

## State-Level Protection for Good-Faith Pharmaceutical Manufacturers

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## I. INTRODUCTION

In 1996, the Michigan legislature enacted a common-sense proposition into law: drug-safety determinations should be made by the Food and Drug Administration (FDA), rather than by judges or juries hearing tort cases. This statute, Michigan Compiled Law § 600.2946(5) (the Michigan FDA Shield Law), provides that, with certain exceptions, drugs approved by FDA and in compliance with FDA requirements cannot be held to be “defective or unreasonably dangerous” in a state-law tort action. Nevertheless, misconceptions regarding the operation of the Michigan FDA Shield Law and the FDA drug-approval process have led some to attack this sensible and well-considered measure.<sup>1</sup>

The FDA drug-approval process is often misunderstood. FDA’s decision to approve a new drug is qualitatively different from decisions made by many other consumer-protection agencies.<sup>2</sup> For example, when the Consumer Product Safety Commission sets minimum standards for lawnmowers or children’s toys, manufacturers are generally permitted to exceed these minimum standards. They may do so either to produce ultra-safe products for consumers willing to pay for that additional safety or out of a business-driven desire to reduce the likelihood that the manufacturer could ultimately be held liable for product-related injuries. By contrast, when FDA approves a new drug, it intends to set not a minimum standard but an optimal

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<sup>1</sup> See, e.g., Dawson Bell, *Group calls for repeal of state drug liability law*, Detroit Free Press, April 12, 2005, available at 2005 WLNR 5675662; Patricia Anstett & Kim Norris, *Cover Story: A Michigan law stirs a national debate*, Detroit Free Press, March 1, 2005, available at <http://www.freep.com>; Patricia Anstett & Kim Norris, *Michigan Rezulin lawsuits tossed*, Detroit Free Press, February 25, 2005, available at 2005 WLNR 2890059.

<sup>2</sup> See, e.g., Leslie Richter, *Shielding drug firms isn’t the state’s job*, LANSING STATE J., Sept. 13, 2005, at 1 (“It doesn’t make sense that drug companies are immune from responsibility when we hold auto makers, toy makers, and everyone else accountable for their products.”) (op-ed by a plaintiff in a suit against Merck).

standard: one that balances the risks associated with the drug against the competing risks associated with not having the drug available.<sup>3</sup>

This difference in regulatory approaches results from a fundamental distinction between pharmaceuticals and other manufactured products. The adverse effects associated with a given drug are almost inevitably not a result of cost-cutting or sloppy manufacturing: rather, they are the result of the drug's composition and are inseparable from the drug's beneficial effects.<sup>4</sup> Accordingly, FDA approval of a drug does not require a determination that the drug is safe in all circumstances. Indeed, such a requirement would prohibit the approval of the vast majority of drugs. Instead, FDA approval of a prescription drug constitutes a determination that, as a matter of public health policy, the drug is sufficiently beneficial to justify its widespread availability to prescribers, despite a (perhaps unavoidable) risk of harm to certain patients.

Unfortunately, the liability regime currently applicable in most states does not account for this aspect of the FDA regulatory process. Even when FDA has concluded that it is better to

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<sup>3</sup> FDA, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 21 C.F.R. §§ 201, 314, 601 (2006) ("FDA, Physician Labeling Rule"), at 41-42 ("Another misunderstanding of the [FDCA] encouraged by State law actions is that FDA labeling requirements represent a minimum safety standard. . . . In fact, FDA interprets the act to establish both a 'floor' and a 'ceiling' . . . ."), available at <http://www.fda.gov/bbs/topics/news/2005/NEW01272.html>; see also *Geier v. American Honda Motor Co.*, 529 U.S. 861, 875-76, 868 (2000) (holding that statute intended to provide automobile manufacturers "with a range of choices among different passive restraint devices" was not simply a "minimum safety standard" and accordingly preempted state-law tort actions requiring additional passive restraints); Michael D. Green, *Statutory Compliance and Tort Liability: Examining the Strongest Case*, 30 U. MICH. J. L. REFORM 461, 468-69 (1997).

<sup>4</sup> See, e.g., *United States v. Rutherford*, 442 U.S. 544, 555 (1979) ("[T]he Commissioner generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use."); FDA, Proposed Recommendations to the Drug Enforcement Administration Regarding the Scheduling Status of Marijuana and Its Components and Notice of a Public Hearing, 47 Fed. Reg. 28141 (proposed June 29, 1982) ("Because no drug is ever completely safe, FDA considers "safe" to mean (in the context of a human drug) that the therapeutic benefits to be derived from the drug outweigh its known and potential risks under the conditions of use in the labeling."); FDA, Report to the FDA Commissioner from the Task Force on Risk Management, Managing the Risks from Medical Product Use (1999), available at <http://www.fda.gov/oc/tfrm/riskmanagement.html> ("A safe product is one that has reasonable risks, given the magnitude of the benefit expected and the alternatives available."); see also Michael D. Green & William B. Schultz, *Tort Law Deference to FDA Regulation of Medical Devices*, 88 GEO. L.J. 2119, 2129-30 (2000).

have a given drug on the market, despite its known adverse effects, state tort regimes often make it possible to recover large damage awards against the drug manufacturer. One notable exception is the state of Michigan. The solution adopted by the Michigan legislature is simple. Absent certain important exceptions, a drug “manufacturer or seller” will not be deemed to have sold a “defective or unreasonably dangerous” drug if: (1) FDA had approved the drug in question “for safety and efficacy”; and (2) “the drug and its labeling were in compliance with [FDA’s] approval at the time the drug left the control of the manufacturer or seller.”<sup>5</sup> Importantly, the Michigan FDA Shield Law protects only those pharmaceutical manufacturers who act in good faith. The law expressly does *not* apply to: (1) any drug “sold in the United States after the effective date of an [FDA order] to remove the drug from the market or to withdraw [FDA’s] approval”;<sup>6</sup> (2) any defendant who intentionally withholds required information from FDA that would have, had it been submitted, resulted in the drug not being approved or FDA withdrawing approval;<sup>7</sup> or (3) any defendant who “makes an illegal payment” to a U.S. official “for the purposes of securing or maintaining approval of the drug.”<sup>8</sup>

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<sup>5</sup> MICH. COMP. LAWS SERV. § 600.2946(5).

<sup>6</sup> *Id.* § 600.2946(5).

<sup>7</sup> *Id.* § 600.2946(5)(a).

<sup>8</sup> *Id.* § 600.2946(5)(b). The relevant section reads in full:

(5) In a product liability action against a manufacturer or seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the United States food and drug administration, and the drug and its labeling were in compliance with the United States food and drug administration's approval at the time the drug left the control of the manufacturer or seller. However, this subsection does not apply to a drug that is sold in the United States after the effective date of an order of the United States food and drug administration to remove the drug from the market or to withdraw its approval. This subsection does not apply if the defendant at any time before the event that allegedly caused the injury does any of the following:

(a) Intentionally withholds from or misrepresents to the United States food and drug administration information concerning the drug that is required to be submitted under the federal food, drug, and cosmetic act, chapter 675, 52 Stat. 1040, 21 USC. 301 to 321, 331 to 343-2, 344 to 346a, 347, 348 to 353, 355 to 360, 360b to 376, and 378 to 395, and the drug would not have been approved, or the United States food and drug administration would have withdrawn approval for the drug if the information were accurately submitted.

(b) Makes an illegal payment to an official or employee of the United States

To avoid constitutional difficulties, the United States Court of Appeals for the Sixth Circuit has held that the fraud and bribery exceptions require an FDA finding that fraud or bribery has occurred.<sup>9</sup> Nonetheless, these exceptions remain important to the overall statutory scheme. A drug manufacturer who misleads FDA by withholding material information remains potentially liable for marketing a defective or unreasonably dangerous product. A manufacturer who ignores an FDA order to withdraw a drug or who bribes a federal official is similarly potentially liable. In other words, the statute provides protection only to drug manufacturers who act in good faith in their dealings with FDA, providing all information material to the agency's decision-making process. Manufacturers that FDA determines did not act in good faith in their dealings with the agency receive no protection from the Michigan FDA Shield Law.<sup>10</sup>

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food and drug administration for the purpose of securing or maintaining approval of the drug.

*Id.* § 600.2946(5).

<sup>9</sup> *Garcia v. Wyeth-Ayerst Labs.*, 385 F.3d 961, 966-67 (6th Cir. 2004). The Sixth Circuit's requirement of an FDA finding should help to ensure the effectiveness of the statutory scheme. Experience with the Vaccine Injury Compensation Program ("VICP") suggests that loopholes in statutory protection for pharmaceutical manufacturers can lead to significant litigation costs for claims not specifically envisioned in the protective statute. In the case of the VICP, it has primarily involved plaintiffs' attempts to avoid the no-fault system of the VICP by arguing that their injuries were caused by Thimerosal, a preservative used in vaccines, rather than by the vaccine itself. *See, e.g.*, Michael L. Williams et al, Association of Trial Lawyers of America, 2 ATLA CONVENTION REFERENCE MATERIALS 2681 (2002) (discussing different strategies lawyers representing Thimerosal plaintiffs have used in their efforts to "intentionally avoid[] the federal [compensation] program" in favor of "class actions and individual claims in state courts"); *cf.* Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 741, 761-62 (2003) ("[R]ecent litigation . . . has shaken some of the confidence that manufacturers have had about the extent of their protection from liability [under the VICP]."). The Sixth Circuit's requirement that FDA explicitly make a finding of fraud or bribery before suit is permitted may help prevent similarly abusive litigation under the Michigan FDA Shield Law.

<sup>10</sup> Manufacturers who mislead FDA do so at their peril. One recent example is the criminal prosecution of Endovascular Technologies, Inc. ("ETV"), a subsidiary of Guidant Corporation. Rather than face trial in the Northern District of California, ETV "pled guilty . . . to ten felonies and agreed to pay \$92.4 million to settle criminal and civil charges that it covered up thousands of incidents in which a medical device used to treat aneurysms in the aorta malfunctioned." Press Release, United States Attorney's Office, Northern District of California June 12, 2003), available at [http://www.usdoj.gov/usao/can/press/html/2003\\_06\\_12\\_endovascular.html](http://www.usdoj.gov/usao/can/press/html/2003_06_12_endovascular.html). This constituted "the second largest criminal and civil settlement in the history of the Northern District of California." *Id.*

Part II, below, explains the comprehensive nature of FDA prescription drug regulation. The strict demands of this regulatory program explain why it is not appropriate to hold pharmaceutical manufacturers to state tort-law requirements that might be inconsistent with FDA determinations. Part III sets out four negative consequences of the pharmaceutical-liability regime currently effective in most states: (1) reduced investment in research; (2) reduced availability of drugs already proven to be effective; (3) higher drug prices; and (4) interference with rational prescribing. Part IV discusses one tactic of FDA that has reduced the negative consequences of the current pharmaceutical-liability regime. By becoming involved in select state-law products-liability actions, FDA has had some success in preventing state tort laws from frustrating federal regulatory efforts. FDA involvement in state-law cases is not an ideal solution, not least because each instance of such involvement involves the costly investment of substantial agency resources.<sup>11</sup> However, FDA's new Physician Labeling Rule<sup>12</sup> provides some hope that direct FDA involvement in state-law tort cases will become less necessary. The preamble to that rule makes an official statement of FDA's views on preemption easily available to courts hearing state-law tort cases. If courts give appropriate deference to this statement of FDA's considered judgment, FDA will not be forced to file briefs in individual cases.

However, given that some courts may fail to give sufficient deference to FDA's views, Part V suggests that state legislatures can play a valuable role in making FDA involvement in product liability lawsuits less necessary. By passing FDA shield laws based on the Michigan model, individual states can help to reduce the negative consequences of the current pharmaceutical-liability regime. In so doing, they would help to encourage the development of new drugs, preserve the availability of existing drugs, reduce upward pressure on drug prices, and assure rational prescribing. They would, thereby, serve the long-term health interests of their citizens.

## II. COMPREHENSIVE REGULATION OF PRESCRIPTION DRUGS BY FDA

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<sup>11</sup> As I have previously noted, *see* Daniel E. Troy, *FDA Involvement in Product Liability Lawsuits*, FDLI UPDATE, Jan.-Feb. 2003, at 4-8, FDA participation in state-law products-liability cases plays some role in preserving agency resources that would otherwise be spent dealing with the confusion created by conflicting state and federal obligations. Nonetheless, each such involvement consumes agency resources that, absent state-law efforts to undermine FDA's authority over prescription drugs, could be spent on other activities.

<sup>12</sup> *See supra* note 3.

Prescription drugs are regulated more heavily than almost any other consumer product.<sup>13</sup> The process of developing and obtaining approval to market a new drug is long and expensive. The process takes close to 15 years.<sup>14</sup> By 2003, it was estimated to cost an average of \$897 million per drug.<sup>15</sup> The last phase of this process is regulatory approval. Under federal law, new drugs must obtain premarket approval from FDA to ensure that they are safe and effective,<sup>16</sup> and not misbranded.<sup>17</sup> FDA approval requires the submission of a New Drug Application,<sup>18</sup> which includes reports on investigations for safety and efficacy,<sup>19</sup> as well as “adequate tests ... to show whether or not [the] drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling.”<sup>20</sup>

FDA’s determination whether to approve a drug is “based not on an abstract estimation of its safety and effectiveness, but rather on a comprehensive scientific evaluation of the product’s risks and benefits under the conditions of use prescribed.”<sup>21</sup> In making its decision, FDA considers both “complex clinical issues related to the use of the product in study populations” and “practical public health issues pertaining to the use of the product in day-to-day clinical practice.”<sup>22</sup> Practical public health issues considered by FDA include “the nature of the disease or condition for which the product will be indicated, and the need for risk management measures to help assure in clinical practice that the product maintains its favorable benefit-risk balance.”<sup>23</sup>

The evaluation of a drug’s safety and effectiveness under federal law is inextricably intertwined with an assessment of its labeling.<sup>24</sup> An applicant seeking approval of a new drug

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<sup>13</sup> Michael D. Green, *Safety as an Element of Pharmaceutical Quality: The Respective Roles of Regulation and Tort Law*, 42 ST. LOUIS U. L.J. 163, 163 (1998).

<sup>14</sup> Richard J. Findlay, *Originator Drug Development*, 54 FOOD & DRUG L.J. 227, 227 (1999).

<sup>15</sup> Press Release, Tufts Ctr. for the Study of Drug Dev., Total Cost to Develop a New Prescription Drug, Including Cost of Post-Approval Research, is \$897 Million (May 13, 2003), available at <http://csdd.tufts.edu/NewsEvents/NewsArticle.asp?newsid=29>.

<sup>16</sup> 21 U.S.C. §§ 355(d), 393(b)(2)(B).

<sup>17</sup> *Id.* § 331(a), (b).

<sup>18</sup> *Id.* § 355(b).

<sup>19</sup> *Id.* § 355(b)(1)(A).

<sup>20</sup> *Id.* § 355(d).

<sup>21</sup> FDA, Physician Labeling Rule, *supra* note 3, at 38-39.

<sup>22</sup> *Id.* at 39.

<sup>23</sup> *Id.*

<sup>24</sup> *Id.* at 39, 171.

must submit a proposed package insert to accompany the product.<sup>25</sup> FDA's regulations establish numerous and specific requirements for this labeling<sup>26</sup>—including requirements for the content and format of information on the drug's risks. This information must be scientifically substantiated and may not be false or misleading.<sup>27</sup> The applicant lawfully may not disseminate any package insert that substantively deviates from the FDA-approved version without first receiving agency approval.<sup>28</sup> False or misleading labeling misbrands the product, which is prohibited,<sup>29</sup> and is subject to a variety of penalties, including withdrawal of approval.<sup>30</sup>

State-law tort actions against companies who have complied with FDA requirements appear to be premised on the belief that drugs can be free of harmful effects. This notion fundamentally misunderstands the nature of pharmaceuticals as well as the FDA approval process. FDA long has recognized that “[t]here is no such thing as absolute safety in drugs. There are some drugs that are less liable to cause harmful reaction than others, but people die every year from drugs generally regarded as innocuous.”<sup>31</sup>

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<sup>25</sup> 21 U.S.C. § 355(b)(1)(F).

<sup>26</sup> 21 C.F.R. § 201.56-57; *see also* FDA, Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81082 (proposed Dec. 22, 2000).

<sup>27</sup> *E.g.*, 21 U.S.C. § 355(d)(7); 21 C.F.R. § 201.57(d) (“Known hazards and not theoretical possibilities shall be listed, e.g., if hypersensitivity to the drug has not been demonstrated, it should not be listed as a contraindication.”).

<sup>28</sup> 21 C.F.R. § 314.70. Although courts and plaintiffs rely on § 314.70(c)(6)(iii)(A) to support their argument that a defendant manufacturer could have revised the risk information in its package insert without explicit permission from FDA, it is well-known that manufacturers seldom, if ever, add or revise risk information unilaterally, as two previous FDA chief counsels in addition to myself have observed. *See* Richard M. Cooper, *Drug Labeling and Products Liability: The Role of the Food and Drug Administration*, 41 FOOD & DRUG L.J. 233, 238 (1986); Thomas Scarlett, *The Relationship Among Adverse Drug Reaction Reporting, Drug Labeling, Product Liability, and Federal Preemption*, 46 FOOD & DRUG L.J. 31, 36 (1991). *See also* FDA, Physician Labeling Rule, *supra* note 3, at 40 (“[I]n practice, manufacturers typically consult with FDA prior to adding risk information to labeling.”).

<sup>29</sup> 21 U.S.C. § 331(a), (b).

<sup>30</sup> *E.g.*, *id.* §§ 332, 333(a), 334(a)

<sup>31</sup> Hearings on Drug Safety Before the Subcomm. on Intergovernmental Relations of the House Comm. on Gov't Operations, 88th Cong., 2d Sess., pt. 1, at 147 (1964) (testimony of former FDA Commissioner George P. Larrick); *see also* *Restatement (Second) of Torts* § 402A cmt. k (1965) (recognizing that many drugs are often “unavoidably unsafe,” even “for their intended and ordinary use”) (emphasis omitted).

The FDA approval process cannot, and does not, require that drugs be risk-free: “If the FDA were to demand absolute proof that no short-term or long-term health risks exist, no drug ever would reach the market.”<sup>32</sup> It would be impossible to implement a drug approval process that sought to prevent all adverse reactions, and costly beyond measure to do so. FDA categorizes an adverse reaction as “rare[]” if it occurs in 1 in 1000 cases.<sup>33</sup> Yet even studies comprising 3000 patients are unable to identify “uncommon side effects, delayed effects, or consequences of long-term drug administration.”<sup>34</sup> Indeed, “to detect the difference between an adverse reaction incidence rate of 1/5000 and 1/10,000, approximately 306,000 patients would have to be observed, which is far more than any study could achieve.”<sup>35</sup> And to insist upon no adverse reactions as a result of the drug would cause immeasurable harm to public health: “To take the drastic step of forbidding marketing of a drug until all long-term consequences and interactions are identified through formal research would impose unacceptable costs in the form of untreated or inadequately treated illness.”<sup>36</sup>

In short, FDA fully contemplates that the drugs it approves will carry some risk. “[S]afety does not mean zero risk.”<sup>37</sup> FDA has long acknowledged that its role is to conduct a risk-benefit analysis to determine what risk is *reasonable*.<sup>38</sup> As another former Chief Counsel to FDA has explained, FDA “weighs the drug’s therapeutic benefits against the potential risks of its use.... In

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<sup>32</sup> Steven R. Salbu, *The FDA and Public Access to New Drugs: Appropriate Levels of Scrutiny in the Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. 93, 147 (1999).

<sup>33</sup> 21 C.F.R. § 201.57(g)(2).

<sup>34</sup> Am. Med. Ass’n, *Reporting Adverse Drug and Medical Device Events: Report of the AMA’s Council on Ethical and Judicial Affairs*, 49 FOOD & DRUG L.J. 359, 359-60 (1994).

<sup>35</sup> *Id.* at 360 (footnote omitted).

<sup>36</sup> *Id.*; accord INST. OF MED., VACCINE SUPPLY AND INNOVATION 8 (1985) (“[T]here is no way totally to avoid injuries caused by current vaccines manufactured according to approved procedures and administered in accordance with recommended medical practices short of the total suspension of vaccine use, which is unacceptable because of the increased risk of morbidity and mortality.”).

<sup>37</sup> FDA, *Managing the Risks from Medical Product Use*, *supra* note 4.

<sup>38</sup> See *United States v. Rutherford*, 442 U.S. 544, 555 (1979) (“[T]he Commissioner generally considers a drug safe when the expected therapeutic gain justifies the risk entailed by its use.”); FDA, *Managing the Risks from Medical Product Use*, *supra* note 4, at 3 (“A safe product is one that has reasonable risks, given the magnitude of the benefit expected and the alternatives available.”).

short, the FDA effectively determines what risks physicians should be permitted to impose upon the patients they treat with therapeutic drugs.”<sup>39</sup>

Despite this comprehensive and finely wrought regulatory regime, mass tort actions against pharmaceutical manufacturers are by now commonplace. Litigation against drug companies has been recognized as a growth industry for some time now.<sup>40</sup> Over one 13-year period, approximately 11,000 such cases were brought in federal court alone.<sup>41</sup> That trend appears to have continued unabated. Merck, the manufacturer of the painkiller Vioxx, withdrew that product from the market more than a year ago. As of February 2005, seventy putative class actions had already been filed, in addition to hundreds of individual suits.<sup>42</sup> Wyeth (formerly American Home Products) has paid billions of dollars to litigate and settle claims stemming from voluntary withdrawal of the diet drug combination Fen-Phen—yet still faces lawsuits from more than 60,000 claimants who opted out of the class-action settlement.<sup>43</sup>

### III. NEGATIVE CONSEQUENCES OF THE CURRENT PHARMACEUTICAL-LIABILITY REGIME

Given the potential for enormous damage awards with any finding of liability, the current tort regime has created undesirable incentives in the pharmaceutical market. Four effects of these suits deserve special mention because they vividly illustrate the way the current liability environment is harming public health. First, this environment appears to stifle innovation in the pharmaceutical industry. Anticipated litigation costs have prevented drug manufacturers from investing in new product development. Specific areas of research (such as vaccines) have been

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<sup>39</sup> Richard A. Merrill, *Compensation for Prescription Drug Injuries*, 59 VA. L. REV. 1, 9 (1973) (footnote omitted).

<sup>40</sup> See Terence Dungworth, *Product Liability and the Business Sector* ix (RAND Inst. for Civil Justice 1988) (“no other defendants in any industry have experienced federal litigation growth comparable to that observed in asbestos or single-product pharmaceutical suits”).

<sup>41</sup> *Id.* at 38.

<sup>42</sup> See Press Release, Merck & Co., *Merck Announces Voluntary Worldwide Withdrawal of VIOXX®* (Sept. 30, 2004), available at [http://vioxx.com/vioxx/documents/english/vioxx\\_press\\_release.pdf](http://vioxx.com/vioxx/documents/english/vioxx_press_release.pdf); Susan Todd, *Vioxx Lawsuits To Be Rolled into One*, NEWARK STAR-LEDGER, Feb. 17, 2005; Robert Steyer, *Vioxx Lawsuits Swamp Merck*, The Street.com, Dec. 14, 2004, available at [http://www.thestreet.com/\\_googlen/stocks/robertsteyer/10199047.html?cm\\_ven=GOOGLLEN&cm\\_cat=FREE&cm\\_ite=NA](http://www.thestreet.com/_googlen/stocks/robertsteyer/10199047.html?cm_ven=GOOGLLEN&cm_cat=FREE&cm_ite=NA).

<sup>43</sup> See Melissa Nann Burke, *Philadelphia Sees 10,000 Fen-Phen Cases in 2004*, NAT’L L.J. (July 20, 2005).

particularly affected. Second, this environment has reduced the availability of drugs. Not only are fewer drugs being researched and created, but also existing beneficial drugs have been removed from the market because of crippling litigation. Third, the current liability environment plays a role in higher drug prices. To turn a profit on the production of any particular drug, the manufacturer must charge prices sufficiently high to cover not only the cost of developing and manufacturing the drug, but also the anticipated cost of future litigation. As the costs of even a successful mass-tort defense have reached astronomical levels,<sup>44</sup> this is a significant product-related expense that drug manufacturers must account for in their pricing decisions. Finally, the current system creates incentives for drug manufacturers to seek FDA approval of labeling that includes indiscriminate and prolix lists of risks, threatening the ability of prescribers to evaluate accurately the risk-benefit profile of a drug for a specific patient. Physicians may reasonably react to such labeling by simply declining to prescribe a drug that is, in fact, appropriate. Or, the physician may underestimate the drug's risks and prescribe it in circumstances in which its risks actually outweigh its benefits.

#### A. *Roadblocks to Innovation*

##### 1. *Reduced Total Investment in Research*

The tort system is “having a profound negative impact on the development of new medical technologies.”<sup>45</sup> “Innovative new products are not being developed or are being withheld from the market because of liability concerns or inability to obtain adequate insurance.”<sup>46</sup> As Justice O'Connor recognized some fifteen years ago, “The threat of ... enormous awards has a detrimental effect on the research and development of new products. Some manufacturers of prescription drugs, for example, have decided that it is better to avoid uncertain liability than to introduce a new pill or vaccine into the market.”<sup>47</sup>

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<sup>44</sup> See W. Kip Viscusi, *Corporate Risk Analysis: A Reckless Act?*, 52 STAN. L. REV. 547, 583-84 (2000) (noting that litigation costs led to withdrawal of Bendectin despite the fact the failure of any jury verdict against the manufacturer to be upheld on appeal).

<sup>45</sup> American Med. Ass'n, Report of the Board of Trustees, Impact of Product Liability on the Development of New Medical Technologies 1 (1988).

<sup>46</sup> *Id.*

<sup>47</sup> *Browning-Ferris Indus. of Vt., Inc. v. Kelco Disposal, Inc.*, 492 U.S. 257, 282 (1989) (O'Connor, J., concurring in part and dissenting in part). Although the *Browning-Ferris* case

This unfortunate effect may reflect a rational response to today's irrational liability environment. The decision to research a new drug and to try to bring it to market involves a calculation of expected benefits and expected costs. Massive tort verdicts can dramatically skew the cost side of that equation. Expenditures on research and development increase when liability costs decrease.<sup>48</sup> And, where the level of risk is high, the risk of liability is inversely related to investment in research and development activity.<sup>49</sup>

## 2. *Skewed Research Agenda*

The current liability regime is a strong disincentive to the production of drugs intended for healthy patients. In such patients, any future disease or disability for which there is not a clear cause can potentially serve as grounds for a lawsuit against a drug manufacturer.<sup>50</sup> Healthy patients who fall into demographic groups likely to be viewed as sympathetic plaintiffs—such as young children<sup>51</sup> and pregnant women<sup>52</sup>—serve as an even stronger disincentive.

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specifically concerned punitive damages, the principles set out in Justice O'Connor's dissent apply to liability more generally.

<sup>48</sup> See Amy Finkelstein, *Health Policy and Technological Change: Evidence from the Vaccine Industry* (Nat'l Bureau of Econ. Research Working Paper No. 9460, 2003), *abstract available at* <http://www.nber.org/papers/w9460>. Finkelstein's research focused on the Vaccine Injury Compensation Fund (VICF), a no-fault product liability system paid for by excise taxes on certain childhood vaccines. That system took the place of tort remedies stemming from those vaccines, and applied a fixed payment schedule for claims. See 42 U.S.C. §§ 300aa-10 to -34; 42 C.F.R. § 100.3. This alternative to the tort system had the salutary effects of reducing risk by normalizing payments and reducing expected liability costs. The result was stark—institution of the Fund led to a statistically significant increase in new clinical trials. Finkelstein, *supra*, at 22-24.

<sup>49</sup> Michael J. Moore & W. Kip Viscusi, *Product Liability Entering the Twenty-first Century: The U.S. Perspective* 25, 27 (2001).

<sup>50</sup> See, e.g., Bernard Wysocki, Jr., *Fearing Avian Flu, Bioterror, U.S. Scrambles to Fill Drug Gap*, WALL ST. J., Nov. 9, 2005, at A1 (“Vaccine makers point to the heavy costs of litigating suits alleging a link between vaccines and autism. Despite scholarly studies that have found no link, some 350 lawsuits have been filed, costing \$200 million, industry executives say. None has yet gone to trial.”).

<sup>51</sup> See *id.*

<sup>52</sup> See PETER W. HUBER, *LIABILITY: THE LEGAL REVOLUTION AND ITS CONSEQUENCES* 155 (1988) (“‘Who in his right mind,’ the president of a major pharmaceutical company asked in 1986, ‘would work on a product today that would be used by pregnant women?’”).

Excessive liability has especially pernicious effects on vaccines, a particularly perverse effect in light of those products' unquestioned public health benefits.<sup>53</sup> The reason for this effect is simple: "Products with less market potential are more vulnerable to a given degree of liability potential."<sup>54</sup> And, where vaccines are concerned, "[t]he profit per dose is low, and yet the perceived liability per dose is high."<sup>55</sup>

Thus, the Institute of Medicine has recognized that "apprehensions [about tort liability] act as a deterrent to vaccine production and thereby threaten the public's health."<sup>56</sup> Indeed, "[r]ising liability costs during the 1980s reduced the number of firms producing vaccines for five serious childhood diseases from thirteen in 1981 to three by the end of the decade."<sup>57</sup> Concerns about liability have slowed the progress of particular identifiable vaccines, including an AIDS vaccine.<sup>58</sup>

#### B. *Decreased Availability of Investigational or Approved Drugs*

In addition to discouraging initial product innovation, the current pharmaceutical-liability regime adversely affects patient access to beneficial pharmaceuticals by causing the

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<sup>53</sup> Am. Med. Ass'n, *supra* note 45, at 6-7.

<sup>54</sup> STEVEN GARBER, *PRODUCT LIABILITY AND THE ECONOMICS OF PHARMACEUTICALS AND MEDICAL DEVICES* 167 (1993).

<sup>55</sup> John P. Wilson, *The Resolution of Legal Impediments to the Manufacture and Administration of an AIDS Vaccine*, 34 SANTA CLARA L. REV. 495, 505 (1994); W. Kip Viscusi & Michael J. Moore, *Rationalizing the Relationship Between Product Liability and Innovation*, in *TORT LAW AND THE PUBLIC INTEREST: COMPETITION, INNOVATION, AND CONSUMER WELFARE*, 105, 111 (Peter H. Schuck ed., 1991); *see also* Scott Hensley and Bernard Wysocki Jr., *As Industry Profits Elsewhere, U.S. Lacks Vaccines, Antibiotics*, WALL ST. J., Nov. 8, 2005, at A1 (noting that the \$12 billion annual revenue produced by Lipitor, a single anticholesterol drug, is larger than the entire vaccine market); *id.* ("The margins were so low that four of the last five years we were on the market, we lost money," says Peter Paradiso, a Wyeth research executive, referring to his company's decision in 2002 to stop making flu vaccine.").

<sup>56</sup> INST. OF MED., *supra* note 36, at 2 (1985).

<sup>57</sup> Viscusi & Moore, *Rationalizing*, *supra* note 55, at 111.

<sup>58</sup> *See* Jon Cohen, *Is Liability Slowing AIDS Vaccines?*, SCIENCE, Apr. 10, 1992. The development of contraceptives has similarly been slowed by liability concerns. Experiences like the forced withdrawal of Bendectin as the result of baseless tort suits (described *infra* Part III.B) have discouraged manufacturers from developing new products indicated for or associated with contraception and pregnancy. *See, e.g.*, Linda Johnson, *Wyeth Won't Resume Norplant Sales*, AP ONLINE, July 26, 2002; Gina Kolata, *Will the Lawyers Kill Off Norplant?*, N.Y. TIMES, May 28, 1995; *see generally* INST. OF MED. & NAT'L RES. COUNCIL, *DEVELOPING NEW CONTRACEPTIVES: OBSTACLES AND OPPORTUNITIES* 118-43 (Luigi Mastroianni, Jr. et al. eds., 1990).

discontinuation of clinical trials, and by forcing already-approved drugs and interested companies from the marketplace.<sup>59</sup>

The signal example of market withdrawal concerns Bendectin, a drug approved by FDA for preventing nausea during pregnancy. Starting in 1969, assertions that Bendectin could produce birth defects began to appear in scientific literature. Yet no sound scientific study ever demonstrated a causal relationship between the drug and birth defects, and FDA continued to affirm its safety. Nevertheless, nearly 1700 lawsuits were brought against the manufacturer. Although the company won most cases, in 1983 it withdrew the drug in the United States because its \$18 million in annual legal costs and insurance had nearly overtaken its \$20 million in annual sales.<sup>60</sup> Yet “[i]t is unlikely that any new drug will be developed to close this therapeutic gap,”<sup>61</sup>—all this despite the fact that, as FDA reaffirmed in 1999, Bendectin was *not* withdrawn for safety reasons.<sup>62</sup>

Given the particular vulnerability of vaccines to liability effects,<sup>63</sup> it is no surprise that tort liability has diminished the availability of this category of FDA-regulated products. Nearly all manufacturers of the diphtheria, pertussis, and tetanus (DPT) vaccine withdrew from the U.S. market due to lawsuits alleging harmful side effects filed in the 1980s.<sup>64</sup> In 1987, the CDC announced that the sole manufacturer of a vaccine to prevent Japanese encephalitis would no longer supply the product in the United States because of product liability concerns.<sup>65</sup> And

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<sup>59</sup> See, e.g., E. Patrick McGuire, *The Impact of Product Liability* 17 (The Conference Bd., Res. Rpt. No. 908, 1988) (quoting a drug manufacturer: “We have been forced to discontinue sale of therapeutically beneficial drugs because of excessive product liability costs.”).

<sup>60</sup> Marvin E. Jaffe, *Regulation, Litigation, and Innovation in the Pharmaceutical Industry: An Equation for Safety*, in *PRODUCT LIABILITY AND INNOVATION: MANAGING RISK IN AN UNCERTAIN ENVIRONMENT* 120, 126 (Janet R. Hunziker & Trevor O. Jonas eds., 1994). As a result, it was reported in 1994 that “treatment for severe nausea during pregnancy now accounts for nearly \$40 million of the nation’s annual hospital bill.” *Id.* at 126.

<sup>61</sup> *Id.*

<sup>62</sup> See FDA, *Determination That Bendectin Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness*, 64 Fed. Reg. 43190 (Aug. 9, 1999); see also Louis Lasagna, *The Chilling Effect of Product Liability on New Drug Development*, in *THE LIABILITY MAZE: THE IMPACT OF LIABILITY LAW ON SAFETY AND INNOVATION* 334, 337-41 (Peter W. Huber & Robert E. Litan eds., 1991) (discussing the withdrawal of Bendectin).

<sup>63</sup> See *supra* Part III.A & n.48.

<sup>64</sup> Lasagna, *supra*, at 341-45; see also *supra* Part III.A.

<sup>65</sup> Lasagna, *supra*, at 344.

commentators discussing the shortage and then surplus of flu vaccine last winter have noted that there remain only two manufacturers licensed to sell the flu vaccine in the United States.<sup>66</sup>

### *C. Increased Drug Prices*

The current liability environment makes drugs cost more than they otherwise would.<sup>67</sup> The mathematics involved are simple. The revenue a pharmaceutical manufacturer generates by selling a drug must be sufficient to cover not only the costs of research, development, and production, but also the future litigation expenses the manufacturer can reasonably expect to incur. The higher these anticipated future expenses, the higher the price the manufacturer must charge to avoid losing money by selling the drug in question. Efforts to generate a profit—a goal which managers of publicly-held companies have a fiduciary duty to pursue—require still-higher prices.

Empirical evidence appears to support this basic mathematical proposition. For example, between 1980 and 1989, most vaccines doubled or tripled in wholesale price—an increase of less than twice the rate of inflation.<sup>68</sup> However, two vaccines with a higher perceived liability potential increased in price at a much higher rate. The oral polio vaccine, which can in some cases cause polio, increased in price “by a factor of almost seven” during the same period.<sup>69</sup> The DPT vaccine increased in price even more dramatically, by a factor of more than forty, as “the pertussis component of this vaccine has long been suspected of carrying a small risk of very

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<sup>66</sup> *E.g.*, Anthony S. Fauci, *A Risky Business*, WASH. TIMES, Nov. 30, 2004, at A17 (column by the Director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health).

<sup>67</sup> *See, e.g.*, Richard L. Manning, *Changing Rules in Tort Law and the Market for Childhood Vaccines*, 37 J. L. & ECON. 247, 273 (1994) [hereinafter Manning, *Childhood Vaccines*] (noting the “dramatic” effect of liability costs on vaccine prices); Richard L. Manning, *Products Liability and Prescription Drug Prices in Canada and the United States*, 40 J. L. & ECONOMICS 203, 234 (1997) [hereinafter Manning, *Canada and the United States*] (analyzing the effect of differing liability regimes on prescription-drug prices in Canada and the United States); GARBER, *supra* note 54, at 122 (1993) (concluding that a high perceived liability potential results in “substantially higher” product prices).

<sup>68</sup> Manning, *Childhood Vaccines*, at 257; Federal Reserve Bank of Minneapolis, *Consumer Price Index, 1913-*, <http://minneapolisfed.org/Research/data/us/calc/hist1913.cfm> (last visited Mar. 8, 2006) (listing annual inflation rates based on the Consumer Price Index); Gina Kolata, *Litigation Causes Huge Price Increase in Childhood Vaccines*, SCIENCE, June 13, 1986.

<sup>69</sup> Manning, *Childhood Vaccines*, at 254-55, 257.

serious side effects.”<sup>70</sup> The price of the diphtheria and tetanus (DT) vaccine, which is similar to the DPT vaccine but does not contain the pertussis component, increased by a factor of just over two during the same period.<sup>71</sup> In other words, vaccine prices seem to be related in some significant manner to perceived liability potential.

#### *D. Interference with Rational Prescribing*

Finally, the current pharmaceutical-liability regime interferes with the basic public-health goal of providing physicians with the information necessary to make rational prescribing decisions. The decision to prescribe a drug is rational when, on the basis of all information reasonably available to the prescribing physician, the benefits associated with the use of the drug outweigh, *for that particular patient*, the risks associated with the use of the drug.<sup>72</sup> In other words, a prescribing decision is not rational unless it is: (1) based on an accurate understanding of the risks and benefits of the drug at issue, considered in relation to other treatment possibilities, and (2) tailored to the unique circumstance of the individual patient.

The effects of the current pharmaceutical-liability regime on rational prescribing decisions must be considered in the context of basic limitations on human ability to consider and process information.<sup>73</sup> Particularly in a modern managed-care environment, practicing physicians are faced with numerous demands on their time and attention. Unless drug labeling makes

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<sup>70</sup> *Id.* at 257.

<sup>71</sup> *Id.* at 254-55, 257-60.

<sup>72</sup> See FDA, Managing the Risks of Medical Product Use, *supra* note 4 (“[A]fter FDA evaluates the risks and benefits for the population, the prescriber is central to managing risks and benefits for the individual.”); FDA, *supra* note 26, at 81105 (“Under the proposed rule, the highlights section would emphasize the drug information that physicians report is the most important for decisionmaking. . . . Consequently, this proposed rule would improve the ability of physicians to select the most safe and effective pharmaceutical treatments for their patients and to administer those treatments in the most safe and effective manner.”); *cf.* 65 Fed. Reg. 59192 (“Regardless of the root causes for the current paucity of information, rational prescribing for the pregnant patient must attempt to ensure that she will have the greatest likelihood of clinical benefit from a medication in exchange for the safest or least exposure of her developing baby.”); Robert Temple, *Legal Implications of the Package Insert*, 58 MEDICAL CLINICS OF NORTH AMERICA 1151, 1151 (1974) (“The preceding papers have emphasized what clinicians have long recognized: not all patients respond to a drug in the same way. Therefore it should be apparent that physicians must always individualize drug therapy.”).

<sup>73</sup> See FDA, Physician Labeling Rule, *supra* note 3, at 27-28.

accurate risk information easily comprehensible to the average physician, prescribing decisions are likely to be made on the basis of an inaccurate understanding of drug risks.

Thus, the current pharmaceutical-liability regime hinders rational prescribing efforts in two distinct ways. First, by creating an incentive for drug manufacturers to seek to include warnings relating to all possible risks, even those that are trivial or extremely rare, it results in the provision of *excessive* risk information that may discourage physicians from prescribing drugs in situation where a decision to prescribe would clearly be rational.<sup>74</sup> Second, by creating an incentive for manufacturers to seek to emphasize all risks equally, it results in the provision of *insufficient or misleading* risk information that may encourage physicians to prescribe a drug in situations where a decision to prescribe is not rational. Yet an effort by drug manufacturers to convince federal regulators to permit overly numerous warning and to emphasize all risks equally is a likely result of permitting state courts to impose liability on drug manufacturers who comply fully with federal regulations.<sup>75</sup>

Two recent federally-funded studies illustrate this point.<sup>76</sup> The FDA currently requires relatively strong suicide-related warnings in the labeling of certain antidepressants.<sup>77</sup> However,

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<sup>74</sup> *Id.* at 42-43 (“FDA has previously found that labeling that includes theoretical hazards not well-grounded in scientific evidence can cause meaningful risk information to ‘lose its significance’ . . . . Overwarning, just like underwarning, can similarly have a negative effect on patient safety and public health. . . . Similarly, State-law attempts to impose additional warnings can lead to labeling that does not accurately portray a product’s risks, thereby potentially discouraging safe and effective use of approved products or encouraging inappropriate use and undermining the objectives of the act.”) (citing FDA, Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37434, 37447 (June 26, 1979)); see also Lars Noah, *The Imperative to Warn: Disentangling the “Right to Know” from the “Need to Know” About Consumer Product Hazards*, 11 YALE J. ON REG. 293, 374-91 (1994).

<sup>75</sup> FDA, Physician Labeling Rule, *supra* note 3, at 43 (noting FDA concern that the current pharmaceutical-liability regime “could encourage manufacturers to propose ‘defensive labeling’ to avoid State liability, which, if implemented, could result in scientifically unsubstantiated warnings and underutilization of beneficial treatments.”).

<sup>76</sup> See Madhukar H. Trivedi et al., *Evaluation of Outcomes with Citalopram for Depression Using Measurement-Based Care in STAR\*D Implications for Clinical Practice*, 163 AM. J. PSYCHIATRY 28 (2006); Gregory E. Simon et al., *Suicide Risk During Antidepressant Treatment*, 163 AM. J. PSYCHIATRY 41 (2006); see also Rob Stein & Marc Kaufman, *Depression Drugs Safe, Beneficial, Studies Say*, WASH. POST, Jan. 1, 2006, at A01; Alex Berenson, *Antidepressants Seem to Cut Suicide Risk in Teenagers and Adults, Study Says*, N.Y. TIMES, Jan. 1, 2006, at 15.

<sup>77</sup> See *infra* Parts IV.A.2, IV.A.4.

these recent studies give support to concerns that these warnings may be causing a failure to prescribe antidepressants to depressed individuals that in turn leads to an even greater risk of suicide. In particular, one of the studies found that for patients treated with newer antidepressant drugs (those included in a March 2004 FDA Public Health Advisory<sup>78</sup>), “risk [of suicide attempts] was highest in the month before starting treatment.”<sup>79</sup> That risk was lower in each of the six months following initiation of treatment than in the month prior to initiation of treatment.<sup>80</sup> In other words, overly strong warnings about suicide-related risks may have the paradoxical effect of increasing suicides by preventing appropriate prescription of antidepressants to those who are genuinely in need of this type of medication. Although these studies did not control for any placebo effect, they suggest at the least a need for caution in issuing any warning about a potential drug side effect that is also a known symptom of the condition the drug is designed to treat.

#### IV. FDA INVOLVEMENT IN STATE-LAW CASES: A PARTIAL SOLUTION

Were state and federal courts to defer sufficiently to FDA determinations of drug safety, the negative consequences of the current liability regime would be much less pronounced. Yet this has often not been the case. In recent years, FDA’s legal authority and scientific expertise over drug labeling and advertising have been implicitly, although repeatedly, questioned in state and federal courts. In response, FDA has intervened in select cases where its authority and expertise may be undermined by state law. In the four cases discussed below, state law claims against drug manufacturers concerning the adequacy of labeling and advertising were allowed to proceed, even though the requested relief, if awarded, would squarely conflict with specific prior determinations made by FDA. In each of these cases, an FDA Shield Law on the Michigan model might well have made FDA involvement unnecessary.

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<sup>78</sup> FDA, Public Health Advisory: Worsening Depression and Suicidality in Patients Being Treated With Antidepressant (March 22, 2004), available at <http://www.fda.gov/cder/drug/antidepressants/AntidepressantPHA.htm>.

<sup>79</sup> Gregory E. Simon et al., *Suicide Risk During Antidepressant Treatment*, 163 AM. J. PSYCHIATRY 44 (2006).

<sup>80</sup> *Id.* at 44-45 & Fig. 6; see also Berenson, *supra* note 76 (noting that the Simon study “found that patients were significantly more likely to attempt or commit suicide in the month before they began drug therapy than in the six months after starting it.”)

More recently, in the preamble to its long-awaited Physician Labeling Rule, FDA explicitly set forth its view that FDA approval of prescription drug labeling preempts most state-law tort claims based on alleged deficiencies in FDA-approved labeling. Nonetheless, it is unclear whether courts hearing state tort cases will give this language an appropriate degree of deference. At least until an authoritative ruling requires all courts in the United States to recognize the validity of FDA's exercise of preemptive authority over drug labeling, state-by-state legal reform will remain an important aspect of efforts to ensure a pharmaceutical-liability regime that serves the long-term health interests of all Americans.

A. *Cases*

1. *Dowhal v. SmithKline Beecham Consumer Healthcare*

In 1999, Paul Dowhal filed a citizen suit in the Superior Court of the State of California, San Francisco County, under the state's Safe Drinking Water and Toxic Enforcement Act (Proposition 65), against manufacturers, distributors, and retailers of over-the-counter nicotine replacement products.<sup>81</sup> California environmental protection authorities had listed nicotine as a developmental and reproductive toxicant.<sup>82</sup> Dowhal argued that the defendants were required to disseminate publicly—through labeling—a statement that the State of California had determined that these products cause birth defects or other reproductive harm.<sup>83</sup>

Specifically, Dowhal sought to require the defendants to label over-the-counter nicotine replacement products with the following statement: “Warning: This product contains a chemical known to the State of California to cause birth defects or other reproductive harm.” Alternatively, the plaintiff sought an injunction requiring the following warning or a comparable one: “If pregnant or breast-feeding, ask a health professional before use. Nicotine, whether from smoking or medication, can harm your baby. First try to stop smoking without the patch.”

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<sup>81</sup> *Dowhal v. SmithKline Beecham Consumer Healthcare*, A094460, 2002 Cal. App. LEXIS 4384, at \*\*\*2 n.1 (Cal. Ct. App. July 12, 2002) (reversing trial court decision granting summary judgment for defendants on preemption grounds), *review granted*, 56 P.3d 1027 (Cal. 2002) (en banc), *judgment reversed*, 88 P.3d 1 (Cal. 2004).

<sup>82</sup> 2002 Cal. App. LEXIS 4384, at \*\*\*3 (citing CAL. CODE REGS. tit. § 12000(c)).

<sup>83</sup> *Id.* at \*\*\*5.

A year after filing his complaint under Proposition 65, Dowhal submitted a citizen petition to FDA. That petition asked FDA to require manufacturers of nicotine replacement products to label their products with a warning like the “harm your baby” warning set forth above. After reviewing the pertinent scientific evidence, FDA rejected the proposal, including the information submitted with the petition. FDA determined that the requested warning was not scientifically supportable. FDA concluded, further, that the Proposition 65 warning could cause pregnant and nursing women to conclude, mistakenly, that using a nicotine replacement therapy product presents health risks that are as grave as those associated with smoking.

Indeed, FDA had prohibited manufacturers from labeling their products voluntarily with a Proposition 65 warning. In January 1997, FDA denied a request from one manufacturer of nicotine replacement products for permission to change the label for its product to add Proposition 65 warning language. The agency advised the manufacturer to use the FDA-approved labeling, which includes a statement encouraging pregnant and nursing women to seek professional advice before using nicotine replacement therapy. In March 2001, FDA confirmed in a letter to other manufacturers that using additional warning language to satisfy Proposition 65 could render their products misbranded under the Federal Food, Drug, and Cosmetic Act (FDCA).<sup>84</sup>

The Superior Court granted summary judgment to the defendants on the ground that Proposition 65 is impliedly preempted by the FDCA. Dowhal appealed to the California Court of Appeal. FDA submitted an *amicus curiae* brief supporting the defendants.<sup>85</sup> The agency’s legal theory rested on the doctrine of conflict preemption: First, the labeling sought by Dowhal was preempted by the FDCA because it would be impossible for the defendants to comply with both Proposition 65 (as interpreted by the plaintiff) and with the FDCA (as applied by FDA). In essence, if the defendants were to adopt the warning language advocated by Dowhal, they would be in violation of the prohibition in the FDCA against selling misbranded drugs.<sup>86</sup> Second, application of Proposition 65 to nicotine replacement products in the manner advocated by

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<sup>84</sup> *Id.* at \*\*\*9.

<sup>85</sup> Amicus Curiae Brief of the United States of America in Support of Defendants/Respondents SmithKline Beecham Consumer Healthcare LP, *et al.*, Dowhal v. SmithKline Beecham, Case No. A094460 (Cal. Ct. App. filed Mar. 22, 2002)

<sup>86</sup> *Id.* at 13.

Dowhal would pose an obstacle to the accomplishment of the full purposes and objectives of the FDCA.

The Court of Appeal reversed the Superior Court's decision in July 2002, finding that in the FDA Modernization Act (FDAMA), Congress intended to exempt Proposition 65 from preemption, and that this disposed of the defendants' preemption arguments.<sup>87</sup> The court refused to resolve whether, by complying with the FDCA and not including the warning language advocated by Dowhal, the defendants exposed themselves to Proposition 65 liability.<sup>88</sup>

In August 2002, the defendants petitioned the Supreme Court of California for review of the Court of Appeal's decision. FDA submitted a letter brief in support of the petition the following month.<sup>89</sup> In October 2002, the Supreme Court of California granted the petition.<sup>90</sup> In August 2004, that court reversed the decision of the Court of Appeal. Concluding that FDA had barred all possible warnings that would have complied with Proposition 65,<sup>91</sup> the Supreme Court of California applied the doctrine of conflict preemption to hold that Proposition 65 was preempted insofar as it conflicted with FDA requirements.<sup>92</sup>

In so deciding, the court explicitly clarified that it was immaterial to the question of preemption whether Dowhal's warning could in some sense be classified as truthful.<sup>93</sup> As the Supreme Court of California correctly explained, FDA's authority is not limited to prohibiting statements that are false.<sup>94</sup> The agency is also charged with prohibiting those statements which, though perhaps formally "true," would be misleading.<sup>95</sup> The Supreme Court of California found that FDA was well within its authority to conclude that the labeling of a nicotine replacement

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<sup>87</sup> 2002 Cal. App. LEXIS 4384, at \*\*\*16-17 (citing 21 U.S.C. § 379r).

<sup>88</sup> *Id.* at \*\*\*29-30.

<sup>89</sup> Letter from Robert D. McCallum, Jr., Ass't Attorney General, *et al.*, to Frederick K. Ohlrich, Supreme Court Clerk/Administrator, *Dowhal v. SmithKline Beecham Consumer Healthcare LP, et al.* (S. Ct. No. S-109306) (filed Sept. 12, 2002).

<sup>90</sup> *Dowhal*, 56 P.3d 1027 (Cal. 2002).

<sup>91</sup> *Dowhal v. SmithKline Beecham Consumer Healthcare*, 88 P.3d 1, 11-12 (Cal. 2004).

<sup>92</sup> *Id.* at 11.

<sup>93</sup> *Id.* at 12.

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

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

product must indicate that it is better for a pregnant woman to use a nicotine replacement product than to continue smoking.<sup>96</sup>

## 2. *Motus v. Pfizer, Inc.*

When FDA specifically considers and rejects language regarding the risk of a particular adverse event allegedly associated with a prescription drug or class of drugs, courts applying state tort law should not allow failure-to-warn claims based on the absence of such language. Yet that is exactly what happened in a lawsuit filed in California against Pfizer Inc. The case involves ZOLOFT (sertraline HCl), a drug in the selective serotonin reuptake inhibitor (SSRI) class used to treat depression.

Pfizer submitted its original new drug application (NDA) for ZOLOFT in 1988. FDA evaluated all relevant scientific data and found no causal link between the drug and an increased risk of suicide. In 1990, FDA convened a meeting of the Psycho-pharmacological Drugs Advisory Committee (PDAC) to assess ZOLOFT.<sup>97</sup> The committee unanimously concluded that the drug was safe when used to treat depression.<sup>98</sup> The original labeling approved with the NDA for ZOLOFT on December 30, 1991, included precautionary language concerning the risk of suicide in depressed patients, but did not specifically warn that the drug increased suicidal ideation or the risk of suicide.<sup>99</sup> ZOLOFT later was approved for use in four other psychiatric disorders.

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<sup>96</sup> *Id.* at 14-15.

<sup>97</sup> *Motus v. Pfizer, Inc.*, 127 F. Supp. 2d 1085, 1088 (C.D. Cal. 2000) [hereinafter *Motus I*], *summary judgment granted*, *Motus v. Pfizer, Inc.*, 196 F. Supp. 2d 984, 986 (C.D. Cal. 2001) [hereinafter *Motus II*], *appeal docketed*, *Motus v. Pfizer, Inc.*, Case Nos. 02-55372 & 02-55498 (9th Cir. Mar. 12, 2002).

<sup>98</sup> *Motus I*, 127 F. Supp. 2d at 1088. The facts of FDA's review of the NDA for ZOLOFT, and its consideration of the need for suicide warnings in the labeling of SSRIs as a class, are recounted *id.* at 1089-90.

<sup>99</sup> The "Precautions" section of the proposed labeling, which FDA instructed Pfizer to use "verbatim," included the following statement:

*Suicide*—The possibility of a suicide attempt is inherent in depression and may persist until significant remission occurs. Close supervision of high risk patients should accompany initial drug therapy. Prescriptions for Zoloft (sertraline) should be written for the smallest quantity of capsules consistent with good patient

On three other occasions, FDA specifically considered and rejected claims that another SSRI causes suicide. In 1990 and 1991, FDA received two citizen petitions alleging a link between the SSRI PROZAC (fluoxetine) and suicide. One petition sought market withdrawal; the other asked FDA to require a “black box warning” in PROZAC’s labeling concerning a putative link between the drug and suicide. FDA examined the data concerning the risk of suicide and other violent behavior and SSRIs, and rejected both petitions. In 1997, FDA declined to grant a third citizen petition requesting additional suicide warning language in the labeling for PROZAC.

FDA also obtained expert advice as to whether antidepressants generally increase patients’ suicide risk. In 1991, FDA requested that the PDAC review the scientific evidence relating to the risk of suicide and the pharmacological treatment of depression. On September 20, 1991, the PDAC determined unanimously that the evidence did not indicate that use of any particular drug or class of drugs to treat depression heightens the risk of suicide. The advisory committee also heard remarks from the then-Director of FDA’s Division of Neuropharmacological Drug Products concerning the risk that modifying the labeling could misleadingly overstate the risk of suicide and cause a reduction in the use of pharmacotherapy to treat depression.

In 2002, FDA conducted yet another internal review of scientific evidence regarding SSRIs and suicide.<sup>100</sup> The review revealed no difference in the risk of suicide between patients using SSRIs and patients on placebo.<sup>101</sup> However, after reviewing further studies the agency refined its position in late 2004 and early 2005.<sup>102</sup> FDA now warns that antidepressants, including Zoloft, “may increase suicidal thoughts and actions in about 1 out of 50 people 18

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management, in order to reduce the risk of overdose.

*Id.* at 1088.

<sup>100</sup> Amicus Brief for the United States in Support of the Defendant-Appellee and Cross-Appellant, and in Favor of Reversal of the District Court’s Order Denying Partial Summary Judgment to Defendant-Appellee and Cross-Appellant, *Motus v. Pfizer, Inc.*, Case Nos. 02-55372 & 02-55498, at 22 (9th Cir. filed Sept. 3, 2002) (citation omitted).

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

<sup>102</sup> Amicus Brief for the United States, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed Sept. 15, 2005).

years or younger,” and that “[s]everal recent publications report the possibility of an increased risk for suicidal behavior in adults who are treated with antidepressant medications.”<sup>103</sup>

Despite FDA’s position prior to October 2002, Pfizer has been a target of state law failure-to-warn claims based on the absence of additional warning language concerning suicide in the labeling for ZOLOFT. Notably, in November 1998, a candidate for the city council and failing businessman named Victor Motus visited his doctor, appearing depressed and frustrated.<sup>104</sup> His physician diagnosed moderate depression and prescribed ZOLOFT 25 mg for seven days, followed by 50 milligrams of ZOLOFT for fourteen days.<sup>105</sup> Six days after visiting his doctor, Motus committed suicide by shooting himself.<sup>106</sup> His wife sued Pfizer, claiming that, under California law, the company had acted negligently by failing to warn adequately in the package insert and marketing materials that ZOLOFT could cause suicide.<sup>107</sup>

The United States District Court for the Central District of California (to which the case had been removed on the ground of diversity) held that federal law did not preempt the plaintiff’s state tort law claims.<sup>108</sup> In making this finding, the court relied on cases finding that FDA’s regulation of labeling did not preempt all tort actions.<sup>109</sup> The court did not carefully analyze whether requiring the additional warning language sought by the plaintiff would conflict with FDA’s conclusion that SSRIs do not heighten the risk of suicide.

FDA filed an *amicus curiae* brief in the United States Court of Appeals for the Ninth Circuit, contending that the plaintiff’s state law claims could not stand.<sup>110</sup> The FDA-approved labeling for ZOLOFT discusses the risk of suicide that accompanies depression, but does not identify ZOLOFT as a potential cause of suicide. The labeling thus reflects FDA’s specific finding that ZOLOFT does not cause suicide, contrary to the language that would be included in the labeling were the plaintiff to prevail.

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<sup>103</sup> *FDA Alert: Suicidal Thoughts or Actions in Children and Adults*, July 2005, <http://www.fda.gov/cder/drug/infopage/sertraline/default.htm>.

<sup>104</sup> *Motus II*, 196 F. Supp. 2d at 986.

<sup>105</sup> *Id.*

<sup>106</sup> *Id.* at 987.

<sup>107</sup> *Id.* at 984.

<sup>108</sup> *Motus I*, 127 F. Supp. 2d at 1087.

<sup>109</sup> *Id.* at 1092.

<sup>110</sup> *Amicus Brief*, *supra* note 100.

In affirming the judgment of the district court, the Ninth Circuit explicitly declined to reach the district court's preemption holding.<sup>111</sup> Instead, the Ninth Circuit rested its conclusion on the prescribing doctor's failure to read Pfizer's warnings or rely on information provided by Pfizer's representatives in making his decision to prescribe ZOLOFT.<sup>112</sup> As the doctor would not have been aware of any warning Pfizer issued, Mrs. Motus could not prevail on a claim that the inadequacy of Pfizer's warnings caused her husband's death.

### 3. *In re PAXIL Litigation*

Where FDA has reviewed a particular prescription drug advertisement and determined that it is not false or misleading, state courts should not second-guess that judgment. For this reason, FDA decided it was necessary to file a statement of interest in a case involving PAXIL (paroxetine HCl), marketed by GlaxoSmithKline (GSK).

PAXIL was approved in 1992 for the treatment of depression. Like ZOLOFT, PAXIL is an SSRI. In reviewing the NDA for PAXIL, FDA found no clinical evidence of drug-seeking behavior associated with use of the drug. FDA concluded that PAXIL is not habit-forming, and did not require language in the approved labeling stating that PAXIL is associated with this risk. The approved labeling does, however, include language regarding discontinuation syndrome: it recommends that physicians gradually reduce dosages rather than abruptly halting use, and that physicians monitor patients discontinuing the drug for syndrome symptoms.

On five separate occasions in 2001 and 2002, DDMAC reviewed advertisements for PAXIL claiming that the product was "non-habit-forming." DDMAC concluded that this statement was not false or misleading because, as FDA previously had found in the NDA review, PAXIL does not induce drug-seeking behavior.<sup>113</sup> DDMAC suggested that GSK adjust the wording of one advertisement to state clearly that a doctor should be consulted before discontinuing PAXIL. DDMAC determined that this additional statement ensured that the

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<sup>111</sup> *Motus v. Pfizer, Inc.*, 358 F.3d 659, 660 (9th Cir. 2004) [hereinafter *Motus III*].

<sup>112</sup> *Motus III*, 358 F.3d at 660.

<sup>113</sup> The discontinuation symptoms associated with PAXIL and other drugs (e.g., beta-blockers and steroids) are distinct from the drug-seeking behavior that is associated with habit-forming drugs, such as narcotics. FDA, therefore, traditionally has limited use of the phrase "habit-forming" to drugs that induce such behavior.

advertisement adequately communicated to patients the appropriate information about discontinuation.

Notwithstanding DDMAC's review of and lack of objection to these precise advertisements, a federal district court judge applying California law in August 2002 granted plaintiffs' motion to enjoin GSK from running advertisements for PAXIL that included the "non-habit-forming" language.<sup>114</sup> The court suggested that whether a drug advertisement was false or misleading could be a different issue under state tort law than under the FDCA.<sup>115</sup>

FDA decided to participate in the case to preserve the agency's important role in regulating prescription drug advertising. With the court's agreement, FDA filed a brief in September 2002 in connection with GSK's Motion for Reconsideration of the preliminary injunction order.<sup>116</sup> FDA's brief contended that the court should have deferred to FDA's determination that the advertisements were not false or misleading.<sup>117</sup> The court later granted GSK's Motion for Reconsideration. It declined to enjoin the advertising on the ground that information submitted by FDA concerning DDMAC's review made the plaintiff less likely to succeed on the merits.<sup>118</sup> The court still could find that state law supports imposing requirements on advertising for PAXIL that are different from those applied by DDMAC.<sup>119</sup>

#### 4. *Kallas v. Pfizer, Inc.*

More recently, FDA filed a brief in another ZOLOFT case, *Kallas v. Pfizer, Inc.*<sup>120</sup> In *Kallas*, the parents of a 15-year-old girl who committed suicide while taking ZOLOFT sued

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<sup>114</sup> Memorandum of Decision re: Preliminary Injunction, *In re PAXIL Litigation*, Case No. CV 01-07937 MRP (C.D. Cal. filed Aug. 16, 2002) [hereinafter PAXIL Injunction], at 10. The injunction never took effect. *See id.*; Minutes of Status Conference, *In re PAXIL Litigation*, Case No. CV 01-07937 MRP (C.D. Cal. filed Aug. 22, 2002); Minutes in Chambers, *In re PAXIL Litigation*, Case No. CV 01-07937 MRP (C.D. Cal. filed Oct. 9, 2002).

<sup>115</sup> PAXIL Injunction, at 6.

<sup>116</sup> Brief of the United States of America, *In re PAXIL Litigation*, Case No. CV 01-07937 MRP (CWx) (C.D. Cal. filed Sept. 4, 2002).

<sup>117</sup> *Id.* at 8-9.

<sup>118</sup> Memorandum of Decision re: Motion for Reconsideration of Order Granting Preliminary Injunction, *In re PAXIL Litigation*, Case No. CV 01-07937 MRP (C.D. Cal. filed Oct. 18, 2002).

<sup>119</sup> *Id.*

<sup>120</sup> Amicus Brief for the United States, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed Sept. 25, 2005).

Pfizer, alleging in part that Pfizer should have warned of an *association* between ZOLOFT and suicide, even if Pfizer was not required to state that ZOLOFT *caused* suicide.<sup>121</sup> Pfizer filed a motion for summary judgment, and after hearing argument on that motion, the U.S. District Court requested that the government file a brief explaining the FDA's position on the case.

The FDA brief emphasized that at the time the young girl took ZOLOFT, Pfizer would not have been permitted to warn of an association between ZOLOFT and suicide.<sup>122</sup> FDA further noted that the agency's "accomplishment of its responsibilities would be disrupted and undermined if, driven in part by concerns about later state law tort liability, drug manufacturers were to engage in their own labeling determinations by adding warnings that, in FDA's judgment, were not based on reasonable scientific evidence of association or causation."<sup>123</sup> The court did not have the opportunity to rule on Pfizer's motion, as the parties settled the case shortly after FDA filed its brief.<sup>124</sup>

### *B. The Physician Labeling Rule*

On January 18, 2006, FDA issued a major policy statement concerning the preemptive effect of its prescription drug labeling determinations on state-law liability. The statement occurs in the preamble accompanying the long-awaited final rule revising 21 C.F.R. §§ 201.56 and 201.57, which establish content and format requirements for prescription drug package inserts.<sup>125</sup> The language provides that FDA's decisions on labeling matters take precedence over conflicting state-law requirements, whether imposed through legislation, regulations, or product liability law.<sup>126</sup>

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<sup>121</sup> Order Requesting Government to Submit Amicus Brief, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed June 30, 2005).

<sup>122</sup> Amicus Brief for the United States, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed Sept. 15, 2005), at 34-36.

<sup>123</sup> *Id.* at 37.

<sup>124</sup> See Notice of Settlement, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed Oct. 13, 2005); Order of Dismissal with Prejudice, *Kallas v. Pfizer, Inc.*, No. 2:04-cv-998 (D. Utah filed Oct. 24, 2005).

<sup>125</sup> FDA, Physician Labeling Rule, *supra* note 3, at 37-47, 169-76.

<sup>126</sup> *Id.* at 38.

FDA had to address preemption in the preamble for legal reasons.<sup>127</sup> But FDA clearly also hopes that, by addressing the relationship of its labeling requirements to state law, the preamble language will reduce the need for the Agency to submit briefs in private lawsuits. The Agency has considered it increasingly necessary to submit such briefs over the past five years because of the growing tendency of product liability lawsuits to encroach upon the Agency's prerogatives. Although FDA's views on preemption are set forth with relative clarity in this important new document, it remains to be seen how much weight will be given the preamble language by courts hearing particular product liability and other state-law actions.

### *1. Background*

On December 22, 2000, FDA published for comment in the Federal Register a proposed rule to amend the Agency's regulations standardizing the content and format of package inserts for prescription drugs (including biological products that are regulated as drugs).<sup>128</sup> The proposed rule would have revised current regulations, codified principally at 21 C.F.R. §§ 201.56 and 201.57, to simplify drug product labeling and reduce medication error risks. The proposed changes included, with respect to new and recently approved products:

- Requiring that the labeling include a "Highlights" section with the most important information relating to safety and effectiveness
- Requiring that the labeling include an index to prescribing information
- Reordering of the sections in labeling to make information easier for health care practitioners to access (e.g., by placing the indication information earlier in the labeling)
- Revising the content requirements for labeling
- Establishing minimum graphical requirements.

For older products, the proposed changes included:

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<sup>127</sup> *Id.* at 169-76.

<sup>128</sup> FDA, *supra* note 26 (proposed Dec. 22, 2000).

- Requiring that certain types of statements currently appearing in labeling be removed if not sufficiently supported
- Eliminating certain unnecessary statements that are currently required to appear on prescription drug product labels
- Moving certain information currently required to be on the label into labeling

In the preamble accompanying the proposed rule, FDA specifically addressed and requested comment on product liability issues. For example, FDA explained that product liability was one of the reasons package inserts had become longer and more complex: “the use of labeling in product liability and medical malpractice lawsuits, together with increasing litigation costs, has caused manufacturers to become more cautious and include virtually all known adverse event information, regardless of its importance or its plausible relationship to the drug.”<sup>129</sup> FDA also asked whether requiring manufacturers to include a Highlights” section in labeling had “a significant effect on manufacturers’ product liability concerns.”<sup>130</sup> If it did, FDA asked how manufacturers’ concerns could be adequately addressed.

FDA received numerous comments from the pharmaceutical industry regarding product liability issues. For that reason, and because Executive Order 13132<sup>131</sup> required the Agency to address the preemptive effect of the rule, FDA included a discussion of preemption of product liability claims in the preamble accompanying the final regulations. Although critics may contend that the preemption discussion amounts to a power grab by FDA, it is hard to see how FDA could have issued the rule without addressing preemption issues.<sup>132</sup> Moreover, this is certainly not the first time FDA has expressed preemptive intent in a preamble.<sup>133</sup>

The final rule itself is extremely regulatory and highly detailed, occupying 275 pages in its prepublication form. Although much of the proposed rule reached the final version intact,

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<sup>129</sup> 65 Fed. Reg. at 81083.

<sup>130</sup> *Id.* at 81086.

<sup>131</sup> Exec. Order No. 13132, 64 Fed. Reg. 43255 (Aug. 4, 1999).

<sup>132</sup> *See, e.g.*, FDA, Physician Labeling Rule, *supra* note 3, at 24, 37 (noting manufacturer concern that the requirement of a highlights section, universally supported by health care providers, would make manufacturers more vulnerable to products liability claims).

<sup>133</sup> *See, e.g., id.* at 43-44.

there are many important changes between the documents of which manufacturers should be aware. To assist in phasing in the changes, FDA included in the rule a staggered implementation schedule. The Agency also announced the availability of four labeling-related guidance documents: (1) a draft guidance on implementing the provisions of the final rule generally;<sup>134</sup> (2) a final version of the draft guidance on the adverse events section of labeling (originally issued in 2000)<sup>135</sup>; (3) a draft guidance addressing the other risk-related sections of labeling (warnings, including boxed warnings, precautions, and contraindications)<sup>136</sup>; (4) and a final version of the guidance on the clinical studies section (originally issued in 2001).<sup>137</sup>

## 2. Preemption Aspects of the Rule

The codified version of the final rule does not itself address preemption. However, the preamble does so in two distinct sections: FDA's responses to comments on the product liability implications of the new "Highlights" requirements,<sup>138</sup> and the discussion of Executive Order 13132.<sup>139</sup>

In the responses to comments section of the preamble, FDA included a discussion of the increasing prevalence of product liability lawsuits threatening the Agency's exclusive authority over the dissemination of risk information for prescription drugs.<sup>140</sup> The preamble describes previous instances in which FDA expressed its intention for its actions to have preemptive effect

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<sup>134</sup> FDA, Guidance for Industry: Labeling for Human Prescription Drug and Biological Products—Implementing the New Content and Format Requirements (2006) (Draft Guidance), *available at* <http://www.fda.gov/OHRMS/DOCKETS/98fr/05d-0011-gdl0001.pdf>.

<sup>135</sup> FDA, Guidance for Industry: Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products—Content and Format (2006), *available at* <http://www.fda.gov/OHRMS/DOCKETS/98fr/01d-0269-gdl0002.pdf>.

<sup>136</sup> FDA, Guidance for Industry: Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products—Content and Format (2006) (Draft Guidance), *available at* <http://www.fda.gov/OHRMS/DOCKETS/98fr/05d-0011-gdl0002.pdf>.

<sup>137</sup> FDA, Guidance for Industry: Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products—Content and Format (2006), *available at* <http://www.fda.gov/OHRMS/DOCKETS/98fr/00d-1306-gdl0002.pdf>.

<sup>138</sup> FDA, Physician Labeling Rule, *supra* note 3, at 37-47.

<sup>139</sup> *Id.* at 169-76.

<sup>140</sup> *Id.* at 40-43.

in preambles in rulemaking proceedings.<sup>141</sup> The preamble also describes the previous private lawsuits in which FDA submitted briefs addressing the relationship of federal and state law. In the most important language in this discussion, FDA expresses its intention that federal labeling requirements will preempt state-law actions according to well-established conflict and obstacle preemption principles, as follows:

. . . FDA believes that at least the following claims would be preempted by its regulation of prescription drug labeling: (1) Claims that a drug sponsor breached an obligation to warn by failing to put in Highlights or otherwise emphasize any information the substance of which appears anywhere in the labeling; (2) claims that a drug sponsor breached an obligation to warn by failing to include in an advertisement any information the substance of which appears anywhere in the labeling, in those cases where a drug's sponsor has used Highlights consistently with FDA draft guidance regarding the "brief summary" in direct-to-consumer advertising . . . ; (3) claims that a sponsor breached an obligation to warn by failing to include contraindications or warnings that are not supported by evidence that meets the standards set forth in this rule, including § 201.57(c)(5) (requiring that contraindications reflect "[k]nown hazards and not theoretical possibilities") and (c)(7); (4) claims that a drug sponsor breached an obligation to warn by failing to include a statement in labeling or in advertising, the substance of which had been proposed to FDA for inclusion in labeling, if that statement was not required by FDA at the time plaintiff claims the sponsor had an obligation to warn (unless FDA has made a finding that the sponsor withheld material information relating to the proposed warning before plaintiff claims the sponsor had the obligation to warn); (5) claims that a drug sponsor breached an obligation to warn by failing to include in labeling or in advertising a statement the substance of which FDA has prohibited in labeling or advertising; and (6) claims that a drug's sponsor breached an obligation to plaintiff by making statements that FDA approved for inclusion in the drug's label (unless FDA has made a finding that the sponsor withheld material information relating to the statement). Preemption would include not only claims against manufacturers as described above, but also against health care practitioners for claims related to dissemination of risk information to patients beyond what is included in the labeling. (See, e.g., *Bowman v. Songer*, 820 P.2d 1110 (Col. 1991).)

. . . FDA's regulation of drug labeling will not preempt all State law actions. The Supreme Court has held that certain State law requirements that parallel FDA requirements may not be preempted (*Medtronic, Inc. v. Lohr*, 518 U.S. 470, 495 (1996) (holding that the presence of a State law damages remedy for violations of FDA requirements does not impose an additional requirement upon medical device manufacturers but "merely provides another reason for manufacturers to comply with \* \* \* federal law")); *id.* at 513 (O'Connor, J., concurring in part and dissenting in part); *id.*). *But see Buckman Co. v. Plaintiffs' Legal Comm.*, 531

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<sup>141</sup> *Id.* at 43-44.

U.S. 341, 352-53 (2001) (holding that “fraud on the FDA” claims are preempted by Federal law); 21 U.S.C. 337(a) (restricting the act enforcement to suits by the United States); *In re Orthopedic Bone Screw Prods. Liability Litig.*, 159 F.3d 817, 824 (3d Cir. 1998) (“Congress has not created an express or implied private cause of action for violations of the FDCA or the MDA [Medical Device Amendments]”).<sup>142</sup>

A comprehensive analysis of FDA’s authority to regulate the risk information provided for prescription drugs also appears in the discussion of the Executive Order.<sup>143</sup>

Notably, although FDA disclaims authority to regulate medical practice, consistent with its well-established policy of noninterference in the practice of medicine, the preamble twice makes clear that FDA intends for its regulation of risk information for prescription drugs to shield health care practitioners from state-law claims.<sup>144</sup>

### 3. *Effect of the Rule in Individual Cases*

The preamble material on preemption should help to mitigate the negative consequences of the current pharmaceutical liability regime. The two discussions of preemption issues resemble a concise version of an FDA amicus curiae brief that defendants in failure-to-warn actions arising under state law can use to explain to a court (and, if necessary, to a jury) that FDA’s regulation of warnings issued with respect to prescription drugs constitutes both a “floor” and a “ceiling.”<sup>145</sup> Indeed, FDA specifically refutes the minimum standards theory of FDA regulation that has been a mainstay of plaintiffs’ attorney argument against preemption in these case.<sup>146</sup>

FDA also squarely rejects the myth that manufacturers are free to add or revise risk information without first obtaining FDA approval. Although the Agency has not revised the sNDA regulation, 21 C.F.R. § 314.70, it does make clear in the preamble that manufacturers generally consult with FDA and await specific authorization before supplementing risk

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<sup>142</sup> *Id.* at 45-47 (emphasis added).

<sup>143</sup> *Id.* at 169-76.

<sup>144</sup> *Id.* at 46-47, 175.

<sup>145</sup> *See id.* at 42.

<sup>146</sup> *Id.* at 41.

information in labeling.<sup>147</sup> The Agency also twice points out that changes being effected (CBE) supplements may not be used under the final rule to make changes to the “Highlights” section.<sup>148</sup>

Questions are likely to arise concerning whether the position set forth by FDA in the preamble applies in existing cases or only prospectively. According to the preamble, “FDA believes that[,] under existing preemption principles, FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law.”<sup>149</sup> By making clear that the discussion of preemption is a reflection of current principles under existing regulations, FDA makes clear its expectation that the preamble discussion will be invoked in pending cases. The cases that are going to be the clearest candidates for preemption are where the plaintiff asserts that a manufacturer was required as a matter of state law to provide risk information that FDA specifically considered and rejected, or where FDA’s regulations clearly prohibit the dissemination of risk information that is allegedly compelled by state law. It is significant that the preamble uses the phrase “at least,”<sup>150</sup> signaling that arguments from field preemption or based on theories of conflict/obstacle preemption not expressly set forth in the preamble are not foreclosed by FDA’s articulation of specific categories of cases in which it intends for its regulations to have preemptive effect.

### C. Discussion

FDA will likely continue to participate in product liability lawsuits<sup>151</sup> brought under state law as necessary to safeguard its considerable expertise in regulating the content of drug labeling and advertising.<sup>152</sup> Nonetheless, this is not a complete solution to the problems created by inappropriate pharmaceutical-liability rules, as FDA lacks the resources to use court submissions as a mechanism for defending its statutory mandate against all cases of state encroachment. The

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<sup>147</sup> *See id.* at 40.

<sup>148</sup> *See id.* at 32, 40.

<sup>149</sup> *Id.* at 38.

<sup>150</sup> *Id.* at 45.

<sup>151</sup> *See id.* at 38 (noting that amicus briefs filed by the Department of Justice on behalf of FDA “represent[] the government’s long standing views on preemption, with a particular emphasis on how that doctrine applies to State laws that would require labeling that conflicts with or is contrary to FDA-approved labeling”).

<sup>152</sup> *Id.* at 43 (“State law actions also threaten FDA’s statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs.”).

new Physician Labeling Rule is helpful, as it may reduce the need for FDA to file individual briefs, but there is a possibility FDA's preemption argument may not be accepted by some courts. Patients are well-served by state-level action to ameliorate the perverse incentives of the current liability regime.

## V. STATE-LEVEL PROTECTION FOR GOOD-FAITH MANUFACTURERS: THE MICHIGAN MODEL

A number of states have recognized the need to provide some type of protection for manufacturers of FDA-approved drugs. Although Michigan's statute is the strongest, several other states provide some lesser degree of protection. For example, Arizona,<sup>153</sup> Ohio,<sup>154</sup> Oregon,<sup>155</sup> and Utah<sup>156</sup> each have some type of prohibition on punitive damages for FDA-approved drugs. In New Jersey, FDA approval creates a rebuttable presumption that a drug warning is adequate,<sup>157</sup> and in North Carolina it is explicitly listed as a factor to be considered in

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<sup>153</sup> ARIZ. REV. STAT. ANN. § 12-701 (2005) (drug manufacturers who comply fully with FDA regulations not liable for punitive or exemplary damages except on a showing of that the manufacturer withheld material information from or misrepresented material information to FDA), *held preempted in part by Kobar ex. rel Kobar v. Novartis*, 378 F. Supp. 2d 1166, 1174-75 (D. Ariz. 2005) (holding that the portion of the Arizona statute permitting punitive damages against a drug company on a showing of fraud on FDA was preempted by the agency's statutory authority to punish fraud).

<sup>154</sup> OHIO REV. CODE ANN. § 2307.80(C) (drug manufacturers who comply fully with FDA regulations not liable for punitive or exemplary damages except on a showing that the manufacturer withheld material information from or misrepresented material information to FDA); *but see Garcia v. Wyeth-Ayerst Labs.*, 385 F.3d 961, 966-67 (6th Cir. 2004) (holding that the fraud and bribery exceptions to the Michigan FDA Shield Law require finding by FDA that fraud or bribery has occurred).

<sup>155</sup> OR. REV. STAT. § 30.927 (2003) (drug manufacturers who comply fully with FDA regulations not liable for punitive damages except on a showing that the manufacturer withheld material information from or misrepresented material information to either FDA or the prescribing physician). It does not appear that any Oregon court has considered whether any part of § 30.927(2) is preempted by the FDCA.

<sup>156</sup> UTAH CODE § 78-18-2 (2005) (drug manufacturers who comply fully with FDA regulations not liable for punitive damages except on a showing that the manufacturer withheld material information from or misrepresented material information to FDA). It does not appear that any Utah court has considered whether any part of § 78-18-2(2) is preempted by the FDCA.

<sup>157</sup> N.J. CODE § 2A:58C-4 (2005) (product manufacturers not liable for failure-to-warn damages when a product contains an adequate warning or instruction; rebuttable presumption that warning or instruction on FDA-approved drug is adequate).

determining whether a manufacturer has acted reasonably.<sup>158</sup> Although each of these state laws helps to reduce the negative effects of the current liability environment, the more comprehensive Michigan statute would be the preferable model for state-by-state reform.

The Michigan statute is more effective at reducing the negative consequences of the current pharmaceutical-liability regime because it provides protection from compensatory as well as punitive damages.<sup>159</sup> Although punitive damages awards play a major role in increasing the severity of the undesirable incentives affecting the pharmaceutical industry, they are not the whole problem. Even without the possibility of punitive damages, mass tort claims would be exceedingly expensive to defend.

Although protection from both compensatory and punitive damages is no doubt troubling to those who make their living suing drug companies, it is entirely appropriate as a matter of public health policy. Recall that prescription drugs are substances that, at our current state of technological achievement, can be modified only in limited ways.<sup>160</sup> In most cases, the beneficial properties of a particular drug are simply not available without the possibility—or even the certainty—of some adverse effect.<sup>161</sup> FDA will approve an individual drug when the agency believes that the benefits of having the drug available to prescribers outweigh the adverse effects that substance may have in some patients.<sup>162</sup> Such an outcome is clearly desirable. To take a dramatic example, it is difficult to imagine that any serious person would suggest that the world would be better off without the oral polio vaccine, even though that vaccine is known to cause polio in some individuals who would not otherwise have been exposed to the disease.<sup>163</sup> Given the nature of the risk/benefit determination involved in FDA approval, it does not make

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<sup>158</sup> N.C. GEN. STAT. § 99B-6(b)(4) (2005) (extent to which the manufacturer of an FDA-approved drug complied with “any applicable government or private standard” is a factor to be considered in determining whether the manufacturer could be held to have acted unreasonably in designing the drug).

<sup>159</sup> See *supra* Part I.

<sup>160</sup> See *supra* Part I.

<sup>161</sup> See *supra* Part I.

<sup>162</sup> See *supra* Part I.

<sup>163</sup> See Center for Disease Control and Prevention, *Polio Vaccine: What You Need To Know*, at 1 (Jan. 1, 2000), available at <http://www.cdc.gov/nip/publications/VIS/vis-IPV.pdf> (noting that the oral polio vaccine causes polio in approximately one in 2.4 million people who receive it). The polio shot does not carry a risk of causing polio, but is less effective as a public health measure in areas where polio is prevalent. *Id.*

sense to allow individual juries to hold drug manufacturers liable for adverse effects inherent in a drug approved by FDA.

Despite the positive effects of the Michigan FDA Shield Law, opponents of the law are seizing on Vioxx-related publicity to mount an effort to roll back this important reform.<sup>164</sup> Michigan legislators should resist this short-sighted effort, and other states should realize that it is in their own citizens' long-term best interests to follow Michigan's lead. As discussed above,<sup>165</sup> the consequences of the present liability regime (i.e., the one applicable in most states other than Michigan) are perverse. In terms of innovation, the current regime deals patients a crippling double-blow. First, by providing disincentives to drug investment more generally, the current regime slows the overall pace at which new medicines are invented.<sup>166</sup> Second, the current regime encourages pharmaceutical companies to direct their scarce research dollars away from products intended for healthy patients.<sup>167</sup> This is the case no matter how socially desirable those products (in particular vaccines) may be. In terms of availability, the current regime has forced pharmaceutical companies to remove beneficial—and, according to FDA, entirely safe—drugs from the U.S. market because the excessive cost of defending those drugs from massive litigation efforts.<sup>168</sup> When no adequate substitute drug is available, such withdrawals can leave patients with no option to treat a particular condition despite the pharmaceutical industry's technical ability to provide treatment. As to price, simple math suggests that the more companies reasonably expect to pay in litigation costs for a particular drug, the more they will be forced to charge for that drug.<sup>169</sup> In regard to rational prescribing, the current regime dilutes the most important drug-related risks by creating an incentive to overemphasize less significant concerns.<sup>170</sup>

As a matter of public policy, the case for providing pharmaceutical companies marketing FDA-approved drugs with some protection from lawsuits is overwhelming. At the present time,

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<sup>164</sup> See, e.g., Bell, *supra* note 1; Anstett & Norris, *A Michigan law stirs a national debate*, *supra* note 1; Anstett & Norris, *Michigan Rezulin lawsuits tossed*, *supra* note 1.

<sup>165</sup> See *supra* Part III.

<sup>166</sup> See *supra* Part III.A.1.

<sup>167</sup> See *supra* Part III.A.2.

<sup>168</sup> See *supra* Part III.B.

<sup>169</sup> See *supra* Part III.C.

<sup>170</sup> See *supra* Part III.D.

state-level reform is an appropriate compliment to FDA efforts to clarify the scope of federal regulation. State legislatures should embrace this opportunity. Each state that passes an FDA shield law on the Michigan model reduces the strength of the perverse incentives currently affecting the pharmaceutical industry. The payoff is particularly high in states with large populations or significant research-based pharmaceutical industries. Were just a few large-population states to adopt an effective FDA shield law, the perverse incentives affecting the industry would be substantially reduced. In states with significant research-based pharmaceutical industries, the effect might be even more significant, as such laws would apply any time choice-of-law rules dictated application of the law of the state where the product was produced. In particular, states that hope to attract or retain research-based pharmaceutical industries would be well-served to adopt an FDA shield law on the Michigan model.