

Number 28 ❖ December 2013

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**We wish to thank New York Law School  
student Mehgan Gallagher for her  
invaluable research assistance.**

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## AMERICA’S UNACCOUNTABLE GENERIC DRUG INDUSTRY: How Legal Immunity Could Be Making You Sick

*By Jocelyn Bogdan, Associate Director*

### INTRODUCTION

Today, when a doctor writes a patient a prescription, it is far more likely than not that the pharmacist will fill their prescription with a generic version of the drug. Usually, health insurers will not pay for the prescription otherwise. In fact, “in many states pharmacists are required to dispense the generic version of a drug unless a doctor specifies otherwise.”<sup>1</sup> What’s more, in some cases, the brand-name versions of drugs no longer exist, having left the market altogether. According to the Institute of Medicine, “In any given month, an estimated 48 percent of Americans take at least one prescription drug”<sup>2</sup> and generic drugs account for over 80 percent of them.<sup>3</sup> Moreover, “[a]mong drugs for which a generic version is available, approximately 94 percent are dispensed as a generic.”<sup>4</sup>

Most people take generic drugs without ever thinking about their safety, assuming that a generic drug is the perfect copy of the equivalent brand-name drug and that it was manufactured safely. However, they would be wrong. While the U.S. Food and Drug Administration (FDA) requires a certain chemical and “bioequivalence” between brand-name and generic drugs, there are differences. It allows drugs to contain lower quality “inactive” ingredients, which can affect how drugs are absorbed, and even different concentrations of “active” ingredients.<sup>5</sup> And the FDA does not independently test generics before allowing them on the market, relying primarily on the company’s word before approving them for sale. As the FDA’s former Generic Drug Office Director Gary Buehler put it, because “drug

applications work on the honor system” and “the FDA relies on data provided by the companies themselves ... ‘We depend on that information to be truthful. ... ‘Otherwise, the whole house of cards will fall down.’”<sup>6</sup>

Sometimes the FDA approves a strength or dosage of a drug that hasn’t been tested at all. Of even more concern – the drugs, once approved, can be manufactured in factories all over the world, some of which have never been inspected. In fact, to keep costs down, generic drugs are much more likely than their brand-name counterparts to be manufactured overseas, in countries like India and China, where the FDA does not have the ability to monitor the manufacturing process. Even worse, generic companies sometimes mislead the FDA by giving them faulty data, compromising consumer safety.

The FDA’s current generic drug labeling regulations also raise significant safety concerns. While specifying that generic companies have an “independent responsibility to ensure that the labeling is accurate and up-to-date,” the regulations say that a generic drug must maintain the same label as the brand name drug even if it knows that label to be unsafe, inaccurate or out-of-date. As noted by the FDA, “Federal law [does] not permit a generic drug manufacturer to ... unilaterally strengthen warnings in its labeling or to issue additional warnings.”<sup>7</sup> Given these potential design, labeling and manufacturing problems, it’s no surprise that a recent study published in *The Annals of Pharmacotherapy* found that “[o]ver 23% of physicians surveyed expressed negative perceptions about efficacy of generic drugs, almost 50% reported negative perceptions about quality of generic medications, and more than one quarter do not prefer to use generics as first-line medication for themselves or for their family.”<sup>8</sup>

Sometimes generic drugs are unsafe; sometimes they cause unexpected adverse reactions in the people who take them. Normally, if someone is harmed or killed by an unsafe product made by a negligent company, they or their family have the option to sue that company in court. The right to sue negligent drug manufacturers under state tort law has long existed, providing patients with both the ability to be compensated for harms and a means to hold irresponsible drug companies directly accountable for causing injuries, often forcing changes in the sale of unsafe drugs. Lawsuits also help uncover important information about dangerous drugs that the understaffed and under-resourced FDA misses and can create widespread publicity about them through the mass media and other means, alerting an unsuspecting public to drug dangers.

The U.S. Supreme Court recognized the important role that lawsuits play in drug cases when it confirmed that brand-name drug companies should be liable for injuring or killing patients in the 2009 case *Wyeth v. Levine*.<sup>9</sup> The Court said, “[S]tate law offers an additional, and important, layer of consumer protection that complements FDA regulation,”<sup>10</sup> noting that “the FDA has limited resources to monitor the 11,000 drugs on the market and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge.”<sup>11</sup> In other words, in 2009 the Court recognized that the FDA has limited resources when it comes to monitoring drugs and that state tort law serves an important purpose, adding a necessary layer of protection for consumers.

Unfortunately, in 2011 and again in 2013, the Court (in two 5-4 decisions)<sup>12</sup> seemed to forget all of that when it came to generic drugs. Resting on a peculiarity in FDA law that obligates generic companies to ensure accurate labeling but prevents them from changing labels even if a “clinically significant hazard” exists, the Court majority held that state tort lawsuits are incompatible with FDA generic drug regulation.<sup>13</sup> Notably, this is even though FDA regulation and state litigation have coexisted for decades<sup>14</sup>. The Court ruled that if a drug consumer is harmed or killed by a generic drug due to the drug’s inadequate labeling<sup>15</sup> or defective design, the manufacturer cannot be held accountable in court. As a result, whether or not an injured patient has any legal recourse depends entirely on whether they have been prescribed a brand-name or generic drug, which even the Court suggested was “bizarre.”<sup>16</sup> As noted by U.S. Senate Judiciary Committee Chair Patrick Leahy, “The result is a two-track system that penalizes consumers of generic drugs – even though many consumers have no control over which drug they take, because state law and their health insurance plan require them to take generics if they are available.”<sup>17</sup>

The underlying presumption in the Court’s 2011 and 2013 decisions – and the general view of most consumers – is that a generic version of a drug is essentially identical to the brand-name drug already on the market, so it should be safe. In fact, the Court reasoned that a generic drug’s only relevant requirement is that it *be* identical in both design and labeling. But are these presumptions really correct and should they be the basis for stripping away the legal rights of 80 percent of U.S. prescription drug consumers? This report finds that in key respects, these presumptions are incorrect or highly misleading. And it concludes that until Congress or FDA regulations change what the Supreme Court has done, the vast majority of those prescribed drugs in this country will have no access to the courts if they are harmed.

Fortunately, the FDA has now taken concrete steps to address this absurd situation by proposing a rule change to place new responsibility on generic companies to immediately “update product labeling promptly to reflect certain types of newly acquired information related to drug safety, irrespective of whether the revised labeling differs from” that of the brand-name drug.<sup>18</sup> Underlying this proposed rule are two main ideas. First, drug labeling has a critical safety function because it “summarizes the essential information needed for the safe and effective use of the drug.”<sup>19</sup> Second, whether a drug is a brand-name or generic, “as a drug is used more widely or under diverse conditions, new information regarding the risks and benefits of a drug may become available,”<sup>20</sup> and this information must be communicated to doctors and consumers.

The rule is not in effect yet. A 60-day comment period ends January 13, 2014<sup>21</sup> and no doubt the generic industry will fight it. But changing the regulations in this manner is exactly the direction in which the Supreme Court pointed the agency, so hopefully it will take effect soon.<sup>22</sup>

## **THE BUSINESS OF GENERIC DRUGS**

The prescription drug business is huge business. According a recent GlobalData report,<sup>23</sup> in 2012 the U.S. pharmaceutical market was worth approximately \$359 billion. Those numbers are expected to increase to \$475 billion by 2020.<sup>24</sup> While the vast majority of

the money is in brand-name drugs, the generic drug industry has itself grown to be a \$43.1 billion industry.<sup>25</sup>

The generic industry spends a fraction of the cost to get their versions on the market. Specifically, before the FDA approves a brand-name drug, it requires lengthy and expensive testing to ensure the safety and effectiveness of the drug. The process of inventing, testing and marketing a new drug can run into the hundreds of millions of dollars.<sup>26</sup> After approval, the drug receives a patent, which means that, until the patent expires, no other company or manufacturer is allowed to make or sell the same drug. Thanks to this lack of competition, “consumers are forced to shoulder a heavy financial burden, or even go without needed medicine, due to the high cost of brand-name drugs.”<sup>27</sup> These patents typically last twenty years. But once they expire, the drug’s ingredients become available to generic manufacturers, who then attempt to recreate the drug and sell it themselves for significantly less money.

Clearly, most consumers benefit financially once these patents expire and generics enter the market. For example, in 2011, Pfizer lost its “\$10-billion-a-year revenue stream” when Lipitor’s patent expired.<sup>28</sup> Before it went generic, Pfizer sold Lipitor for “\$3.50 a pill and up.”<sup>29</sup> Today, as a generic, it costs less than 50 cents a pill.<sup>30</sup> Sometimes, brand-name drug companies try to avoid this by engaging in “pay-for-delay” schemes whereby “a brand-name drug company pays off a would-be competitor to delay it from selling a generic version of the drug [and] without any competition, the brand-name company can continue demanding high prices for its drug.”<sup>31</sup> In June 2013, the U.S. Supreme Court ruled that the Federal Trade Commission could sue to invalidate these schemes as antitrust violations, a decision that is “likely to increase the number of generic drugs in the marketplace and benefit consumers” but also “shift an important balance of power to the generic companies.”<sup>32</sup>

Sometimes when the patent on a brand-name drug expires, the company removes the brand-name version from the market altogether. As Public Citizen explains in its recent report, *Generic Drug Labeling*, “Whether because of price competition or other reasons, it is not uncommon for the brand-name manufacturer to exit the market entirely after generic entry, leaving generic products as the only marketed versions of the drug.”<sup>33</sup> Public Citizen found 434 approved generic drugs that lack a brand-name alternative.<sup>34</sup>

In sum, there’s no question that consumers benefit from cheaper generic versions of a drug. Good reasons exist as to why 80 percent of all drug prescriptions are filled by generic drugs today. However, no consumer saves money if a generic drug is unsafe and they are medically harmed as a result. Unfortunately this does happen and under current law, injured generic drug consumers have no recourse.

## **GENERIC DRUG DESIGN AND TESTING – KEEPING IT CHEAP BUT NOT NECESSARILY SAFE**

The FDA used to “[require] generic drug manufacturers to obtain approval of their products as if they were completely new drugs, including through new clinical studies of safety and effectiveness.”<sup>35</sup> Since generics were supposed to be copies of brand-name

drugs already on the market,<sup>36</sup> this kind of lengthy and expensive testing seemed to make little sense.

So in 1984, Congress passed the Hatch-Waxman Amendments,<sup>37</sup> which intended to get generic drugs into the market more quickly and ensure that they were more affordable by simplifying their approval process.<sup>38</sup> The Hatch-Waxman Amendments allowed “the FDA to approve a generic drug based on a showing of bioequivalence to an approved drug without requiring additional clinical testing for safety and effectiveness....”<sup>39</sup> The goal of the Amendments, according to U.S. Representative Waxman, was to “[protect] consumers by ‘provid[ing] low-cost, generic drugs for millions of Americans,’ resulting in ‘a significant savings to people who purchase drugs.’”<sup>40</sup>

Now, rather than putting generic versions of drugs through a lengthy approval process<sup>41</sup> that brand-name drugs must undergo, usually involving 10-15 years of research and testing on animals and human subjects, generic companies submit an Abbreviated New Drug Application, which simply shows that their drugs are equivalent in “dosage, form, safety, strength, route of administration, quality, performance characteristics and intended use.”<sup>42</sup> More specifically, the drug must:

- contain the same active ingredients as the innovator drug (inactive ingredients may vary)
- be identical in strength, dosage form, and route of administration
- have the same use indications
- be bioequivalent
- meet the same batch requirements for identity, strength, purity, and quality
- be manufactured under the same strict standards of FDA’s good manufacturing practice regulations required for innovator products.<sup>43</sup>

Or to put it another way, companies need to “scientifically demonstrate that their product ... performs in the same manner as the innovator drug.”<sup>44</sup> They can do this by measuring “the time it takes the generic drug to reach the bloodstream in 24 to 36 healthy, volunteers,”<sup>45</sup> (as opposed to tens of thousands of people, as brand-name drug companies typically must do).

However, determining “bioequivalence” is not as simple as it sounds and the FDA’s process is far from perfect. For example, when the FDA approves a generic drug, it typically recommends “that the highest strength of a drug be used to establish bioequivalence.”<sup>46</sup> However, in cases where the highest dosage of the drug may lead to complications in otherwise healthy test subjects, the FDA allows a lower dosage of the drug to be used to determine bioequivalence in a process called “waiving up.”<sup>47</sup> This means that a stronger dosage of a drug, which may behave differently than a lower dosage, can be approved as bioequivalent without any study ever being conducted. As illustrated in the section below discussing Wellbutrin and Budeprion, “waiving up” can have serious health and safety consequences.

And there are other problems. When the patent on the brand-name drug expires, generic drug manufacturers gain access to the ingredients in the brand-name drug. This is a huge

step in replicating the drugs. However, the patent does not explain how the drug is made or put together. Thus, the generic companies have to figure out on their own how to create “copies” of brand-name drugs. As *Fortune Magazine* points out, “[M]anufacturing a generic requires reverse engineering, and the result is an approximation rather than a duplicate of the original.”<sup>48</sup>

Some generic companies have to go even further. Ten percent of the pharmaceutical market is made up of time-release drugs, or extended release drugs. Time-release drugs slowly release the active ingredients of their medication into a patient’s bloodstream, allowing patients to take their medications less frequently.<sup>49</sup> Brand-name manufacturers acquire patents for their drug’s time-release mechanism just like they acquire patents over the drugs themselves.<sup>50</sup> Yet while the patents on time-release drugs, like all other pharmaceuticals, expire after about twenty years, the patent on the time-release mechanism can outlast the drug’s patent. Thus, a generic drug company may be eligible to design a version of the drug before the time-release patent expires – but they do so without information from the brand-name company on how the time-release mechanism in the brand-name drug works. As the *New York Times* pointed out, “[S]ome critics say the generic companies don’t always succeed at mimicking the longer-acting effects of the brands, and the FDA does not do a good enough job of evaluating them.”<sup>51</sup>

And finally, generics are all allowed to deviate from brand names “in characteristics such as tablet shape, scoring, packaging, excipients (e.g. colors, flavors, and preservatives), and expiration dating or storage conditions.”<sup>52</sup> The assumption may be that these differences should not raise safety issues. However, evidence shows that they can.

According to *Fortune Magazine*, generic companies often use inactive ingredients that are lower in quality:

Those differences can affect what’s called bioavailability – the amount of the drug that could be absorbed into the bloodstream. As the American Heart Association recently noted, “Some additives traditionally thought to be inert, such as alcohol sugars, cyclodextrans, and polysorbate-80, may alter a drug’s dissolution, thereby impacting its bioavailability.”<sup>53</sup>

As noted above, differences also occur because generics are not told how brand-name drugs are put together. Because the brand-name drug companies do not tell generic companies how their drugs are made, generic drug companies have to guess how make their drugs.<sup>54</sup> The FDA is aware of this and allows for certain differences. As *Fortune Magazine* notes, the FDA’s “definition of bioequivalence is surprisingly broad: A generic’s maximum concentration of active ingredient in the blood must not fall more than 20% below or 25% above that of the brand name. This means a potential range of 45%, by that measure, among generics labeled as being the same.”<sup>55</sup>

Even small design differences between generic and brand-name drugs can have real health consequences. Over the years, *The People’s Pharmacy* – a consumer website run by pharmacologist Joe Graedon and his wife Terry, who together host an NPR radio program<sup>56</sup> – has collected many stories from people who have experienced adverse

effects after switching from brand-name drugs to generics or from one generic to another. For example:

- One victim switched from one generic form of Xanax (for epilepsy) to another and experienced his first seizure in over two years. *The People's Pharmacy* pointed out that he was not the only person to report seizures after taking generic anticonvulsant medicine and noted that “[t]he question of whether anti-epilepsy drugs are truly bioequivalent is controversial among doctors as well as patients (*The Lancet Neurology*, March, 2010; *Annals of Pharmacotherapy*, Nov. 2011).”<sup>57</sup>
- Another user of epilepsy medication wrote about his switch from a brand-name drug to a generic form of the same drug. After years of having his epilepsy under control, he experienced several seizures in two weeks. His doctor switched him back to the brand name but he is terrified of what will happen if his insurance company insists he switches back, stating, “I will have to stop driving and become housebound.”<sup>58</sup>
- Another victim wrote that he had “horrific side effects” and withdrawal when he was switched from one generic diazepam, the generic form of Valium, to another. Side effects included feeling as though he’d been shocked by electricity, having seizures and having out of body experiences.<sup>59</sup>
- *The People's Pharmacy* received many stories from users of a generic form of Coreg, one of the most popular beta blockers on the market. Consumers who were switched from the brand-name to the generic wrote in with fatigue, suddenly elevated blood pressure, sore throat, pains in extremities, headaches and more. Some who switched back to the brand name saw these side effects completely disappear.<sup>60</sup>

### **Wellbutrin/Budeprion**

In 2006, Beth Hubbard, a 34-year-old newly married housewares designer who suffered from mild depression, dealt with her condition by taking Wellbutrin XL. Her health was otherwise fine and her depression was under control until she went to refill her prescription and the pharmacy gave her a generic form of Wellbutrin called Budeprion XL. Suddenly everything changed. “Within a month, she had gained 15 pounds, couldn’t sleep well, developed gastrointestinal problems, and felt such extreme fatigue and lack of motivation that she thought about quitting her job.”<sup>61</sup> Her doctor referred her to specialists who “diagnosed her alternatively with severe allergies, a heart murmur, a slow thyroid, irritable bowel syndrome, gluten intolerance, mononucleosis and chronic pain.”<sup>62</sup> She was given a variety of drugs to treat these ailments and she stayed on the Budeprion.<sup>63</sup>

After eight months of suffering, she told a friend that she needed to refill her anti-depressant prescription. Her friend, who had recently stopped taking Wellbutrin herself, offered Beth her extra pills.<sup>64</sup> A week after taking her friend’s brand-name Wellbutrin tablets, all of Beth’s health problems disappeared. When she called her doctor’s office

and asked if she could get a prescription specifically for the brand-name drug, the nurse informed her that she could and also told her that it was a common request.<sup>65</sup>

Beth Hubbard was not alone. In 2007, *The People's Pharmacy* began receiving messages from readers and listeners taking Budeprion XL. The messages complained of severe depression, suicidal thoughts, migraines, weight gain, insomnia, nausea and anxiety.<sup>66</sup> Many noted that when they went back on Wellbutrin, their symptoms disappeared. *The People's Pharmacy's* Joe and Terry Graedon "immediately reported these cases to officials at the [FDA] who assured [them] that the FDA would look into the issue."<sup>67</sup>

When the FDA failed to act, the Graedons took action themselves. They turned to independent lab ConsumerLab.com and "suggested that it initiate laboratory testing to see whether there was any measurable difference between the generic formulation and the originator product."<sup>68</sup> The Graedons were "stunned to learn [from the testing] that the generic's active ingredient dissolved four times more quickly in the first two hours than that of the brand name because of a different time-release mechanism."<sup>69</sup> Despite this, the FDA continued to dismiss complaints about Budeprion for years. While Joe Graedon pushed for the FDA to release results from the generic drug companies' own pharmacological studies, the FDA refused, claiming the data were proprietary.<sup>70</sup>

But after enough pressure the FDA asked companies distributing the generic drug to conduct tests. However, the tests never happened because the companies ultimately cancelled them, claiming they couldn't find enough participants.<sup>71</sup> The FDA finally stepped in and conducted its own tests to determine bioequivalence in 2010. The agency learned that patients' problems were stemming from the 300 milligram version of the drug, which had been approved without any direct study in patients.<sup>72</sup> Explained the FDA,

[I]n the case of extended-release [Budeprion] the 300mg strength of the drug was not used in bioequivalence studies due to concerns that this higher strength of the drug could cause seizures in healthy adult volunteers. Therefore the FDA granted [the manufacturer] a waiver, pursuant to which the company was not required to perform a bioequivalence study at the 300 mg strength but, instead, performed its bioequivalence studies on the next lower strength, 150mg.<sup>73</sup>

In other words, the FDA had "waived up" the drug,<sup>74</sup> never requiring that the higher dosage be tested for bioequivalence at all.

In 2009, patients who had experienced adverse effects started bringing lawsuits against Teva Pharmaceuticals and Impax Laboratories, the distributor and manufacturer of Budeprion XL, the generic form of Wellbutrin XL<sup>75</sup> that had harmed Beth Hubbard. Eventually the cases were consolidated and transferred to the Eastern District of Pennsylvania. Among those injured: Andrew Richards, a lead plaintiff in the lawsuit, who "suffered his seizure in March 2008 after his pharmacy switched him to the Teva generic. Within a few days of starting the new pills, he said he started to experience jolts and jerks."<sup>76</sup> As he told ProPublica, "'Sometimes when you're falling asleep, you get what's called a sleep start.... Well, I would get that but I was awake.' Then the seizure hit."<sup>77</sup>

The patients argued that after the generic drug was approved, the companies learned about material differences between the generic and brand name – namely that the two drugs’ time-release mechanism functioned differently<sup>78</sup> – and they “had a duty to disclose this information.”<sup>79</sup> When patients taking the generic switched back to brand name Wellbutrin XL, they saw their side effects immediately improve.<sup>80</sup> They argued that even though the companies knew there were problems, “they failed to disclose this information or warn patients and doctors about the differences between the medications.”<sup>81</sup> Further, “to protect their market share [the companies] continued to misrepresent that the release profile of their products was identical to those of the name brand product.”<sup>82</sup> They “sued under California’s Unfair Competition Law based on the omission and misrepresentations surrounding [the companies’] products.”<sup>83</sup>

In July 2012, the court approved a class action settlement on behalf of victims.<sup>84</sup> Notably, between the start of the case and the settlement, the Supreme Court decided *PLIVA, Inc. v. Mensing*, which likely would have prevented their lawsuit from proceeding at all.<sup>85</sup> Although Teva and Impax later asked the court to dismiss the case based on *PLIVA*, they ultimately agreed to a mediation session with the patients and, after an 11-hour session, both sides decided to settle the claims.<sup>86</sup> However, the court pointed out that the patients were “leaving this litigation with much less than they sought when these cases were originally filed,”<sup>87</sup> acknowledging that *PLIVA* made establishing liability much more difficult, and emphasized the number of similar cases thrown out by “numerous courts” since the *PLIVA* decision.<sup>88</sup>

Meanwhile, it took two years for the FDA to complete its study of the 300 mg Budeprion; during that time the drug remained on the market. Finally, in October 2012, the FDA announced that Budeprion XL 300 mg was not therapeutically equivalent to Wellbutrin XL 300 mg and required it be taken off the market.<sup>89</sup> The FDA has still not performed tests on any other forms of generic Wellbutrin at 300 mg strength. However, it did ask other manufacturers to conduct and complete their own studies by March 31, 2013.<sup>90</sup>

The FDA finally finished its review in October 2013. While three companies produced generic products that were acceptable, the FDA found that one company, Watson, was producing a generic form of Wellbutrin that was not therapeutically equivalent to the brand name. As a result, Watson agreed to “withdraw this product from the distribution chain”<sup>91</sup> and the FDA recoded Watson’s product, stating that the “data are insufficient to determine therapeutic equivalence....”<sup>92</sup>

Despite the outcome, this case clearly highlights the deficiencies in FDA oversight of generic drugs and how litigation can be crucial to patients harmed by manufacturer and FDA inaction and delay.

## **MANUFACTURING IN FARAWAY, UNINSPECTED FACTORIES**

When patients are prescribed medication, or when they go to the drug store and pick up a painkiller, they do so assuming the drug they are about to take has been manufactured in a clean, government-approved facility. Many people probably even assume that their

drug was made in a U.S. facility. They would be wrong on all counts. What's more, if a drug is manufactured abroad, it is nearly impossible to hold that manufacturer accountable in U.S. courts, providing yet another kind of immunity for the pharmaceutical industry.<sup>93</sup>

In general, the number of drugs manufactured abroad has doubled since 2002,<sup>94</sup> with most overseas drugs being manufactured in India and China.<sup>95</sup> By 2007, "half of the aspirin used worldwide [came] from China, as [did] 35 percent of the painkiller acetaminophen [*e.g.*, Tylenol] ... India's pharmaceutical imports into [the United States] increased 2,400 percent, to \$789 million, from 1996 to 2006, making it the fastest-growing drug importer."<sup>96</sup> By 2013, "[m]ore than 80 percent of active pharmaceutical ingredients for all U.S. drugs [came] from overseas, as [did] 40 percent of finished pills and capsules."<sup>97</sup>

The overseas manufacturing phenomenon is even more significant when it comes to generic drugs. Since overhead costs in overseas factories are much lower than in the U.S., generic drugs are far more likely than brand-name drugs to be manufactured overseas.<sup>98</sup> And many of these factories are not inspected by the FDA.

As Marcia Crosse, Director of Health Care at the Government Accountability Office (GAO), notes,

Although inspections of foreign drug manufacturing establishments – which are intended to assure that the safety and quality of drugs are not jeopardized by poor manufacturing practices – are an important element of FDA's oversight of the supply chain... FDA conducts relatively few inspections of the establishments that it considers subject to inspection.<sup>99</sup>

Indeed, the difference between the number of foreign and domestic manufacturing plant inspections is startling. While the "FDA inspects domestic establishments approximately once every 2.5 years,"<sup>100</sup> in 2009 the agency "inspected 11 percent of foreign establishments subject to inspection,"<sup>101</sup> meaning that "it would take FDA about 9 years to inspect all such establishments at this rate."<sup>102</sup>

And once the FDA inspects a foreign manufacturer, "it is unlikely that the agency will inspect it again, as the majority of foreign inspections FDA conducts are to inform decisions about the approval of new drugs before they are marketed for sale in the United States."<sup>103</sup>

Additionally, the foreign inspections that do occur do not include all parts of the supply chain. Instead they "generally limit [their] inspections to manufacturers of the finished product and APIs [*i.e.*, active pharmaceutical ingredients]"<sup>104</sup> In other words, an "inactive" ingredient that might affect a drug's absorption into the bloodstream can make it into a generic drug even though it is produced in a facility that the government has absolutely no way of knowing is safe or not.

Further, the GAO points out that there are a number of challenges the FDA faces while conducting foreign inspections. Unlike in the United States where inspectors can arrive

at manufacturing plants unannounced, when conducting foreign inspections, inspectors typically have to notify the manufacturer of their intention to inspect and may need advanced permission from the government before conducting an inspection.<sup>105</sup> This advanced warning means they “may not observe an accurate picture of the manufacturer’s day-to-day operations.”<sup>106</sup> Additionally, they can be denied access to entire sections of the manufacturing plants,<sup>107</sup> preventing them, again, from gaining an accurate picture of the plant. While unannounced domestic inspections last up to six weeks, foreign inspections are sometimes less than a week in length.<sup>108</sup>

Because inspections are so rare, when they do happen the FDA can make horrifying discoveries. For example, a July 2013 FDA inspection of a factory in India that makes metoprolol (a generic version of the popular heart pill Toprol-XL) found that the factory was really “a jumble of dilapidated buildings with blighted windows connected by flaking pipes and capped by a rusty roof.”<sup>109</sup> A *Bloomberg* report states that the FDA found “urine spilling over open drains, soiled uniforms and mold growing in a raw-material storage area.”<sup>110</sup> Wockhardt, who owns the factory, controls over one-quarter of the U.S. market for metoprolol.

*Bloomberg* goes on to note,

A check of the linen room found worker uniforms crusted with dirt. Raw-material storage areas had “significant mold growth” and the men’s toilets and toilets for the manufacturing gowning areas had urinals with inadequate drainage piping, with urine found to fall directly on the floor where it was collected in open drains and causing an odor...

Inspectors found tablets stored at the wrong temperature, raw materials and finished drugs kept in makeshift storage areas with no cleaning or temperature procedures, and condensate droplets falling from an overhead air handling unit onto shipping containers of pills....<sup>111</sup>

While some may worry that the biggest safety concerns stemming from the lack of FDA oversight abroad are dilapidated, dirty factories and mistakes and errors that may accidentally slip through the cracks, the actual truth is even worse. With so many generics being produced overseas in factories and plants that are not frequently, if ever, inspected by the FDA, opportunities exist for companies to engage in misconduct that puts consumers at additional risk. Often the wrongdoing goes undetected by the FDA until a whistleblower comes forward – meaning that the FDA sometimes approves and unknowingly allows fraudulent drugs on the market.

## **Ranbaxy**

Ranbaxy is “the sixth-largest generic-drug maker in the country, with more than \$1 billion in U.S. sales [in 2012]. The company... sells its products in more than 150 countries and has 14,600 employees.”<sup>112</sup> In the United States, Ranbaxy is “the fourth-fastest-growing pharmaceutical company ... both by sales and number of prescriptions.”<sup>113</sup> However, for years, Ranbaxy engaged in outright safety-related fraud

in connection with their manufacturing facilities in India, putting consumers at substantial risk.

Specifically, “[t]he company manipulated almost every aspect of its manufacturing process to quickly produce impressive-looking data that would bolster its bottom line.”<sup>114</sup> Among other things, Ranbaxy fabricated data, skipped steps while testing their drugs for bioequivalence and stability and, in some cases, substituted brand-name drugs for their own generics in their bioequivalence studies.<sup>115</sup> They lied to regulators, backdated documents and engaged in forgery. “The company even forged its own standard operating procedures, which FDA inspectors rely on to assess whether a company is following its own policies.”<sup>116</sup>

The FDA did not uncover this information on its own. It took a whistleblower coming forward with proof that Ranbaxy “had lied to regulators and falsified data.”<sup>117</sup> Even then, it took years for the FDA to stop approving the compromised Ranbaxy drugs. As *The People’s Pharmacy* points out,

What makes this story so astonishing is that the FDA did *NOT* discover the problems at Ranbaxy on its own. Had it not been for [a whistleblower], it is entirely possible that the FDA would be unaware of the fraud to this day. The FDA was apparently incapable of detecting forged data. Crucial tests had never been performed and the FDA didn’t discover that its house of cards was teetering dangerously. In fact, agency inspectors gave Ranbaxy a clean bill of health during an inspection in December, 2004. That was after key Ranbaxy executives had concluded “that crucial testing data for many of the company’s drugs did not actually exist and submissions to regulators had been forged.”<sup>118</sup>

A *Fortune Magazine* investigation, which uncovered the full extent of Ranbaxy’s misconduct, noted:

As the Ranbaxy story makes vividly clear, generic-drug makers intent on breaking the rules – especially those operating abroad – can easily do so. Drug applications work on the honor system: The FDA relies on data provided by the companies themselves. “We depend on that information to be truthful,” Gary Buehler, who headed the FDA’s office of generic drugs for 10 years, said in 2009.... The approval system “requires the behavior of the applicant,” he said. Otherwise, “the whole house of cards will fall down.”<sup>119</sup>

Perhaps more alarming, as *Fortune’s* investigation points out, were the FDA’s actions after the information came to light. While the agency did ultimately stop reviewing new drug applications from the manufacturing site, “until Ranbaxy proved their truthfulness”<sup>120</sup> and stopped the import of 30 different drugs from Ranbaxy’s two implicated Indian plants, they continued to let Ranbaxy operate and sell drugs in the U.S.<sup>121</sup>:

For all the actions taken by federal authorities, there is a deeply troubling aspect to the government’s role in the saga of Ranbaxy. Even as ever more details of the

company's long-running misconduct emerged, drug regulators permitted Ranbaxy to keep on selling many of its products.

Indeed, the FDA – charged with protecting the safety and health of Americans – went even further. Despite the agency's finding of fraud and misconduct, it granted Ranbaxy lucrative rights to sell new generic drugs. In the most high-profile example, in November 2011 the FDA allowed the company to maintain its exclusive first dibs on making the generic version of a medicine taken by tens of millions of Americans: Lipitor. In the first six months, this privilege allowed Ranbaxy to generate \$600 million in sales of generic atorvastatin, as nonbranded Lipitor is known.

Should the FDA have been surprised then, when problems emerged just a year later? In November 2012, Ranbaxy had to recall millions of pills after tiny glass particles were discovered in some of them. Even that, it turns out, was enough for only a temporary suspension, and the FDA permitted the company to resume sales in March.<sup>122</sup>

## Heparin

In 2008, federal officials linked heparin, a blood thinner being produced in China, to up to 149 deaths in the United States<sup>123</sup> and hundreds of allergic reactions.<sup>124</sup> The FDA determined that the contaminated heparin, sold by Baxter, was the result of “economically motivated adulteration,”<sup>125</sup> in other words, intentional fraud for economic gain. After the heparin crisis came to light, the FDA “increased its frequency of inspections of Chinese firms associated with [the heparin] contamination in the United States.”<sup>126</sup> But for the 20 months leading up to the crisis, there had not been any inspections of heparin firms in China.<sup>127</sup>

The reason for the lack of inspections goes beyond the FDA's inability to inspect foreign manufacturers in a timely manner and highlights another problem with FDA inspections. “Heparin is made from the mucous membranes of the intestines of slaughtered pigs that, in China, are often cooked in unregulated family workshops.”<sup>128</sup> While the FDA tries to inspect finished products and active pharmaceutical ingredients, crude heparin manufacturers producing raw ingredients did not fall into either of these categories. The contaminated ingredients were produced earlier in the supply chain.

As the GAO explains, “FDA officials told us that prior to the contaminated heparin crisis, the agency did not usually inspect crude heparin manufacturers and instead focused on API [active pharmaceutical ingredient] manufacturing facilities.”<sup>129</sup> Though here it may not have made any difference, as the GAO also said, “According to FDA's heparin-related inspections reports, there were both crude and API Chinese heparin firms that had never been previously inspected.”<sup>130</sup>

Passage of the Foreign Manufacturers Legal Accountability Act of 2013 (H.R.1910) would clearly help establish accountability for these drugmakers, though it should be noted that the U.S. Supreme Court has made it difficult to bring “fraud on the FDA” claims.<sup>131</sup> *The People's Pharmacy* also maintains that Congress should act on the

following consumer safety-related recommendations in light of overseas manufacturing problems<sup>132</sup>:

- “Country of origin labeling. You should know where your medicine comes from!”
- “The name of the manufacturer of your medicine should be on the label.”
- “We must demand unannounced inspections in all countries that wish to export pharmaceuticals to the U.S. market.”
- “Every foreign drug manufacturing company must be inspected every two years, just as U.S. manufacturers are inspected.”

## **THE CONSEQUENCES OF GENERIC DRUG INDUSTRY IMMUNITY**

As has been noted throughout this report, in addition to the difficulty holding foreign manufacturers accountable in U.S. courts,<sup>133</sup> two recent U.S. Supreme Court decisions immunized the generic drug industry for harm caused by the product’s inadequate labeling or defective design.<sup>134</sup> To understand the impact of generic drug industry immunity, it is important to examine the many ways lawsuits can – and have – led to safety improvements as the last line of defense against unsafe drugs.<sup>135</sup> Often, companies that are hit with large verdicts or settlements act immediately to change their unsafe product or practice. Sometimes it may take several large verdicts before a company acts.

Lawsuits can also have a tremendously beneficial role spurring medical research and alerting the public, and ultimately pressuring regulators to act on larger health risks and problems. As former FDA Commissioner David A. Kessler testified during a 2008 U.S. House Oversight and Government Reform Committee hearing on the prospect of immunity for medical products manufacturers:

many [FDA doctors and scientists] believe that the FDA lacks sufficient resources to protect the public health, and many worry that the FDA is not adequately monitoring the safety of drugs once they are on the market. The FDA has long been hamstrung by resource limitations. Even if FDA’s funding were doubled or tripled, its resources and ability to detect emerging risks on the thousands of marketed drugs and devices would still be dwarfed by those of the drug and device companies who manufacture those products.

For that reason, the tort system has historically provided a critical incentive to drug and device companies to disclose important information to physicians, patients, and the FDA about newly emerging risks.<sup>136</sup>

Zyprexa is a good example of the importance of litigation. In 1996, the FDA approved the antipsychotic drug Zyprexa, which quickly became the top seller for manufacturer Eli Lilly<sup>137</sup> until it was discovered that some patients taking the drug were also developing

diabetes.<sup>138</sup> Over 30,000 people sued Eli Lilly and during the course of litigation, patients uncovered disturbing information that Lilly had evidence, even during the clinical trials, that some patients taking Zyprexa had experienced significant weight gain and high blood sugar – symptoms that frequently lead to diabetes. According to internal documents released during litigation, Eli Lilly officials had instructed its sales representatives to downplay these possible side effects because it “might cause unwarranted fear among patients that will cause them to stop taking their medication.”<sup>139</sup>

Had it been up to FDA oversight alone, this misconduct would never have been uncovered. The FDA simply cannot exercise proper oversight of pharmaceutical companies and the drugs they market. Indeed, in 2012, the Institute of Medicine issued a new report, finding that the “FDA’s current approach to drug oversight in the postmarketing setting is not sufficiently systematic and does not ensure that it assesses the benefits and risks of drugs consistently over a drug’s life cycle.”<sup>140</sup>

The health consequences can be life-threatening. Every year there are over 2 million serious adverse drug reactions (ADRs). Of this total, an estimated 100,000 people die from ADRs, making it the fourth leading cause of death in the United States.<sup>141</sup> As one team of medical researchers concluded, “Many serious ADRs are discovered only after a drug has been on the market for years. Only half of newly discovered serious ADRs are detected and documented in the *Physicians’ Desk Reference* within seven years after drug approval.”<sup>142</sup>

Similarly, David C. Vladeck, Professor of Law at Georgetown University and former Director of the Federal Trade Commission’s Bureau of Consumer Protection, has written:

[The] FDA does not have the resources to perform the monumental task of monitoring the performance of every drug on the market. The FDA regulates products that amount to one-quarter of consumer spending in the United States, but it has only 9,000 employees nationwide.... [The] FDA’s Office of Drug Safety, the unit charged with monitoring adverse events associated with the 3,000 prescription drugs (and 11,000 drugs altogether) on the market, has about 100 professional employees....

[S]tate damages litigation helps uncover and assess risks that are not apparent to the agency during a drug’s approval process, and this ‘feedback loop’ enables the agency to better do its job.<sup>143</sup>

In the 2009 case *Wyeth v. Levine*,<sup>144</sup> the U.S. Supreme Court agreed with this analysis, ruling that brand-name drug companies should not be immune from liability for injuring or killing patients. The Court explained that the “FDA has limited resources to monitor the 11,000 drugs on the market and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge,”<sup>145</sup> and the “FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation.”<sup>146</sup>

In recognizing this, the Court looked to congressional intent, stating,

Congress did not provide a federal remedy for consumers harmed by unsafe or ineffective drugs.... Evidently, it determined that widely available state rights of action provided appropriate relief for injured consumers. It may also have recognized that state-law remedies further consumer protection by motivating manufacturers to produce safe and effective drugs and to give adequate warnings.<sup>147</sup>

Further, in terms of state tort law, the Court acknowledged that “[s]tate tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly”<sup>148</sup> and that such suits “serve a distinct compensatory function that may motivate injured persons to come forward with information.”<sup>149</sup>

As noted earlier, however, this same reasoning did not hold for the two U.S. Supreme Court generic drug cases that followed *Wyeth: PLIVA, Inc. v. Mensing* (2011) and *Mutual Pharmaceutical Co. v. Bartlett* (2013). *PLIVA* was brought by two women who were prescribed Reglan – a drug that treats digestive tract problems like gastroesophageal reflux disorder – yet given the generic version when pharmacists filled their prescriptions.<sup>150</sup> After several years on the medication, both women developed tardive dyskinesia, “a severe irreversible neurological disorder, characterized by ‘grotesque involuntary movements of the mouth, tongue, lips, and extremities, involuntary chewing movements, and a general sense of agitation.’”<sup>151</sup> They sued the manufacturers, asserting that the drugmakers did not provide adequate warnings regarding the risk of the neurological disorder from long-term drug use.<sup>152</sup> Even though there was mounting evidence that long use of the drug could lead to their disorder, the manufacturers did not change their labels to warn of the danger.<sup>153</sup>

However, the Court threw out this suit, holding that, regardless of the evidence, the victims could not sue the generic manufacturers. Why? Because while the FDA holds brand-name drug companies responsible for the adequacy and accuracy of their warning labels, FDA regulations specify that generic drug companies are only responsible for ensuring that their warning labels are the same as the brand-name labels.<sup>154</sup> The Court reasoned that generic drug companies cannot independently change their warning labels and therefore cannot be responsible when the labels are inadequate.<sup>155</sup>

The Court went even further in the 2013 case *Mutual Pharmaceutical Co. v. Bartlett*.<sup>156</sup> Karen Bartlett was prescribed a generic version of the drug sulindac for shoulder pain. “Within weeks of taking the drug, her skin began to slough off until nearly two-thirds of it was gone. She spent almost two months in a burn unit, and months more in a medically induced coma. The reaction permanently damaged her lungs and esophagus and rendered her legally blind.”<sup>157</sup> Bartlett sued the drug company, claiming there was a design-defect with the drug. A jury awarded her \$21 million in damages.

The Court invalidated the jury verdict, reasoning that because generic drug companies have a responsibility to mimic the composition of their brand-name counterparts and cannot independently alter their drugs’ composition, they cannot be sued for design-defect claims. The decision left Karen Bartlett (and anyone else who suffers injury after taking a defectively designed generic drug) empty-handed.

The dissent, infuriated by the decision, pointed out that Congress never intended for generic drug companies to operate with legal immunity and stated that the majority's reasoning "has the 'perverse effect' of granting broad immunity 'to an entire industry that, in the judgment of Congress, needed more stringent regulation.'"<sup>158</sup> And as was noted earlier in the *PLIVA* dissent,

[A] drug consumer's right to compensation for inadequate warnings now turns on the happenstance of whether her pharmacist filled her prescription with a brand-name drug or a generic. If a consumer takes a brand-name drug, she can sue the manufacturer.... If, however, she takes a generic drug, as occurs 75 percent of the time, she now has no right to sue. ...In some States, pharmacists must dispense generic drugs absent instruction to the contrary from a consumer's physician. Even when consumers can request brand-name drugs, the price of the brand-name drug or the consumers' insurance plans may make it impossible to do so. As a result, in many cases, consumers will have no ability to preserve their state-law right to recover for injuries caused by inadequate warnings.<sup>159</sup>

The dissents in both *PLIVA* and *Bartlett* made other important points. Congress clearly did not intend to leave victims with no recourse or access to the courts.<sup>160</sup> The holdings in those cases directly interfere with state police power to protect its own citizens<sup>161</sup> – powers that are "not to be superseded [without] the clear and manifest purpose of Congress,"<sup>162</sup> which does not apply here since these cases have existed for decades and Congress had said nothing at all about it. State law does not regulate generic drugs but rather provides a generic company a choice: cover its liability for marketing an unsafe drug by paying compensation to victims<sup>163</sup> or stop selling the drug.<sup>164</sup>

In *Bartlett*, Justice Sotomayor's dissent spelled out the safety implications of the majority decision:

State design-defect laws play an important role not only in discovering risks, but also in providing incentives for manufacturers to remove dangerous products from the market promptly. "The tort system can encourage FDA regulatory vigor and competence"...If manufacturers of products that require preapproval are given *de facto* immunity from design-defect liability, then the public will have to rely exclusively on imperfect federal agencies with limited resources and sometimes limited legal authority to recall approved products. And consumers injured by those products will have no recourse.<sup>165</sup>

And in *PLIVA*, she noted:

Today's decision eliminates the traditional state-law incentives for generic manufacturers to monitor and disclose safety risks. When a generic drug has a brand-name equivalent on the market, the brand-name manufacturer will remain incentivized to uncover safety risks. But brand-name manufacturers often leave the market once generic versions are available, meaning that there will be no manufacturer subject to failure-to-warn liability. As to those generic drugs, there will be no "additional...layer of consumer protection."<sup>166</sup>

As to this point, the FDA is clearly in agreement. In its new proposed rule, the agency clearly acknowledges that just because a generic drug matches a brand-name drug, its safety is not guaranteed and safety problems can still arise. In fact, the FDA emphasizes that *PLIVA* “alters the incentives for generic drug manufacturers to comply with current requirements to conduct robust postmarketing surveillance, evaluation, and reporting, and to ensure that the labeling for their drugs is accurate and up-to-date.”<sup>167</sup> To help close this safety gap, the new rule would restore parity between brand-name and generic drug companies when it comes to their responsibilities for maintaining safe and up-to-date warning labels. The agency notes,

This proposal is also intended to ensure that generic drug companies actively participate with FDA in ensuring the timeliness, accuracy, and completeness of drug safety labeling in accordance with current regulatory requirements. If this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs.<sup>168</sup>

After the proposed rule was announced, Dr. Sidney Wolfe, founder and Senior Adviser of Public Citizen’s Health Research Group, which filed the original rule change petition with the FDA, said in a statement that, “[w]hen finalized, the revisions will fill a regulatory gap that poses a risk to patient safety” and “[w]hen finalized after public comments, it will provide added protection to the tens of millions of people who regularly use generic drugs.”<sup>169</sup>

## CONCLUSION

There is no question that consumers benefit from cheaper generic versions of drug. There are good reasons why 80 percent of all drug prescriptions are filled by generic drugs today. However, no consumer benefits if a generic drug is unsafe and he or she is medically harmed as a result - and then has no recourse in the courts. Generic drugs are often do not match their brand name counterparts and patients who take them can suffer serious health consequences due to unsafe design, labeling and manufacturing. As the law now stands, whether or not an injured patient has legal recourse in court depends entirely on whether they have been prescribed a brand name or generic drug. This situation needs an urgent solution, which the FDA is fortunately pursuing.

## NOTES

<sup>1</sup> Katie Thomas, “Why the Bad Rap on Generic Drugs,” *New York Times*, October 5, 2013, <http://www.nytimes.com/2013/10/06/sunday-review/why-the-bad-rap-on-generic-drugs.html>.

<sup>2</sup> Institute of Medicine, *Ethical and Scientific Issues in Studying the Safety of Approved Drugs*, May 1, 2012, <http://www.iom.edu/Reports/2012/Ethical-and-Scientific-Issues-in-Studying-the-Safety-of-Approved-Drugs.aspx>.

<sup>3</sup> Katherine Eban, “Are generics really the same as branded drugs?” *Fortune*, January 14, 2013, <http://management.fortune.cnn.com/2013/01/10/generic-drugs-quality/>.

<sup>4</sup> “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Federal Register Doc. 2013-26799, November 13, 2013, at 67988, <http://www.gpo.gov/fdsys/pkg/FR-2013-11-13/pdf/2013-26799.pdf>.

<sup>5</sup> U.S. Food and Drug Administration, “Facts about Generic Drugs,” September 19, 2012, <http://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm>.

<sup>6</sup> Katherine Eban, “Dirty Medicine,” *Fortune*, May 15, 2013, <http://features.blogs.fortune.cnn.com/2013/05/15/ranbaxy-fraud-lipitor/>.

<sup>7</sup> “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Federal Register Doc. 2013-26799, November 13, 2013, at 67988, <http://www.gpo.gov/fdsys/pkg/FR-2013-11-13/pdf/2013-26799.pdf>.

<sup>8</sup> William H. Shrank et al., “Physician Perceptions About Generic Drugs,” *Annals of Pharmacotherapy* (January 2011), [http://scholar.harvard.edu/nkc/files/2011\\_physician\\_perceptions\\_about\\_generic\\_drugs\\_annals\\_pharmacotherapy.pdf](http://scholar.harvard.edu/nkc/files/2011_physician_perceptions_about_generic_drugs_annals_pharmacotherapy.pdf)

<sup>9</sup> *Wyeth v. Levine*, 555 U.S. 555 (2009).

<sup>10</sup> *Id.* at 579 (footnote omitted).

<sup>11</sup> *Id.* at 578-9 (footnote omitted).

<sup>12</sup> *Mutual Pharmaceutical Co. v. Bartlett*, 570 U. S. \_\_\_, 133 S. Ct. 2466 (2013); *PLIVA, Inc. v. Mensing*, 564 U.S. \_\_\_, 131 S.Ct. 2567 (2011).

<sup>13</sup> Together these cases immunize generic drug companies for deaths and injuries caused by either a defect in a drug’s defective or inadequate warning label or a drug’s design. (“On June 24, 2013, the U.S. Supreme Court held 5-4 in *Mutual Pharmaceutical Co. v. Bartlett* that federal law preempted a state-law design-defect damages claim against a manufacturer of generic prescription drugs. *Mutual* follows on the heels of two related U.S. Supreme Court rulings, *Wyeth v. Levine*, decided in 2009, and *PLIVA, Inc. v. Mensing*, decided in 2011. In *Wyeth*, the Court held that federal law generally does not preempt state law failure-to-warn claims against manufacturers of *brand-name* prescription drugs. In *PLIVA*, however, the Court concluded that federal law generally does preempt failure-to-warn claims against manufacturers of *generic* prescription drugs because federal law prohibits generic manufacturers from unilaterally amending their drug labels, and instead requires them invariably to use the label of the brand-name drug on which the generic product is based.” Brian Wolfman and Anne Warren King, “*Mutual Pharmaceutical Co. v. Bartlett* and Its Implications,” *United States Law Week* (2013), at 1 (emphasis in original)(footnotes omitted), <http://ssrn.com/abstract=2350930>).

<sup>14</sup> The current generic drug regulatory scheme was established by the 1984 Hatch-Waxman Amendments to the Federal Food, Drug and Cosmetic Act. 21 U.S.C. Food and Drugs, Chapter 9 § 301 et seq. Even before that, “the legislative history of the [1938] 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.” *Mutual Pharmaceutical v. Bartlett*, 133 S. Ct. 2466, 2485 (2013)(Sotomayor, dissenting).

<sup>15</sup> Drug labels are how the FDA communicates safety information to doctors and patients, specifically, “FDA-approved drug labeling summarizes the essential information needed for the safe and effective use of the drug, and reflects FDA’s finding regarding the safety and effectiveness of the drug under the labeled conditions of use.”

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“Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Federal Register Doc. 2013-26799, November 13, 2013, at 67986, <http://www.gpo.gov/fdsys/pkg/FR-2013-11-13/pdf/2013-26799.pdf>.

<sup>16</sup> “We acknowledge the unfortunate hand that federal drug regulation has dealt Mensing, Demahy, and others similarly situated. But ‘it is not this Court’s task to decide whether the statutory scheme established by Congress is unusual or even bizarre.’” *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2581-2 (2011)(footnote omitted).

<sup>17</sup> Press release from the Office of U.S. Senator Patrick Leahy, “Leahy To Introduce Bill to Protect Consumers Who Take Generic Drugs,” March 26, 2012, <http://www.leahy.senate.gov/press/leahy-to-introduce-bill-to-protect-consumers-who-take-generic-drugs>. In 2012, Senator Leahy introduced the Patient Safety and Generic Labeling Improvement Act (S. 2295, 112th Congress), <https://www.govtrack.us/congress/bills/112/s2295>, noting, “The Patient Safety and Generic Labeling Improvement Act will promote consumer safety by ensuring that generic drug companies can improve the warning information for their products in the same way that brand name manufacturers can under existing law.” The FDA has now proposed a new rule that, if passed, may make this legislation redundant.

<sup>18</sup> On November 5, 2013, the FDA issued a proposed new rule that addresses *PLIVA* directly. Noting that the Court found in *PLIVA* “that Federal law did not permit a generic drug manufacturer to ... unilaterally strengthen warnings in its labeling or to issue additional warnings,” and because “the difference between [brand-name and generic companies’] ability to independently change product labeling ... leads to different outcomes on whether Federal labeling requirements preempt State law failure-to-warn claims,” the agency would enable generic drug companies “to update product labeling promptly to reflect certain types of newly acquired information related to drug safety, irrespective of whether the revised labeling differs from” that of the brand-named drug. Under the new rule, “when new information becomes available that causes information in labeling to be inaccurate” a generic company “must take steps to change the content of its labeling...” “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Federal Register Doc. 2013-26799, November 13, 2013, at 67986-8, <http://www.gpo.gov/fdsys/pkg/FR-2013-11-13/pdf/2013-26799.pdf>.

<sup>19</sup> According to the FDA, “The primary purpose of labeling (commonly referred to as the ‘package insert’ or ‘prescribing information’) for prescription drugs is to provide health care practitioners with the essential scientific information needed to facilitate prescribing decisions, thereby enhancing the safe and effective use of prescription drug products and reducing the likelihood of medication errors. Prescription drug labeling is directed to health care practitioners, but may include FDA-approved patient labeling (see § 201.57(c)(18) (21 CFR 201.57(c)(18)) and 21 CFR 201.80(f)(2)). The over-the-counter (OTC) *Drug Facts* labeling is directed to consumers and conveys information in a clear, standardized format to enable patient self-selection of an appropriate drug and enhance the safe and effective use of the drug (see 21 CFR 201.66).” *Id.* at 67986.

<sup>20</sup> According to the FDA, “In the current marketplace, in which approximately 80 percent of drugs dispensed are generic and, as we have learned, brand name drug manufacturers may discontinue marketing after generic drug entry, FDA believes it is time to provide [generic drug companies] with the means to update product labeling to reflect data obtained through postmarketing surveillance, even though this will result in temporary labeling differences among products. In a study of FDA safety-related drug labeling changes made in 2010, FDA found that the median time from initial approval of the drug product to the time of making the safety-related labeling change was 11 years, which confirms that data supporting labeling changes may become available after approval of generic versions of the drug product (see Ref. 2). FDA found that ‘[t]he most critical safety-related label changes, boxed warnings and contraindications, occurred a median 10 and 13 years after drug approval (and the range spanned from 2 to 63 years after approval), underscoring the importance of persistent and vigilant postmarket drug safety surveillance’ (Ref. 2).” *Id.* at 67988.

<sup>21</sup> *Id.* at 67985.

<sup>22</sup> The Court in *PLIVA* said, “[I]t is not this Court’s task to decide whether the statutory scheme established by Congress is unusual or even bizarre.” ... As always, Congress and the FDA retain the authority to change the law and regulations if they so desire.” 131 S. Ct. 2567, 2582.

<sup>23</sup> GlobalData, “CountryFocus: Healthcare, Regulatory and Reimbursement Landscape – US ” (May 2013), <http://www.researchandmarkets.com/research/hl8vbr/countryfocus>.

<sup>24</sup> *Ibid.*

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- <sup>25</sup> Steven E. Kuehn, “Generics Industry: Under Pressure,” *PharmaManufacturing.com*, June 4, 2013, <http://www.pharmamanufacturing.com/articles/2013/1306-generics-industry/>.
- <sup>26</sup> Ranit Mishori, “Why are generic drugs cheaper than brand-name ones?” *Washington Post*, July 11, 2011, [http://articles.washingtonpost.com/2011-07-11/national/35267296\\_1\\_generic-drugs-manufacturers-of-brand-name-drugs-pharmaceutical-companies](http://articles.washingtonpost.com/2011-07-11/national/35267296_1_generic-drugs-manufacturers-of-brand-name-drugs-pharmaceutical-companies).
- <sup>27</sup> U.S. PIRG, “Top Twenty Pay-For-Delay Drugs: How Drug Industry Payoffs Delay Generics, Inflate Prices and Hurt Consumers,” July 11, 2013, <http://www.uspirg.org/reports/usp/top-twenty-pay-delay-drugs>.
- <sup>28</sup> Duff Wilson, “Drug Firms Face Billions in Losses in ’11 as Patents End,” *New York Times*, March 6, 2011, <http://www.nytimes.com/2011/03/07/business/07drug.html>.
- <sup>29</sup> Arthur Caplan and Zachary Caplan, “How Big Pharma rips you off on drugs,” *CNN*, April 25, 2013, <http://www.cnn.com/2013/04/25/opinion/caplan-prescription-drugs/>.
- <sup>30</sup> *Ibid.*
- <sup>31</sup> “Top Twenty Pay-For-Delay Drugs: How Drug Industry Payoffs Delay Generics, Inflate Prices and Hurt Consumers,” *U.S. PIRG*, July 11, 2013, <http://www.uspirg.org/reports/usp/top-twenty-pay-delay-drugs>.
- <sup>32</sup> Edward Wyatt, “Supreme Court Lets Regulators Sue Over Generic Drug Deals,” *New York Times*, June 17, 2013, <http://www.nytimes.com/2013/06/18/business/supreme-court-says-drug-makers-can-be-sued-over-pay-for-delay-deals.html>.
- <sup>33</sup> Public Citizen, “Generic Drug Labeling”(June 2013), at 11, <http://www.citizen.org/documents/2138.pdf>.
- <sup>34</sup> *Ibid.*
- <sup>35</sup> Brief of Amici Curiae Senator Tom Harkin and Representative Henry A. Waxman in Support of Respondent, *Mutual Pharmaceutical Company, Inc. v. Karen L. Bartlett*, No. 12-142 (February 2013), at 10, [http://www.americanbar.org/content/dam/aba/publications/supreme\\_court\\_preview/briefs-v2/12-142\\_resp\\_amcu\\_th\\_hw.authcheckdam.pdf](http://www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-142_resp_amcu_th_hw.authcheckdam.pdf).
- <sup>36</sup> *Ibid.*
- <sup>37</sup> 21 U.S.C. Food and Drugs, Chapter 9 § 301 et seq.
- <sup>38</sup> Brief of Amici Curiae Senator Tom Harkin and Representative Henry A. Waxman in Support of Respondent, *Mutual Pharmaceutical Company, Inc. v. Karen L. Bartlett*, No. 12-142 (February 2013), at 10, [http://www.americanbar.org/content/dam/aba/publications/supreme\\_court\\_preview/briefs-v2/12-142\\_resp\\_amcu\\_th\\_hw.authcheckdam.pdf](http://www.americanbar.org/content/dam/aba/publications/supreme_court_preview/briefs-v2/12-142_resp_amcu_th_hw.authcheckdam.pdf).
- <sup>39</sup> *Id.* at 11.
- <sup>40</sup> *Ibid.*
- <sup>41</sup> Brand-name drug applications “must include evidence showing the drug can be safely used and is effective in the proposed patient population. Such evidence may require testing in hundreds of animals and the treatment of tens of thousands of patients before a brand-name drug can be approved by the FDA.” Costas H. Kefalas and Arthur A. Ciociola, “The FDA’s Generic-Drug Approval Process: Similarities to and Differences From Brand-Name Drugs,” *American Journal of Gastroenterology* (2011), at 1019, [http://d2j7fjepcxuj0a.cloudfront.net/wp-content/uploads/2012/04/AJG\\_June11\\_FDAGeneric-DrugApprovalProcess.pdf](http://d2j7fjepcxuj0a.cloudfront.net/wp-content/uploads/2012/04/AJG_June11_FDAGeneric-DrugApprovalProcess.pdf).
- <sup>42</sup> U.S. Food and Drug Administration, “Facts about Generic Drugs,” September 19, 2012, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/default.htm>.
- <sup>43</sup> U.S. Food and Drug Administration, “Generic Drugs: Questions and Answers,” September 3, 2013, <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm>.
- <sup>44</sup> U.S. Food and Drug Administration, “Abbreviated New Drug Application (ANDA): Generics,” July 17, 2013, <http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/default.htm>.
- <sup>45</sup> *Ibid.*
- <sup>46</sup> U.S. Food and Drug Administration, “Questions and Answers Regarding Market Withdrawal of Budeprion XL 300mg Manufactured by Impax and Marketed by Teva,” October 3, 2012, <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm322160.htm>

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- <sup>47</sup> *Ibid.*
- <sup>48</sup> Katherine Eban, "Are generics really the same as branded drugs?" *Fortune*, January 14, 2013, <http://management.fortune.cnn.com/2013/01/10/generic-drugs-quality/>.
- <sup>49</sup> Katie Thomas, "An Increase in Scrutiny for Generics," *New York Times*, October 31, 2012, <http://www.nytimes.com/2012/11/01/business/fda-increases-scrutiny-of-some-generic-drugs.html>.
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- <sup>51</sup> Katie Thomas, "An Increase in Scrutiny for Generics," *New York Times*, October 31, 2012, <http://www.nytimes.com/2012/11/01/business/fda-increases-scrutiny-of-some-generic-drugs.html>.
- <sup>52</sup> Costas H. Kefalas and Arthur A. Ciociola, "The FDA's Generic-Drug Approval Process: Similarities to and Differences From Brand-Name Drugs," *American Journal Gastroenterology* (2011), at 1018, [http://d2j7fjepcxuj0a.cloudfront.net/wp-content/uploads/2012/04/AJG\\_June11\\_FDAGeneric-DrugApprovalProcess.pdf](http://d2j7fjepcxuj0a.cloudfront.net/wp-content/uploads/2012/04/AJG_June11_FDAGeneric-DrugApprovalProcess.pdf).
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- <sup>56</sup> See, "About the Graedons," *The People's Pharmacy*, <http://www.peoplespharmacy.com/about/>.
- <sup>57</sup> "Seizures after Drug Switch," *The People's Pharmacy*, July 15, 2013, <http://www.peoplespharmacy.com/2013/07/15/seizures-after-drug-switch/>.
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- <sup>69</sup> Katherine Eban, "Are generics really the same as branded drugs?" *Fortune*, January 14, 2013, <http://management.fortune.cnn.com/2013/01/10/generic-drugs-quality/>.
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<sup>76</sup> Charles Seife and Rob Garver, “No Substitute: When a Generic Drug Isn’t What it Seems,” *ProPublica*, <http://www.propublica.org/article/no-substitute-when-a-generic-drug-isnt-what-it-seems>.

<sup>77</sup> *Ibid.*

<sup>78</sup> Wellbutrin XL peaked 5 hours after taking the drug whereas the generics peaked after 2 hours – and the “amount and rate of the active chemical released into the body from Defendants’ drugs depended upon factors like food and alcohol consumption, other medications, and other [gastro intestinal issues].” None of this was an issue with the brand name. *In Re: Budeprion XL Marketing & Sales Litigation*, 09-md-2107, MDL No. 2107 (E.D. Pa. memorandum, July 2, 2012), at 3, [http://www.gpo.gov/fdsys/pkg/USCOURTS-paed-2\\_09-md-02107/pdf/USCOURTS-paed-2\\_09-md-02107-2.pdf](http://www.gpo.gov/fdsys/pkg/USCOURTS-paed-2_09-md-02107/pdf/USCOURTS-paed-2_09-md-02107-2.pdf).

<sup>79</sup> *Id.* at 4.

<sup>80</sup> *Ibid.*

<sup>81</sup> *Ibid.*

<sup>82</sup> *Ibid.*

<sup>83</sup> *Id.* at 7.

<sup>84</sup> The settlement provided injunctive relief, meaning that the companies agreed to make changes in the way they monitored, marketed and sold their drug. *Id.* at 9.

<sup>85</sup> *Id.* at 7, 26-29 (citing *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011)).

<sup>86</sup> *Id.* at 7.

<sup>87</sup> *Id.* at 24.

<sup>88</sup> *Id.* at 29.

<sup>89</sup> U.S. Food and Drug Administration, “Questions and Answers Regarding Market Withdrawal of Budeprion XL 300mg Manufactured by Impax and Marketed by Teva,” October 3, 2012, <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm322161.htm>.

<sup>90</sup> *Ibid.*

<sup>91</sup> *Ibid.*

<sup>92</sup> *Ibid.*

<sup>93</sup> *See, e.g.*, James Bickford, “Opinion analysis: No jurisdiction over foreign companies,” *SCOTUSblog*, June 30, 2011, <http://www.scotusblog.com/2011/06/opinion-analysis-no-jurisdiction-over-foreign-companies/>. Legislation has been introduced in Congress to try to fix this problem. It would direct the FDA and other agencies “to require foreign manufacturers and producers of such products (or components used to manufacture them), in excess of a minimum value or quantity, to establish a registered agent in the United States authorized to accept service of process on their behalf for the purpose of any state or federal regulatory proceeding or civil action in state or federal court.” “Summary: H.R.1910 – 113th Congress (2013-2014),” <http://beta.congress.gov/bill/113th/house-bill/1910>.

<sup>94</sup> Statement of U.S. Government Accountability Office Health Care Team Director Marcia Crosse before the U.S. Senate Committee on Health, Education, Labor and Pensions, “DRUG SAFETY: FDA Faces Challenges Overseeing the Foreign Drug Manufacturing Supply Chain,” September 14, 2011, at 1, <http://www.gao.gov/assets/130/126943.pdf>.

<sup>95</sup> *Ibid.*

<sup>96</sup> Nancy Shute, “Are Your Drugs Safe?” *U.S. News & World Report*, October 5, 2007, <http://health.usnews.com/health-news/managing-your-healthcare/healthcare/articles/2007/10/05/are-your-drugs-safe>.

<sup>97</sup> Katherine Eban, “Dirty Medicine,” *Fortune Magazine*, May 15, 2013, <http://features.blogs.fortune.cnn.com/2013/05/15/ranbaxy-fraud-lipitor/>.

<sup>98</sup> Bernadine Healy, “Generic Drugs: Cheaper, Yes; Same Quality, Maybe Not,” *U.S. News & World Report*, December 3, 2008, <http://health.usnews.com/health-news/blogs/heart-to-heart/2008/12/03/generic-drugs-cheaper-yes-same-quality-maybe-not>.

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<sup>100</sup> *Id.* at 6.

<sup>101</sup> *Id.* at 5.

<sup>102</sup> *Ibid.*

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<sup>109</sup> Ketaki Gokhale, “Urine Spills Staining Image of Wockhardt’s Generic Drugs,” *Bloomberg News*, September 27, 2013, <http://www.bloomberg.com/news/2013-09-27/urine-spills-staining-image-of-wockhardt-s-generic-drugs.html>.

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<sup>115</sup> *Ibid.*

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<sup>117</sup> “FDA Fails to Catch Generic Drug Disasters,” *The People’s Pharmacy*, May 15, 2013, <http://www.peoplespharmacy.com/2013/05/15/fda-fails-to-catch-generic-drug-disasters-1/>

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<sup>120</sup> *Ibid.*

<sup>121</sup> *Ibid.*

<sup>122</sup> *Ibid.*

<sup>123</sup> Alexander Gaffney, “With Eye on Tainted Chinese Heparin Scandal, FDA Finalizes Quality Monitoring Guidance,” *Regulatory Focus*, June 26, 2013, <http://www.raps.org/focus-online/news/news-article-view/article/3684.aspx>.

<sup>124</sup> Jennifer Corbett Dooren, “Suppliers Linked to Impure Heparin,” *Wall Street Journal*, February 23, 2012, <http://online.wsj.com/news/articles/SB10001424052970203960804577239624228625522>.

<sup>125</sup> U.S. Government Accountability Office Report to the Ranking Member, Committee on Energy and Commerce, House of Representatives, “Food and Drug Administration Response to Heparin Contamination Helped Protect Public Health; Controls That Were Needed for Working With External Entities Were Recently Added” (October 2012), at 2, <http://www.gao.gov/assets/320/311879.pdf>.

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<sup>127</sup> *Id.* at 13.

<sup>128</sup> Gardiner Harris, “U.S. Identifies Tainted Heparin in 11 Countries,” *New York Times*, April 22, 2008, <http://www.nytimes.com/2008/04/22/health/policy/22fda.html>.

<sup>129</sup> U.S. Government Accountability Office Report to the Ranking Member, Committee on Energy and Commerce, House of Representatives, “Food and Drug Administration Response to Heparin Contamination Helped Protect Public Health; Controls That Were Needed for Working With External Entities Were Recently Added” (October 2012), at 12 (note 17), <http://www.gao.gov/assets/320/311879.pdf>.

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<sup>133</sup> See, e.g., James Bickford, “Opinion analysis: No jurisdiction over foreign companies,” *SCOTUSblog*, June 30, 2011, <http://www.scotusblog.com/2011/06/opinion-analysis-no-jurisdiction-over-foreign-companies/>. Legislation has been introduced in Congress to try to fix this problem. It would direct the FDA and other agencies “to require foreign manufacturers and producers of such products (or components used to manufacture them), in excess of a minimum value or quantity, to establish a registered agent in the United States authorized to accept service of process on their behalf for the purpose of any state or federal regulatory proceeding or civil action in state or federal court.” “Summary: H.R.1910 – 113th Congress (2013-2014),” <http://beta.congress.gov/bill/113th/house-bill/1910>.

<sup>134</sup> *Mutual Pharmaceutical Co. v. Bartlett*, 570 U. S. \_\_\_\_ , 133 S. Ct. 2466 (2013); *PLIVA, Inc. v. Mensing*, 564 U. S. \_\_\_\_ , 131 S.Ct. 2567 (2011).

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<sup>137</sup> Matthew Herper, “Lilly Ferociously Defends Its Top Seller,” *Forbes.com*, September 9, 2004, [http://www.forbes.com/healthcare/2004/09/09/cx\\_mh\\_0909lly.html](http://www.forbes.com/healthcare/2004/09/09/cx_mh_0909lly.html).

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<sup>144</sup> *Wyeth v. Levine*, 555 U.S. 555 (2009).

<sup>145</sup> *Id.* at 578-9 (footnote omitted).

<sup>146</sup> *Id.* at 579 (footnote omitted).

<sup>147</sup> *Id.* at 574 (footnote omitted).

<sup>148</sup> *Id.* at 579.

<sup>149</sup> *Ibid.*

<sup>150</sup> *PLIVA v. Mensing*, 564 U.S. \_\_\_\_ , 131 S. Ct. 2567 (2011).

<sup>151</sup> Respondents’ Brief, *PLIVA, Inc. v. Mensing*, February 23, 2011, at 4 (citation omitted), [http://www.americanbar.org/content/dam/aba/publishing/previewbriefs/Other\\_Brief\\_Updates/09-993\\_Respondent.authcheckdam.pdf](http://www.americanbar.org/content/dam/aba/publishing/previewbriefs/Other_Brief_Updates/09-993_Respondent.authcheckdam.pdf).

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- <sup>153</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2573 (2011).
- <sup>154</sup> *Id.* at 2574.
- <sup>155</sup> *Id.* at 2577-8.
- <sup>156</sup> *Mutual Pharmaceutical Co. v. Bartlett*, 570 U. S. \_\_\_\_, 133 S. Ct. 2466 (2013).
- <sup>157</sup> Katie Thomas, “Justices to Take Up Case on Generic Drug Makers’ Liability,” *New York Times*, March 4, 2013, <http://www.nytimes.com/2013/03/05/business/justices-to-take-up-case-on-generic-drug-makers-liability.html>.
- <sup>158</sup> 133 S. Ct. 2466, 2495 (2013)(Sotomayor, dissenting)(citations omitted).
- <sup>159</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2592 (2011)(Sotomayor, dissenting).
- <sup>160</sup> “[T]he 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.” *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466, 2486 (2013)(Sotomayor, dissenting)(citations omitted); “Given the longstanding existence of product liability actions, including for failure to warn, ‘[i]t is difficult to believe that Congress would, without comment, remove all means of judicial recourse for those injured by illegal conduct.’” *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2592 (2011)(Sotomayor, dissenting)(citations omitted).
- <sup>161</sup> “[I]t is a choice that a sovereign State may impose to protect its citizens from dangerous drugs or at least ensure that seriously injured consumers receive compensation.” *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466, 2491 (2013)(Sotomayor, dissenting).
- <sup>162</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2586 (2011) (Sotomayor, dissenting)(citations omitted).
- <sup>163</sup> “New Hampshire’s design-defect law did not require Mutual to do anything other than to compensate consumers who were injured by an unreasonably dangerous drug.” *Mutual Pharmaceutical Co. v. Bartlett*, 133 S. Ct. 2466, 2489 (2013)(Sotomayor, dissenting).
- <sup>164</sup> “When a manufacturer cannot change the label or when doing so would not make the drug safe, the manufacturer may still choose between exiting the market or continuing to sell while knowing it may have to pay compensation to consumers injured by the product.” *Id.* at 2491 (endnote omitted).
- <sup>165</sup> *Id.* at 2495 (citations omitted).
- <sup>166</sup> *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567, 2592-3 (2011)(Sotomayor, dissenting)(citations omitted).
- <sup>167</sup> “Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products,” Federal Register Doc. 2013-26799, November 13, 2013, at 67988-9, <http://www.gpo.gov/fdsys/pkg/FR-2013-11-13/pdf/2013-26799.pdf>.
- <sup>168</sup> *Id.* at 67989.
- <sup>169</sup> Public Citizen, “FDA Proposal to Revise Drug Labeling Regulations is Welcome News, Will Improve Drug Safety,” July 3, 2013, <http://www.citizen.org/pressroom/pressroomredirect.cfm?ID=3930>.