

# AN ADVERSE REACTION: FDA REGULATION OF GENERIC DRUG LABELING

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*Thanks to a streamlined approval process under the 1984 Hatch-Waxman Act, generic drugs have largely helped make prescription medications in the United States more affordable by providing an essentially identical product at a lower price. While generics may appear to be a perfect substitute for brand-name pharmaceuticals, consumers injured by prescription drugs may encounter an unexpected difference: because federal regulations severely restrict the ability of generic manufacturers to unilaterally update their warning labels, the Supreme Court has held that many products liability claims against generic manufacturers are preempted. At the same time, the Court has held that identical claims against brand name manufacturers remain viable. In response, the Federal Food and Drug Administration (FDA) has recently proposed a rule that would purportedly “fix” this asymmetry by allowing generic manufacturers to make labeling changes without prior FDA approval, even if it results in a brand-name drug and its generic “equivalent” bearing different warning labels.*

*This Note argues that the FDA’s response, while well intentioned, loses the forest for the trees by overvaluing compensation for injured consumers at the expense of low-cost generic drugs and accurate, consistent information for consumers. Instead, both the Agency and consumers injured by generic drugs should focus on discrepancies that already exist—that violate FDA regulations—between generic and brand name labels. Such cases not only present an information problem that should be corrected, but they may also provide a viable avenue for litigating products liability claims. While there is currently a circuit split on the issue, this Note explains why these failure-to-update claims should not be preempted. Moreover, given that such differences may occur in a majority of generic drug labels, these claims offer the possibility of recovery for a significant number of consumers.*

INTRODUCTION .....	2155
I. THE DOCTRINAL DICHOTOMY OF <i>LEVINE</i> AND <i>MENSING</i> .....	2158
A. <i>Federal Preemption</i> .....	2159
1. <i>Preemption Platitudes</i> .....	2160
2. <i>Normative Values at Stake</i> .....	2161
B. <i>The FDA and State Failure-to-Warn Claims</i> .....	2162

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- 1. *Federal Regulation* ..... 2163
- 2. *State Tort Law* ..... 2166
- C. *Preemption of Failure-to-Warn Claims Against Brand Name Drugs* ..... 2168
- D. *Preemption of Failure-to-Warn Claims Against Generic Drugs* ..... 2170
- II. THE FDA’S PROPOSED RULE ON GENERIC DRUG LABELING ..... 2171
  - A. *Legality of the Proposed Rule*..... 2175
  - B. *Effects on Labeling* ..... 2176
  - C. *Costs* ..... 2179
- III. FAILURE-TO-UPDATE TORT CLAIMS ..... 2181
  - A. *Desirability of Failure-to-Update* ..... 2182
  - B. *Legal Viability of Failure-to-Update Claims* ..... 2184
- CONCLUSION ..... 2190

INTRODUCTION

In April 2000, Diana Levine had a friend drive her to a medical clinic in Plainfield, Vermont.<sup>1</sup> Plagued by an especially virulent migraine, Levine was given Phenergan, a brand-name anti-nausea drug manufactured by Wyeth.<sup>2</sup> After the first dose, administered by intramuscular injection, failed to relieve Levine’s symptoms, the clinic administered a second dose via the “IV-push” method, which meant injecting the drug directly into Levine’s vein.<sup>3</sup> Phenergan could also be administered using the “IV-drip” method, where the drug is introduced into a saline solution and delivered intravenously through a catheter.<sup>4</sup> Though Phenergan’s warning label stated that the IV-drip method was “usually preferable,” it did not mention that the reason for this preference was that the IV-push method involved a heightened risk that the drug would enter the patient’s artery and cause the onset of gangrene—which is exactly what happened to Levine.<sup>5</sup> Eventually, doctors had to amputate her right forearm.<sup>6</sup>

The year after Levine’s amputation procedure, Gladys Mensing—like many patients who suffered from chronic gastroesophageal reflux disorder (GERD) in the late 1990s and early 2000s—was prescribed

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<sup>1</sup> Dave Gram, *Amputee Awaits High Court, Wants Musical Glow Back*, USA TODAY (Oct. 30, 2008, 10:35 AM), [http://usatoday30.usatoday.com/news/washington/2008-10-30-842691671\\_x.htm](http://usatoday30.usatoday.com/news/washington/2008-10-30-842691671_x.htm).

<sup>2</sup> *Id.*

<sup>3</sup> *Wyeth v. Levine*, 555 U.S. 555, 559 (2009).

<sup>4</sup> *Id.*

<sup>5</sup> *Id.* at 559–60.

<sup>6</sup> Gram, *supra* note 1.

Reglan, a brand-name metoclopramide tablet also manufactured by Wyeth.<sup>7</sup> At the time, Reglan's warning label stated that tardive dyskinesia, an incurable neurological disorder causing involuntary and repetitive facial movements, was a potential side effect.<sup>8</sup> An insert in the package further cautioned that use for more than twelve weeks had not been evaluated and could not be recommended.<sup>9</sup> That warning, however, had been approved in 1985,<sup>10</sup> and it had since become increasingly evident that tardive dyskinesia was a significant risk associated with long-term use of metoclopramide, with an incidence rate approaching 30% in patients taking the drug for more than two-and-a-half years.<sup>11</sup> After taking metoclopramide for several years, Mensing was diagnosed with tardive dyskinesia.<sup>12</sup>

Both Levine and Mensing were prescribed brand name prescription pharmaceuticals manufactured by Wyeth. Both suffered permanent, debilitating injuries as a result of the drugs they were given. Both brought suits for damages that were appealed all the way to the U.S. Supreme Court,<sup>13</sup> but only Levine was ultimately successful.

The reason was that Mensing's pharmacy had not dispensed Reglan, as was written on her doctor's prescription, but rather a generic version of metoclopramide manufactured by PLIVA. The pharmacy was required to do so under Minnesota's generic substitution law because Mensing's physician had not written "Dispense as Written" or "DAW" on the prescription.<sup>14</sup> As the Supreme Court later explained, Mensing would have been able to recover damages had her prescription been filled with Wyeth's brand-name

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<sup>7</sup> See *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2572–73 (2011) (noting that Reglan was "commonly used to treat digestive tract problems such as diabetic gastroparesis and gastroesophageal reflux disorder").

<sup>8</sup> *Id.* at 2572.

<sup>9</sup> *Id.*

<sup>10</sup> *Id.*

<sup>11</sup> *McNeil v. Wyeth*, 462 F.3d 364, 370 n.5 (5th Cir. 2006) (noting a study finding a 29% incidence of tardive dyskinesia in a patient population with an average exposure to metoclopramide of 2.6 years), cited in *Mensing*, 131 S. Ct. at 2572.

<sup>12</sup> *Mensing*, 131 S. Ct. at 2573.

<sup>13</sup> *Id.* at 2567; *Wyeth v. Levine*, 555 U.S. 555, 559 (2009).

<sup>14</sup> See MINN. STAT. § 151.21 (2001) (describing when and how pharmacists must dispense a generic drug in lieu of the one prescribed). All fifty states, the District of Columbia, and Puerto Rico, have some form of generic substitution law, though they may differ on whether substitution is required or purely permissive. See *Generic Drug Substitution Requires Pharmacist Attention to Ensure Compliance with State Laws and Regulations*, 42 NAT'L ASS'N OF BDS. OF PHARMACY NEWSLETTER 135, 135–36 (2013) (noting that fourteen of those jurisdictions have "mandatory" substitution laws, while the other thirty-eight have "permissive" substitution laws).

metoclopramide, Reglan.<sup>15</sup> However, the Court held that federal law preempted her claim for damages<sup>16</sup> because it was impossible for PLIVA to simultaneously comply with the federal “duty of sameness”—which requires that the labeling for PLIVA’s generic metoclopramide match the warning label of the brand name, Reglan<sup>17</sup>—and the duty imposed by state tort law to provide a more adequate warning.<sup>18</sup> Cases like *Mensing* thus represent a significant failure—in terms of both labeling regulation and victim compensation—of the FDA’s generic drug program.

Notwithstanding the apparent underenforcement of the existing sameness requirements,<sup>19</sup> the FDA responded to *Mensing* by introducing a proposed rule that aims to provide compensation to the Gladys Mensings. The rule would eliminate the duty of sameness and allow generic manufacturers to make certain labeling changes unilaterally and without prior FDA approval. By removing the mutual exclusivity from compliance with both state and federal law, the rule would theoretically expose generic manufacturers to tort liability.

This Note thus argues that the FDA’s response to these regulatory failures has been neither measured nor focused, resulting in a proposed rule that creates more problems than it solves and threatens to undercut many of the benefits of the generic drug scheme envisioned by Congress. Diverted resources from both industry and consumer groups have been siphoned off by a regulatory battle that, as this Note goes to publication, is entering its third year. And the rule itself, if implemented, would exacerbate rather than mitigate the safety risks faced by consumers, to say nothing of the inevitable costly litigation challenging the rule. Indeed, the mere specter of the rule may already be contributing to product shortages and price jumps in generic drugs.

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<sup>15</sup> *Mensing*, 131 S. Ct. at 2581 (noting that if *Mensing* had “taken Reglan . . . [her] lawsuit] ] would not be pre-empted”).

<sup>16</sup> See *id.* at 2580 (“When . . . federal law blocks a private party from independently accomplishing what state law requires, that party has established pre-emption.”).

<sup>17</sup> *Id.* at 2574–75 (“The FDA . . . interprets its regulations to require that the warning labels of a brand-name drug and its generic copy must always be the same—thus, generic drug manufacturers have an ongoing federal duty of sameness.” (internal quotation marks omitted)).

<sup>18</sup> See *Mensing*, 131 S. Ct. at 2573 (“Under Minnesota law, which applies to *Mensing*’s lawsuit, ‘where the manufacturer . . . of a product has actual or constructive knowledge of danger to users, the . . . manufacturer has a duty to give warning of such dangers.’” (quoting *Frey v. Montgomery Ward & Co.*, 258 N.W.2d 782, 788 (Minn. 1977))).

<sup>19</sup> See Jon Duke et al., *Consistency in the Safety Labeling of Bioequivalent Medications*, 22 PHARMACOEPIDEMOLOGY & DRUG SAFETY 294, 301 (2013) (“[Equivalent drugs] from different manufacturers often differ in their safety labeling. This variation stands in contrast to the expectations of providers, the FDA, and, more recently, the United States Supreme Court.”).

A superior alternative to enforce labeling standards for at least some generics exists in a “new breed of state-law torts” pursued by some enterprising products liability plaintiffs in the wake of the Supreme Court’s ruling against Gladys Mensing.<sup>20</sup> Failure-to-update tort claims target generic drugs that have failed to update their warning labels following a revision by the corresponding brand-name drug, as required by generic drug manufacturers’ “duty of sameness.”<sup>21</sup> These lawsuits compensate victims and enforce the federal regulatory scheme, but without the deleterious tradeoffs of the FDA’s proposed rule. Failure-to-update claims are a viable alternative in a significant number of cases that the proposed FDA rule targets, because “the majority of drugs show[ ] some variation within their labeling, and the majority of generic manufacturers hav[e] produced labels discrepant from the reference brand.”<sup>22</sup>

This Note proceeds as follows. Part I explains the preemption of most product liability claims against generic manufacturers. Part II examines shortcomings of the FDA’s response: a proposed rule, though seemingly delayed indefinitely, which would strip generic manufacturers of their de facto immunity to state tort claims. Such a move may achieve short-term compensation for a handful of injured plaintiffs, but sacrifices many of the consumer benefits (including lower prices and heightened product safety) of generic drugs that would otherwise be realized over the long term. Part III introduces the newly-minted class of failure-to-update claims and argues that these suits should not be preempted because they function as a beneficial vehicle for parallel state enforcement of federal regulations.

## I

### THE DOCTRINAL DICHOTOMY OF *LEVINE* AND *MENSING*

Although the Supreme Court held that Gladys Mensing’s tort claims were preempted, it was not unsympathetic to her injury and inability to sue for damages. The Court “acknowledge[d] the unfortunate hand that federal drug regulation has dealt Mensing.”<sup>23</sup> Justice Thomas, the author of the majority opinion, went as far as to suggest that the result “ma[de] little sense.”<sup>24</sup>

Perhaps what inspired Justice Thomas to describe the outcome as nonsensical was the fact that Mensing’s claims were only preempted

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<sup>20</sup> Catherine M. Sharkey, *Tort-Agency Partnerships in an Age of Preemption*, 15 THEORETICAL INQUIRIES L. 359, 364 (2014).

<sup>21</sup> *Mensing*, 131 S. Ct. at 2576.

<sup>22</sup> Duke et al., *supra* note 19, at 299.

<sup>23</sup> *Mensing*, 131 S. Ct. at 2581.

<sup>24</sup> *Id.*

because she was not given, and consequently did not take, the very drug her physician had actually prescribed: Reglan.<sup>25</sup> Indeed, just two years earlier in *Levine*, the Court found no preemption in a case that similarly centered on a plaintiff's claim that the defendant drug manufacturer "failed to provide an adequate warning."<sup>26</sup> Yet in *Mensing*, "because pharmacists, acting in full accord with state law, substituted generic metoclopramide instead, federal law preempt[ed]" the claims.<sup>27</sup>

### A. Federal Preemption

Federal preemption involves the "displacement" of state law by federal law by virtue of the Supremacy Clause of the Constitution.<sup>28</sup> Preemption taxonomy divides the doctrine into two categories: express preemption and implied preemption. Express preemption encompasses cases in which a federal statute explicitly proscribes some category of state regulation, such as by prohibiting a state from enacting regulations that supplement or diverge from federal regulations.<sup>29</sup>

Implied preemption is further subdivided into field preemption and conflict preemption. In implied preemption, by contrast, there is often no explicit proscription of state regulation; rather, something about the nature of the federal regulation leads a court to conclude that state law is meant to be preempted. The first subcategory of implied preemption, field preemption, involves federal occupation of an entire field of regulation, such that there is no space for state regulation of any kind.<sup>30</sup> Field preemption precludes "not only competing state regulatory standards, but remedies for violation of federal stan-

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<sup>25</sup> See *id.* ("Had [plaintiffs] taken Reglan, the brand-name drug prescribed by their doctors, . . . their lawsuits would not be pre-empted.").

<sup>26</sup> *Wyeth v. Levine*, 555 U.S. 555, 558 (2009) (holding that a plaintiff's failure-to-warn claims were not preempted by either the federal Food, Drug, and Cosmetic Act (FDCA) or FDA regulations).

<sup>27</sup> *Mensing*, 131 S. Ct. at 2581 (noting that federal law prohibits generic drug manufacturers from altering their warning, in direct conflict with state labeling duties).

<sup>28</sup> Thomas W. Merrill, *Preemption and Institutional Choice*, 107 Nw. U. L. REV. 727, 730 (2008).

<sup>29</sup> See, e.g., *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 316 (2008) (finding plaintiff's product liability claims preempted under the express preemption provision of the 1976 Medical Device Amendments to the FDCA, which forbids enforcement of state requirements for medical devices "different from, or in addition to, any [federal] requirement" (quoting 21 U.S.C. § 360k(a) (2006))).

<sup>30</sup> See *Arizona v. United States*, 132 S. Ct. 2492, 2502 (2012) ("Where Congress occupies an entire field, as it has in the field of alien registration, even complementary state regulation is impermissible. Field preemption reflects a congressional decision to foreclose any state regulation in the area, even if it is parallel to federal standards." (citing *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 249 (1984))).

dards as well.”<sup>31</sup> The second subcategory, implied conflict preemption, comes in two flavors: broad and narrow.<sup>32</sup> The broader form, known as obstacle preemption, occurs when state law impedes “the accomplishment and execution of the full purposes and objectives of Congress.”<sup>33</sup> The other, “vanishingly narrow” variety is called impossibility preemption,<sup>34</sup> which results—as the name implies—when state regulation is literally “incompatible with the federal dictates” on the topic.<sup>35</sup>

### 1. Preemption Platitudes

Two recurring platitudes pervade modern preemption jurisprudence. One is the (in)famous “presumption against preemption.”<sup>36</sup> Justice Douglas first framed this paradigm in *Rice v. Santa Fe Elevator Corp.*, and explained that where Congress legislates “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.”<sup>37</sup> Despite its ubiquity, it is unclear whether the presumption is anything more than a rhetorical device,<sup>38</sup> let alone an interpretive canon of sufficient caliber to displace what would otherwise be the Court’s preferred interpretation of the law at issue.

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<sup>31</sup> Sharkey, *supra* note 20, at 362. While field preemption is a relative rarity in products liability cases, *id.*, such an approach is not without any defenders, *see, e.g.*, Richard A. Epstein, *Why the FDA Must Preempt Tort Litigation: A Critique of Chevron Deference and a Response to Richard Nagareda*, 1 J. TORT L. 5, Dec. 2006, at 5, 1 (“[F]ederal preemption of state tort actions for pharmaceuticals is long overdue, both under current law and as a matter of sound legal policy.”).

<sup>32</sup> *See* Catherine M. Sharkey, *Products Liability Preemption: An Institutional Approach*, 76 GEO. WASH. L. REV. 449, 456 n.21 (2008) (“[C]onflict preemption occurs where the federal interest conflicts with underlying state law, either in the narrow sense that an actor would find it impossible to comply with both commands or, in the broader sense, that compliance with the state law command would pose an obstacle to . . . federal regulatory purposes . . . .” (internal quotation marks and citations omitted)).

<sup>33</sup> *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941) (holding Pennsylvania’s alien registration law to be preempted by a similar federal statute and thus unenforceable).

<sup>34</sup> Caleb Nelson, *Preemption*, 86 VA. L. REV. 225, 228 (2000).

<sup>35</sup> Sharkey, *supra* note 20, at 360.

<sup>36</sup> *See* Cipollone v. Liggett Grp., Inc., 505 U.S. 504, 524 (1992) (construing an express preemption clause narrowly “in light of the strong presumption against pre-emption”).

<sup>37</sup> 331 U.S. 218, 230 (1947).

<sup>38</sup> *E.g.*, Sharkey, *supra* note 32, at 458 (“Here, I join a veritable chorus of scholars pointing out the Court’s haphazard application of the presumption. In the realm of products liability preemption, the presumption does yeoman’s work in some cases while going AWOL altogether in others.”); *id.* at 459 (“On either normative or empirical grounds alone, then, one might defend setting aside the presumption against preemption. The fall of this interpretive canon, moreover, would make way for alternative organizing principles.”).

The second truism is that “the purpose of Congress is the ultimate touchstone in every preemption case.”<sup>39</sup> Much like the presumption against preemption, this cliché sporadically appears in and vanishes from the current Court’s preemption jurisprudence. On the one hand, despite the growing influence of textualism on both the Court and the federal judiciary in general, purposive arguments remain the dominant currency in the preemption law realm. This holds true for express preemption—where the intent to preempt is stated explicitly—and implied preemption—which, by its very nature, looks to legislative purpose.<sup>40</sup> At the same time, with the ever-expanding regulatory state, administrative agencies have come to play an increasingly important role in preemption cases involving statutes they administer or enforce, often supplementing or even supplanting the purpose of Congress.<sup>41</sup>

## 2. *Normative Values at Stake*

Because every preemption case requires the Court to calibrate the appropriate balance of power between states and the federal government,<sup>42</sup> “preemption decisions always entail policy choices.”<sup>43</sup> As Justice Breyer noted:

[T]he Court has recognized the practical importance of preserving local independence, at retail, i.e., by applying pre-emption analysis with care, statute by statute, line by line, in order to determine how best to reconcile a federal statute’s language and purpose with federalism’s need to preserve state autonomy. Indeed, in today’s world, filled with legal complexity, the true test of federalist principle may lie, not in the occasional constitutional effort to trim Congress’ commerce power at its edges, or to protect a State’s treasury from a private damages action, but rather in those many statutory cases

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<sup>39</sup> *Wyeth v. Levine*, 555 U.S. 555, 565 (2009) (internal quotation marks omitted) (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996)).

<sup>40</sup> See Daniel J. Meltzer, *Preemption and Textualism*, 112 MICH. L. REV. 1, 10 (2013) (“[E]ven though many of the justices are generally attracted to textualist premises, the Court has tended to rest its preemption decisions on a much more open-ended, purposive approach to interpretation—both in reading preemption clauses (where they exist) and in interpreting statutes that include no such clause.”).

<sup>41</sup> See Catherine M. Sharkey, *Inside Agency Preemption*, 110 MICH. L. REV. 521, 523 (2012) (“[W]hile courts reiterate that congressional intent is the touchstone of preemption analysis, they increasingly rely on the views propounded by federal agencies either in regulations or else in preambles or litigation briefs.”).

<sup>42</sup> See Catherine M. Sharkey, *Against Freewheeling, Extratextual Obstacle Preemption: Is Justice Clarence Thomas the Lone Principled Federalist?*, 5 N.Y.U. J.L. & LIBERTY 63, 64 (2012) (“Federal preemption of state tort law unequivocally alters the allocation of authority between the states and the national government.”).

<sup>43</sup> Catherine M. Sharkey, *What Riegel Portends for FDA Preemption of State Law Products Liability Claims*, 103 Nw. U. L. REV. 437, 439 (2009).



where courts interpret the mass of technical detail that is the ordinary diet of the law.<sup>44</sup>

Whether one merely acknowledges “the capacity of federalism to promote various policy values” or believes the protection of state autonomy is required as a matter of “constitutional fidelity,”<sup>45</sup> evaluating competing state and federal regulatory interests at stake in preemption cases—for example, weighing costs and benefits of federalized uniformity in prescription drug labeling—is a valuable normative consideration.<sup>46</sup> Such a utility-maximizing approach is not necessarily at odds—and, indeed, may very well align—with the purposes that federalism is designed to advance.<sup>47</sup> Moreover, homing in on “a more concrete federalism value, namely, giving heed to state regulatory interests and how they interact with federal regulatory schemes,”<sup>48</sup> may sharpen the debate within a doctrinal area that is famously a “muddle.”<sup>49</sup>

### B. *The FDA and State Failure-to-Warn Claims*

As suggested by the discussion above, preemption analysis accordingly directs courts to focus on the “tension between federal and state law.”<sup>50</sup> If this tension reaches impermissible levels, state law is preempted and displaced by the competing federal regulation. The first task of a court faced with a preemption question is therefore to

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<sup>44</sup> Egelhoff v. Egelhoff, 532 U.S. 141, 160–61 (2001) (Breyer, J., dissenting) (internal citations omitted). As though it were a fate worse than death, Ernest Young laments that this valuable insight into federalism and preemption is “condemned to the hopeless obscurity of an ERISA case.” Ernest A. Young, “*The Ordinary Diet of the Law*”: *The Presumption Against Preemption in the Roberts Court*, 2011 SUP. CT. REV. 253, 254 (2011).

<sup>45</sup> Ernest A. Young, *Executive Preemption*, 102 Nw. U. L. REV. 869, 872 (2008).

<sup>46</sup> See Merrill, *supra* note 28, at 743–44 (noting that relevant factors in assessing whether the tension between state and federal law warrants preemption “include both larger traditions about the appropriate division of authority between the federal government and the states, and the pragmatics of the particular issue under consideration, most notably determining whether the application of state law would interfere with maintaining a single national market”).

<sup>47</sup> See, e.g., Abigail R. Moncrieff, *Cost-Benefit Federalism: Reconciling Collective Action Federalism and Libertarian Federalism in the Obamacare Litigation and Beyond*, 38 AM. J.L. & MED. 288, 308 (2012) (“The best federalist balance is the one that optimizes the benefits of regulatory efficiency within the constraint of libertarian costs (or, the same rule, that optimizes the benefits of individual liberty within the constraint of efficiency costs.”). The centralization of regulation, according to Professor Moncrieff, should continue whenever social benefits exceed or are equal to social costs, “where the costs are measured in terms of the liberty lost and the benefits in terms of the efficiency gained.” *Id.*

<sup>48</sup> Catherine M. Sharkey, *Federalism Accountability: “Agency-Forcing” Measures*, 58 DUKE L.J. 2125, 2147–48 (2009).

<sup>49</sup> Nelson, *supra* note 34, at 232.

<sup>50</sup> Merrill, *supra* note 28, at 752.

“compare federal and state law.”<sup>51</sup> In an implied conflict preemption analysis, a category that covers substantially all of the prescription drug preemption cases,<sup>52</sup> “courts scrutinize whether the state tort law poses either an irreconcilable (impossibility preemption) or formidable (obstacle preemption) tension with the federal regulatory scheme.”<sup>53</sup>

### 1. Federal Regulation

At the center of one of the most rigorous regulatory frameworks for pharmaceuticals anywhere in the world is a single agency: the FDA.<sup>54</sup> A bit more than a century old, the Agency’s regulatory authority has steadily expanded in size, scope, and complexity.<sup>55</sup> In the context of pharmaceuticals, the FDA functions not only as a regulator, but also as a gatekeeper. Each and every new drug must be approved by the FDA before the drug’s manufacturer can introduce it into the U.S. market.<sup>56</sup>

Submitting and obtaining approval of a “New Drug Application” (NDA), however, is an incredibly costly undertaking. In addition to the sunk costs of years of research and development, the company must perform extensive testing and clinical trials, the results of which must be documented and included with the NDA.<sup>57</sup> The average total cost of developing and securing FDA approval for a NDA is more than two billion dollars.<sup>58</sup>

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<sup>51</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2573 (2011).

<sup>52</sup> As a general matter, “[f]ield preemption is not common in the products liability realm.” Sharkey, *supra* note 20, at 362. Nor do pharmaceutical cases fall under express preemption. Sharkey, *supra* note 43, at 452 (noting “a key statutory distinction between the realms of medical devices and drugs: a preemption clause applies to the former, but not the latter”).

<sup>53</sup> Sharkey, *supra* note 20, at 363.

<sup>54</sup> See Carl Tobias, *FDA Regulatory Compliance Reconsidered*, 93 CORNELL L. REV. 1003, 1008 (2011) (“[The FDA’s] technical demands, review procedures, and scientific quality make U.S. pharmaceutical regulation one of the world’s most stringent regimes.”).

<sup>55</sup> See Wallace F. Janssen, *The Story of the Laws Behind the Labels*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/AboutFDA/WhatWeDo/History/Overviews/ucm056044.htm> (last updated Mar. 11, 2014).

<sup>56</sup> See 21 U.S.C. § 355(a) (2012) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug.”).

<sup>57</sup> See Peter Barton Hutt, *The Regulation of Drug Products by the US Food and Drug Administration*, in *THE TEXTBOOK OF PHARMACEUTICAL MEDICINE* 461, 482 (John P. Griffin et al. eds., 7th ed. 2013) (“After the sponsor has completed all non-clinical and clinical testing necessary to demonstrate the safety and effectiveness of the drug, the test results must be compiled in an NDA for submission . . . . The typical NDA comprises tens of thousands or even hundreds of thousands of pages.”).

<sup>58</sup> See PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, *FOOD AND DRUG LAW* 643 (4th ed. 2014).

Until 1984, the NDA process generally applied to *all* drug manufacturers, meaning that the FDA required generic manufacturers to duplicate the preclinical and clinical testing already performed by brand-name manufacturers prior to submitting their NDAs.<sup>59</sup> In light of these barriers to entry, it is unsurprising that generic drugs played a fairly marginal role in the marketplace.<sup>60</sup> In 1983, the average market share for generic drugs was 13%,<sup>61</sup> and generic versions were available for only 35% of eligible off-patent drugs.<sup>62</sup>

Many of these obstacles were diminished or eliminated in 1984, when Congress passed the Drug Price Competition and Patent Term Restoration Act.<sup>63</sup> Commonly known as the Hatch-Waxman Act, the Act completely overhauled the generic drug approval process.<sup>64</sup> Under Hatch-Waxman, generic drugs are submitted for FDA approval

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<sup>59</sup> See David M. Dudzinski & Aaron S. Kesselheim, *Scientific and Legal Viability of Follow-on Protein Drugs*, 358 NEW ENG. J. MED. 843, 844 (2008) (“Before [1984], most manufacturers that wanted to distribute generic versions of brand-name drugs had to undertake a full set of clinical trials proving the safety and efficacy of their products, and as a result, few generic products were available on the U.S. market.”). *But see* Edward Tabor, *Generic Drug Approvals in the US Prior to the Hatch-Waxman Act*, REG. FOCUS, Sept. 2008, at 50 (“In fact, the [FDA] . . . approved many generic drugs before 1984, using three separate approval mechanisms: the Abbreviated New Drug Application (ANDA) for drugs originally approved before 1962; the paper NDA . . . for generic copies of drugs approved after 1962; and the monograph system for generic antibiotics and insulin.” (footnotes omitted) (internal quotation marks omitted)).

<sup>60</sup> See CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 29 (July 1998) [hereinafter CBO, GENERIC DRUGS] (“Before 1984 . . . , competition from generic drugs in terms of price and market share was limited primarily to antibiotics.”).

The comparative prevalence of generic antibiotics was due to the fact that a separate approval mechanism had been in place since the 1940s. See Irving L. Wiesen, *FDA’s Antibiotic Regulatory Scheme: Then and Now*, in THE PHARMACEUTICAL REGULATORY PROCESS 131, 131–33 (Ira R. Berry & Robert P. Martin eds., 2d ed. 2008) (describing the distinct history and development of antibiotics regulation in the United States up until 1997); Tabor, *supra* note 59, at 50 (“Generic copies of antibiotics and insulin were approved under a monograph system from 1945 to 1997.”).

<sup>61</sup> CBO, GENERIC DRUGS, *supra* note 60, at xiii. This figure excludes antibiotics, *id.*, for reasons described in the previous footnote.

<sup>62</sup> See *id.* at 29 (“Excluding antibiotics and drugs approved before 1962 (for which an abbreviated generic-drug approval process existed), only 18 out of 52 top-selling drugs with expired patents had generic versions available.”).

<sup>63</sup> Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 21 U.S.C. § 355(j) (2012) and 35 U.S.C. §§ 156, 271(e) (2012)).

<sup>64</sup> See Hutt, *supra* note 57, at 487 (“All of the regulations and requirements for an abbreviated NDA developed by FDA . . . were eliminated when Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (often referred to as the Hatch-Waxman Act). The 1984 Act established detailed requirements that supersede everything that went before.”).

using an “Abbreviated New Drug Application” (ANDA).<sup>65</sup> The Act simplified the application process for manufacturers of generic versions of pharmaceuticals that the Agency had previously approved—essentially allowing such manufacturers to free-ride on research and development (as well as safety and effectiveness trials) already performed during the NDA process.<sup>66</sup> As a tradeoff, the Act also created an extended period of market exclusivity for branded manufacturers, which may extend beyond the protection period afforded by a patent.<sup>67</sup>

Generic drugs must meet three general requirements for FDA approval, all of which are linked to the reference listed drug (RLD) being “copied.”<sup>68</sup> First, they must contain the same active ingredient(s)<sup>69</sup> and have the same “route of administration, dosage form, and strength” as the RLD.<sup>70</sup> Second, though the inactive ingredients may differ, the generic drug must be “bioequivalent” to the RLD.<sup>71</sup>

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<sup>65</sup> See *Abbreviated New Drug Application (ANDA): Generics*, U.S. FOOD AND DRUG ADMIN., <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm> (last updated Sept. 18, 2014) (describing the ANDA process).

<sup>66</sup> See Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL’Y L. & ETHICS 717, 737 (2005) (noting that generic drugs can free-ride on prior studies after patents expire).

<sup>67</sup> The time-consuming nature of the NDA process typically reduces the effective patent term to less than the twenty-year period theoretically provided by statute. See 35 U.S.C. § 156 (2012) (describing the conditions under which a patent term will be extended). However, under Hatch-Waxman the patent term may be extended by “the time between the effective date of the investigational new drug application and the submission of the NDA, plus the entire time lost during FDA approval of the NDA.” WENDY H. SCHACHT & JOHN R. THOMAS, CONG. RESEARCH SERV., RL30756, PATENT LAW AND ITS APPLICATION TO THE PHARMACEUTICAL INDUSTRY: AN EXAMINATION OF THE DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984 (“THE HATCH-WAXMAN ACT”) (2005); see also § 156(b)–(c) (limiting time restored to a maximum of five years and providing that total length of restored patent term may not exceed fourteen years).

<sup>68</sup> The RLD is “the listed drug identified by FDA as the drug product upon which an applicant relies in seeking approval of its abbreviated application [or ANDA].” 21 C.F.R. § 314.3 (2015); see also Basis for an ANDA Submission, 57 Fed. Reg. 17,950, 17,958 (Apr. 28, 1992) (“Generally, the reference listed drug will be the NDA drug product for a single source drug product. For multiple source NDA drug products or multiple source drug products without an NDA, the reference listed drug generally will be the market leader as determined by FDA . . .”).

<sup>69</sup> 21 C.F.R. § 314.94(a)(5) (2015).

<sup>70</sup> *Id.* § 314.94(a)(6).

<sup>71</sup> *Id.* § 314.94(a)(7). Bioequivalence looks to whether the generic drug interacts with the human body in essentially the same way as the RLD. See *id.* § 320.1(e) (“*Bioequivalence* means the absence of a significant difference in the rate and extent to which the active ingredient or active moiety . . . becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.”).

Finally, the warning label on the generic pharmaceutical must match the FDA-approved warning for the RLD.<sup>72</sup>

## 2. *State Tort Law*

This federal regulatory scheme sits in tension with “warning defect”<sup>73</sup> claims under state products liability law.<sup>74</sup> Such claims essentially allege that a product “is defective because of inadequate instructions or warnings.”<sup>75</sup> As these claims sound primarily in tort,<sup>76</sup> strict liability<sup>77</sup> and negligence<sup>78</sup> are the primary theories of liability.

There are two important practical similarities between negligence and strict liability in the context of a failure-to-warn claim. First, regardless of how a jurisdiction characterizes a warning defect claim, courts tend to apply a virtually identical framework.<sup>79</sup> Even in jurisdictions that nominally treat liability for product defects as inherently

<sup>72</sup> *Id.* § 314.94(a)(8)(iii). This is the federal “sameness” requirement discussed earlier. See *supra* note 17 and accompanying text.

<sup>73</sup> DAVID G. OWEN & MARY J. DAVIS, OWEN & DAVIS ON PRODUCTS LIABILITY 834 (4th ed. 2014) (defining a warning defect as instructions that either fail to provide adequate warning of a risk or fail to explain how to reduce the risk).

<sup>74</sup> A manufacturer may be liable in tort when an individual is injured because of a defective or misrepresented product. See DAVID G. OWEN, PRODUCTS LIABILITY LAW 1 (3d ed. 2005) (“Products liability law governs liability for the sale or other commercial transfer of a product that causes physical harm because it is defective or its properties are falsely represented.”).

<sup>75</sup> RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 (AM. LAW INST. 1998) [hereinafter RESTATEMENT (THIRD)]; see also RESTATEMENT (SECOND) OF TORTS § 402A cmt. h (AM. LAW INST. 1965) [hereinafter RESTATEMENT (SECOND)] (noting that in certain cases a manufacturer or seller “may be required to give adequate warning . . . , and a product sold without such warning is in a defective condition”).

<sup>76</sup> See MARK A. GEISTFELD, PRODUCTS LIABILITY LAW 1 (2012) (“The rules are largely ones of tort law.”).

While breach of warranty is another viable theory of liability in some jurisdictions, its independent utility in products liability cases involving personal injury is primarily in “jurisdictions that have not adopted strict tort liability.” OWEN & DAVIS, *supra* note 73, at 866–67. Moreover, unlike a tort claim, “the seller may defend the warranty claim with the defenses of lack of privity, contractual assumption of the risk, express disclaimer or express limitation of remedy.” *Id.* at 867.

<sup>77</sup> See OWEN, *supra* note 74, at 244 (“The doctrine of strict liability in tort, from the 1970s into the early 2000s, was widely considered the principal theory of recovery in modern products liability law—as it still is thought to be in many American jurisdictions today.”).

<sup>78</sup> See *id.* at 58 (noting that negligence was the “principal basis of recovery in products liability cases” until the 1960s and remains “the classic products liability claim in American law”).

<sup>79</sup> See, e.g., MICHAEL I. KRAUSS, PRINCIPLES OF PRODUCTS LIABILITY 142 (2d ed. 2014) (“[C]ourts have increasingly admitted that the test for informational defect is negligence-based.”); OWEN & DAVIS, *supra* note 73, at 836 (“Most jurisdictions have reached the conclusion that there is no material distinction between a claim in negligent failure to warn and strict tort liability failure to warn.”). Even if analytically equivalent, where plaintiffs have a choice “[s]trict liability continues to be the theory of choice because of the ability to

strict, the warning defect test has all the trappings of a rule of negligence.<sup>80</sup> Second, the distinction—whether doctrinal or superficial—between negligence and strict liability for warning defects has no bearing on preemption analysis, at least for generic drug labeling. This is because an allegation of liability under either theory necessarily contends that the defendant has breached an affirmative duty.<sup>81</sup> Indeed, the Court in *Mensing* focused solely on the duty imposed by state tort law, conducting its preemption analysis without reference to any theory of liability.<sup>82</sup>

Reflecting this general state of the law, the Restatement (Third) of Torts: Products Liability takes a functionalist view of warning defects and frames the analysis “without regard to doctrinal application of negligence, warranty, or strict tort liability principles.”<sup>83</sup> Typically, “the plaintiff identifies a safety instruction that is not in the allegedly defective warning, and shows that an instruction to this effect would alert the ordinary consumer to the need to take the precaution while using the product, thereby reducing risk in a cost-effective manner.”<sup>84</sup> While in the context of prescription drugs the warning will often be analyzed from the perspective of the patient’s physician

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pursue non-manufacturing sellers such as retailers and others.” OWEN & DAVIS, *supra* note 73, at 853.

<sup>80</sup> See OWEN & DAVIS, *supra* note 73, at 838 (“[M]any jurisdictions using a strict liability theory for warning claims developed a test that devolved to a familiar negligence-like balancing . . .”). While some courts still refuse to concede that the warning-defect test is one of negligence, they nonetheless have acknowledged that “any posited distinction between strict liability and negligence principles is illusory.” KRAUSS, *supra* note 79, at 142 (quoting *Olson v. Proscoco, Inc.*, 522 N.W.2d 284, 289 (Iowa 1994)). Indeed, “[e]ven staunch defenders of strict liability have concluded that informational defect case law is hard to reconcile with their vision.” *Id.* (citing *Anderson v. Owens-Corning Fiberglas Corp.*, 810 P.2d 549, 563 (Cal. 1991) (Mosk, J., concurring in part and dissenting in part) (“We should consider the possibility of holding that failure to warn actions lie solely on a negligence theory.”)).

<sup>81</sup> See *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2474 n.1, 2480 (2013) (noting “most common law causes of action for negligence and strict liability do not exist merely to spread risk, but rather impose affirmative duties” and finding plaintiff’s product liability claim against a generic manufacturer preempted under *Mensing*).

<sup>82</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2577 (2011) (describing the case based on a theory of preemption, without any use of the words “strict liability” or “negligence”).

<sup>83</sup> OWEN & DAVIS, *supra* note 73, at 838 (citing RESTATEMENT (THIRD), *supra* note 75, § 2(c) (“A product . . . is defective because of inadequate instructions or warnings when the foreseeable risks of harm posed by the product could have been reduced or avoided by the provision of reasonable instructions or warnings . . . and the omission of the instructions or warnings renders the product not reasonably safe.”)).

<sup>84</sup> MARK A. GEISTFELD, *TORT LAW: THE ESSENTIALS* 345 (2008). However, in failure-to-update cases, see discussion *infra* Part III, a plaintiff need only point to the updated warning on the brand-name drug for the source of the missing safety instructions.

rather than an ordinary consumer,<sup>85</sup> at bottom the inquiry is whether “reasonable instructions or warnings regarding foreseeable risks of harm” were provided.<sup>86</sup>

### C. Preemption of Failure-to-Warn Claims Against Brand Name Drugs

Returning to the opening storyline, after a Vermont jury awarded \$7.4 million to Levine, Wyeth appealed the verdict all the way to the U.S. Supreme Court.<sup>87</sup> As Wyeth noted, the FDA had sanctioned the initial warning label for Phenergan when it approved the drug in 1955.<sup>88</sup> Over the next forty-five years, the FDA approved various changes to the label as a result of supplemental applications from, and correspondence with, Wyeth, and a “new” label was approved just two years before the drug was administered to Levine.<sup>89</sup>

The Court, however, was unconvinced by Wyeth’s impossibility and obstacle preemption arguments,<sup>90</sup> concluding that “the FDA’s approvals [do not] provide Wyeth with a complete defense to Levine’s tort claims.”<sup>91</sup> Justice Stevens, writing for the majority, first noted that while Wyeth was generally prohibited from altering Phenergan’s warning label unilaterally, an FDA regulation known as “changes being effected” (CBE) did permit labeling changes “to ‘add or

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<sup>85</sup> This is the “learned intermediary doctrine” under which “the pharmaceutical manufacturer’s duty to warn is satisfied by conveying adequate warnings to the prescribing physician or other health care provider as informed intermediaries.” OWEN & DAVIS, *supra* note 73, 887–88. The Restatement (Third) requires that the necessary warning be provided to “health-care providers who are in a position to reduce the risks of harm in accordance with the instructions or warnings” unless “the manufacturer knows or has reason to know that health-care providers will not be in a position to reduce the risks of harm in accordance with the instructions or warnings,” in which case the warning should be given to the patient. RESTATEMENT (THIRD), *supra* note 75, § 6(d)(1)–(2). Though the doctrine is often thought to be “generally accepted,” *id.* § 6 cmt. e, there is admittedly some dispute. Compare *In re Norplant Contraceptive Prods. Liab. Litig.*, 215 F. Supp. 2d 795, 806 (E.D. Tex. 2002) (concluding that forty-eight states, the District of Columbia, and Puerto Rico “apply the learned intermediary doctrine to define a pharmaceutical company’s duty to warn of risks associated with the use of a prescription drug”), with *State ex rel. Johnson & Johnson Corp. v. Karl*, 647 S.E.2d 899, 903–04 (W. Va. 2007) (acknowledging the figure from *In re Norplant* but concluding that “the total number of jurisdictions recognizing the learned intermediary doctrine, either by decision of the highest court or by statute, is only twenty-two”).

<sup>86</sup> RESTATEMENT (THIRD), *supra* note 75, § 6(d).

<sup>87</sup> *Wyeth v. Levine*, 555 U.S. 555, 558 (2009).

<sup>88</sup> *Id.* at 561 (“The FDA first approved injectable Phenergan in 1955.”).

<sup>89</sup> See *id.* at 561–62 (describing various changes to Phenergan’s label that were made between 1955 and 1998).

<sup>90</sup> See *id.* at 581 (“We conclude that it is not impossible for Wyeth to comply with its state- and federal-law obligations and that Levine’s common-law claims do not stand as an obstacle to the accomplishment of Congress’ purposes in the FDCA.”).

<sup>91</sup> *Id.* at 558–59.

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'" without prior FDA approval.<sup>92</sup> Although the FDA could have rejected such a change, the Court declined to find impossibility preemption—particularly in light of the “demanding” nature of such a defense<sup>93</sup>—“absent clear evidence that the FDA would not have approved a change to Phenergan’s label.”<sup>94</sup>

The Court similarly concluded that state tort law did not frustrate the federal regulatory scheme.<sup>95</sup> The Court found that the Food, Drug, and Cosmetic Act (FDCA) does *not* constitute “both a floor and a ceiling for drug regulation.”<sup>96</sup> Pointing to the fact that Congress had included an express preemption clause in the Medical Device Amendments but had neglected to add one for prescription drugs across multiple amendments to the FDCA over several decades,<sup>97</sup> the majority found no congressional intent to preempt state products liability claims.<sup>98</sup> Furthermore, the Court rejected the argument—advanced by both Wyeth and the United States as amicus—“that, because the FDCA requires the FDA to determine that a drug is safe and effective under the conditions set forth in its labeling,” the FDA’s approval of the Phenergan label resulted from an exacting cost-benefit analysis and “established a specific labeling standard that leaves no room for different state-law judgments.”<sup>99</sup> Finding the Government’s position contradictory to the purposes of Congress<sup>100</sup> and undeserving of any administrative deference,<sup>101</sup> the Court held that Levine’s state

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<sup>92</sup> *Id.* at 568 (quoting 21 C.F.R. § 314.70(c)(6)(iii)(A), (C) (2008)). For a more detailed discussion of the CBE process and the FDA’s regulation of generic drugs, see *infra* notes 115–17.

<sup>93</sup> *Id.* at 573.

<sup>94</sup> *Id.* at 571.

<sup>95</sup> *Id.* at 580.

<sup>96</sup> *Id.* at 573.

<sup>97</sup> See *id.* at 574–75 (“Congress could have applied the pre-emption clause [in the 1976 Medical Device Amendments] to the entire FDCA. It did not do so, but instead wrote a pre-emption clause that applies only to medical devices.” (quoting *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 327 (2008))).

<sup>98</sup> See *id.* at 575 (“[Congress’s] silence on the issue, coupled with its certain awareness of the prevalence of state tort litigation, is powerful evidence that Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness.”).

<sup>99</sup> *Id.*

<sup>100</sup> *Id.* at 577.

<sup>101</sup> See *id.* at 581 (“[T]he FDA’s recently adopted position that state tort suits interfere with its statutory mandate is entitled to no weight.”). The Agency’s new stance on the purportedly preemptive effect of its drug approvals first appeared in the preamble to a 2006 FDA regulation. See 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) (“FDA believes that under existing preemption



tort claims did not interfere with—and therefore were not preempted by—federal regulations.<sup>102</sup>

#### *D. Preemption of Failure-to-Warn Claims Against Generic Drugs*

Two years later, the Court reached a seemingly contradictory result in Gladys Mensing's case.<sup>103</sup> Writing for a majority of five, Justice Thomas explained that it was not possible for PLIVA, a manufacturer of generic metoclopramide, to simultaneously comply with its duties under both federal and state law.<sup>104</sup> The Court thus held that, although federal law had not barred Levine's failure-to-warn suit against Wyeth, Mensing's analogous claims against a generic manufacturer were preempted.<sup>105</sup>

This result turned entirely on what the Court believed were material differences between the federal regulations governing brand-name drugs and those governing generics.<sup>106</sup> Deferring to the FDA's interpretation of the Agency's own regulations, the Court noted that "the warning labels of a brand-name drug and its generic copy must always be the same—thus, generic drug manufacturers have an ongoing federal duty of sameness."<sup>107</sup> Indeed, under FDA regulations, the Agency may withdraw approval from a generic drug whose labeling "is no longer consistent with" the RLD.<sup>108</sup> The FDA also "interpret[ed] the CBE regulation to allow changes to generic drug labels only when a generic drug manufacturer changes its label to match an updated brand-name label or to follow the FDA's instructions."<sup>109</sup> As such, it

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principles, FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law."). Finding that the FDA, "without offering States or other interested parties notice or opportunity for comment, articulated a sweeping position on the FDCA's pre-emptive effect," the Court found the FDA's views "inherently suspect." *Levine*, 555 U.S. at 577.

<sup>102</sup> See *Levine*, 555 U.S. at 581 (affirming the Vermont Supreme Court's judgment for *Levine*).

<sup>103</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011).

<sup>104</sup> *Id.* at 2578.

<sup>105</sup> See *id.* at 2581 ("Here, state law imposed a duty on the Manufacturers to take a certain action, and federal law barred them from taking that action. . . . [Conversely,] the federal regulations applicable to Wyeth allowed the company, of its own volition, to strengthen its label in compliance with its state tort duty.").

<sup>106</sup> *Id.* at 2582 ("[T]he federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers.").

<sup>107</sup> *Id.* at 2574–75 (internal quotation marks omitted).

<sup>108</sup> 21 C.F.R. § 314.150(b)(10) (2015).

<sup>109</sup> *Mensing*, 131 S. Ct. at 2575.

was not possible for PLIVA to comply with federal labeling laws while also providing a reasonably safe warning as required by state law.<sup>110</sup>

## II THE FDA'S PROPOSED RULE ON GENERIC DRUG LABELING

In 2013, the FDA decided to use its rulemaking authority to counteract *Mensing*.<sup>111</sup> The Agency has proposed amendments to existing regulations that would allow generic manufacturers to make certain updates to their warning labels unilaterally. These warning updates could be made without prior FDA review or approval and “irrespective of whether the revised labeling differs from that of the [reference listed drug].”<sup>112</sup> The Agency proposes to allow generic manufacturers to utilize a supplemental application process commonly known as “changes being effected supplements” or “CBE-0 supplements.”<sup>113</sup>

A CBE labeling supplement is a special mechanism—already used by brand-name manufacturers—that permits the manufacturer of an FDA-approved drug to circumvent the usual requirement that changes to the approved label can only be made upon *prior* FDA approval of a supplemental application.<sup>114</sup> More specifically, a CBE-0

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<sup>110</sup> *Id.* at 2577–76; *see also id.* at 2577 (describing PLIVA’s duty under state tort law “to adequately and safely label their products”). The FDA, arguing against preemption, pressed that PLIVA nonetheless had a federal duty to ask the FDA to help strengthen the Reglan/metoclopramide warning label. *Id.* at 2576–78. The Court noted that even if such a duty existed, requesting FDA assistance would fulfill only PLIVA’s federal duty and not the “state tort-law duty to provide adequate labeling.” *Id.* at 2578. While the “possibility of impossibility,” *id.* at 2581 n.8 (quoting *id.* at 2587 (Sotomayor, J., dissenting)), was insufficient to establish preemption in *Levine*, Justice Thomas concluded that the mere “possibility of *possibility*” did not defeat preemption in *Mensing, id.*

For a discussion of how state courts have interpreted *Mensing* narrowly to find that certain tort claims are not preempted (including the failure-to-update claims discussed in this Note, *see infra* Part III), see Arlen W. Langvardt, *Generic Pharmaceuticals and the “Unfortunate Hand” Dealt to Harmed Consumers: The Emerging State Court Resistance*, 17 *MINN. J.L. SCI. & TECH.* (forthcoming 2016).

<sup>111</sup> *See* Brief for the United States as Amicus Curiae Supporting Petitioner, *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013) (No. 12-142), 2013 WL 314460, at \*15 n.2 (“Th[e] Office [of the Solicitor General] has been informed that FDA is considering a regulatory change that would allow generic manufacturers, like brand-name manufacturers, to change their labeling in appropriate circumstances. If such a regulatory change is adopted, it could eliminate preemption of failure-to-warn claims against generic-drug manufacturers.”).

<sup>112</sup> Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,986 (proposed Nov. 13, 2013) (to be codified at 21 C.F.R. pts. 314, 601) (emphasis added).

<sup>113</sup> *Id.* at 67,986–87.

<sup>114</sup> Under FDA regulations, “major changes,” 21 C.F.R. § 314.70(b) (2015), to an approved application require prior FDA approval. *Id.* § 314.70(b)(3). This encompasses all changes that have “a substantial potential to have an adverse effect on the identity,

supplement permits the manufacturer to effectuate a labeling change—and begin distributing products with the revised label—as soon as the FDA receives the supplemental application.<sup>115</sup> Certain labeling changes that “reflect newly acquired information” can currently be made using a CBE-0 supplement.<sup>116</sup>

The primary change in the proposed rule expands the applicability of a narrow subpart of the CBE process, presently section 314.70(c)(6)(iii) of the Code of Federal Regulations, to ANDA holders.<sup>117</sup> This would allow ANDA holders to make labeling changes unilaterally, upon submission of a supplement to both the FDA and the NDA holder for the RLD, “to reflect newly acquired information” in order to accomplish any of five permissible purposes listed in the regulation.<sup>118</sup> These purposes are:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under §201.57(c) of this chapter;

(B) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdose;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.<sup>119</sup>

Though the FDA’s notice of proposed rulemaking states that the purpose of the rule is to place generic and brand-name drug manufacturers on a level playing field with respect to “safety-related labeling

strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product,” *id.* § 314.70(b)(1), and presumptively includes most labeling changes, *id.* § 314.70(b)(2)(v).

<sup>115</sup> *Id.* § 314.70(c)(6). The CBE-0 is actually a special exception to the application process for “moderate changes” under section 314.70(c), commonly referred to as “CBE-30.” A CBE-30—so named because, absent other action by the FDA, the change may be effected thirty days after the FDA receives the supplemental application, *id.* § 314.70(c)(4)—is required for changes having “a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product.” *Id.* § 314.70(c).

<sup>116</sup> *Id.* § 314.70(c)(6)(iii).

<sup>117</sup> See Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. at 67,998 (proposing the creation of section 314.70(c)(8), which would allow ANDA holders to submit CBE-0 applications).

<sup>118</sup> *Id.*

<sup>119</sup> 21 C.F.R. § 314.70(c)(6)(iii)(A)–(E) (2015).

changes,”<sup>120</sup> there seems little doubt that “[t]he rule was proposed in response to” *Mensing*.<sup>121</sup> The notice of proposed rulemaking explicitly details the disparate treatment of failure-to-warn tort claims against generic and brand-name manufacturers that resulted from the Supreme Court’s decisions in *Levine* and *Mensing*.<sup>122</sup> It also acknowledges that “[i]f this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs.”<sup>123</sup> Even more telling is the sole justification provided under the heading “Need for Regulation” in the FDA’s Preliminary Regulatory Impact Analysis on the proposed rule: “As a result of [*Levine* and *Mensing*] . . . , access to the courts is dependent on whether an individual is dispensed a ‘brand name’ or generic drug.”<sup>124</sup>

It is uncertain when, or even if, the rule will be finalized and implemented.<sup>125</sup> While the proposed rule was first published in the Federal Register on November 13, 2013, the Agency announced on December 27 of that year that the initial sixty-day comment period would be extended an additional sixty days, to March 13, 2014.<sup>126</sup> The final rule was expected to be published in December 2014, but one month before the scheduled date the Agency disclosed that it was

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<sup>120</sup> Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. at 67,985.

<sup>121</sup> Ed Silverman, *Lawmakers Ask White House to Review FDA Rule for Generic Label Changes*, WALL ST. J. PHARMALOT (June 26, 2014, 1:19 PM), <http://blogs.wsj.com/pharmalot/2014/06/26/lawmakers-ask-white-house-to-review-fda-rule-for-generic-label-changes/>; *see also* Brief for the United States as Amicus Curiae Supporting Petitioner, *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013) (No. 12-142), 2013 WL 314460, at \*15 n.2 (“FDA is considering a regulatory change that . . . could eliminate preemption of failure-to-warn claims against generic-drug manufacturers.”).

<sup>122</sup> Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. at 67,988–89.

<sup>123</sup> *Id.* at 67,989.

<sup>124</sup> *See* U.S. FDA, FDA-2013-N-0500, SUPPLEMENTAL APPLICATIONS PROPOSING LABELING CHANGES FOR APPROVED DRUGS AND BIOLOGICAL PRODUCTS: PRELIMINARY REGULATORY IMPACT ANALYSIS; INITIAL REGULATORY FLEXIBILITY ANALYSIS; UNFUNDED MANDATES REFORM ACT ANALYSIS 5 (2013) [hereinafter FDA PRELIMINARY REGULATORY IMPACT ANALYSIS], available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/UCM375128.pdf>.

<sup>125</sup> In 2014, the FDA suggested that “the final rule may differ in some respects from the proposal to reflect public comments.” *Examining Concerns Regarding FDA’s Proposed Changes to Generic Drug Labeling: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 113th Cong. (2014) (statement of Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration), available at <http://docs.house.gov/meetings/IF/IF14/20140401/101823/HHRG-113-IF14-Wstate-WoodcockJ-20140401.pdf>.

<sup>126</sup> Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products; Correction and Extension of Comment Period, 78 Fed. Reg. 78,796 (Dec. 27, 2013).

delaying publication of the final rule until September 30, 2015.<sup>127</sup> Responding to requests from industry groups and Congress, the FDA announced that it would hold a public hearing on the proposed rule on March 27, 2015, and that it was reopening the comment period until April 27, 2015.<sup>128</sup> At the time of writing, September 30, 2015 has come and gone with no indication of when or if a final rule will be published.<sup>129</sup>

The proposed rule raises several concerns. First, any such rule seems almost certain to face legal challenges over the FDA's ability to eliminate the sameness requirement. Jay Lefkowitz, who argued on behalf of the generic manufacturer before the Supreme Court in *Mensing*, opined that the proposed rule "expressly conflicts with the Hatch Waxman Act" and contradicts the way in which the Act has consistently been interpreted for the past quarter century.<sup>130</sup> Second, the rule is likely to reduce the effectiveness of prescription drug labeling. Forcing generic manufacturers to update labels, independent of brand manufacturers, will lead to disparate warning labels on purportedly identical products, confusing both consumers and healthcare providers. Compounding this problem is the potential for generic manufacturers to include a profusion of unnecessary warnings as a defense against tort liability.<sup>131</sup> Finally, the FDA's proposed scheme may prove incredibly costly to administer and implement, further frustrating the express purpose of the Hatch-Waxman Act "to make available more low cost generic drugs by establishing a generic drug

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<sup>127</sup> Bronwyn Mixer, *FDA Delays Publication of Final Rule on Generic Drug Labeling Until Fall 2015*, 12 PHARM. L. & INDUS. REP. 1601, 1601 (2014).

<sup>128</sup> Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products; Public Meeting; Request for Comments; Reopening of the Comment Period, 80 Fed. Reg. 8577, 8577-78 (Feb. 18, 2015).

<sup>129</sup> In the meantime, the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Generic Pharmaceutical Association (GPhA)—the leading organizations representing brand-name and generic pharmaceutical companies, respectively—have put forward an "alternative solution" called "Expedited Agency Review (EAR)," which would completely eliminate the CBE-0 and require prior FDA approval of any safety-related labeling change. Letter from Ralph G. Neas, President & CEO, GPhA & John J. Castellani, President & CEO, PhRMA, to Margaret Hamburg, Comm'r, Food & Drug Admin. (Nov. 14, 2014), [http://www.gphaonline.org/media/cms/EAR\\_letter\\_to\\_FDA.pdf](http://www.gphaonline.org/media/cms/EAR_letter_to_FDA.pdf). The proposal would require the FDA, either on its own initiative or on the request of a brand-name or generic manufacturer, to determine on an expedited basis whether a labeling change is required for a particular drug. *Id.*

<sup>130</sup> Ed Silverman, *FDA Rule Change on Generic Labeling Is a Problem: Lefkowitz Explains*, WALL ST. J. PHARMALOT (Oct. 23, 2014, 10:28 AM), <http://blogs.wsj.com/pharmalot/2014/10/23/fda-rule-change-on-general-labeling-is-a-problem-lefkowitz-explains/>. Lefkowitz similarly anticipates that, if the FDA rule is finalized, "a lawsuit will be filed immediately seeking to prevent the regulation from taking effect." *Id.*

<sup>131</sup> See discussion *infra* Part II.B.

approval procedure . . . .”<sup>132</sup> The rule will likely expose generic manufacturers to state tort liability by abrogating *Mensing*.<sup>133</sup> Those burdens—along with any costs associated with preparing, submitting, and implementing revised warnings—seem likely to be borne by consumers in the form of higher generic drug prices.

### A. *Legality of the Proposed Rule*

An initial hurdle that any final rule will have to clear is whether the rule is within the FDA’s statutory authority. The FDA has previously interpreted its own regulations to mean that a generic drug manufacturer may not submit a CBE-0 labeling supplement except either to effectuate a labeling update to conform with the approved labeling for the brand-name drug or in response to the FDA’s specific request that a labeling change be submitted utilizing the CBE-0 process.<sup>134</sup> A number of commentators, however, have argued that this requirement stems from FDCA itself—specifically, the Hatch-Waxman Act.<sup>135</sup> While the statutory text is largely directed at the content of the new drug application,<sup>136</sup> some language in *Mensing* suggests there is ambiguity as to whether the sameness requirement stems from the FDCA and not merely from FDA regulations.<sup>137</sup> Moreover, such a change in regulatory policy might make the validity of the Agency’s interpretation subject to a heightened standard of review under the Administrative Procedure Act.<sup>138</sup>

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<sup>132</sup> H.R. REP. NO. 98-857, pt. 1, at 14 (1984).

<sup>133</sup> See Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,989 (Nov. 13, 2013) (“If this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs.”).

<sup>134</sup> *Id.* at 67,988.

<sup>135</sup> See Greg Ryan, *FDA’s Generic-Drug Plan Will Live or Die on Sameness Rule*, LAW360 (July 8, 2013, 10:07 PM), <http://www.law360.com/articles/455523/fda-s-generic-drug-plan-will-live-or-die-on-sameness-rule> (“Opponents of a regulatory change argue that the Hatch-Waxman Amendments to the FDCA mandate that the labels must always match.”).

<sup>136</sup> See 21 U.S.C. § 355(j)(2)(A)(v) (describing the requirements for FDA approval of a generic drug, including “information to show that the labeling proposed for the new drug is the same as the labeling approved for the [RLD]”).

<sup>137</sup> See *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2575 (2011) (deferring to the FDA’s view “that CBE changes unilaterally made to strengthen a generic drug’s warning label would violate *the statutes* and regulations requiring a generic drug’s label to match its brand-name counterpart’s” (emphasis added)).

<sup>138</sup> See *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 514–15 (2009) (noting that an agency’s “rescission of a prior regulation” or “prior action” will sometimes require “a more detailed justification than what would suffice for a new policy created on a blank slate” in order to withstand judicial scrutiny).

### B. *Effects on Labeling*

The proposed rule may also adversely affect the quality and quantity of information contained in generic warning labels in two distinct ways. First, by permitting labeling differences between the brand-name and generic versions of the same drug, the proposed rule undercuts Hatch-Waxman's goal of fostering generic competition to drive down prescription drug prices.<sup>139</sup> Generic competition would obviously have the greatest impact on brand-name prices if consumers selected between a brand-name drug and a generic equivalent based solely on price, but the biggest obstacle for generics in the United States has always been convincing consumers that they are equivalent to and just as safe as brand-name drugs. Even if they cleared the heightened regulatory barriers that existed before Hatch-Waxman, early generics faced an uphill battle against public opinion.<sup>140</sup> In contrast to the overwhelming prevalence of modern generic substitution laws,<sup>141</sup> less than half a century ago nearly all states had some form of prohibition against generic substitution.<sup>142</sup> Even today, the FDA acknowledges that consumers' primary concern about generic drugs is whether their "quality and performance" are comparable to brand-name drugs.<sup>143</sup> Warning discrepancies, even if temporary, between a brand-name drug and a generic "equivalent"—or across generic substitutes—"may cause patient and provider confusion" and "may

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<sup>139</sup> See Letter from Twenty-Eight Members of Congress to Margaret A. Hamburg, Comm'r, FDA 2 (Jan. 22, 2014) ("The labeling on the generic products should be identical to the labeling on the branded product so providers and patients are comfortable with the risks and benefits of the product they are using regardless of the name of the company on the bottle or vial.").

<sup>140</sup> See *supra* note 14 (describing state generic substitution laws).

<sup>141</sup> See BUREAU OF CONSUMER PROT., DRUG PRODUCT SELECTION: STAFF REPORT TO THE FEDERAL TRADE COMMISSION 150 (1979) ("By 1972, virtually every jurisdiction except the District of Columbia had enacted some form of antisubstitution law or regulation.").

<sup>142</sup> See Victor E. Schwartz, Phil Goldberg & Cary Silverman, *Warning: Shifting Liability to Manufacturers of Brand-Name Medicines When the Harm Was Allegedly Caused by Generic Drugs Has Severe Side Effects*, 81 FORDHAM L. REV. 1835, 1839 (2013) ("In the early twentieth century, consumers had . . . broad concerns that generic drugs could be counterfeit or have wide variations in quality from their brand-name counterparts."). In contrast to the overwhelming prevalence of generic substitution laws today, see *supra* note 14 (describing state generic substitution laws), less than half a century ago nearly all states had some form of prohibition against generic substitution, see BUREAU OF CONSUMER PROT., *supra* note 141, at 150 ("By 1972, virtually every jurisdiction except the District of Columbia had enacted some form of antisubstitution law or regulation.").

<sup>143</sup> CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FDA, *GENERIC DRUGS 5*, available at <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm127615.pdf>.

undermine confidence in FDA-approved generics.”<sup>144</sup> Indeed, the FDA’s amicus brief in *Mensing* stressed that the Agency “places a very high priority [on] assuring consistency in labeling, so as to minimize any cause for confusion among health care professionals and consumers as well as to preclude a basis for lack of confidence in the equivalency of generic versus brand name products.”<sup>145</sup> By eliminating the duty of sameness and permitting greater labeling discrepancy between a brand-name drug and its generic equivalent(s), the proposed rule creates a visible distinction that unnecessarily complicates the purchasing decision.

Second, regardless of labeling discrepancies across purportedly bioequivalent drugs, the proposed rule may undermine individual warning labels themselves. While the FDA predicts that “[e]mpowering generic drug companies to update their own drug safety information” will induce such companies to “more actively participate with FDA in ensuring the timeliness, accuracy, and completeness” of their warning labels,<sup>146</sup> this overvalues the free flow of such information and ignores the potentially perverse incentives the proposed rule creates for generic manufacturers. Expanding the availability of the CBE-0 mechanism circumvents *Mensing* preemption analysis by giving generic manufacturers a means of unilaterally complying with their duty under state tort law.<sup>147</sup> But because utilizing the CBE-0 may shield a generic manufacturer from future liability, one

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<sup>144</sup> Ohio Public Employees Retirement System, Comment Letter on Proposed Rule “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” FDA-2013-N-0500, at 1 (Mar. 10, 2014). “This confusion could undermine acceptance of interchangeability and reduce the collective confidence of patients, prescribers, and payers in generic drugs’ safety and efficacy.” *Id.* at 2; *see also* California Public Employees’ Retirement System, Comment Letter on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, at 1–2 (Mar. 12, 2014) (expressing a similar concern that multiple labels could cause consumer confusion).

<sup>145</sup> Brief for the United States as Amicus Curiae Supporting Respondents at 4, *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011) (No. 09-993), 2011 WL 741927, at \*4 (internal quotation marks omitted) (alteration in original); *see also* Abbreviated New Drug Application Regulations, 57 Fed. Reg. 17,950, 17,961 (Apr. 28, 1992) (“Consistent labeling will assure physicians, health professionals, and consumers that a generic drug is as safe and effective as its brand-name counterpart.”).

<sup>146</sup> *See* Janet Woodcock, *Working to Improve the Communication of Important Drug Safety Information About Generic Drugs*, FDA VOICE (Nov. 8, 2013) <http://blogs.fda.gov/fdavoices/index.php/2013/11/working-to-improve-the-communication-of-important-drug-safety-information-about-generic-drugs/#sthash.pixpjeHV.dpuf> (“Faster safety updates and easier access to this information should be a win-win for all involved.”).

<sup>147</sup> *See* Ralph F. Hall & Michelle Mercer, *Rethinking Lohr: Does “SE” Mean Safe and Effective, Substantially Equivalent, or Both?*, 13 MINN. J.L. SCI. & TECH. 737, 764 (2012) (“Cases such as *Wyeth* and *Mensing* turned on whether the company could modify the product in question or the product labeling without prior FDA approval.”).



would expect a deluge of updates resulting in overwarning that might actually render the warning labels *less* safe.<sup>148</sup>

While some have raised empirical questions about the actual occurrence or harm of overwarning,<sup>149</sup> the concern may be more legitimate in the context of the proposed FDA rule because of several key differences between the respective markets for brand name and generic drugs. Certain incentives exist that discourage brand-name manufacturers from overwarning. For instance, competitive marketing among brand-name drugs means that labeling full of “superfluous safety information not tethered to science but merely intended to shield [manufacturers] from lawsuits” is merely fodder for the competition.<sup>150</sup> In contrast, such market-based incentives against overwarning do not apply to generic drugs, as they are typically not marketed based on their labeling and instead “usually compete solely on distribution and price.”<sup>151</sup>

Moreover, even if the proposed rule incentivized generic manufacturers to meaningfully utilize the CBE process to provide adequate

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<sup>148</sup> See GEISTFELD, *supra* note 84, at 346 (“Information costs can cause a new disclosure to crowd out or obscure other, potentially more important safety instructions or hazard warnings.”); James A. Henderson, Jr. & Aaron D. Twerski, *Doctrinal Collapse in Products Liability: The Empty Shell of Failure to Warn*, 65 N.Y.U. L. REV. 265, 297 n.135 (1990) (“Overwarning causes users and consumers to discount or ignore warnings that should be heeded, leading to higher accident costs which, though very real, are not before the court in failure-to-warn litigation. Overwarning also may scare some worthwhile users away, resulting in wastefully high avoidance costs.”).

<sup>149</sup> See, e.g., *Examining Concerns Regarding FDA’s Proposed Changes to Generic Drug Labeling: Hearing Before the Subcomm. on Health of the H. Comm. on Energy and Commerce*, 113th Cong. (2014) (statement of Rep. Henry A. Waxman, Ranking Member, H. Comm. on Energy and Commerce) (“We heard the exact same claims about overwarning and drug company economic distress six years ago when the Supreme Court decided the *Wyeth v Levine* case. . . . But since then we have not seen any of these dire predictions come to pass.”); Catherine M. Sharkey, State Farm “*With Teeth*”: *Heightened Judicial Review in the Absence of Executive Oversight*, 89 N.Y.U. L. REV. 1589, 1597 (2014) (discussing a 2008 incident where the FDA argued that a CBE regulation “should preempt conflicting state law requirements, so as to mitigate or prevent overwarning by drug manufacturers,” but later admitted that “of more than [3000 CBEs], the FDA had rejected the proposed warnings in only four instances and none on the basis of threatened harm to the public”).

<sup>150</sup> Scott Gottlieb, Alex Brill & Robert W. Pollock, *Proposed FDA Generic Drug Regulation: Higher Prices, No Public Health Benefit*, AM. ENTER. INST. (Mar. 12, 2014, 8:44 AM), <http://www.aei.org/publication/proposed-fda-generic-drug-regulation-higher-prices-no-public-health-benefit/> (explaining that brand-name manufacturers are incentivized against superfluous warnings because “[i]f they load their labels with superfluous safety information not tethered to science but merely intended to shield themselves from lawsuits, competing drug makers with similar medicines could use any labeling discrepancies in competitive marketing”).

<sup>151</sup> *Id.*

warning labels, they might not be capable of doing so.<sup>152</sup> For example, in objecting to the proposed rule, the National Conference of State Legislatures (NCSL) questioned, among other things, “the ability of generic drug manufacturers to *comply* with the research and labeling requirements contained in the proposed rule.”<sup>153</sup> In particular, the NCSL seemed to doubt whether those manufacturers possessed “the capacity to perform the necessary research and to comply with the other requirements established in the rule.”<sup>154</sup> These concerns seem well-founded, in part because generic manufacturers simply do not have the same sort of data and resources as brand name producers.<sup>155</sup> Unlike brand name manufacturers, generic manufacturers are generally not required to conduct detailed studies before receiving FDA approval, and are held to much less demanding post-approval monitoring and reporting requirements.<sup>156</sup>

### C. Costs

The proposed rule also seems likely to impose immense costs on both the FDA and generic manufacturers—costs which, at least in part, will likely be borne by consumers. As mentioned above, it is quite possible that the FDA will face a deluge of CBE-0 supplements if the proposed rule is finalized. Additionally, generic manufacturers will be exposed to a broad range of potential compliance and liability costs.

The FDA estimates that the costs of the rule will be minimal. Including costs to manufacturers of reviewing and submitting applications, the FDA “estimates the net annual social costs to be between

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<sup>152</sup> See National Conference of State Legislatures, Comment Letter on Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products at 1 (Mar. 13, 2014) (raising a concern about “the ability of generic drug manufacturers to comply with the research and labeling requirements contained in the proposed rule”).

<sup>153</sup> *Id.* (emphasis added).

<sup>154</sup> *Id.* The NCSL also expressed concern that the costs of compliance would ultimately be paid by consumers in the form of higher prices. *Id.*

<sup>155</sup> Marsha Blackburn, Opinion, *A Threat to Affordable Medicine*, U.S. NEWS & WORLD REP. (Apr. 7, 2014, 8:00 AM), <http://www.usnews.com/opinion/articles/2014/04/07/fda-rule-on-generic-labeling-disregards-safety-and-undermines-congress> (“Generic drug manufacturers do not have the luxury of research and development data, or post market surveillance from the time that brand products were under patent . . .”).

<sup>156</sup> Stacey B. Lee, PLIVA v. Mensing: *Generic Consumers' Unfortunate Hand*, 12 YALE J. HEALTH POL'Y L. & ETHICS 209, 221 (2012) (“[T]he FDA does not require generic manufacturers to conduct post-approval clinical studies as a condition of ANDA approval, nor do FDA regulations require generic manufacturers to perform the same postmarketing surveillance, review, and data collection activities as brand-name manufacturers.”).

\$4,237 and \$25,852.”<sup>157</sup> These figures, however, have been the subject of considerable debate.<sup>158</sup>

Regardless of the actual cost, several observers have argued that the proposed rule will inevitably impose *some* cost on generic manufacturers as a result of the potential exposure to liability.<sup>159</sup> In a comment on the proposed rule, one state pension fund openly predicted that “[t]he additional costs – in direct expenses and in possible litigation – for generic manufacturers to implement the proposed requirements will ultimately be borne by patients, large employers, and public programs like Medicare and Medicaid.”<sup>160</sup> Additionally, prices for generic pharmaceuticals have been “[s]kyrocketing” in recent months.<sup>161</sup> From November 2013 to November 2014, roughly half of all generics increased in price.<sup>162</sup> While these increases have largely been attributed to supply shortages,<sup>163</sup> one commentator has testified before Congress that these price hikes are at least in part a response

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<sup>157</sup> FDA PRELIMINARY REGULATORY IMPACT ANALYSIS, *supra* note 124.

<sup>158</sup> A study sponsored by the GPhA provided “a conservative estimate” of a \$4 billion increase in annual spending on generics based solely on costs associated with product liability due to the proposed rule. ALEX BRILL, MATRIX GLOBAL ADVISORS, FDA’S PROPOSED GENERIC DRUG LABELING RULE: AN ECONOMIC ASSESSMENT 1 (2014), available at <http://www.matrixglobaladvisors.com/GenericLabelingRule.pdf>. Critiquing Brill’s statistical methods and calling the \$4 billion estimate “completely unrealistic,” California Western School of Law Professor Robert A. Bohrer arrived at \$685 million as “a generous estimate of the average annual total liability expenses of the *brand name* pharmaceutical industry,” and concluded that the potential liability of the generic industry under the proposed rule was likely even less than that. Bob Bohrer, *An Estimate of Pharmaceutical Industry Product Liability Costs*, PHARMACEUTICAL POL’Y (Mar. 14, 2014, 5:42 PM), [http://pharmaceuticalpolicy.blogspot.com/2014/03/an-estimate-of-pharmaceutical-industry\\_14.html](http://pharmaceuticalpolicy.blogspot.com/2014/03/an-estimate-of-pharmaceutical-industry_14.html) (emphasis added).

<sup>159</sup> See, e.g., Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, 78 Fed. Reg. 67,985, 67,989 (Nov. 13, 2013) (to be codified at 21 C.F.R. pts. 314 and 601) (“If this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs.”).

<sup>160</sup> See, e.g., Ohio Public Employees Retirement System, Comment Letter on Proposed Rule “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” FDA-2013-N-0500, at 2 (Mar. 10, 2014), <http://www.regulations.gov/#!documentDetail;D=FDA-2013-N-0500-0024>.

<sup>161</sup> See, e.g., Ed Silverman, *How Much? Some Generic Drug Prices Are Skyrocketing: Analysis*, WALL ST. J. PHARMALOT (Aug. 14, 2014, 2:44 PM), <http://blogs.wsj.com/pharmalot/2014/08/14/how-much-some-generic-drug-prices-are-skyrocketing-analysis/> (“[O]ver the past 12 months . . . , the prices paid by pharmacies more than doubled for one out of 11 generics.”).

<sup>162</sup> Adam J. Fein, *In the Third Quarter, Retail Generic Drug Inflation Kept on Truckin’*, DRUG CHANNELS (Nov. 18, 2014), <http://www.drugchannels.net/2014/11/in-third-quarter-retail-generic-drug.html>. While the other approximately 50% of generic drugs declined in cost, the median decline of -6.6% was far exceeded by the median increase of +13.9%. *Id.*

<sup>163</sup> See, e.g., David Lazarus, *What’s Behind the Huge Price Jump for Some Generic Drugs?*, L.A. TIMES (Oct. 20, 2014, 6:14 PM), <http://www.latimes.com/business/la-fi-lazarus-20141021-column.html> (“Shortages of raw materials frequently are cited as a reason for higher drug prices.”).

to the proposed rule as generic manufacturers anticipate greater liability exposure.<sup>164</sup>

### III FAILURE-TO-UPDATE TORT CLAIMS

In lieu of fundamentally altering generic drug labeling regulations that have been in place for thirty years, an alternative enforcement mechanism has emerged in the form of what have been termed failure-to-update claims.<sup>165</sup> Such claims rely on the generic manufacturer's "ongoing federal duty of sameness,"<sup>166</sup> which, according to the FDA, requires that "the warning labels of a brand-name drug and its generic copy must always be the same."<sup>167</sup> Essentially the invention of enterprising products liability attorneys, this theory of liability appears to key off of language in *Mensing* suggesting that "federal law would permit [generic drug m]anufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so."<sup>168</sup>

There is currently a circuit split on whether failure-to-update claims are preempted.<sup>169</sup> The two federal courts of appeals that have split on this issue have both done so in cases involving PLIVA—a generic manufacturer of the reflux drug metoclopramide (under the brand name Reglan). In 2004, following an application by the brand-name manufacturer, the FDA approved a proposed labeling change from "Therapy longer than 12 weeks has not been evaluated and cannot be recommended" to "Therapy should not exceed 12 weeks in duration."<sup>170</sup> This new warning was not added to PLIVA's

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<sup>164</sup> See *Why Are Some Generic Drugs Skyrocketing in Price?: Hearing Before the Subcomm. on Primary Health and Aging of the S. Comm. on Health, Educ., Labor, and Pensions*, 113th Cong. 6 (2014) (testimony of Scott Gottlieb, M.D., American Enterprise Institute), available at <http://www.help.senate.gov/imo/media/doc/Gottlieb2.pdf> ("[The proposed FDA rule] would expose generic firms to the same large torts that are targeted to branded drug firms. The action may undermine some of the key public health benefits that generic drugs provide by substantially raising the industry's costs, in the process reducing access to low cost generic medicines.").

<sup>165</sup> See, e.g., *In re Darvocet, Darvon, & Propoxyphene Prods. Liab. Litig.*, 756 F.3d 917, 927–31 (6th Cir. 2014) (affirming dismissal of plaintiff's claim that generic manufacturers failed to update drug label on the ground that claim was not properly pleaded).

<sup>166</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2575 (2011).

<sup>167</sup> *Id.* at 2574–75.

<sup>168</sup> *Id.* at 2578.

<sup>169</sup> After inviting briefing from the Solicitor General, the Supreme Court denied certiorari in a failure-to-update case. See *Teva Pharm. USA, Inc. v. Superior Court*, 158 Cal. Rptr. 3d 150 (Ct. App. 2013), cert. denied, 135 S. Ct. 1152 (2015).

<sup>170</sup> *Fulgenzi v. PLIVA, Inc.*, 711 F.3d 578, 580 (6th Cir. 2013) (emphasis omitted).

metoclopramide label.<sup>171</sup> It was not until February 2009 that the Agency ordered the strongest form of warning.<sup>172</sup>

Despite holding that the plaintiffs had not adequately pleaded a failure-to-update claim, the Fifth Circuit in *Morris v. PLIVA, Inc.* went on to explain that such a claim would necessarily fail on two grounds. First, as the *Morris* plaintiffs also claimed the updated brand-name label was inadequate, the court held that “[t]ort liability does not arise for failure to attach an inadequate label.”<sup>173</sup> Second, the court read the failure-to-update claim as alleging a breach of FDA labeling requirements, and found that the “obligation sounds exclusively in federal (not state) law, and is preempted.”<sup>174</sup>

In contrast, the Sixth Circuit in *Fulgenzi v. PLIVA, Inc.* held that a failure-to-update claim was not preempted. It did note, however, that the plaintiff could “argue only that PLIVA’s warning was inadequate *to the extent* that it did not include the language contained in the updated Reglan label from 2004.”<sup>175</sup> Though the plaintiff had also argued in the district court that the updated label was inadequate, the Sixth Circuit also rejected PLIVA’s argument that the failure-to-update claim could not succeed where the alleged breach consisted of a failure to update a warning that was also inadequate under state law. While the court noted that it would be more challenging to prove the element of proximate cause under these circumstances, it pointed out that “there is no reason to believe that a severely inadequate warning would never cause an injury that a moderately inadequate warning would have prevented.”<sup>176</sup> Although *Fulgenzi* was decided after *Morris*, it did not cite or mention *Morris*.

#### A. *Desirability of Failure-to-Update*

These failure-to-update claims offer many of the same purported benefits of the FDA’s proposed rule, as well as some additional ones, but do not suffer from many of the serious drawbacks that plague the rule. First, no intricate review process by the FDA is necessary for enforcement. The current brand-name labeling is readily accessible for both generic manufacturers to consult when creating their own

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<sup>171</sup> *Id.*

<sup>172</sup> *Id.*

<sup>173</sup> *Morris v. PLIVA, Inc.*, 713 F.3d 774, 777 (5th Cir. 2013).

<sup>174</sup> *Id.* (citing 21 U.S.C. § 337(a) (2012)) (limiting suits to enforce the FDCA to those brought by the United States and, in certain circumstances, the states); *see also* *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 349 n.4 (2001) (holding that private parties cannot bring claims under the FDCA).

<sup>175</sup> *Fulgenzi*, 711 F.3d at 584.

<sup>176</sup> *Id.* at 587.

labels and for courts to examine alongside the generic labeling.<sup>177</sup> Given the FDA's failure to enforce the sameness requirements already in effect,<sup>178</sup> along with the Agency's backlog in reviewing ANDAs,<sup>179</sup> a regulatory scheme that can rely heavily on private enforcement—and minimally on the FDA—is highly desirable. Second, while failure-to-update claims will not allow as many individuals to recover as the proposed FDA rule would,<sup>180</sup> and it may be debated whether a more comprehensive compensatory scheme is needed that would cover *all* consumers harmed by generic drugs, the failure-to-update scheme may provide a path to individual recovery in a significant number of cases.<sup>181</sup> Finally, the liability imposed by failure-to-update claims actually furthers rather than hinders the overall goal of a less expensive and more efficient marketplace for generic drugs. Any increased costs imposed upon generic manufacturers in these suits are almost certainly offset by efficiency gains that result from curing and deterring inconsistencies between the brand-name and generic labeling.

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<sup>177</sup> The FDA already maintains a browseable and searchable database with labeling information for all approved drugs. *Drugs @ FDA: FDA Approved Drug Products*, U.S. FDA, <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm> (last visited Aug. 15, 2015).

<sup>178</sup> See Duke et al., *supra* note 19, at 296 (finding that more than two-thirds of drugs with multiple manufacturers had some discrepancy in their labeling).

<sup>179</sup> See Letter from Curtis Rooney, President, Healthcare Supply Chain Ass'n, to Stephen Ostroff, Acting Comm'r, FDA (May 21, 2015) ("The U.S. healthcare system has lost billions in estimated savings from generic approval delays which, according to private sector industry surveys, are facing 50-month approval times for first-time generic applications.").

<sup>180</sup> The nature of a plaintiff's failure-to-warn claim is necessarily narrower than a traditional warning defect claim, which could theoretically make recovery more difficult. See *Fulgenzi*, 711 F.3d at 588 ("Fulgenzi's claims are viable only to the extent PLIVA's actions were permitted by federal law. Thus she must argue that PLIVA should have included the language contained in the updated Reglan label by soon after July 2004, and that the failure to include that language proximately caused her injuries."). However, under the so-called "heeding presumption," there is a rebuttable presumption that the plaintiff would have heeded a warning that the defendant had a duty to provide (since it would make little sense to say that tort law imposed a duty to warn where it is more likely than not that the warning would not have altered consumer behavior in a way that would have avoided some harm). See *GEISTFELD*, *supra* note 76, at 380–87 (providing an overview of and rationales for the heeding presumption).

<sup>181</sup> While the viability of any particular failure-to-update claim will depend on the specific discrepancies between the brand-name and generic warning labels, it seems reasonable to conclude that a substantial number of failure-to-update claims could be advanced given the overall prevalence of such labeling discrepancies. See Duke et al., *supra* note 19, at 296 (finding that more than two-thirds of drugs with multiple manufacturers had some discrepancy in their labeling).

### B. *Legal Viability of Failure-to-Update Claims*

Failure-to-update cases are grounded in product liability claims of defective warnings.<sup>182</sup> The unilateral changes a generic manufacturer may make to its labeling, however, are limited. Under federal law, when a generic drug manufacturer initially seeks FDA approval, it must ensure that its warning label is virtually identical to the brand-name drug.<sup>183</sup> Moreover, under the FDA's interpretation of its own regulations, "generic drug manufacturers have an ongoing federal duty of sameness."<sup>184</sup> Though the Agency's CBE regulation permits brand-name drug manufacturers to provide superior warning labels by merely notifying the FDA, the Agency "interprets the CBE regulation to allow changes to generic drug labels only when a generic drug manufacturer changes its label to match an updated brand-name label or to follow the FDA's instructions."<sup>185</sup>

Although in the wake of *Mensing* it might verge on malpractice not to argue for preemption against any state tort claim involving the warning label on a generic drug, the preemption questions posed by failure-to-update claims are quite distinct from those raised by more general warning defect claims against generic manufacturers. In the case of general warning defect claims, any state law requirement to strengthen a warning label creates an impossibility preemption scenario: Because generic manufacturers are generally prohibited from making unilateral changes to their warning labels, they cannot simultaneously conform to the state tort duty and federal regulations.<sup>186</sup> Failure-to-update claims, however, would appear to successfully skirt the impossibility issue. Instead of independently formulating a safety instruction that state tort law arguably requires, the plaintiff merely identifies the updated warning added by the brand-name manufacturer.<sup>187</sup> In such a scenario, the manufacturer not only may, but is

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<sup>182</sup> See *supra* notes 73–86 and accompanying text (explaining the basic framework of a defective warning claim).

<sup>183</sup> See, e.g., 21 U.S.C. § 355(j)(2)(A)(v), (4)(G) (2012); 21 C.F.R. §§ 314.94(a)(8), 314.127(a)(7) (2014).

<sup>184</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2575 (2011) (citations omitted) (internal quotation marks omitted).

<sup>185</sup> *Id.* (citations omitted).

<sup>186</sup> See *id.* at 2577–78 ("We find impossibility [preemption] here. It was not lawful under federal law for the Manufacturers to do what state law required of them. And even if they had fulfilled their federal duty to ask for FDA assistance, they would not have satisfied the requirements of state law.")

<sup>187</sup> See Mark A. Geistfeld, *Tort Law in the Age of Statutes*, 99 IOWA L. REV. 957, 984 (2014) (explaining that courts may defer to a statute or regulation as a basis of tort liability even when the black-letter rule of negligence per se is not satisfied); cf. *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 354 (2001) (Stevens, J., concurring) (suggesting that a fraud-on-the-FDA claim neither would nor should be preempted where the agency had

arguably *required* to, cure the alleged breach of the state tort duty because of a “parallel requirement” that exists under federal law.<sup>188</sup>

Having successfully navigated “the Scylla of contemporary preemption analysis” by alleging a parallel requirement, the primary substantive challenge to failure-to-update claims becomes the “looming Charybdis”<sup>189</sup> of implied preemption under *Buckman Co. v. Plaintiffs’ Legal Committee*.<sup>190</sup> The plaintiffs in *Buckman* alleged that a manufacturer of bone screws had made fraudulent misrepresentations to the FDA.<sup>191</sup> On the theory that absent such fraud the FDA would not have approved the screws, the plaintiffs alleged that the “fraud-on-the-FDA” was the cause of their injuries.<sup>192</sup> A unanimous Supreme Court held that such claims were preempted.<sup>193</sup>

The precise scope of *Buckman*, however, remains unclear. Focusing on some of the broader statements made in the opinion, one might conclude that *Buckman* is a fairly sweeping opinion that dramatically expands the preemptive force of federal law. For example, the Court noted there was conflict preemption because “the federal statutory scheme amply empowers the FDA to punish and deter fraud against the Administration, and . . . this authority is used by the Administration to achieve a somewhat delicate balance of statutory objectives”—a balance that could “be skewed by allowing fraud-on-

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made a prior determination of fraud because, in such a case, “state damages remedies would not encroach upon, but rather would supplement and facilitate, the federal enforcement scheme”); Catherine M. Sharkey, *The Fraud Caveat to Agency Preemption*, 102 Nw. U. L. REV. 841, 849 (2008) (“By requiring an antecedent determination . . . by the FDA, the approach [to preemption endorsed by Justice Stevens in *Buckman*] effectively eliminates the substantial federal interest in adjudicating state claims that entail interpreting the FDCA.”). Still, of course, “causation and damages need [to] be proved.” Sharkey, *supra* note 20, at 363 n.8.

<sup>188</sup> The concept of “parallel requirements” originated in the context of the Medical Devices Amendment to the FDCA, which expressly preempts requirements imposed by state law that are “different from, or in addition to” certain federal requirements. 21 U.S.C. § 360k(a)(1) (2012). The Supreme Court has repeatedly held that § 360k(a)(1) nonetheless permits a state to “provid[e] a damages remedy for claims premised on a violation of FDA regulations” because “the state duties in such a case ‘parallel,’ rather than add to, federal requirements.” *Riegel v. Medtronic, Inc.*, 552 U.S. 312, 330 (2008) (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 495 (1996)). As Catherine Sharkey has observed, failure-to-update claims “can be viewed as affirmative efforts on plaintiffs’ part to enforce ‘parallel requirements.’” Sharkey, *supra* note 20, at 366.

<sup>189</sup> Sharkey, *supra* note 20, at 369.

<sup>190</sup> 531 U.S. 341 (2001).

<sup>191</sup> *Id.* at 343.

<sup>192</sup> *Id.* at 342.

<sup>193</sup> Though the Medical Device Amendments contain an express preemption provision, the Court explicitly noted that it was solely conducting an implied preemption analysis and took no position on express preemption. *See id.* at 348 n.2 (“[W]e express no view on whether these claims are subject to express pre-emption . . .”).



the-FDA claims under state tort law.”<sup>194</sup> Moreover, the Court pointed to the express prohibition on private rights of action under the FDCA as “clear evidence that Congress intended” for the Medical Device Amendments to be “enforced exclusively by the Federal Government.”<sup>195</sup> Thus, the plaintiffs sought to bring claims that “exist[ed] solely by virtue of the FDCA disclosure requirements” rather than “relying on traditional state tort law which had predated the federal enactments in questions [sic].”<sup>196</sup>

At its narrowest, however, *Buckman* might simply be labeled a case of field preemption.<sup>197</sup> The opinion underscores the exclusively federal domain of “fraud-on-the-agency” claims,<sup>198</sup> and describes the regulation at issue as “a comprehensive scheme.”<sup>199</sup> Far from pre-saging preemption in any case where state law affects federal regulation, and notwithstanding some of the case’s broadest rhetoric,<sup>200</sup> the

<sup>194</sup> *Id.* at 348.

<sup>195</sup> *Id.* at 352 (citing 21 U.S.C. § 337(a)).

<sup>196</sup> *Id.* at 353.

<sup>197</sup> See Sharkey, *supra* note 187, at 846 (“The narrow view confines *Buckman* to . . . field preemption—taking the position that the Court was content to treat the FDA as the master of this limited domain of agency fraud claims only because policing fraud against federal agencies is not ‘a field which the States have traditionally occupied.’” (quoting *Buckman*, 531 U.S. at 347)). While field preemption is usually a more sweeping proscription against state regulation in a broad field, see, e.g., *Arizona v. United States*, 132 S. Ct. 2492, 2502 (2012) (“[T]he Federal Government has occupied the field of alien registration.”), the “field preemption view of *Buckman*” essentially confines the field to “stand-alone fraud-on-the-agency claims,” Sharkey, *supra* note 187, at 853. As Professor Sharkey notes, *id.*, this was the approach taken by Judge Calabresi in *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 93–96 (2d Cir. 2006), *aff’d by an equally divided Court sub nom.* *Warner-Lambert Co. v. Kent*, 552 U.S. 440 (2008) (per curiam).

<sup>198</sup> See *Buckman*, 531 U.S. at 347 (“[T]he relationship between a federal agency and the entity it regulates is inherently federal in character because the relationship originates from, is governed by, and terminates according to federal law.” (citing *Boyle v. United Techs. Corp.*, 487 U.S. 500, 504–05 (1988) (finding federal common law preempted state law where the case implicated “uniquely federal” interests))).

<sup>199</sup> *Buckman*, 531 U.S. at 348. This is classic field preemption language. See, e.g., *Arizona*, 132 S. Ct. at 2503 (finding field preemption of an Arizona statute providing state law penalties for violations of federal alien registration law in light of “the comprehensive scheme” established by Congress); *Hillsborough Cty. v. Automated Med. Labs., Inc.*, 471 U.S. 707, 713 (1985) (“In the absence of express pre-emptive language, Congress’ intent to pre-empt all state law in a particular area may be inferred where the *scheme* of federal regulation is sufficiently *comprehensive* to make reasonable the inference that Congress ‘left no room’ for supplementary state regulation.” (emphasis added) (quoting *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947))); *Hines v. Davidowitz*, 312 U.S. 52, 66–67 (1941) (“[W]here the federal government, in the exercise of its superior authority in this field, has enacted a *complete scheme of regulation* . . . , states cannot, inconsistently with the purpose of Congress, conflict or interfere with, curtail or complement, the federal law, or enforce additional or auxiliary regulations.” (emphasis added)).

<sup>200</sup> See *supra* note 194 and accompanying text; see also *Buckman*, 531 U.S. at 353 (“[T]his sort of litigation would exert an extraneous pull on the scheme established by Congress, and it is therefore pre-empted by that scheme.”). In *Chamber of Commerce v.*

Court has distinguished *Buckman* as involving a “uniquely federal area[] of regulation”<sup>201</sup>—that is, “fraud on a federal agency.”<sup>202</sup> The field preemption theory is also consistent with the Court’s subsequent interpretations of *Buckman*; indeed, the Court’s two most recent field preemption decisions have cited *Buckman* in this way.<sup>203</sup>

Also illuminating is the treatment of *Buckman* in *Levine*. Recall that *Levine* centered on whether the FDCA preempted a warning defect suit against a brand-name pharmaceutical manufacturer that *could* unilaterally update its labeling.<sup>204</sup> Citing *Buckman*, the dissent argued that “[w]here the FDA determines, in accordance with its statutory mandate, that a drug is on balance ‘safe,’ our conflict pre-emption cases prohibit any State from countermanding that determination.”<sup>205</sup> Justice Stevens, writing for the majority, found “[t]he dissent’s reliance on *Buckman* . . . especially curious.”<sup>206</sup> In particular, *Levine* noted that *Buckman* “involved state-law fraud-on-the-agency claims” and had “distinguished state regulation of health and safety as matters to which the presumption [against preemption] does apply.”<sup>207</sup>

Ultimately, it seems likely that the scope of *Buckman* is somewhere between these two extremes. Even beyond the doctrine of field preemption, *Buckman* embraces considerations of policy and institutional comparative advantage. For example, the Court noted that the FDA had been given an array of tools to combat fraud committed against itself,<sup>208</sup> and expressed its concern that fraud-on-the-FDA claims would “exert an extraneous pull on the scheme established by Congress.”<sup>209</sup> Yet, despite such rhetoric, the Court’s opinion is plainly

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*Whiting*, 131 S. Ct. 1968, 1983 (2011), the Court rejected Petitioners’ attempt to rely on the language just quoted.

<sup>201</sup> *Whiting*, 131 S. Ct. at 1983.

<sup>202</sup> *Id.*

<sup>203</sup> Most recently, the Court declined to apply the presumption against preemption to the National Voter Registration Act because, in light of the Elections Clause, U.S. CONST. art. I, § 4, cl. 1, “the States’ role in regulating congressional elections—while weighty and worthy of respect—has always existed subject to the express qualification that it ‘terminates according to federal law.’” *Arizona v. Inter Tribal Council of Ariz., Inc.*, 133 S. Ct. 2247, 2257 (2013) (quoting *Buckman*, 531 U.S. at 347). One year earlier in *Arizona v. United States*, the Court cited *Buckman* in support of its holding that an Arizona statutory provision was preempted notwithstanding its apparent consistency with federal objectives. 132 S. Ct. at 2502. The Court noted that where “the Federal Government has occupied the field of [regulation],” any state regulation necessarily creates an impermissible conflict. *Id.*

<sup>204</sup> See *supra* notes 87–102 and accompanying text.

<sup>205</sup> *Wyeth v. Levine*, 555 U.S. 555, 609 (2009) (Alito, J., dissenting).

<sup>206</sup> *Id.* at 566 n.3 (majority opinion).

<sup>207</sup> *Id.* (citing *Buckman*, 531 U.S. at 347–48).

<sup>208</sup> *Buckman*, 531 U.S. at 349.

<sup>209</sup> *Id.* at 353.

not so broad as to preclude all claims that might rub elbows with the FDA's authority and discretion to enforce its own regulations. This is not only confirmed by the Court's characterization of *Buckman* in subsequent opinions,<sup>210</sup> but *Buckman* itself also acknowledged that a wide array of state law claims remained viable. Indeed, *Buckman* distinguished a prior medical device case, *Medtronic, Inc. v. Lohr*,<sup>211</sup> and reaffirmed that *Medtronic* "can be read to allow certain state-law causes of actions that parallel federal safety requirements."<sup>212</sup>

Justice Stevens's separate concurrence in *Buckman* similarly embodies a more nuanced view of that case.<sup>213</sup> Unlike the majority, he readily acknowledged that *Buckman* "does not fit neatly into our pre-existing pre-emption jurisprudence."<sup>214</sup> Essentially advocating deference to the policy determination of the Agency, Justice Stevens argued that the plaintiffs' claim would necessarily fail as a matter of law because—in light of the FDA's failure to take the screws off the market even after it was made aware of the fraud—they could not establish that the screws would not have survived FDA scrutiny.<sup>215</sup> However, he would find that the test for causation had been met if the Agency had previously determined that the manufacturer had made fraudulent misrepresentations that necessitated pulling the device.<sup>216</sup>

A further consideration in products liability preemption, which Justice Stevens also noted in his *Buckman* concurrence, is whether individuals harmed by unlawful conduct can still obtain compensation or some other form of relief if state law is preempted.<sup>217</sup> This is relevant because federal and state regulations may have distinct purposes:

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<sup>210</sup> See *supra* notes 200–07 and accompanying text (describing the Court's analysis of *Buckman*).

<sup>211</sup> *Buckman*, 531 U.S. at 352 ("Notwithstanding the fact that *Medtronic* did not squarely address the question of implied pre-emption, it is clear that the *Medtronic* claims arose from the manufacturer's alleged failure to use reasonable care in the production of the product, not solely from the violation of FDCA requirements." (citing *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 481 (1996)).

<sup>212</sup> *Id.* at 353.

<sup>213</sup> See *id.* (Stevens, J., concurring in judgment).

<sup>214</sup> *Id.* at 353 n.1.

<sup>215</sup> See *id.* at 353 (arguing that FDA cannot prove "an essential link in the chain of causation" because it "has done nothing to remove the devices from the market, even though it is aware of the basis for the fraud allegations").

<sup>216</sup> See *id.* at 354 ("[I]f FDA had determined that petitioner had committed fraud . . . and had then taken the necessary steps to remove the harm-causing product from the market . . . a plaintiff would be able to establish causation without second-guessing the FDA's decisionmaking . . .").

<sup>217</sup> See *id.* at 355 ("Under the pre-emption analysis the Court offers today, however, parties injured by fraudulent representations to federal agencies would have no remedy even if recognizing such a remedy would have no adverse consequences upon the operation or integrity of the regulatory process.").

“‘[U]nlike most administrative and legislative regulations,’ common-law claims ‘necessarily perform an important remedial role in compensating accident victims.’”<sup>218</sup> Indeed, this insight has pervaded a number of the Court’s preemption decisions.<sup>219</sup> Additionally, as Justice Sotomayor recently observed, in the context of pharmaceuticals “the legislative history of the FDCA suggests that Congress chose not to create a federal cause of action for damages precisely because it believed that state tort law would allow injured consumers to obtain compensation.”<sup>220</sup>

In sum, failure-to-update claims should survive *Buckman* implied preemption. Analyzed under the narrower view of *Buckman*, regulating defective product warnings is hardly an area of exclusive federal concern, and indeed is “a field which the States have traditionally occupied.”<sup>221</sup> Even taking a broader reading of *Buckman*, while the FDA may be entrusted to determine what the content of a generic drug label should be, a failure-to-update claim “would not depend upon speculation as to the FDA’s behavior in a counterfactual situation but would be grounded in the agency’s explicit actions.”<sup>222</sup> Similarly, failure-to-update claims neatly “parallel federal safety requirements” as required by *Buckman*.<sup>223</sup> Moreover, the fact that the update can be made unilaterally<sup>224</sup> means that the impossibility preemption analysis should follow *Levine* rather than *Mensing*.<sup>225</sup>

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<sup>218</sup> *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2485 (2013) (Sotomayor, J., dissenting) (quoting *Sprietsma v. Mercury Marine*, 537 U.S. 51, 64 (2002)).

<sup>219</sup> *See, e.g., Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005) (“The long history of tort litigation against manufacturers of poisonous substances adds force to the basic presumption against pre-emption. If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly.”); *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 251 (1984) (“It is difficult to believe that Congress would, without comment, remove all means of judicial recourse for those injured by illegal conduct.”).

<sup>220</sup> *Bartlett*, 133 S. Ct. at 2485 (Sotomayor, J., dissenting) (citing *Wyeth v. Levine*, 555 U.S. 555, 574–75 & n.7 (2009)).

<sup>221</sup> *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947), quoted in *Buckman*, 531 U.S. at 347 (arguing that in each case—whether Congress may take unto itself all regulatory authority of entities engaged in foreign commerce, share the task with states, or adopt the state scheme as federal policy—the question is what Congress’s purpose was).

<sup>222</sup> *Buckman*, 531 U.S. at 354 (Stevens, J., concurring in judgment).

<sup>223</sup> *Id.* at 353.

<sup>224</sup> *See supra* notes 117–19 and accompanying text.

<sup>225</sup> *See PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2581 n.8 (2011) (noting that a drug manufacturer’s ability to unilaterally make a labeling change required by state law generally defeats a preemption defense, even if the FDA can later revoke those changes, absent proof by the manufacturer that the FDA would in fact have done so).

### CONCLUSION

The distinct regulatory treatment by the FDA of brand name and generic pharmaceutical manufacturers presently imposes unique restrictions on the ability of generic manufacturers to update their warning labels. This leaves generic drugs, but not brand-name drugs, unable to comply with their state tort law duties to provide an adequate warning whenever such a warning in any way departs from the FDA-approved warning for the brand-name equivalent. This impossibility has resulted in the preemption of many failure-to-warn claims against generic manufacturers. Not only are many consumers given generic drugs by virtue of state substitution laws or their insurance plans, but a scant few have any idea that failing to insist upon a brand-name drug is tantamount to foregoing insurance or waiving liability.

While the FDA has proposed a rule to alleviate this narrow gap in compensation and deterrence between generic and brand-name drugs, the rule entails a number of costly tradeoffs with respect to both the pricing of generics, consumer confidence in generics, and the overall efficacy of consumers and their healthcare providers to make informed choices about pharmaceuticals.

Newly conceived failure-to-update claims may represent a more viable and desirable means of imposing liability on generic drug manufacturers, and ensuring both safety and consistency across generic and brand-name drug labeling. Such claims help fill an existing gap in regulatory enforcement, as well as provide an alternative avenue for otherwise uncompensated individuals. Though the preemption of failure-to-warn claims against generic manufacturers who maintain updated warning labels may still warrant a regulatory solution, such a plan should seek to preserve rather than obliterate existing private enforcement mechanisms that are much more efficient and do not entail such serious tradeoffs.