inadequate warnings and ensure that generic manufacturers pay their fair share. Finally, with no generic preemption, the proposed rule will

as the brand-name manufacturer. This process will ensure that the brand-name manufacturer is promptly advised of the new safety information. Upon submission of a CBE supplement to the FDA, the generic manufacturer could distribute the revised safety labeling to the public, resulting in at least temporary differences in safety-related labeling between brand-name and generic drugs. While such differences are currently prohibited by law, the proposed rule would create an exception for generic drug labeling that is temporarily inconsistent with its brand-name counterpart due to safety-related labeling changes submitted via the CBE supplement process.

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While the FDA’s proposed rule has received support from many consumer advocacy groups, the proposal has not been without critics. Since its release, the proposed rule has come under fire by generic and brand-name manufacturers, as well as some members of Congress. Critics of the proposed rule argue that differing labels in the market will create confusion among doctors and consumers, jeopardizing patient safety and undermining public confidence in generic drugs. If passed, the proposal will also result in additional tort liability for manufacturers and healthcare providers, driving up the cost of generic drugs. Finally, critics contend that the proposed rule is unlawful under the 1984 Hatch-Waxman Act because it would allow for temporary differences in labeling between generic and brand-name drugs, undermining the law’s “sameness” requirement.

**ECONOMIC IMPACT**

The FDA states that the proposed rule will “generate little cost,” estimating the net increase to be between $4,237 and $25,852 per year. The FDA’s cursory economic assessment, however, focuses primarily on the cost manufacturers will incur in submitting and reviewing CBE supplements, and ignores the expected increase in product liability litigation. It also gives no consideration to factors like higher insurance premiums, manufacturers who may exit or decline to enter the market for products carrying increased liability risk, insurance companies who may leave the market when faced with insurer against greater risk, or generic manufacturers who may have to bear the cost of duplicating brand companies’ efforts to monitor for safety-related issues.

In response to the FDA’s cost analysis, the Generic Pharmaceutical Association (GPhA) commissioned economist and policy advisor Alex Brill to perform a separate economic assessment of the FDA’s proposed rule. In contrast to the FDA’s projections, Brill estimates that new product liability risks arising from the proposed rule could “increase spending on generic drugs by $4 billion per year.” According to Brill, these additional costs will be passed on to consumers, causing the price of generic drugs to increase and forcing manufacturers out of the market. While Brill’s assessment has already been criticized as “fundamentally mistaken” by an economist sponsored by the American Association for Justice (formerly the Association of Trial Lawyers of America), both sides agree that the proposed rule will generate additional costs for generic manufacturers. The critical question, then, is how much?

**INFLUENCE OF PLAINTIFFS’ BAR**

Given the potential tort liability that would result if the rule is finalized, it is no surprise that the FDA’s proposal has received strong support from plaintiff attorneys. In fact, the involvement of plaintiff attorneys in the development of the proposed rule has been so pronounced that some members of Congress have expressed “significant questions” about the FDA’s “primary motivation” for the proposal. Members of Congress have also suggested that FDA Commissioner Margaret Hamburg was less than truthful with them when she testified in front of a House Appropriations Subcommittee meeting in March of 2014 the FDA had met with the generic drug industry during development of the proposed rule. In truth, the only outside interest group the FDA had consulted with at the time was the American Association of Justice.

After coming under fire from Congress, the FDA held a public meeting on March 27, 2015 to “promote transparency” and receive input on the proposed rule. Present at the meeting were FDA personnel, individual stakeholders, consumer advocates, attorneys, pharmaceutical manufacturers and others. Four plaintiff attorneys and nine individuals sponsored by the American Association for Justice were among the speakers who provided comments in support of the FDA’s proposal. A central theme of the commentary was holding generic manufacturers legally accountable for inadequate warnings. Representatives from the pharmaceutical industry were also present at the meeting and voiced their opposition to the proposed rule. They and others against the proposal expressed concerns about the rule and urged FDA officials to consider adopting an alternative proposal.

**EXPEDITED AGENCY REVIEW: AN ALTERNATIVE PROPOSAL**

In response to the FDA’s proposed rule, the GPhA and Pharmaceutical Research and Manufacturers of America (PhRMA) teamed up and created an alternative proposal known as the Expedited Agency Review (EAR). The EAR proposal, which would apply to both brand-name and generic manufacturers, would replace the CBE process for safety-related labeling changes with an FDA-led system. The proposal is intended to accomplish the FDA’s basic goal of ensuring that manufacturers diligently report and publish important safety information, while avoiding any conflict with Hatch-Waxman’s “sameness” requirement.

Under this alternative proposal, an expedited review may be initiated by a brand or generic manufacturer, or by the FDA. Once initiated, the FDA would review all available safety data and engage all manufacturers in a discussion regarding the potential label change. If the FDA determines that a label change is required after reviewing all available safety data, the FDA will inform the brand and generic manufacturers of the content of the final labeling within 15 days, and instruct the manufacturers to update their labeling within 30 days through e-labeling. By using e-labeling, a process whereby manufacturers can distribute updated information electronically instead of in paper form, users will be provided with immediate access to the latest safety information.
Supporters of the FDA’s proposal argue that the rule will improve patient safety, hold generic manufacturers legally accountable for inadequate warnings and incentivize robust pharmacovigilance.

JUSTIFICATION FOR THE EAR

According to its creators, the EAR proposal is premised on the belief that manufacturers are “poorly situated” to recommend safety changes in product labeling because they each comprise only a small share of the market, and no manufacturer has access to all available data.62 In contrast, the FDA “possesses all the significant clinical trial data on a pharmaceutical product and all the adverse event and periodic reports from all manufacturers,” and is the “primary repository of safety information for pharmaceutical products through creation of the Sentinel System,” the FDA’s national electronic system used to track the safety of marketed drugs.63

Critics to the EAR proposal disagree and argue that manufacturers, not the FDA, are best situated to track and evaluate safety information.64 As noted by the Supreme Court in Wyeth, the FDA “has limited resources to monitor and periodic reports from all manufacturers,”65 and no manufacturer has access to all available data.66 In contrast, the FDA “possesses all the significant clinical trial data on a pharmaceutical product and all the adverse event and periodic reports from all manufacturers,” and is the “primary repository of safety information for pharmaceutical products through creation of the Sentinel System,” the FDA’s national electronic system used to track the safety of marketed drugs.67

Critics argue that the EAR proposal is simply an attempt by generic manufacturers to minimize their responsibility for postmarketing vigilance and expand immunity in product liability cases to brand-name manufacturers.68 By replacing the CBE process with FDA oversight, the EAR proposal essentially “embed[s] a conflict with the current proposal.69

In the event the FDA approves the rule in its current form, generic manufacturers will likely see an increase in tort-liability to generic manufacturers and imposes greater drug-labeling responsibility on the FDA – two outcomes in conflict with the current proposal.

With the public hearing and comment period complete, generic manufacturers must now await the FDA’s final decision. The FDA hopes to have a rule finalized by September 2015.70

AWAITING FDA ACTION


2. Id.
4. Id. at 570-71.
6. Id. at 2575-76.
7. Id. at 2571.
8. Id. at 2581, 2583.
9. Id. at 2582.
12. Id. at 67997.
13. Id. at 67997, 67998.
14. Per 21 C.F.R. § 314.61 ("only acquired information") is not just new data, but also includes "new analyses of previously submitted data." Id.
16. Id.
17. Id. at 67986.
18. Id.
19. Id. at 67989.
20. Id. at 67994-95.
21. Id. at 67994.
22. Id.
23. Id.
24. Id. at 67994.
25. Id. at 67994.
26. Id.
27. Id. at 67993.
28. Id. at 67986.
29. Id. at 67987-88.
30. Id. at 67998.
31. Id. at 67986-87, 67989.
34. Id.
35. Id.
36. Id.
38. Id.
39. Id.
40. Id. 41. Supplemental Applications: Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. at 67997.
42. Id.
44. Id. at 1, 12.
45. Id. at 1.
46. Id. at 6.
48. Id. at 55-57, 255-65, 279-86.
50. Id.
51. Id.
54. Id. at 36-55, 58-64, 238-25, 246-56, 253-274.
55. Id.
56. Id. at 108-39, 314-201.
59. Id.
60. Id.
61. Id.
62. Id.
63. Elec. Distribution of Prescribing Info. for Human Prescription Drugs, Including Biopolitical Drugs, 79 Fed. Reg. 75180 (proposed Dec. 18, 2014) (to be codified at 21 C.F.R. pts. 201, 505, 506 and 602); The FDA has already endorsed the use of labeling under limited circumstances. On December 18, 2014, the FDA issued a final rule on the voluntary electronic distribution of the prescribing information intended for healthcare professionals, which is currently distributed in paper form or as within the package from which a prescription drug or biological product is dispensed. The rule would “not apply to patient labeling (including patient and Medication Guides), or to prescribing information accompanying promotional labeling, which would continue to be provided in paper form.” Id. at 570-71.
64. Id.
66. Id.
68. Wyeth, 555 U.S. at 579.
69. Id. at 570-571.
71. Id.
72. Id.