FDA Preemption:
The Battle for Supremacy

Featuring
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February 10, 2015

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Wyeth, Inc. v. Weeks, --- So.3d ----, 2014 WL 4055813 (Ala. Aug. 15, 2014).

PLIVA, Inc. v. Mensing, 131 S. Ct. 2567 (2011).

Wyeth v. Levine, 555 U.S. 555 (2009).

Riegel v. Medtronic, Inc., 552 U.S. 312 (2008).

78 FR 67985 - Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products

73 FR 49603 - Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices

Paul D. Clement, *Legal Reform, The Framers and First Principles*, U.S. CHAMBER INSTITUTE FOR LEGAL REFORM, Oct. 2013.

2014 WL 4055813
Only the Westlaw citation is currently available.

NOT YET RELEASED FOR PUBLICATION.

Supreme Court of Alabama.

WYETH, INC.,[1] et al.
v.
Danny WEEKS and Vicki Weeks.

1101397. | Aug. 15, 2014.

Synopsis
Background: Consumer brought action against drug manufacturers for injuries allegedly suffered as a result of his long-term use of the generic drug metoclopramide. The United States District Court for the Middle District of Alabama, No. 1:10–cv–602, 2011 WL 6988047, certified question.

[Holding:] On application for rehearing, the Supreme Court, Bolin, J., held that brand-name manufacturer could be held liable for fraud or misrepresentation based on statements it made in connection with the manufacture of the drug in an action brought by consumer who was allegedly injured by generic version of drug.

Question answered.

Shaw, J., concurred specially with opinion.

Moore, C.J., filed dissenting opinion.

Parker, J., filed dissenting opinion.

Murdock, J., filed dissenting opinion.

On Application for Rehearing

BOLIN, Justice.

***1** The opinion of January 11, 2013, is withdrawn, and the following is substituted therefor.

The United States District Court for the Middle District of Alabama, Southern Division ("the district court"), has certified to this Court the following question pursuant to Rule 18, Ala. R.App. P.:

> "Under Alabama law, may a drug company be held liable for fraud or misrepresentation (by misstatement or omission), based on statements it made in connection with the manufacture or distribution of a brand-name drug, by a plaintiff claiming physical injury from a generic drug manufactured and distributed by a different company?"

Facts and Procedural History

In its certification to this Court, the district court provided the following background information:

> "Plaintiffs Danny and Vicki Weeks filed this action against five current and former drug manufacturers for injuries that Mr. Weeks allegedly suffered as a result of his long-term use of the prescription drug product metoclopramide, which is the generic form of the brand-name drug Reglan.® The Weekses claim that two companies—Teva Pharmaceuticals USA and Actavis Elizabeth, LLC—manufactured and sold the generic metoclopramide that Mr. Weeks ingested.
>
> "The Weekses concede that Mr. Weeks did not ingest any Reglan® manufactured by the three brand-name defendants, Wyeth LLC, Pfizer Inc., and Schwarz Pharma, Inc. The Weekses nonetheless assert that the brand-name defendants are liable for Mr. Weeks's harm on fraud, misrepresentation, and/or suppression theories because they at different times manufactured or sold brand-name Reglan® and purportedly either misrepresented or failed adequately to warn Mr. Weeks or his physician about the risks of using Reglan® long-term. The brand-name defendants moved to dismiss the claims against them, arguing, among other things, (1) that the Weekses' claims, however pled, are in fact product liability claims that are barred for failure of 'product identification' and (2) that they had no duty to warn about the risks associated with ingestion of their competitors' generic products. The Weekses responded to the brand-name defendants' motion, and the defendants replied. On March 31, 2011, this Court

granted in part and denied in part the brand-name defendants' motion, holding that the Weekses might be able to state a claim for relief under Alabama law if they could prove that the brand-name manufacturers had a duty to warn Mr. Weeks's physician about the risks associated with long-term use of brand-name Reglan® and, further, that the Weekses, as third parties, had a right to enforce an alleged breach of that duty.

"Within the last year alone, federal district courts in this State have issued four decisions addressing the question whether brand-name Reglan® manufacturers can be held liable on fraud, misrepresentation, and/or suppression theories for physical injuries allegedly caused by plaintiffs' ingestion of generic metoclopramide. The first two courts answered no; however, this Court held otherwise, thereby creating an intrastate split. *Compare Simpson v. Wyeth, Inc.*, No. 7:10–CV–01771–HGD (N.D.Ala. Dec. 9, 2010) [not reported in F.Supp.2d], *report and recommendation adopted* (N.D.Ala. Jan. 4, 2011) [not reported in F.Supp.2d] (holding that a brand-name manufacturer has no duty under Alabama law to warn of the risks associated with a competitor's generic product); *Mosley v. Wyeth, Inc.*, 719 F.Supp.2d 1340 (S.D.Ala.2010)(same), *with Weeks v. Wyeth, Inc.*, No. 1:10–cv–602 (M.D.Ala. Mar. 31, 2011) [not reported in F.Supp.2d](denying brand-name manufacturers' motion to dismiss on the ground that the plaintiffs there had pleaded a claim 'that defendants perpetrated a fraud on the physician'); *see also Barnhill v. Teva Pharm. USA, Inc.*, No. Civ. 06–0282–CB–M (S.D.Ala. Apr. 24, 2007) [not reported in F.Supp.2d](holding that a brand-name manufacturer of the drug Keflex® has no duty under Alabama law to warn of the risks associated with a competitor's generic product). Since this Court's decision, another district court in Alabama has followed the earlier decisions. *See Overton v. Wyeth, Inc.*, No. CA 10–0491–KD–C (S.D.Ala. Mar. 15, 2011) [not reported in F.Supp.2d], *report and recommendation adopted* (S.D.Ala. Apr. 7, 2011)[not reported in F.Supp.2d].

***2** "Certification is appropriate here to resolve the disagreement among the federal district courts within Alabama and to prevent both federal courts within the State and state courts around the country from having to 'mak[e] unnecessary *Erie* guesses' about unsettled questions of Alabama law. *Tobin v. Michigan Mut. Ins. Co.*, 398 F.3d 1267, 1274 (11th Cir.2005); *see also*, e.g., *Lehman Bros. v. Schein*, 416 U.S. 386, 391, 94 S.Ct. 1741, 40 L.Ed.2d 215 (1974)(noting that certification often 'save[s] time, energy, and resources and helps build a cooperative judicial federalism')."Because the only authoritative voice on Alabama law is the Alabama Supreme Court, it is axiomatic that that court is the best one to decide issues of Alabama law.'*Blue Cross & Blue Shield of Ala., Inc. v. Nielsen*, 116 F.3d 1406, 1413 (11th Cir.1997).

"The question framed ... satisfies the requirements of Ala. R.App. P. 18(a): first, it presents a pure question of Alabama law; second, it is 'determinative' of this case in the sense that a negative answer would require dismissal of the Weekses' claims against the brand-named defendants; and third, although two Alabama trial courts have addressed the question whether a brand-name manufacturer can ever be held liable for physical harm caused by a generic product and answered it in the negative,[1] the Alabama Supreme Court has never considered or resolved either that question or the subsidiary question whether a plaintiff claiming physical injury can prevail on fraud, misrepresentation, and/or suppression theories under these facts.

"Considerations of judicial efficiency likewise counsel certification. During the last year, the number of Reglan®/metoclopramide cases nationwide ballooned from 250 to approximately 3500. Current estimates suggest that among the 3500 cases there are at least 250 Alabama-resident plaintiffs and that most (if not all) of these plaintiffs assert the fraud, misrepresentation, and/or suppression theories asserted here. The Alabama Supreme Court's definitive resolution of the question presented will therefore affect not only cases pending (or that might later arise) in this State, but also the scores of Alabama-resident cases pending in courts around the country—particularly in large consolidated actions pending in California, New Jersey, and Pennsylvania. Moreover, the question's significance extends well beyond the Reglan® litigation—and for that matter, even beyond pharmaceutical litigation. It is likely to recur any time a brand-name manufacturer (of any product) is sued on fraud, misrepresentation, and/or suppression theories by a plaintiff who claims to have been injured while using a generic-equivalent product.

"....

" [1]*See Buchanan v. Wyeth Pharm., Inc.*, No. CV–2007–900065, Order at 1 (Ala.Cir.Ct. Oct. 20, 2008); *Green v. Wyeth Pharm., Inc.*, No. CV–06–3917 ER (Ala.Cir.Ct. May 14, 2007)."

Discussion

[1] At the outset, we limit the question posed to manufacturers of prescription drugs and not to any distributors thereof.[2]The Weekses' complaint alleges that three brand-name manufacturers, Wyeth, Pfizer, Inc., and Schwarz Pharma, Inc. (hereinafter collectively referred to as "Wyeth"), falsely and deceptively misrepresented or knowingly suppressed facts about Reglan or metoclopramide such that Danny Weeks's physician, when he prescribed the drug to Danny, was materially misinformed and misled about the likelihood that the drug would cause the movement disorder tardive dyskinesia and related movement disorders.[3]The Weekses contend that Wyeth had a duty to warn Danny's physician about the risks associated with the long-term use of metoclopramide and that the Weekses, as third parties, have a right to hold Wyeth liable for the alleged breach of that duty.

***3** [2] [3] A fraudulent-misrepresentation action is governed by § 6–5–101, Ala.Code 1975, which provides that "[m]isrepresentations of a material fact made willfully to deceive, or recklessly without knowledge, and acted on by the opposite party, or if made by mistake and innocently and acted on by the opposite party, constitute legal fraud."A claim of fraudulent misrepresentation comprises the following elements: "(1) a false representation (2) concerning a material fact (3) relied upon by the plaintiff (4) who was damaged as a proximate result."*Fisher v. Comer Plantation*, 772 So.2d 455, 463 (Ala.2000) (quoting *Baker v. Bennett*, 603 So.2d 928, 935 (Ala.1992))."An essential element of fraudulent-misrepresentation and fraudulent-suppression claims is a duty to disclose."*Nesbitt v. Frederick*, 941 So.2d 950, 955 (Ala.2006).

[4] We recognize that Wyeth argues that the Weekses' claims are, in essence, "products-liability" claims. In *Atkins v. American Motors Corp.*, 335 So.2d 134 (Ala.1976), in conjunction with *Casrell v. Altec Industries, Inc.*, 335 So.2d 128 (Ala.1976), this Court adopted the Alabama Extended Manufacturer's Liability Doctrine ("AEMLD"). The AEMLD is "a judicially created accommodation of Alabama law to the doctrine of strict liability for damage or injuries caused by allegedly defective products."*Keck v. Dryvit Sys., Inc.*, 830 So.2d 1, 5 (Ala.2002). This Court has explained that the AEMLD did not subsume a common-law negligence or wantonness claim. *Tillman v. R.J. Reynolds Tobacco Co.*, 871 So.2d 28 (Ala.2003); *Vesta Fire Ins. Corp. v. Milam & Co. Constr.*, 901 So.2d 84 (Ala.2004).

> "It must be remembered, ... that the AEMLD, as established in *Casrell* and *Atkins*, supra, is 'an example of judicial legislation,' not of legislative enactment. *Keck v. Dryvit Sys., Inc.*, 830 So.2d 1, 8 (Ala.2002). This Court warned last year in *Keck* that '[j]udicial decision-making should not be seen as the opportunity to legislate.'830 So.2d at 8. Alabama remains a common-law state, and therefore common-law tort actions 'so far as [they are] not inconsistent with the Constitution, laws and institutions of this state ...*shall continue in force*, except as from time to time ... may be altered or repealed by the Legislature.'§ 1–3–1, Ala.Code 1975. We will not presume to so define the boundaries of the judicially created AEMLD so that it subsumes the common-law tort actions of negligence and wantonness against the retailer defendants."

Tillman, 871 So.2d at 34–35. We have also recognized that fraudulent suppression is a claim separate from an AEMLD claim. *Keck*, supra.Accordingly, for purposes of this certified question, we will not treat the Weekses' claims as AEMLD claims governed by the principles of the AEMLD.

Wyeth argues, based on *Pfizer, Inc. v. Farsian*, 682 So.2d 405 (Ala.1996), that a plaintiff who in substance alleges physical injury caused by a product has a products-liability claim, no matter the label or labels he uses in his complaint, and that, in a products-liability claim, the plaintiff must prove that the defendant manufactured the product the plaintiff claims injured him or her. We recognize that in *Farsian* this Court contended that the plaintiff's claim was in substance a products-liability claim and not a fraud claim as he had asserted. In *Farsian*, a heart-valve recipient's valve had not malfunctioned, although the valves in some other patients who had received the valve made by the manufacturer had malfunctioned. The federal court where the action was filed certified the following question to this Court:

> ***4** " 'Does a heart valve implantee have a valid cause of action for fraud under Alabama law if he asserts that the valve's manufacturer fraudulently induced him to have the valve implanted when the damages he asserts do not include an injury-producing malfunction of the product because the valve has been and is working properly?' "

682 So.2d at 406. The manufacturer argued that, although the plaintiff had alleged a risk of possible future malfunction of the valve, it was uncontroverted that his

valve was and had been working properly. The manufacturer contended that the plaintiff was really asserting a products-liability claim and that, as such, the action did not accrue until there was an injury-producing malfunction. The manufacturer further argued that an allegation of fraud did not relieve the plaintiff from having to prove an injury-producing malfunction. The plaintiff argued that his fraud claim was not subsumed by products-liability law and that he could recover damages even if he could not prove that his valve was not yet malfunctioning.

In addressing the question, we stated:

> "The question certified to this Court concerns whether [the plaintiff] may maintain a fraud claim under Alabama law. We conclude that he may not.
>
> "Regardless of how [the plaintiff] pleads his claim, his claim is in substance a product liability/personal-injury claim—[the plaintiff] seeks damages because of the risk that his heart valve may one day fail. Alabama courts have never allowed a recovery based on a product that, like [the plaintiff]'s valve, is and has been working properly. Each of our prior cases in which fraud or other intentional conduct was alleged has involved a failure, a malfunction, or an accident that involved the defendant's products and which injured the plaintiff. See *Quality Homes Co. v. Sears, Roebuck & Co.*, 496 So.2d 1 (Ala.1986); *Treadwell Ford, Inc. v. Campbell*, 485 So.2d 312, 313 (Ala.1986), *appeal dismissed*,486 U.S. 1028, 108 S.Ct. 2007, 100 L.Ed.2d 596 (1988)."

682 So.2d at 407. Ultimately, we stated:

> "[The plaintiff]'s heart valve has not failed. Instead, it has been working properly and as intended by its manufacturer.... Although the parties see different theories of this case—[the plaintiff] relying upon Alabama fraud law, while [the manufacturer] argues in the context of product liability law—we conclude that the answer to the certified question, whether it is couched in terms of fraud law or in terms of product liability law, must be that [the plaintiff] does not now have a cause of action for damages, because the valve has not failed."

682 So.2d at 408. *Farsian* is distinguishable. This Court's holding there was that, under either a fraud theory or a products-liability theory, the plaintiff did not have a valid cause of action because fear that the valve could fail in the future was not, without more, a legal injury sufficient to support his claim. In the present case, the Weekses are arguing that Wyeth fraudulently misrepresented or suppressed facts to Danny's physician regarding the dangers of the long-term use of Reglan and that, as a result, Danny was injured. This is not a claim that the drug ingested by Danny was defective; instead, it is a claim that Wyeth fraudulently misrepresented or suppressed information about the manner in which (i.e., the duration) the drug was to be taken. In short, the Weekses' claim is based on what Wyeth said or did not say about Reglan and their assertion that those statements or omissions caused Danny's injuries. *Farsian* does not support a conclusion by this Court that the Weekses' claim is in substance a products-liability claim.

***5** [5] We note that Alabama's Pharmacy Act, § 34–23–1 et seq., Ala.Code 1975, permits a pharmacist to select in place of a brand-name drug a less expensive drug product that is the pharmaceutical and therapeutical equivalent of the brand-name drug and that contains the same active ingredient or ingredients and is the same dosage-form strength, unless the prescribing physician indicates otherwise on the prescription. § 34–23–8, Ala.Code 1975. In the present case, it appears that Danny's prescription did not prohibit the pharmacist from substituting a generic drug for the brand-name drug. "Currently all states have some form of generic substitution law."*PLIVA, Inc. v. Mensing*, 564 U.S. ——, ——, 131 S.Ct. 2567, 2583, 180 L.Ed.2d 580 (2011)(Sotomayor, J., dissenting). That a pharmacist acted under § 34–23–8 and gave Danny a generic drug does not preclude Danny's ability to assert a fraudulent-misrepresentation claim against the brand-name manufacturer of the drug. Additionally, many insurance plans are structured to promote the use of generic drugs. *PLIVA*, 564 U.S. at —— n. 2, 131 S.Ct. at 2584 n. 2. We now turn to the federal laws governing prescription drugs.

Prescription drugs are unique because of the extensive federal regulation of that product by the Food and Drug Administration ("the FDA")."Congress has established a comprehensive regulatory scheme, administered by the FDA, to control the design and distribution of prescription drugs."*Blackmon v. American Home Prods. Corp.*, 328 F.Supp.2d 659, 665 (S.D.Tex.2004)(citing 21 U.S.C. §§ 301–393). The FDA has the ultimate authority to determine whether a new prescription drug is safe and effective for use. 21 U.S.C. §§ 355(a) and (d) (prohibiting the distribution of a new drug without FDA approval of a new-drug application showing the drug to be safe and effective). The approval process begins with an

investigational new-drug application ("IND") submitted to the FDA, which includes information about the chemistry, manufacturing, pharmacology, and toxicology of the drug. See 21 U.S.C. § 355(b); 21 C.F.R. § 312.21. The IND also includes pre-clinical data (animal pharmacology and toxicology), and protocols for human testing must be detailed.[4]

After clinical trials on humans have been completed, the manufacturer may submit a new-drug application ("NDA") to the FDA. The manufacturer must present "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling."21 U.S.C. § 355(d)(5). The NDA shall include: (1) reports of the clinical trials and testing done to determine the safety and effectiveness of the drug; (2) the complete ingredients or components of the drug; (3) the composition of the drug; (4) a complete description of the manufacturing, processing, and packaging methods and controls; (5) samples of the drug and its components (if requested); and (6) samples of the proposed labeling. 21 U.S.C. § 355(b)(1). The NDA also must disclose all the investigators who worked in clinical trials of the drug, as well as their reports. Also, an NDA must include the patent number and expiration dates for any patents related to or impacted by the drug. 21 U.S.C. § 355(b)(1). The patent is generally good for 20 years, giving the manufacturer (drug developer) the exclusive right to make and sell the drug during that period. 35 U.S.C. § 154(a)(2). The manufacturer make seek a five-year extension of the patent under 35 U.S.C. § 156(g)(6)(A).

***6** When the patent on a brand-name drug expires, generic manufacturers may seek to replicate a generic version. Generic versions of brand-name drugs contain the same active ingredient as the brand-name original. *United States v. Generix Drug Corp.*, 460 U.S. 453, 103 S.Ct. 1298, 75 L.Ed.2d 198 (1983). To expedite the approval process for generic drugs in order to bring prescription-drug costs down while at the same time preserving patent protections for brand-name drugs, Congress adopted the Drug Price Competition and Patent Term Restoration Act of 1984. 21 U.S.C. § 355. This Act, also known as the Hatch–Waxman Act, provides for an abbreviated new-drug-application ("ANDA") process for the approval of generic versions of brand-name drugs. The ANDA relies on the FDA's previous determination that the brand-name drug is safe and effective. See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 675, 110 S.Ct. 2683, 110 L.Ed.2d 605 (1990)("The ANDA applicant can substitute bioequivalence data for the extensive animal and human studies of safety and effectiveness that must accompany a full new drug application."). This allows an applicant for a generic version of a drug to avoid the costly and time-consuming process associated with an NDA,[5] which allows the dissemination of low-cost generic drugs. See H.R.Rep. No. 98–857 (Part I) at 14 (June 21, 1984). A generic manufacturer is not entitled to all data in the master file controlled by the FDA because some data may constitute trade secrets belonging to the brand-name manufacturer. 21 C.F.R. § 314.430. At the same time, Congress sought to protect brand-name manufacturers whose patent rights could be threatened by the marketing of generic versions of their patented innovations. See *American Bioscience, Inc. v. Thompson*, 243 F.3d 579, 580 (D.C.Cir.2001); *Purepac Pharm. Co. v. Thompson*, 238 F.Supp.2d 191 (D.D.C.2002).

Brand-name manufacturers have a duty to supply the FDA with "postmarketing reports," which include reports of any serious and unexpected adverse reactions suffered by a user of a drug. 21 C.F.R. § 314.80. The brand-name manufacturer must also submit annual reports to the FDA on significant information, including information that might affect the safety, effectiveness, or labeling of the product. 21 C.F.R. § 314.81. A generic manufacturer is likewise required to submit these reports to the FDA. 21 C.F.R. § 314.98. However, brand-name manufacturers and generic manufacturers have different federal drug-labeling responsibilities.

> "A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. See, *e.g.*,21 U.S.C. §§ 355(b)(1), (d); *Wyeth [v. Levine*, 555 U.S. 555], 570–571 [(2009)]. A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's. See, *e.g.*,§ 355(j)(2)(A)(v); § 355(j)(4)(G); 21 CFR §§ 314.94(a)(8), 314.127(a)(7)."

PLIVA, 564 U.S. at ——, 131 S.Ct. at 2574. "Drug labels are subject to change. New risks may become apparent only after the drug has been used more widely and for longer periods."*Mensing v. Wyeth, Inc.*, 588 F.3d 603, 606 (8th Cir.2009), reversed on other grounds, *PLIVA*, supra.Under the "Changes Being Effected" or "CBE" rule, a brand-name manufacturer, upon discovering a clinically significant hazard, may modify its label to "add or strengthen a contraindication, warning, precaution, or adverse reaction" without FDA approval. 21 C.F.R. §

314.70(c)(6)(iii)(A). Ultimately, the FDA will review any CBE modification to a label. 21 C.F.R. § 314.70(c)(7). If the FDA rejects the change, it may order the manufacturer to cease distribution of the drug with the revised label. 21 C.F.R. § 314.70(c)(7).

***7** [6] A "label" is defined as "a display of written, printed, or graphic matter upon the immediate container of any article...."21 U.S.C. § 321(k)." '[L]abeling' means all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article."21 U.S.C. § 321(m). The FDA interprets "labeling" broadly, to include:

> "Brochures, booklets, mailing pieces, file cards, bulletins, calendars, price lists, catalogs, house organs, letters, motion picture films, film strips, lantern slides, sound recordings, exhibits, literature, and reprints and similar pieces of printed, audio, or visual matter descriptive of a drug and references published (for example, the 'Physicians Desk Reference') for use by medical practitioners, pharmacists, or nurses, containing drug information supplied by the manufacturer, packer, or distributor of the drug...."

21 C.F.R. § 202.1(1)(2). The FDA includes in its interpretation of labeling "Dear Doctor" letters, *PLIVA*, 564 U.S. at ——, 131 S.Ct. at 2576, which are letters drug manufacturers send to health-care providers informing them of critical newly discovered risks or side effects of a medication.

[7] [8] [9] The FDA has determined that a generic manufacturer cannot unilaterally strengthen a warning label for a generic drug or send a "Dear Doctor" letter under the CBE rule because doing so would violate the statutes and regulations requiring the label of a generic drug to match the brand-name manufacturer's label. *PLIVA*, 564 U.S. at ——, 131 S.Ct. at 2575.

> "Federal regulations applicable to generic drug manufacturers directly conflict with, and thus preempt, state laws that hold generic drug manufacturers liable for inadequate warning labels on their products.*Mensing*, 131 S.Ct. at 2578. Under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., a manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate. 21 U.S.C. § 355(b)(1). By contrast, under the Drug Price Competition and Patent Term Restoration Act, known as the Hatch–Waxman Amendments, generic drug formulations can gain FDA approval by showing bioequivalence to a reference-listed drug that has already been approved by the FDA. 21 U.S.C. § 355(j)(2)(A). A generic drug application must also show that 'the labeling proposed for the new drug is the same as the labeling approved for the listed drug.'21 U.S.C. § 355(j)(2)(A)(v).*Therefore, rather than a duty to warn, 'generic manufacturers have an ongoing federal duty of sameness' regarding their warning labels. Mensing,* 131 S.Ct. at 2574. Under the same rules, *generic drug manufacturers may not issue additional warnings through Dear Doctor letters, nor may they imply in any way that there is a therapeutic difference between their product and the name-brand drug.Id.* at 2576."

***8** *Phelps v. Wyeth, Inc.*, 857 F.Supp.2d 1114, 1133 (D.Or.2012) (emphasis added). According to the FDA, if a generic manufacturer believes that stronger warnings are needed, then the manufacturer is required to propose such changes to the FDA, and, if the FDA agrees that such changes are necessary, the FDA will work with the brand-name manufacturer to create a new label for both the brand-name and generic drug. *PLIVA*, 564 U.S. at ——, 131 S.Ct. at 2576.

The Supreme Court, in two cases, has addressed the extent to which manufacturers may change their labels after FDA approval. We note that, because of the extensive federal regulations, both the manufacturers of brand-name drugs and generic drugs in those cases argued that the federal regulations preempted state-law claims. In *Wyeth v. Levine*, 555 U.S. 555, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009), the plaintiff developed gangrene and her forearm had to be amputated when a physician's assistant injected her artery with the anti-nausea drug Phenergan by using the "IV push" method of intravenous injection. She sued Wyeth, the manufacturer of Phenergan, for failing to provide an adequate warning about the different risks involved with the various methods of administering the drug. She relied on common-law negligence and strict-liability theories. A jury found that Wyeth had failed to provide an adequate warning about the risks involved when Phenergan is administered by the IV push method. On appeal, Wyeth argued that the plaintiff's failure-to-warn claims were preempted by federal regulations regarding drug labeling because it was impossible for a manufacturer to comply with both state laws and federal-labeling obligations. Wyeth also argued that recognition of state-law suits would undermine Congress's intent to entrust labeling to

the expertise of the FDA. The Supreme Court rejected both contentions and held that there was no preemption. The Supreme Court concluded that Wyeth failed to demonstrate that it was impossible for it to comply with both federal and state requirements, and it noted that state-law claims are an important complement to the FDA's regulation of prescription drugs. The Supreme Court stated:

> "In keeping with Congress' decision not to pre-empt common-law tort suits, it appears that the FDA traditionally regarded state law as a complementary form of drug regulation. The FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge. State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. Failure-to-warn actions, in particular, lend force to the [Federal Food, Drug, and Cosmetic Act]'s premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times. Thus, the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation."

***9** 555 U.S. at 578–79, 129 S.Ct. 1187 (footnote omitted).

PLIVA, supra, also involved a preemption claim regarding labels, but the manufacturer there produced the generic version of a brand-name drug. "The question presented [was] whether federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, these state-law claims."564 U.S. at ——, 131 S.Ct. at 2572. The FDA had issued a labeling requirement regarding Reglan, the brand name of metoclopramide, the generic drug at issue in the present case. The plaintiffs in *PLIVA* were prescribed Reglan but received the generic form of the drug, which contained the same labeling information the FDA had approved for the brand-name drug. According to the FDA, 57 Fed.Reg. 17961 (1992) requires a generic-drug manufacturer's labeling to be the same as the brand-name-drug manufacturer's labeling because the brand-name drug is the basis for the FDA's approval of the generic drug. 564 U.S. at ——, 131 S.Ct. at 2575. By 2009, the FDA had ordered a "black box" warning for Reglan concerning the dangers associated with its long-term use. The plaintiffs had suffered severe neurological reactions from taking the generic form of the drug and had brought state-law tort claims against the manufacturers of the generic form of the drug for failing to warn them of such danger. The basis of the plaintiffs' claims was that the warning labels for the generic drug were inadequate and that the generic manufacturers had a duty to strengthen their warning labels under the FDA's CBE process. 564 U.S. at ——, 131 S.Ct. at 2575. The Supreme Court found that the FDA's federal-labeling requirement preempted the plaintiffs' state-law claims against the manufacturers of the generic drug because it would have been impossible for the generic manufacturers to change their warning labels without violating the federal requirement that the warning on a generic drug match the warning on its brand-name counterpart.

> "[B]rand-name and generic drug manufacturers have different federal drug labeling duties. A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. See, *e.g.*,21 U.S.C. §§ 355(b)(1), (d); *Wyeth [v. Levine]*, [555 U.S. 555] at 570–571, 129 S.Ct. 1187 [(2009)]. A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's. See, *e.g.*,§ 355(j)(2)(A)(v); § 355(j)(4)(G); 21 C.F.R. §§ 314.94(a)(8), 314.127(a)(7)."

564 U.S. at ——, 131 S.Ct. at 2574. The Supreme Court held that because the FDA prevented the generic manufacturers from independently changing the safety label on their generic drugs, "it was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal law duty to keep the label the same."564 U.S. at ——, 131 S.Ct. at 2578.

The Supreme Court recognized in *PLIVA* the seeming contradiction in preempting claims against a generic manufacturer in *PLIVA* but allowing state-law tort claims in *Wyeth:*

> ***10** "We recognize that from the perspective of [the plaintiffs], finding pre-emption here but not in *Wyeth* makes little sense. Had [the plaintiffs] taken Reglan, the brand-name drug prescribed by their doctors, *Wyeth* would control and their lawsuits would not be pre-empted. But because pharmacists, acting in full accord with state law, substituted generic metoclopramide instead, federal law pre-empts these lawsuits. See, *e.g.*,Minn.Stat. § 151.21 (2010)

(describing when pharmacists may substitute generic drugs); La.Rev.Stat. Ann. § 37:1241(A)(17) (West 2007) (same). We acknowledge the unfortunate hand that federal drug regulation has dealt [the plaintiffs] and others similarly situated.[9]

"But 'it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre.'*Cuomo v. Clearing House Assn., L.L.C.*, 557 U.S. 519, 556, 129 S.Ct. 2710, 174 L.Ed.2d 464 (2009) (Thomas, J., concurring in part and dissenting in part) (internal quotation marks and brackets omitted). It is beyond dispute that the federal statutes and regulations that apply to brand name manufacturers are meaningfully different than those that apply to generic drug manufacturers. Indeed, it is the special, and different, regulation of generic drugs that allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public. But different federal statutes and regulations may, as here, lead to different pre-emption results. We will not distort the Supremacy Clause in order to create similar pre-emption across a dissimilar statutory scheme. As always, Congress and the FDA retain the authority to change the law and regulations if they so desire.

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" [9]That said, the dissent overstates what it characterizes as the 'many absurd consequences' of our holding. *Post,* [131 S.Ct.] at 2592. First, the FDA informs us that '[a]s a practical matter, genuinely new information about drugs in long use (as generic drugs typically are) appears infrequently.'U.S. Brief 34–35. That is because patent protections ordinarily prevent generic drugs from arriving on the market for a number of years after the brand-name drug appears. Indeed, situations like the one alleged here are apparently so rare that the FDA has no 'formal regulation' establishing generic drug manufacturers' duty to initiate a label change, nor does it have any regulation setting out that label-change process. *Id.*, at 20–21. Second, the dissent admits that, even under its approach, generic drug manufacturers could establish pre-emption in a number of scenarios. *Post,* [131 S.Ct.] at 2588–2589."

564 U.S. at ——, 131 S.Ct. at 2581–82.

As noted in the facts set out in the certified question, other federal courts applying Alabama law have held that Alabama law does not allow a person who consumed a generic version of a brand-name drug to sue the brand-name manufacturer based on fraudulent misrepresentation. In *Mosley v. Wyeth, Inc.*, 719 F.Supp.2d 1340 (S.D.Ala.2010), the plaintiffs did not ingest Reglan but took a generic equivalent manufactured by a generic manufacturer. They sued the brand-name manufacturers of Reglan alleging, among other things, negligent and fraudulent misrepresentation regarding the warnings contained in the labels the plaintiffs argued the brand-name manufacturers knew would be relied upon by generic manufacturers in generating the warning labels for the generic version of the drug. The federal court held that the plaintiffs could not rely on any allegedly negligent misrepresentations made by the brand-name manufacturers to support their claim of negligent misrepresentation because the brand-name manufacturers did not owe a duty to the plaintiffs, who had ingested a generic version. The court also stated that the plaintiffs' claim of negligent misrepresentation should fail because the brand-name manufacturers did not engage in any business transaction with the plaintiffs. With regard to fraudulent misrepresentation, the court held that the plaintiffs failed to present any binding authority for the assertion that a brand-name manufacturer owed a duty to the consumer of a generic version of its product and failed to cite any binding authority for the contention that an injury resulting from consuming a generic drug could be considered to be proximately caused by a brand-name manufacturer's alleged misrepresentation regarding the brand-name version of the generic drug. The court also noted that the fact that federal law allowed a generic manufacturer to streamline the approval process by relying on the initial warning labels provided by the brand-name manufacturers did not create a duty between the brand-name manufacturers and the consumer of the generic version because, after the ANDA process, generic manufacturers become responsible for their own warning labels and any necessary revisions to those labels.

***11** *Mosley* is distinguishable from the present case. The Weekses are not arguing that Wyeth owed them a duty. Instead, they are arguing that Wyeth owed Danny Weeks's physician a duty and that, under the learned-intermediary doctrine, the Weekses are entitled to rely on the representations made to Danny's physician. Also, we note that *Mosley* was issued before the United States Supreme Court in *PLIVA*, supra, expressly found that because it was impossible for the generic manufacturers to comply with both their state-law duty to change the drug label to a safer label adequately warning of the dangers inherent in long-term use and their federal-law duty to keep the label the same as the brand-name manufacturer's label, any state-law claims against a generic manufacturer were preempted. Reliance upon the reasoning in *Mosley* that a generic manufacturer is responsible for its own warning labels and revisions of those labels is unsound.

In *Overton v. Wyeth, Inc.* (No. CA 10–0491–KD–C, March 15, 2011) (S.D.Ala.2011) (not reported in F.Supp.2d), the brand-name manufacturers filed a motion to dismiss the plaintiffs' state-law claims of breach of warranty, fraudulent misrepresentation, and negligent misrepresentation where the plaintiffs had ingested the generic versions of the brand-name drug. The plaintiffs argued that the brand-name manufacturers placed false and misleading information in their labels, when they knew the labels would be relied upon by the generic manufacturers in generating their own labels, and that their doing so was a direct and proximate cause of the plaintiffs' injuries. The federal court stated that the dispositive issue on the plaintiffs' misrepresentation claims was whether the brand-name manufacturers owed any duty to plaintiffs who ingested the generic version of their brand-name drug. The federal court held that the plaintiffs presented no evidence indicating that the brand-name manufacturers owed a duty to consumers of the generic version of the drug so that the plaintiffs' injuries could be considered to have been a proximate consequence of a brand-name manufacturers' alleged misrepresentation regarding the brand-name drug. The court noted that FDA regulations could not provide the requisite duty element because federal law allows a generic manufacturer to streamline the approval process by relying on the initial warning labels provided by the brand-name manufacturer, but that the generic manufacturer still had the burden of showing that its warning label adequately described the risk associated with the drug. "In other words, after the initial approval (ANDA approval), the generic manufacturers become responsible for their own warning labels and any necessary revisions."Note 9. *Overton* was issued before the Supreme Court decided *PLIVA.*Accordingly, the federal court's conclusion in *Overton* that a generic manufacturer becomes responsible for its own warning label after the ANDA process is incorrect.

***12** In *Simpson v. Wyeth, Inc.* (No. 7:10–cv–01771–HGD, December 9, 2010) (N.D.Ala.2010) (not reported in F.Supp.2d), the federal court held that the plaintiffs, who had ingested only the generic version of Reglan, could not recover for the alleged fraudulent misrepresentations made to the plaintiffs' doctor by the manufacturers of Reglan. The brand-name manufacturers argued that, because they did not manufacture the product the plaintiffs had ingested and that allegedly had caused their injuries, the brand-name manufacturers could not be held liable. The plaintiffs alleged that their claim against the brand-name manufacturers was based on the damage caused by the product as a result of the brand-name manufacturers' misinformation to the prescribing doctors, and the plaintiffs argued that they could recover from the brand-name manufacturers even though they were third parties to the alleged deceit or concealment because, they argued, the deceit and concealment perpetrated against the plaintiffs' prescribing doctors proximately caused their damage. In support of their argument, the *Simpson* plaintiffs relied on *Delta Health Group, Inc. v. Stafford,* 887 So.2d 887 (Ala.2004), which held that in certain circumstances a plaintiff may properly state a fraud claim even though the defendant's false representation is made to a third party, rather than to the plaintiff. In discussing *Delta Health*, the federal court noted that *Delta Health* went on to hold that a plaintiff must establish that he or she relied on the misrepresentation.

The federal court in *Simpson* stated that the problem with the plaintiffs' reliance argument was that Alabama courts have repeatedly rejected a theory of liability when the plaintiffs have attempted to hold a brand-name manufacturer responsible for damage caused by a generic brand of its drug, citing *Mosley*, supra.The federal court also relied on the fact that the FDA regulation did not require a brand-name manufacturer to ensure that the label of the generic version is accurate, citing *Swicegood v. PLIVA, Inc.*, 543 F.Supp.2d 1351 (N.D.Ga.2008)."Thus, it is the duty of the generic drug manufacturer to correctly advise a physician using its product of any associated risks, not the brand name manufacturer."*Simpson.*

The federal court in *Simpson* went on to address the learned-intermediary doctrine:

> "Likewise, '[u]nder the learned intermediary doctrine, a manufacturer's duty to warn is limited to an obligation to advise a prescribing physician of any potential dangers that may result from the use of *its product.'Walls v. [Alpharma] USPD, [Inc.],* 887 So.2d [881,] 883 [(Ala.2004)]. Thus, the duty to warn of risks related to the use of a drug is owed to the prescribing physician by the drug manufacturer, not some other manufacturer of the same or a similar product. As a matter of law, the manufacturers of Reglan have no duty to communicate any information regarding the risks of taking this product to anyone other than their own customers."

***13** Like *Mosley* and *Overton*, *Simpson* was issued before *PLIVA* was decided, and the federal court's conclusion in *Simpson*—that generic manufacturers have their own duty to correctly advise a physician of risks associated with the generic drug regardless of the fact that a generic label is required to be the same as the brand-name label—is questionable. Also, the plaintiffs in *Simpson* argued that they should be allowed to recover from the brand-name manufacturers even though they were third parties to the

alleged fraud perpetrated by those manufacturers upon the plaintiffs' prescribing physicians. The *Simpson* court stated that, even if the plaintiffs, under the learned-intermediary doctrine, could prove that their physicians had relied upon the brand-name manufacturer's warning, the plaintiffs still had to demonstrate that the brand-name manufacturer owed the plaintiffs a duty before the brand-name manufacturer could be liable.

We recognize that other jurisdictions,[6] primarily relying on *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994), have concluded that a brand-name manufacturer does not owe a duty to users of the generic version of the prescription drug to warn those users of the dangers associated with the drug.[7]In *Foster*, the plaintiffs' daughter died as a result of taking the generic form of Phenergan, a brand-name drug. They sued the brand-name manufacturer of Phenergan, alleging negligent misrepresentation and strict liability. The federal district court dismissed the strict-liability claim because the brand-name manufacturer had not manufactured the generic version taken by the daughter. However, the court allowed the negligent-misrepresentation claim to proceed. The brand-name manufacturer appealed. The federal appeals court noted that, under Maryland law, a plaintiff had to prove that the product in question was defective, attribute that defect to the seller of the product, and prove that there was a causal relationship between the defect and the plaintiff's injury. The federal appeals court stated that the plaintiffs were attempting to hold the brand-name manufacturer liable for injuries caused by another manufacturer's product and that Maryland courts would reject an effort to circumvent the necessity that a defendant be shown to have manufactured the product that caused the injury before the defendant could be held liable for such injury. The court held that the brand-name manufacturer did not owe a duty of care to the plaintiffs, even though the plaintiffs alleged that it was foreseeable to the brand-name manufacturer of Phenergan that statements contained in its label for the drug could result in injury to a user of a generic version of the drug. The court stated:

> "We do not accept the assertion that a generic manufacturer is not responsible for negligent misrepresentations on its product labels if it did not initially formulate the warnings and representations itself. When a generic manufacturer adopts a name brand manufacturer's warnings and representations without independent investigation, it does so at the risk that such warnings and representations may be flawed. In cases involving products alleged to be defective due to inadequate warnings, 'the manufacturer is held to the knowledge and skill of an expert.... The manufacturer's status as expert means that at a minimum he must keep abreast of scientific knowledge, discoveries, and advances and is presumed to know what is imparted thereby.'*Owens–Illinois v. Zenobia*, 325 Md. 420, 601 A.2d 633, 639 (Md.1992) (quoting *Borel v. Fibreboard Paper Prods. Corp.*, 493 F.2d 1076, 1098 (5th Cir.1973), *cert. denied*,419 U.S. 869, 95 S.Ct. 127, 42 L.Ed.2d 107 (1974)). The same principle applies in the instant case; as an expert, a manufacturer of generic products is responsible for the accuracy of labels placed on its products. Although generic manufacturers must include the same labeling information as the equivalent name brand drug, they are also permitted to add or strengthen warnings and delete misleading statements on labels, even without prior FDA approval. 21 C.F.R. § 314.70 (1993). The statutory scheme governing premarketing approval for drugs simply does not evidence Congressional intent to insulate generic drug manufacturers from liability for misrepresentations made regarding their products, or to otherwise alter state products liability law. Manufacturers of generic drugs, like all other manufacturers, are responsible for the representations they make regarding their products.
>
> ***14** "We also reject the contention that a name brand manufacturer's statements regarding its drug can serve as the basis for liability for injuries caused by another manufacturer's drug. Name brand manufacturers undertake the expense of developing pioneer drugs, performing the studies necessary to obtain premarketing approval, and formulating labeling information. Generic manufacturers avoid these expenses by duplicating successful pioneer drugs and their labels. Name brand advertising benefits generic competitors because generics are generally sold as substitutes for name brand drugs, so the more a name brand drug is prescribed, the more potential sales exist for its generic equivalents. There is no legal precedent for using a name brand manufacturer's statements about its own product as a basis for liability for injuries caused by other manufacturers' products, over whose production the name brand manufacturer had no control. This would be especially unfair when, as here, the generic manufacturer reaps the benefits of the name brand manufacturer's statements by copying its labels and riding on the coattails of its advertising. The premarketing approval scheme Congress established for generic equivalents of previously approved drugs cannot be construed to create liability of a name brand manufacturer when another manufacturer's drug has been consumed."

Foster, 29 F.3d at 169–70.

The plaintiffs in *Foster* argued that the brand-name manufacturers owed a duty because it was foreseeable that misrepresentations regarding Phenergan could result in personal injury to the users of the generic equivalents of Phenergan. The *Foster* court concluded that to impose duty in that case would be to stretch the concept of foreseeability too far. "The duty required for the tort of negligent misrepresentation arises when there is 'such a relation that one party has the right to rely for information upon the other, and the other giving information owes a duty to give it with care,' " and the court concluded that no such relationship existed between the plaintiff who was injured by a product that was not manufactured by the brand-name manufacturer. 29 F.3d at 171 (quoting *Weisman v. Connors*, 312 Md. 428, 443–44, 540 A.2d 783, 790 (1988)).

A few courts have held otherwise. In *Conte v. Wyeth, Inc.*, 168 Cal.App.4th 89, 85 Cal.Rptr.3d 299 (2008), the California Court of Appeals, applying state negligence law, held as a matter of first impression that a manufacturer of a brand-name drug may be held liable for injuries suffered by a consumer who purchased a generic form of the drug if the consumer's injuries were foreseeably caused by the negligence of or an intentional misrepresentation by the brand-name manufacturer that developed the drug. Conte, the plaintiff in that case, sued the brand-name manufacturer and three generic manufacturers of Reglan and its generic version, metoclopramide, alleging that her use of metoclopramide over a four-year period caused her to develop tardive dyskinesia. Conte had ingested only the generic drug. "The crux of Conte's claims against all of the drug company defendants [was] that she was injuriously overexposed to metoclopramide due to their dissemination of false, misleading and/or incomplete warnings about the drug's side effect."168 Cal.App.4th at 95, 85 Cal.Rptr.3d at 305. The trial court entered a summary judgment for all the defendant drug manufacturers, and Conte appealed. The California appellate court reversed the summary judgment in favor of the brand-name manufacturer after concluding that Conte had presented a material factual dispute as to whether her doctor had in fact relied on information disseminated by the brand-name manufacturer of Reglan. Specifically, the appellate court held that the brand-name manufacturer knew or should have known "that a significant number of patients whose doctors rely on its product information for Reglan are likely to have generic metoclopramide prescribed or dispensed to them" and that the brand-name manufacturer's "duty of care in disseminating product information extends to those patients who are injured by generic metoclopramide as a result of prescriptions written in reliance on [the brand-name manufacturer's] product information for Reglan."168 Cal.App.4th at 107, 85 Cal.Rptr.3d at 315. The appellate court affirmed the summary judgment in favor of each of the three generic manufacturers on the ground that Conte had conceded on appeal that there was no evidence indicating that the generic manufacturers had disseminated any information concerning their generic product.

***15** In *Kellogg v. Wyeth*, 762 F.Supp.2d 694 (D.Vt.2010), the Vermont federal district court held that a brand-name manufacturer of a drug has a duty to use reasonable care to avoid causing injury to consumers who have been prescribed the generic bioequivalent of its drug. Kellogg, the plaintiff in that case, sued the brand-name manufacturer and generic manufacturers of metoclopramide, alleging that her long-term ingestion of metoclopramide caused her to develop tardive dyskinesia; Kellogg had ingested only the generic drug. The crux of Kellogg's argument was that all the defendant manufacturers were liable because, she argued, they failed to adequately warn her doctors about the risks associated with the long-term use of metoclopramide. Both the brand-name manufacturer and each of the generic manufacturers filed a motion for a summary judgment on Kellogg's failure-to-warn claim; the federal district court denied the motions. The court held that, because all the parties agreed that the defendant drug manufacturers owed a duty to provide adequate warning to Kellogg's prescribing physicians, a jury question existed as to whether the defendant drug manufacturers had provided accurate and adequate warnings. The federal district court further held that the defendant drug manufacturers were not entitled to summary judgments for lack of a triable issue on proximate cause. Specifically, the court stated that "[a] reasonable jury could conclude that inadequate, misleading and inaccurate information provided by the [defendant drug manufacturers] was a proximate cause of [Kellogg's] injury." 762 F.Supp.2d at 702. The federal district court finally denied the summary-judgment motion filed by the brand-name manufacturer on Kellogg's negligent-misrepresentation, fraud, and fraud-by-concealment claims in which Kellogg alleged that the brand-name manufacturer of Reglan was liable for failing to use due care in disseminating information about the drug to physicians, thereby causing the physicians to over-prescribe metoclopramide to her. The brand-name manufacturer agreed that it had a duty to provide adequate warnings about Reglan to physicians. However, it contended that it owed no duty to a doctor who prescribes Reglan if the pharmacy fills the doctor's prescription with a generic brand of the drug. Applying Vermont's negligence law, the federal district court noted that "a brand-name manufacturer owes a duty to use

reasonable care to avoid causing injury to consumers of the generic bioequivalents of its drugs,"762 F.Supp.2d at 706, because "it is reasonably foreseeable that a physician will rely upon a brand name manufacturer's representations—or the absence of representations—about the risk of side effects of its drug, when deciding to prescribe the drug for a patient, regardless of whether the pharmacist fills the prescription with a generic form of the drug."762 F.Supp.2d at 709. The federal district court therefore held that Kellogg had presented triable issues of fact regarding whether "her doctors relied on inaccurate and misleading information—or the absence of accurate information—from [the brand-name manufacturer] concerning the risks and effects of long-term use of [metoclopramide]."762 F.Supp.2d at 710.

***16** In looking at the reasoning in *Foster* and *Conte*, we note that the *Foster* court relied on the finding that a generic manufacturer of a prescription drug is responsible for the accuracy of labels placed on its product. *Foster* was issued before the Supreme Court decided *PLIVA*, in which it held that a generic manufacturer's label must be identical to the brand-name label and that a generic manufacturer cannot unilaterally change its label to update a warning. The *Foster* court's finding that manufacturers of generic drugs are responsible for the representations they make in their labeling regarding their products is flawed based on the "sameness" requirement subsequently discussed in *PLIVA*.

Moreover, the analysis in *Foster* confuses strict liability and tort law. The *Foster* court stated that there is "[n]o legal precedent for using a name brand manufacturer's statements about its own product as a basis for liability for injuries caused by other manufacturers' products, over whose production the name brand manufacturer had no control."29 F.3d at 170. If a plaintiff brought a strict-liability claim and the issue was one of a defect in production of the product, then the *Foster* court's reasoning would be sound. Certainly, a manufacturer will not be held liable for another manufacturer's production, design, or manufacturing defect. However, the *Foster* court's reasoning that a brand-name manufacturer does not owe a duty to persons taking the generic version of their drug *because* the brand-name manufacturer did not manufacture that drug is flawed when the cause of action relates to the warnings contained in the labeling relating to the drug and sound in tort. In *Foster*, the plaintiffs alleged that it was the inadequate warning that caused their daughter's death, not how the drug itself was produced. Because a warning label is not a part of the manufacturing process, we do not agree that the fact that a brand-name manufacturer did not produce the version of the drug ingested by the plaintiff bars the plaintiff's tort action when the plaintiff is arguing that he or she was injured by a failure to warn.

[10] We recognize that the holding in *PLIVA* did not address foreseeability as the *Foster* court did. However, the Supreme Court concluded in *PLIVA* that the labeling for a generic drug is required by federal regulations to be the same as the labeling for the brand-name drug. Therefore, an omission or defect in the labeling for the brand-name drug would necessarily be repeated in the generic labeling, foreseeably causing harm to a patient who ingested the generic product. A brand-name manufacturer is well aware of the expiration of its patent and well aware that a generic version of the drug will be made when that patent expires. It is recognized that generic substitutions are allowed in all 50 states. A brand-name manufacturer could reasonably foresee that a physician prescribing a brand-name drug (or a generic drug) to a patient would rely on the warning drafted by the brand-name manufacturer even if the patient ultimately consumed the generic version of the drug.

***17** We now turn to the issue whether Wyeth owed a duty to the Weekses as third parties to the alleged fraud in failing to adequately warn of the risks of Reglan in its labeling. The Weekses rely on *Delta Health Group, Inc. v. Stafford*, supra, which involved an alleged misrepresentation made to a third party. Tim Stafford and Lana Stafford alleged that Delta Health Group and its insurer, Lumbermens Mutual Casualty Company, had falsely accused Tim Stafford of pilfering from a nursing home owned by Delta Health building material for use on the Staffords' personal residence. After Delta Health filed a claim with Lumbermens for its alleged loss and assigned its rights to Lumbermens, Lumbermens sued Tim Stafford, alleging conversion. The Staffords then sued Delta Health and Lumbermens, alleging, among other things, fraudulent misrepresentation. This Court held that under limited circumstances a plaintiff may properly state a fraud claim based on a false representation to a third party rather than to the plaintiff. This Court stated:

> "We agree with Stafford that in certain limited circumstances not relevant here a plaintiff may properly state a fraud claim even though the defendant makes a false representation to a third party rather than to the plaintiff. However, we do not read *Thomas [v. Halstead*, 605 So.2d 1181 (Ala.1992),] as excusing a plaintiff from the requirement of establishing his reliance upon that misrepresentation. *Thomas* appears to contemplate that the plaintiff, in fact, has relied on the defendant's misrepresentation, even though the misrepresentation was made to another party. Neither have we located any other authority that purports to

> excuse a plaintiff in a fraud action from establishing the element of reliance.
>
> "In this case, the record is devoid of any evidence tending to establish that Stafford relied to his detriment on any of the alleged misrepresentations made by Delta Health to Lumbermens. For this reason, we conclude that Stafford failed to produce sufficient evidence to create a jury question on each of the elements necessary for his fraud claim. Therefore, the trial court erred in denying Delta Health's motion for a judgment as a matter of law regarding Stafford's fraud claim; that claim should not have been submitted to the jury."

887 So.2d at 899.

Delta Health is not the first time this Court has addressed a fraud claim based on misrepresentations made not to a plaintiff but to a third party. In *Thomas v. Halstead*, 605 So.2d 1181 (Ala.1992), a patient sued his dentist alleging fraud, specifically alleging that the dentist had obtained payment from the patient's insurer for services that were never rendered. The patient had gone to see the dentist, who took several X-rays of his mouth and told him he needed additional dental work. The patient claimed that the dentist was to submit a form to the patient's insurer to determine the insurance coverage. Instead, the dentist submitted a claim for the additional work on the patient's teeth, which had never been done. The patient argued that, even if the misrepresentation was not made directly to him, "a misrepresentation, made to his insurance carrier, which is legally obligated to pay valid claims submitted to it for dental expenses incurred by him, is sufficient to satisfy the misrepresentation element of fraud."605 So.2d at 1184. "While generally '[a] stranger to a transaction ... has no right of action [for fraud],' there is an exception to this general rule: 'If a third person is injured by the deceit, he may recover against the one who made possible the damages to him by practicing the deceit in the first place.'37 C.J.S. *Fraud* § 60, p. 344 (1943), see *Sims v. Tigrett*, 229 Ala. 486, 158 So. 326 (1934)."605 So.2d at 1184.

***18** *Sims v. Tigrett*, 229 Ala. 486, 158 So. 326 (1934), involved deceit in the selling of bonds. This Court stated:

> "But we may observe that if defendant caused the representations to be made, and the public were intended to be thereby induced to act upon them, and plaintiff was within the class of those so contemplated, the action for deceit against defendant may be maintained by plaintiff, though defendant did not sell the bonds to plaintiff, but sold them to another, and he to plaintiff, both in reliance on the truth of the representations. *King v. Livingston Mfg. Co.*, 180 Ala. 118, 126, 60 So. 143 [(1912)]; 26 C.J. 1121, §§ 47, 48."

229 Ala. at 491, 158 So. at 330.

Wyeth argues that *Delta Health* is distinguishable because this Court has never extended third-party fraud beyond the economic realm to claims alleging physical harm. We recognize that *Delta Health*, *Thomas*, and *Sims* did not involve a claim of physical injury. However, physical harm suffered by a consumer of prescription medication would have been reasonably contemplated by a manufacturer who made fraudulent statements on the warning label related to that medication.

Wyeth also argues that this Court has never extended third-party-fraud liability to a defendant who did not manufacture the product about which the plaintiff is complaining. We again note that prescription medication is unlike other consumer products. Unlike "construction machinery," "lawnmowers," or "perfume," which are "used to make work easier or to provide pleasure," a prescription drug "may be necessary to alleviate pain and suffering or to sustain life."*Brown v. Superior Court of San Francisco*, 44 Cal.3d 1049, 1063, 245 Cal.Rptr. 412, 420, 751 P.2d 470, 479 (1988). Prescription medication is heavily regulated by the FDA. It can be obtained only through a health-care provider who can make a determination as to the benefits and risks of a drug for a particular patient. Also, the Weekses' claims are not based on the manufacturing of the product but instead allege that the label—drafted by the brand-name manufacturer and required by federal law to be replicated verbatim on the generic version of the medication—failed to warn. Moreover, the brand-name manufacturer is under a continuing duty to supply the FDA with postmarketing reports of serious injury and can strengthen its warnings on its own accord. *Wyeth v. Levine*, supra; 21 C.F.R. § 201.57(c)(6)(I); 21 C.F.R. § 201.56(a)(2)-(b)(1). In contrast, a generic manufacturer's label must be the same as the brand-name manufacturer's label, and the generic manufacturer cannot unilaterally change its warning label.

[11] [12] We recognize that the plaintiff in *Delta Health* did not succeed in his fraud claim because he failed to present evidence indicating that he relied to his detriment on any of the alleged misrepresentations made by his employer to the employer's insurer. In a fraud case, detrimental reliance is an essential aspect of showing that the injury

suffered was caused by the fraud. "[A] fraud claim fully accrues once any legally cognizable damage has proximately resulted, i.e., once the plaintiff has 'detrimentally' relied on the fraud."*Ex parte Haynes Downard Andra & Jones, LLP*, 924 So.2d 687, 694 (Ala.2005). In the present case, the Weekses have alleged that Danny's physician reasonably relied on the representations made by Wyeth regarding the long-term use of Reglan in prescribing Reglan to Danny. In other words, the Weekses are arguing that if a defendant's misrepresentation to a third party causes the third party to take actions resulting in the plaintiff's injuries, then the factual causation link is satisfied and that, here, a misrepresentation to Danny's physician would directly impact the medical care received by Danny.

***19** [13] [14] In *Stone v. Smith, Kline & French Laboratories*, 447 So.2d 1301 (Ala.1984), this Court adopted the learned-intermediary doctrine in a case addressing whether a manufacturer's duty to warn extends beyond the prescribing physician to the physician's patient who would ultimately use the drugs. The principle behind the learned-intermediary doctrine is that prescribing physicians act as learned intermediaries between a manufacturer of a drug and the consumer/patient and that, therefore, the physician stands in the best position to evaluate a patient's needs and to assess the risks and benefits of a particular course of treatment for the patient. A consumer can obtain a prescription drug only through a physician or other qualified health-care provider. 21 U.S.C. § 353(b)(1). Physicians are trained to understand the highly technical warnings required by the FDA in drug labeling. 21 C.F.R. § 201.56. The learned-intermediary doctrine was established in *Marcus v. Specific Pharmaceuticals*, 191 Misc. 285, 77 N.Y.S.2d 508 (N.Y.Sup.Ct.1948), as an absolute defense for "failure to warn" cases. Mitesh Bansilal Shah, Commentary, *As a Matter of Fact or a Matter of Law: The Learned Intermediary Doctrine in Alabama*, 53 Ala. L.Rev. 1299, 1301 (2002).

> "Prescription drugs are likely to be complex medicines, esoteric in formula and varied in effect. As a medical expert, the prescribing physician can take into account the propensities of the drug, as well as the susceptibilities of his patient. His is a task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a knowledge of both patient and palliative."

Reyes v. Wyeth Labs., 498 F.2d 1264, 1276 (5th Cir.1974).

[15] [16] The learned-intermediary doctrine recognizes the role of the physician as a learned intermediary between a drug manufacturer and a patient. As the United States Court of Appeals for the Eleventh Circuit has explained:

> "In cases involving complex products, such as those in which pharmaceutical companies are selling prescription drugs, the learned intermediary doctrine applies. Under the learned intermediary doctrine, a manufacturer's duty to warn is limited to an obligation to advise the prescribing physician of any potential dangers that may result from the use of its product. This standard is 'an understandable exception to the Restatement's general rule that one who markets goods must warn foreseeable ultimate users of dangers inherent in his products.'As such, we rely on the expertise of the physician intermediary to bridge the gap in special cases where the product and related warning are sufficiently complex so as not to be fully appreciated by the consumer....'[U]nder the "learned intermediary doctrine" the adequacy of [the defendant's] warning is measured by its effect on the physician, ... to whom it owed a duty to warn, and not by its effect on [the consumer].' "

***20** *Toole v. Baxter Healthcare Corp.*, 235 F.3d 1307, 1313–14 (11th Cir.2000) (citations omitted).

[17] [18] A prescription-drug manufacturer fulfills its duty to warn the ultimate users of the risks of its product by providing adequate warnings to the learned intermediaries who prescribe the drug. Once that duty is fulfilled, the manufacturer has no further duty to warn the patient directly. However, if the warning to the learned intermediary is inadequate or misrepresents the risk, the manufacturer remains liable for the injuries sustained by the patient. The patient must show that the manufacturer failed to warn the physician of a risk not otherwise known to the physician and that the failure to warn was the actual and proximate cause of the patient's injury. In short, the patient must show that, but for the false representation made in the warning, the prescribing physician would not have prescribed the medication to his patient.

Wyeth argues that there is no relationship between Wyeth and the Weekses so as to create a duty on Wyeth's part to adequately warn the Weekses and that the simple fact that it may be foreseeable that a physician would rely on Wyeth's representations in its warning label in determining whether a prescription drug originally

manufactured by Wyeth was appropriate for a particular patient did not create a relationship between Wyeth and the patient. Wyeth argues:

> "Here, the brand-name defendants had absolutely no relationship with the Weekses. The Weekses never met with any representative of the brand-name defendants, transacted any business with the brand-name defendants, or did anything else that could have established the necessary relationship. Most significantly, the Weekses concede that Mr. Weeks didn't use the brand-name defendants' products. That concession is fatal. Without some product-use link, the Weekses can't establish a relationship; and without a relationship, they can't prove a duty."

Wyeth's brief, p. 42.

Wyeth's argument completely ignores the nature of prescription medication. The Weekses cannot obtain Reglan or any other prescription medication directly from a prescription-drug manufacturer.[8]The only way for a consumer to obtain a prescription medication is for a physician or other medical professional authorized to write prescriptions (i.e., a learned intermediary) to prescribe the medication to his or her patient. This Court has adopted the learned-intermediary doctrine, which provides that a prescription-drug manufacturer fulfills its duty to warn users of the risk associated with its product by providing adequate warnings to the learned intermediaries who prescribe the drug and that, once that duty is fulfilled, the manufacturer owes no further duty to the ultimate consumer. When the warning to the prescribing health-care professional is inadequate, however, the manufacturer is directly liable to the patient for damage resulting from that failure. The substitution of a generic drug for its brand-name equivalent is not fatal to the Weekses' claim because the Weekses are not claiming that the drug Danny ingested was defective; instead, the Weekses' claim is that Wyeth fraudulently misrepresented or suppressed information concerning the way the drug was to be taken and, as discussed, the FDA mandates that the warning on a generic-drug label be the same as the warning on the brand-name-drug label and only the brand-name manufacturer may make unilateral changes to the label.[9]

***21** In support of its argument regarding lack of a relationship, Wyeth cites *Keck v. Dryvit Systems, Inc.*, 830 So.2d 1 (Ala.2002); *State Farm v. Owen*, 729 So.2d 834 (Ala.1998); *DiBiasi v. Joe Wheeler Electric Membership Corp.*, 988 So.2d 454 (Ala.2008); and *Thompson–Hayward Chemical Co. v. Childress*, 277 Ala. 285, 169 So.2d 305 (1964).*Keck* addressed the question whether faux stucco was a fixture attached to a house or part of the house in order to determine whether the AEMLD applied when the faux stucco failed. Because the faux stucco was not a "product" under the AEMLD, this Court turned to the Uniform Commercial Code to determine if it was a "good" and held that it was not. In short, this Court treated the faux stucco as part of the house, and because the plaintiffs, who were not the first purchasers of the house, purchased the house "as is," they had no claim against the manufacturer of the faux stucco because there was no duty to disclose.

Owen held that an insurer had no duty to disclose that, although premiums on homeowners' insurance were based on the appraisal value of the insured property, the insurer would pay no more than replacement value in the event of a loss. *DiBiasi* involved an electrocution victim who was injured when he grabbed electrical transmission lines hanging over the roof of a house. The utility company that owned the pole to which the lines were attached argued that it owed no duty (the city supplied the electrical power) to the victim, who was inspecting the roof of the house when, among other things, there was no relationship shown between the owner of the utility pole and the victim. The wire that electrocuted the victim was owned by the city. In *Thompson–Hayward*, a case that predates the judicial adoption of the AEMLD, this Court held that the plaintiff's complaint failed to allege that the defendant had manufactured an injurious herbicide or to allege that the defendant sold the herbicide to the plaintiffs.

These cases are easily distinguishable from this case. Here, Wyeth authored the label with its warnings, and the generic manufacturers, as required by FDA regulations, copied that label verbatim. Wyeth continues to treat the Weekses' fraud claim as a products-liability claim where privity is needed.

[19] In *Carter v. Chrysler Corp.*, 743 So.2d 456 (Ala.Civ.App.1998), the Court of Civil Appeals, quoting *Hines v. Riverside Chevrolet–Olds, Inc.*, 655 So.2d 909 (Ala.1994),[10] noted:

> " 'Our case law, however, makes it very clear that in an action alleging suppression of a material fact, *a duty to disclose may be owed to a person with whom one has not had a contractual relationship or other*

dealings....

" 'The extent of a legal duty not to make a false representation or to suppress a material fact informs our analysis of whether two parties have a sufficient relationship on which to base a duty to disclose. In *Colonial Bank v. Ridley & Schweigert*, 551 So.2d 390, 396 (Ala.1989), this Court stated:

***22** " ' "There can be no actionable fraud without a breach of a legal duty owed by the defendant to the plaintiff.

" ' "*There is a duty not to make a false representation to those to whom a defendant intends, for his own purposes, to reach and influence by the representation; to those to whom he has a public duty created by statute or pursuant to a statute; and to those members of a group or class that the defendant has special reason to expect to be influenced by the representation.*W. Prosser, Misrepresentation and Third Persons, 19 Vand. L.Rev. 231, 254 (1966)."'

"655 So.2d at 919–20 (emphasis added, footnote omitted).

"The Court in *Hines* then applied these principles to the particular question of the manufacturer's duty to disclose the repairs to the plaintiffs in the case before it:

" 'It is evident from these principles and our case law that the fact that two parties have had no contractual relationship or other dealings does not preclude the finding of a legal duty not to make a material misrepresentation or to suppress a material fact. The absence of a contractual relationship or other dealings, therefore, likewise does not preclude the finding of a relationship on which to base a duty to disclose. Whether a duty to disclose exists must be determined by examining the particular facts of each case.

" '....'

"655 So.2d at 920."

Carter, 743 So.2d at 461–62 (some emphasis added). Stated again, there is a duty not to make a false representation (1) to those to whom a defendant intends, for his own purposes, to reach and influence by the representation; (2) to those to whom the defendant has a public duty created by statute or pursuant to a statute; and (3) to those members of a group or class that the defendant has special reason to expect will be influenced by the representation.

Clearly, prescription drugs differ from lawnmowers, automobiles, and other products because of the FDA's unprecedented control and regulation of prescription drugs; the FDA has the responsibility of weighing (in terms of extremes) the potential benefit of lifesaving medication against potential severe side effects. Those side effects might not become apparent until after a drug has been on the market, and even then the benefits of the drug may outweigh the risks. Wyeth cannot argue that it owes no duty to the Weekses because it lacks a relationship with them.

Conclusion

[20] We answer the certified question as follows: Under Alabama law, a brand-name-drug company may be held liable for fraud or misrepresentation (by misstatement or omission), based on statements it made in connection with the manufacture of a brand-name prescription drug, by a plaintiff claiming physical injury caused by a generic drug manufactured by a different company. Prescription drugs, unlike other consumer products, are highly regulated by the FDA. Before a prescription drug may be sold to a consumer, a physician or other qualified health-care provider must write a prescription. The United States Supreme Court in *Wyeth v. Levine* recognized that Congress did not preempt common-law tort suits, and it appears that the FDA traditionally regarded state law as a complementary form of drug regulation: The FDA has limited resources to monitor the approximately 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge; state-law tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly and serve a distinct compensatory function that may motivate injured persons to come forward with information. *Wyeth v. Levine*, 555 U.S. at 578–79, 129 S.Ct. 1187.

***23** FDA regulations require that a generic manufacturer's labeling for a prescription drug be exactly the same as the brand-name manufacturer's labeling. The Supreme Court in *PLIVA* held that it would have been impossible for the generic manufacturers to change their warning labels without violating the federal requirement that the warning on a generic drug must match the warning on the brand-name version, preempting failure-to-warn claims against generic manufacturers.

[21] In the context of inadequate warnings by the

brand-name manufacturer placed on a prescription drug manufactured by a generic manufacturer, it is not fundamentally unfair to hold the brand-name manufacturer liable for warnings on a product it did not produce because the manufacturing process is irrelevant to misrepresentation theories based, not on manufacturing defects in the product itself, but on information and warning deficiencies, when those alleged misrepresentations were drafted by the brand-name manufacturer and merely repeated, as allowed by the FDA, by the generic manufacturer.

In answering the question of law presented to us by the federal court, we emphasize the following: We are not turning products-liability law (or tort law for that matter) on its head, nor are we creating a new tort of "innovator liability" as has been suggested. Instead, we are answering a question of law involving a product that, unlike any other product on the market, has unprecedented federal regulation. Nothing in this opinion suggests that a plaintiff can sue Black & Decker for injuries caused by a power tool manufactured by Skil based on labeling or otherwise. The unique relationship between brand-name and generic drugs as a result of federal law and FDA regulations, combined with the learned-intermediary doctrine and the fact that representations regarding prescription drugs are made not to the plaintiff but to a third party, create the sui generis context in which we find prescription medication. Again, the fraud or misrepresentation claim that may be brought under Alabama law against a drug manufacturer based on statements it made in connection with the manufacture of a brand-name prescription drug by a plaintiff claiming physical injury caused by a generic drug manufactured by a different company is premised upon liability not as a result of a defect in the product itself but as a result of statements made by the brand-name manufacturer that Congress, through the FDA, has mandated be the same on the generic version of the brand-name drug.[11]

APPLICATION OVERRULED; OPINION OF JANUARY 11, 2013, WITHDRAWN; OPINION SUBSTITUTED; QUESTION ANSWERED.

STUART, MAIN, WISE, and BRYAN, JJ., concur.

SHAW, J., concurs specially.

MOORE, C.J., and PARKER and MURDOCK, JJ., dissent.

SHAW, Justice (concurring specially).

I concur fully in the Court's answer to the certified question. I write specially to note the following.

First, some preliminary observations:

***24** 1. The certified question is not posed within the context of a defective-product case. See note 13, infra. Our answer to the certified question in no way holds that a manufacturer of a product may be held liable, under general products-liability jurisprudence, for a product manufactured by another.

2. The certified question calls for an explanation of, and our answer applies, current Alabama law. We are not creating new law or doing something novel; we are applying established law to a factual and legal scenario that has never been addressed *by this Court.*Concomitant with that, we discuss Alabama law as it exists, not how some perceive it should exist.

3. Given the nature of the federal government's pervasive regulation of the prescription-drug industry, our answer is extremely narrow in scope and cannot conceivably apply outside that context.

4. No decision of any other jurisdiction addresses the precise question of Alabama law discussed in our answer.[12]

The certified question asks this Court to apply current Alabama law as it relates to fraud.[13]For purposes of examining the purely legal issue presented in this certified question, I believe that we must accept the factual allegations of the plaintiffs, Danny Weeks and Vicki Weeks, as true. Those allegations are summarized as follows: Wyeth produced the brand-name drug Reglan, which is metoclopramide, and, through its "labeling" of the drug, misrepresented or failed to provide important facts to Danny Weeks's doctor about how metoclopramide is to be taken properly.[14]

When Wyeth's ability to produce and sell metoclopramide exclusively lapsed, generic-drug companies became able to manufacture and sell metoclopramide. Those generic-drug companies may have wished to give Danny's doctor different facts or instructions about the use of metoclopramide, but, for all intents and purposes relevant in this case, the federal government will not allow them to do so. Essentially, federal law requires that those generic-drug companies repeat Wyeth's alleged misrepresentations or omissions. Wyeth knew that the generic-drug companies are required to do this; Wyeth knew that its instructions on the use of metoclopramide would be repeated by the generic-drug companies. The federal government has declared that

generic-drug companies cannot be sued if a doctor prescribes and a patient takes metoclopramide manufactured by a generic-drug company in the manner in which Wyeth represented that it should be taken. In other words, the generic-drug companies must repeat Wyeth's purportedly fraudulent conduct and cannot be sued for doing so if Wyeth's misconduct ultimately harms the patient.

In this context, we look to see whether, "[u]nder Alabama law, [Wyeth may] be held liable for fraud or misrepresentation (by misstatement or omission), based on statements it made" about metoclopramide. As discussed below, Alabama law allows a plaintiff to sue a defendant based on the defendant's fraudulent conduct directed to a third person. *A prior relationship between the two parties is not necessary.*Two factors have been the focus of this case: foreseeability and duty. Although a controlling issue in other jurisdictions, I see no dispute as to foreseeability. As even Justice Murdock's dissenting opinion agrees, it is "eminently" foreseeable "that a generic version of a brand-name drug will be consumed in reliance upon labeling disseminated by the brand-name manufacturer for its brand-name drug."[15] —— So.3d at ——.

***25** In cases where fraudulent conduct is directed to third parties, this State's caselaw generally holds that a duty to disclose may be owed to a person with whom the defendant has had no prior dealings, specifically, where there is a "duty" not to make a false representation:

> 1. To those to whom a defendant intends, for his or her own purposes, to reach and influence by the representation;
>
> 2. to those to whom the defendant has a public duty created by statute or pursuant to a statute; and
>
> 3. to those members of a group or class that the defendant has special reason to expect to be influenced by the representation.

Hines v. Riverside Chevrolet–Olds, Inc., 655 So.2d 909, 919–20 (Ala.1994),[16] and *Carter v. Chrysler Corp.*, 743 So.2d 456, 461 (Ala.Civ.App.1998); see also generally *Potter v. First Real Estate Co.*, 844 So.2d 540, 553 (Ala.2002), and *Colonial Bank of Alabama v. Ridley & Schweigert*, 551 So.2d 390, 396 (Ala.1989).

In *Hines*, this Court held that an automobile manufacturer had a duty to disclose to subsequent purchasers of an automobile it had manufactured that the automobile had been repainted, even though the manufacturer had no relationship with the later purchasers, "[b]ecause the [subsequent purchasers] were members of a group or class of persons who [the manufacturer] expected or had special reason to expect would be influenced by its decision not to disclose information...."655 So.2d at 920. Thus, they "had a sufficient relationship on which to base a duty to disclose."*Id.* In *Carter*, an automobile manufacturer repurchased under the Lemon Law an automobile that was allegedly defective. This fact was disclosed to the party to whom the automobile was next sold. The Court of Civil Appeals held, however, that the Lemon Law created a duty to ensure that the fact that the automobile had been repurchased was disclosed to those who would *later* purchase the automobile from the second buyer, even though the manufacturer had no relationship with those later purchasers.

In both *Carter* and *Hines* there was a duty to not misrepresent or omit facts to those with whom the automobile manufacturers never had contact. Although those cases involved products that were actually manufactured by the defendants, the logic behind the creation of the duty has nothing to do with that fact. Here, federal law has created a scheme in which persons who purchased metoclopramide manufactured by generic-drug companies would have to rely on *Wyeth's* representations about metoclopramide. Thus, Wyeth had a "special reason to expect" that purchasers of the generic metoclopramide "would be influenced" by its labeling information because that information—owing to federal law—would be the *only* information purchasers of both brand-name and generic metoclopramide would receive. That the metoclopramide was made by another manufacturer creates no distinction: for purposes of this case, metoclopramide is the same no matter who produced it. *As required by federal law*, Wyeth's alleged misrepresentations or omissions concerning metoclopramide also applied to metoclopramide manufactured by a generic-drug company. What Wyeth allegedly said (or failed to say) in its "labeling" about metoclopramide was intended to "reach and influence" users (through doctors or other health professionals) of metoclopramide, which, at that time, was manufactured only by Wyeth. This labeling, as required by federal law, also reached and influenced purchasers of generic metoclopramide. This federal law gave Wyeth "special reason to expect" that all users of metoclopramide would be influenced by its labeling.

***26** Our answer to this certified question on original submission has generated many responses, some of which expressed valid concerns, while others either shamefully misrepresented our holding or bordered on the hysterical. Our answer, however, is extraordinarily narrow in scope. The posture in which the certified question is asked

(assuming a fraud cause of action), the facts of this case, and the impact of strict federal regulation on the prescription-drug industry drastically confine our holding and wholly remove the facts of this case from situations where parties are allegedly being held liable under general products-liability theories for products they did not make. I cannot see our answer to the certified question as in any way speaking to the applicability of Alabama law outside the narrow context created by federal law in this case.

I must disagree with the implication that our answer is based on a motivation other than stating current Alabama law. Nothing in our answer suggests that this Court is trying to "correct" a "wrong" "with a second 'wrong" or to "correct" "unfairness" created by the federal government. —— So.3d at —— (Murdock, J., dissenting). Although the members of this Court might respectfully disagree as to what Alabama tort law does or should require, our answer does nothing more than apply established Alabama decisions (which have not been challenged) to a difficult and unique factual and legal scenario.

I also respectfully reject the implication that our answer, applying as it does established Alabama tort law providing a remedy for fraudulent conduct, might "create a climate in which trade and business innovation" cannot flourish or that it prevents "Americans [from] work[ing] hard to produce innovative goods and services that have benefited not only themselves, but also their children, their communities, and America as a whole." —— So.3d at —— (Murdock, J., dissenting). Allowing fraudulent or tortious conduct in the marketplace to go unchecked—if that is what has occurred in this case—would not seem to promote this policy. The legal analysis set forth in this Court's answer, in my view, creates no new law, enforces existing law, and epitomizes the kind of judicial restraint that should be expected of an appellate court.

MOORE, Chief Justice (dissenting).

***26** I respectfully dissent because I do not think that this Court should accept a certified question when critical facts are not before the Court.

I was not a member of this Court when the certified question from the United States District Court for the Middle District of Alabama was answered on original submission. However, I note that Danny Weeks and Vicki Weeks, the plaintiffs in the federal case, urged this Court at that time to decline to answer. Weekses' brief on original submission (hereinafter "Weekses' original brief"), at 8–13. One of the grounds urged was that "the answer would not be determinative of the cause, which is the purpose of certification."*Id.* at 13. I believe this suggestion points to the proper resolution of this application for rehearing.

***27** The Alabama rule that provides for answering certified questions from the federal courts reads as follows:

> "When it shall appear to a court of the United States that there are involved in any proceeding before it questions or propositions of law of this State *which are determinative of said cause* and that there are no clear controlling precedents in the decisions of the Supreme Court of this State, such federal court may certify such questions or propositions of law of this State to the Supreme Court of Alabama for instructions concerning such questions or propositions of state law, which certified question the Supreme Court of this State, by written opinion, may answer."

Rule 18(a), Ala. R.App. P. (emphasis added). This Court consented to answer the certified question on October 17, 2011. However, that decision is subject to reconsideration. See *Palmore v. First Unum*, 841 So.2d 233 (Ala.2002) (declining to answer a certified question from a federal court that had erroneously been accepted).

Rule 18(a) allows a federal court to certify to this Court "questions or propositions of law of this State which are determinative of said cause," namely the proceeding pending before the federal court. In support of this requirement, the certifying court stated that " '[t]he question framed ... is "determinative" of this case in the sense that a negative answer would require dismissal of the Weekses' claims against the brand-named defendants....' " —— So.3d at ——. The certifying court's statement omits any mention of whether a positive answer would also be determinative of the outcome of the case. If this Court's answer to the certified question is "no," the Weekses' claims must be dismissed for failure to state a claim. However, an answer of "yes," as proposed by the majority, will not be "determinative of said cause." In that event, the Weekses may proceed with their cause of action for misrepresentation, but the ultimate success of their claims will depend upon facts not before us. For example, if Danny Weeks's prescribing physician did not

rely on the Reglan labeling when prescribing the drug, then the Weekses will have failed to prove causation and their claims will fail. According to the Weekses, neither Danny's prescribing physician nor his other medical providers have yet been deposed. Weekses' original brief, at 3–4.

Additionally, as the Weekses stated in urging this Court to decline to answer the certified question, both Wyeth, Inc., and Schwarz Pharma, Inc., two of the three brand-name defendants,[17] apparently no longer had an interest in the Reglan brand at the time Danny Weeks's physician diagnosed him with tardive dyskinesia in 2009.[18]Wyeth sold its interest in Reglan to Schwarz Pharma on December 27,2001, and ceased manufacturing or selling Reglan after that date. Schwarz Pharma in turn sold its interest in Reglan to another company in February 2008. Weekses' original brief, at 10–12. According to the Weekses, Wyeth and Schwarz Pharma are both raising a federal-preemption defense, arguing that, after selling their interest in Reglan, they lost all ability to change Reglan's labeling. See *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011) (holding that state-law claims of misrepresentation in labeling were preempted by federal law when the defendant had no control over labeling of the product alleged to have injured the plaintiff).

***28** Whether the federal-preemption defense will succeed is unknown, but its presence in the case renders an answer of "yes" to the certified question *in* determinative of the cause. As the Weekses have argued, the certified question "should not be decided because it raises a federal question better addressed by the federal court."Weekses' original brief, at 13. See *Palmore*, 841 So.2d at 235 (declining to answer a nondispositive certified question "lest our answer resemble an opinion on an abstract point of law irrelevant to the underlying case"). See also *Stewart Title Guar. Co. v. Shelby Realty Holdings, LLC*, 83 So.3d 469, 472 (Ala.2011) (holding that the "determinative of said cause" requirement of Rule 18(a) prohibits the Court from answering a certified question that "would necessitate our fashioning a broad rule with the possibility that it would have no application to the particular facts presented"); *Harrison v. Jones*, 880 F.2d 1279, 1283 n. 4 (11th Cir.1989) (refusing to certify a question of law to the Alabama Supreme Court because the question "would not be dispositive" and noting that under Rule 18(a) "questions certified must be determinative").

The problem of factual uncertainty is most likely to occur, as in this case, in the context of a question certified from a federal trial court. Because the question of law before us was certified after the denial of the defendants' motion to dismiss, factual development is still incomplete in the federal case.

> "[W]e think it will be incumbent upon us to respond to questions only when it is apparent from the certification itself that all material facts have been either agreed upon or found by the court and that the case is in such posture in all respects that our decision as to the applicable [state] law will in truth and in fact be 'determinative of the cause' as the statute conferring jurisdiction upon us requires."

In re Richards, 223 A.2d 827, 833 (Me.1966) (construing Me.Rev.Stat. Ann., tit. 4, § 57). In this case, however, the facts have yet to be determined. See *Hanchey v. Steighner*, 549 P.2d 1310, 1310–11 (Wyo.1976) (finding that a certified question from a federal trial court was "premature" when the case was "merely in the pleading stage" and "[i]t does not clearly appear that even if the question were answered, how the answer would be determinative of the cause pending in the federal court").

The United States Court of Appeals for the Fourth Circuit, considering certifying a question of state law to the Maryland Court of Appeals, addressed a situation somewhat like the one currently before this Court. If the state court answered "no" to the question, the case would be over, but if it answered "yes," "further proceedings would still be necessary in a federal tribunal and those proceedings might result in an adjudication which would render the certification and the opinion of the [state] court a futile, academic exercise with respect to final disposition of this case."*Boyter v. Commissioner*, 668 F.2d 1382, 1385 (4th Cir.1981). In those circumstances the Fourth Circuit declined to certify the question of law for determination by the Maryland Court of Appeals "unless and until it appears that the answer is dispositive of the federal litigation or is a necessary and inescapable ruling in the course of the litigation."*Id.* Similarly, in this case, we should decline to answer a question that may likely not be determinative of the federal case and thus fails to conform to the mandate of Rule 18 that creates our jurisdiction to answer such questions.[19]

***29** I also believe that imposing an industry-wide duty on brand-name manufacturers through the procedural mechanism of a certified question is unwise. I would far prefer to address this issue, if necessary, on a complete record following a final judgment in a state trial court that resolved all factual questions.

For the reasons stated above, I believe that this Court's acceptance of the certified question was in error and that we should decline to answer the certified question. *Palmore*.

PARKER, Justice (dissenting).

Congressional legislation and regulations of the Food and Drug Administration have created a maze this Court has to navigate to determine the effect of federal preemption on the bedrock legal principles of this State's jurisprudence. As Justice Murdock so comprehensively demonstrated in his dissenting opinion in this case, our legal principles of duty based on privity, *see e.g.*, *State Farm Fire and Casualty Co. v. Owen*, 729 So.2d 834 (Ala.1998),[20] have not been expressly subsumed by the federal legislation and regulations in this area in regard to a consumer of a generic drug vis-à-vis the originator/manufacturer of the brand-name drug.

This Court's modification of its bedrock legal principles in view of federal legislation and regulations in one area could have grave and unforseen effects in other areas. To guard against this, it is incumbent upon this Court to scrutinize any claim of federal preemption to determine the express wording of the limitations of such preemption.

Nothing in federal legislation or regulations at issue here requires this Court to ignore, modify, or override our bedrock legal principles of duty and privity with regard to the originator of a pharmaceutical drug and a consumer who has not consumed a drug manufactured by the originator of the drug.*PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011), and *Mutual Pharmaceutical Co. v. Bartlett*, —— U.S. ——, 133 S.Ct. 2466, 186 L.Ed.2d 607 (2013), have made clear that such a consumer is left without a remedy absent a legislative change by Congress. The United States Supreme Court addressed this implausible result when it stated:

> "But 'it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre.'*Cuomo v. Clearing House Assn., L.L.C.*, 557 U.S. 519, —— (2009) (THOMAS, J., concurring in part and dissenting in part) (internal quotation marks and brackets omitted). It is beyond dispute that the federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers. Indeed, it is the special, and different, regulation of generic drugs that allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public. But different federal statutes and regulations may, as here, lead to different pre-emption results. We will not distort the Supremacy Clause in order to create similar pre-emption across a dissimilar statutory scheme. As always, Congress and the [Food and Drug Administration] retain the authority to change the law and regulations if they so desire."

***30** *PLIVA*, 564 U.S. at ——, 131 S.Ct. at 2582.

Based on the foregoing, I respectfully dissent.

MURDOCK, Justice (dissenting).

There is no good outcome in this case. In fairness to the main opinion, this Court has been put in a position from which it cannot give an answer that yields a just result for both plaintiffs and defendants in cases such as this. My understanding of certain bedrock principles of tort law and of the economic realities underlying those principles, however, compels me to dissent and to explain fully my concerns.

I.

A.

From the beginning, what Alexander Hamilton referred to as "[t]he spirit of enterprise, which characterizes the commercial part of America,"[21] has animated Americans to work hard to produce innovative goods and services that have benefited not only themselves, but also their children, their communities, and America as a whole. An enterprising spirit alone, however, is not enough. The law must protect the fruits of enterprise and create a climate in which trade and business innovation can flourish. Concomitantly, the law must justly allocate risks that are a function of that free trade and innovation.

These dual needs have resulted in an economic and legal system that always has coupled the rewards from the sale of a good or service with the costs of tortious injury resulting from the same. Indeed, this and the corollary notion that parties are responsible for their own products, not those of others, are so organic to western economic and legal thought that they rarely find need of expression.

The path the Court takes today is in conflict with these

notions. Impetus to take this path comes from a newfound and admittedly legitimate concern left in the wake of the United States Supreme Court's holding in *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011), that state-law tort claims against manufacturers of generic drugs are preempted by federal law. The resulting concern is that, if manufacturers of brand-name drugs are not responsible under state law for injuries caused by defects in generic drugs and their related labeling, then no one will be.

To see our way clear to placing such responsibility upon brand-name manufacturers, however, we must distance ourselves from the foregoing notions. We must overlook a foundational element of tort law that these notions inform and in which they find voice: the necessity of a "duty" arising from a sufficient "relationship," or nexus, between the injured party and the defendant. We must focus on the role of "foreseeability" in the creation of a duty to the exclusion of "relationship." In doing so, this Court creates a precedent that poses danger for the prescription-medicine industry and, by extension, for all industry.

B.

As discussed in Part II of this writing, almost every one of the 47 reported cases decided before the United States Supreme Court's decision in *PLIVA*, including cases decided by two United States Circuit Courts of Appeals, held that a manufacturer of a brand-name drug has no duty to the consumer of a generic drug manufactured and sold by another company. Since the Supreme Court's 2011 decision in *PLIVA*, every one of the two dozen cases that have addressed the issue, including decisions by six United States Circuit Courts of Appeals, has reached this same conclusion.

***31** As these numbers indicate, the Supreme Court's holding in *PLIVA*—that state-law claims against *generic*-drug manufacturers are preempted by the federal regulatory scheme—did nothing to undermine the essential rationale in the plethora of pre- and post-*PLIVA* decisions holding that *brand-name* manufacturers are not liable for injuries caused by deficient labeling of generic drugs they neither manufactured nor sold. In fact, as discussed below, the opinion in *PLIVA* expressly says as much, and opinions in post-*PLIVA* cases are even more explicit in saying so.

It does indeed appear unfair—an "unfortunate hand" in the words of the United States Supreme Court—that a consumer harmed by a generic drug cannot seek compensation from the entity that manufactured and sold that drug. If this is unfair, however, it is an unfairness created by Congress and the Food and Drug Administration ("the FDA") in return for the perceived societal benefit of less expensive generic drugs, or perhaps instead by the manner in which the United States Supreme Court subsequently has applied the preemption doctrine to the legislative and regulatory scheme structured by those entities. It is not an unfairness created by the brand-name manufacturer. The just answer then, if there is to be one, must come from a change of federal policy or preemption jurisprudence. It is not to come from ignoring age-old, elemental precepts of tort law in order to impose liability on an entity with whom the plaintiff has no relationship, in regard to a product that that entity did not manufacture or sell.

Having itself laid the blame for the present unfairness at the feet of Congress and the FDA, the United States Supreme Court concludes in *PLIVA* that this is not a problem for that Court to correct. If this is so, then, a fortiori, it is not a problem for this or any other state court to correct. And it certainly is not a "wrong" that this or any court should attempt to correct with a second "wrong."

II.

"The concept of duty does not exist in a vacuum."*State Farm Fire & Cas. Co. v. Owen*, 729 So.2d 834, 839 (Ala.1998). It requires a sufficient "relationship," or nexus, between two or more parties. *Id.* The duty this Court recognizes today is one based solely on "foreseeability." Given the existing federal regulatory scheme, I agree that it is "foreseeable"—indeed, eminently so—that a generic version of a brand-name drug will be consumed in reliance upon labeling disseminated by the brand-name manufacturer for its brand-name drug. But this foreseeability alone is not enough to create a duty. There also must be a "relationship" or nexus between the parties.

For example, it might be foreseeable that one manufacturer would copy the design of an unpatented machine of some nature, which, unbeknownst to that manufacturer, was originally designed in a defective manner, and that a user of the copied device might be injured as a result of a replicated design defect. Nonetheless, the designer of the original machine did not manufacture or sell the copied machine. The law therefore recognizes the lack of any nexus between that designer

and the injured party in relation to the machine that caused the injury and thus recognizes no duty on the part of that designer to the injured party.

***32** The same principle applies to claims of misrepresentation and suppression. A viable claim depends upon the existence of a duty on the part of the defendant to the plaintiff. See, e.g., *Nesbitt v. Frederick*, 941 So.2d 950, 955 (Ala.2006) ("An essential element of fraudulent-misrepresentation and fraudulent-suppression claims is a duty to disclose.").

In *Thompson–Hayward Chemical Co. v. Childress*, 277 Ala. 285, 291–92, 169 So.2d 305, 312 (1964), the Alabama Supreme Court addressed a common-law claim alleging failure to warn of the dangerous nature of a herbicide:

> "The breach of duty charged against defendants is the failure to give notice to or warn plaintiffs of the dangerous nature of the vine killer. Do the facts alleged in the complaint show that the defendant, Bertolla, owed a duty to warn plaintiffs? As plaintiffs candidly admit in brief, it is not alleged that plaintiffs purchased the vine killer from Bertolla. It is not alleged that Bertolla ever had possession of or any connection whatsoever with the particular substance which plaintiffs sprayed and which allegedly caused the death of plaintiffs' cattle. The rule, upon which plaintiffs' right to recover is based, imposes the duty on one who, with knowledge of its dangerous quality, manufactures or sells an imminently dangerous article and fails to warn. *It is not alleged that Bertolla manufactured the dangerous article. It is not alleged that Bertolla sold it. How, then, did Bertolla owe a duty to warn?* "

(Emphasis added.)

In a case in which it was foreseeable to the owner of a power pole that a defective power line hanging from its pole could injure someone in the plaintiff's position, this Court held that the lack of any relationship between the owner of the power pole and the injured party meant that no duty to warn of the danger existed:

> "In addition to foreseeability, Alabama courts look to a number of factors to determine whether a duty exists, including ' "(1) the nature of the defendant's activity; (2) *the relationship between the parties;* and (3) the type of injury or harm threatened." ' *Taylor [v. Smith]*, 892 So.2d [887,] 892 [(Ala.2004)] (quoting *Morgan v. South Cent. Bell Tel. Co.*, 466 So.2d 107, 114 (Ala.1985)).
>
> "[The plaintiff] argues that 'once [Joe Wheeler Electric Membership Corp.] had actual or constructive knowledge of the deadly hazard, it had a duty to require the removal of the hazard,' and she asserts that 'notice or knowledge of a dangerous condition can give rise to a duty of care.' [Plaintiff's] brief at 29 (citing *[Alabama Power Co. v.] Cantrell*, 507 So.2d [1295,] 1297 [(Ala.1986)] (' " 'The duty of an electric company, in conveying a current of high potential, to exercise commensurate care under the circumstances, requires it to insulate its wires, and to use reasonable care to keep the same insulated wherever it may reasonably be anticipated that persons, pursuing business or pleasure, may come in contact therewith.' " ' (quoting *[Alabama Power Co. v.] Brooks*, 479 So.2d [1169,] 1172 [(Ala.1985)], quoting in turn *Bush [v. Alabama Power Co.]*, 457 So.2d [350,] 353 [(Ala.1984)]))).
>
> ***33** "The holding of *Cantrell* is not as broad as [the plaintiff] posits. *Cantrell* imposes a specific duty on utilities to insulate *their own lines*, in specific circumstances, whenever it is reasonably anticipated that people may come into contact with *those* lines. 507 So.2d at 1297. Although the duty imposed on the utility companies in *Cantrell* is triggered when the utility company is aware that individuals may come in contact with *its* lines, *Cantrell* does not stand for the proposition that notice of a dangerous condition alone is sufficient to give rise to a duty of care. Further, none of the other cases cited by DiBiasi support her position. *See...Dominici v. Wal–Mart Stores, Inc.*, 606 So.2d 555, 559 (La.Ct.App.1992) ([stating that] ... '[a]ctual or constructive knowledge of a risk or injury gives rise to a duty to take reasonable steps to protect against injurious consequences resulting from the risk,' but noting that '*whether a legal duty is owed by one party to another depends upon the facts and circumstances of the case and the relationship of the parties....*') ...; *cf. Alabama Dep't of Corr. v. Thompson*, 855 So.2d 1016, 1021–22, 1025 (Ala.2003) (noting that ' " '[i]t is the general rule in Alabama that absent special relationships or circumstances, a person has no duty to protect another from criminal acts of a third party' " '

(quoting *Hail v. Regency Terrace Owners Ass'n*, 782 So.2d 1271, 1274 (Ala.1999), quoting in turn *Moye v. A.G. Gaston Motels, Inc.*, 499 So.2d 1368, 1372 (Ala.1986)), and holding that 'state correctional officers owe a general duty to the public, not a duty to a specific person, to maintain custody of inmates').

"*Although it may be true that foreseeability is a key factor in determining whether a duty exists in a particular circumstance, and knowledge of a dangerous condition may establish foreseeability, Alabama caselaw does not hold that knowledge, by itself, is sufficient to impose a duty.*"

DiBiasi v. Joe Wheeler Elec. Membership Corp., 988 So.2d 454, 461–62 (Ala.2008) (emphasis added; footnote omitted). See also, e.g., David G. Owen et al., *Madden & Owen on Products Liability* § 2:9 (3d ed. 2000) ("As is true in tort law generally, foreseeability, although necessary, is not in itself a sufficient criterion for negligence in products liability cases.").[22]

***Prescription–Drug Cases Decided Before* PLIVA**

In the leading case involving the question of liability on the part of the manufacturer of a brand-name drug for harm caused by deficient labeling of the generic version of the drug, the United States Court of Appeals for the Fourth Circuit recognized not only the necessity of a duty owed by the defendant to the plaintiff, but also that the source of that duty must be *a relationship created by the plaintiff's consumption of the defendant's product.*In *Foster v. American Home Products Corp.*, 29 F.3d 165, 167 (4th Cir.1994), the Court expressly held that "a name brand manufacturer cannot be held liable on a negligent misrepresentation theory for injuries resulting from use of another manufacturer's product."

***34** The plaintiffs attempt to discount *Foster* and other cases that reach the same conclusion. According to the plaintiffs, the opinions in those cases were based on the assumption that generic manufacturers were available to bear the liability for any deficiencies in the labeling that accompanies their products. Such an assumption, they note, is no longer viable in light of the Supreme Court's decision in *PLIVA.*

The issue of the generic manufacturer's liability, however, was not the issue in *Foster* and the dozens of similar cases decided before *PLIVA.*Although the courts in some of those cases might have taken some comfort in the availability of a generic manufacturer as a responsible party, the conclusion reached by the *Foster* court and other courts as to the lack of liability on the part of brand-name manufacturers for injuries caused by deficient labeling of generic drugs was not dependent upon that availability. Thus, after expressing in dicta its views as to the potential liability of generic manufacturers, the *Foster* court proceeded to explain separately as follows:

> "We *also* reject the contention that a name brand manufacturer's statements regarding its drug can serve as the basis for liability for injuries caused by another manufacturer's drug. Name brand manufacturers undertake the expense of developing pioneer drugs, performing the studies necessary to obtain premarketing approval, and formulating labeling information. Generic manufacturers avoid these expenses by duplicating successful pioneer drugs and their labels. Name brand advertising benefits generic competitors because generics are generally sold as substitutes for name brand drugs, so the more a name brand drug is prescribed, the more potential sales exist for its generic equivalents. *There is no legal precedent for using a name brand manufacturer's statements about its own product as a basis for liability for injuries caused by other manufacturers' products*, over whose production the name brand manufacturer had no control. This would be especially unfair when, as here, the generic manufacturer reaps the benefits of the name brand manufacturer's statements by copying its labels and riding on the coattails of its advertising. *The premarketing approval scheme Congress established for generic equivalents of previously approved drugs cannot be construed to create liability of a name brand manufacturer when another manufacturer's drug has been consumed.*"

29 F.3d at 170 (emphasis added).

Furthermore, in a separate portion of its opinion, the court explains unequivocally, and without any reference to the prospects for liability on the part of the generic manufacturer, that a brand-name manufacturer simply has no "duty" to the consumer of a generic drug the brand-name manufacturer did not produce or distribute and that, therefore, the brand-name manufacturer cannot be liable under a negligent-misrepresentation theory:

> "The Fosters' *negligent misrepresentation action against Wyeth also fails because Wyeth is under no duty of care to the Fosters.... An action for negligent misrepresentation will not lie unless the defendant owes the plaintiff a duty of care. Weisman v. Connors,* 312 Md. 428, [442–47,] 540 A.2d 783, 790–92 (1988)."

***35** 29 F.3d at 171. The court then expressly rejects the same foreseeability argument urged upon us by the plaintiffs in this case, explaining that foreseeability alone is not enough to create a duty and that a relationship between the parties is necessary:

> "*The Fosters contend that a duty exists in this case because it was foreseeable to Wyeth that misrepresentations regarding Phenergan could result in personal injury to users of Phenergan's generic equivalents.*They point to *Jacques v. First National Bank*, a negligence action, which noted:
>
> > " 'Where the failure to exercise due care creates a risk of economic loss only, courts have generally required an intimate nexus between the parties as a condition to the imposition of tort liability. This intimate nexus is satisfied by contractual privity or its equivalent. By contrast, where the risk created is one of personal injury, no such direct relationship need be shown, and the principal determinant of duty becomes foreseeability.'
>
> "307 Md. 527, [534–35,] 515 A.2d 756, 759–60 (1986). We think to impose a duty in the circumstances of this case would be to stretch the concept of foreseeability too far. *The duty required for the tort of negligent misrepresentation arises when there is 'such a relation that one party has the right to rely for information upon the other, and the other giving the information owes a duty to give it with care.' Weisman v. Connors,* 312 Md. 428, 540 A.2d [783] at 790 [(1988)] (quoting *Holt v. Kolker,* 189 Md. 636, [640,] 57 A.2d 287, 288 (1948)).*There is no such relationship between the parties to this case, as Brandy Foster was injured by a product that Wyeth did not manufacture.*As *Wyeth has no duty to the users of other manufacturers' products*, a negligent misrepresentation action cannot be maintained against it on the facts of this case."

29 F.3d at 171 (emphasis added).

By my count,[23] from the time *Foster* was decided until the issuance of the Supreme Court's decision in *PLIVA*, 43 reported cases applying the law of 18 states were decided in accordance with the *Foster* decision.[24]Aside from the decision of the court certifying the question in this case, *only two courts held to the contrary*—an intermediate state appeals court in California and a district court in Vermont.[25]

The United States Court of Appeals for the Eighth Circuit is the court from which the *PLIVA* case came and to which it was returned on remand by the United States Supreme Court. See *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 612–14 (8th Cir.2009), rev'd in part on other grounds sub nom., *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011). Before the Supreme Court weighed in, the Eighth Circuit Court of Appeals held that state-law claims against generic-drug manufacturers were *not* preempted by federal law. 588 F.3d at 611. In the same opinion, however, that court was called upon to decide whether a brand-name manufacturer could be held liable for injuries caused by generic metoclopramide manufactured and sold by another party. In a soundly reasoned opinion, that court answered in the negative:

> ***36** "*[R]egardless of whether her doctor relied upon the Reglan label, Mensing must show that the name brand manufacturers owed her a duty of care.*Duty is a threshold requirement for all of the tort claims Mensing asserts. *See, e.g., Noble Systems Corp. v. Alorica Central, LLC,* 543 F.3d 978, 985 (8th Cir.2008) (finding that under Minnesota law *negligent misrepresentation requires the plaintiff to 'prove some relationship that is sufficient to create a duty owed by the defendant to the plaintiff '*).
>
> "Such a duty of care does not extend to all potential Reglan consumers.'Minnesota common law ... requires a stronger relationship and a direct communication.'*Flynn [v. American Home Prods.*

> *Corp.*], 627 N.W.2d [342,] 350 [(Minn.Ct.App.2001)].*Since Mensing'did not purchase or use [the name brand defendants'] product, ... there was no direct relationship between them, let alone a fiduciary relationship that gave rise to a duty.'Id.* at 350. *Mensing focuses on the foreseeability of harm from the defendants' action. Like the Fourth Circuit, we conclude that holding name brand manufacturers liable for harm caused by generic manufacturers 'stretch[es] the concept of foreseeability too far.'Foster,* 29 F.3d at 171."

588 F.3d at 613–14 (some emphasis added; footnote omitted).

In a footnote, the Eighth Circuit also provided this instructive insight:

> "*Mensing's attempt to characterize her fraud claim as a type requiring no proof of a duty of care is unavailing.*A plaintiff claiming fraud in Minnesota *must show that the defendant intended to induce another to act in reliance on its fraudulent statement. Specialized Tours, Inc. v. Hagen,* 392 N.W.2d 520, 532 (Minn.1986). Mensing's relationship with the Reglan manufacturers is too attenuated, and she has cited no Minnesota case in which the court imposed liability for fraud on a defendant who did not intend to communicate with the plaintiff. *The Reglan manufacturers intended to communicate with their customers, not the customers of their competitors."*

588 F.3d at 613 n. 9 (emphasis added).

Among the other pre-*PLIVA* decisions are four decisions from federal district courts in Alabama applying Alabama law: *Mosley v. Wyeth, Inc.,* 719 F.Supp.2d 1340 (S.D.Ala.2010); *Simpson v. Wyeth, Inc.,* No. 7:10–CV–01771–HGD (N.D.Ala. Dec. 9, 2010) (not reported in F.Supp.2d); *Overton v. Wyeth, Inc.,* No. CA 10–0491–KD–C (S.D.Ala. Mar. 15, 2011) (not reported in F.Supp.2d); and *Barnhill v. Teva Pharm. USA, Inc.,* No. 06–0282–CB–M (S.D.Ala.2007) (not reported in F.Supp.2d). In all four of these cases, the court held that claims could not be maintained under Alabama law against the manufacturer of a brand-name drug for injuries resulting from a consumer's use of a generic version of that drug manufactured and sold by another company. The first of these, *Mosley,* is representative of the other Alabama federal district court decisions, as well as the other district court decisions identified above. As the federal district court in *Mosley* explained regarding precisely the same drug, the same defendants, and the same legal issue as are presented in the case at hand:

> ***37** "The argument is not that Defendants' product caused Plaintiff harm, but rather that their dissemination of false and misleading information, which they knew would be relied upon by the generic manufacturers in generating their own labels, was the direct and proximate cause of Plaintiff's injuries."

719 F.Supp.2d at 1344–45. The court rejected this argument because, under Alabama law, no "relationship" existed between the manufacturer of the brand-name drug and the consumer of the generic drug, and thus no "duty" was owed. 719 F.Supp.2d at 1346–47.

Contrary to the main opinion, but consistent with all the foregoing authority, Wyeth's argument does not "ignore[ ] the nature of prescription medication." —— So.3d at ——. Obviously, a duty must be understood to run from a drug manufacturer to a consumer if that consumer is to be able to state a claim against the manufacturer. (If the duty ran only to an intermediary or other third party, such as a physician or pharmacist, then only the intermediary or third party would have a cause of action and be a proper plaintiff.) The controlled nature of prescription drugs, see 21 U.S.C. § 353(b)(1), simply means that the drug manufacturer fulfills its duty of disclosure to the consumer by making disclosures to the consumer's physician and/or pharmacist, who receives the disclosures and acts upon them on behalf of the consumer. In essence, the consumer's physician serves as the agent of the consumer for purposes of receipt of and reliance upon the disclosures, or omissions, of the manufacturer. See, e.g., *Stone v. Smith, Kline & French Labs.,* 447 So.2d 1301, 1305 (Ala.1984) (quoting *Reyes v. Wyeth Labs.,* 498 F.2d 1264, 1276 (5th Cir.1974)):

> " 'As a medical expert, the prescribing physician can take into account the propensities of the drug as well as the susceptibilities of his patient. His is the task of weighing the benefits of any medication against its potential dangers. The choice he makes is an informed one, an individualized medical judgment bottomed on a

> knowledge of both patient and palliative. *Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a "learned intermediary" between manufacturer and consumer.'"*

(Emphasis added.)[26]

Wyeth's position fully accommodates the notion that a prescription drug is consumed only if it is prescribed by a physician and dispensed by a pharmacist, and that the physician and pharmacist act as agents of the consumer of a generic drug for purposes of receiving and acting upon whatever warnings and representations the drug's manufacturer intends for that consumer. The fact that there is such a "learned intermediary" acting in this manner on behalf of the ultimate consumer does not in itself create a relationship between the brand-name manufacturer and the consumer. Regardless of the fact of, or content of, a given prescription, if a person consumes a generic drug, the nexus created is with the manufacturer of the generic drug. The physician's involvement does nothing to create some sort of relationship between the consumer and some different entity. The consumer has no more relationship with the brand-name manufacturer in such a scenario than he or she would have if the learned intermediaries were not involved and the consumer purchased the generic drug directly from the generic manufacturer.

***38** As the Eighth Circuit Court of Appeals indicated in *Mensing*, perhaps there is confusion resulting from the fact that, in prescribing or dispensing a generic drug, physicians or pharmacists might in fact rely upon labeling that previously was published by a brand-name manufacturer in conjunction with the marketing by it of its own brand-name drug. As that court also pointed out, however, the labeling of the brand-name manufacturer is not intended for that purpose; it is published by the brand-name manufacturer solely for the purpose of fulfilling the brand-name manufacturer's own duty to provide adequate labeling to the consumers of *its* product. *To say that a physician's or pharmacist's reliance upon a brand-name manufacturer's labeling in prescribing or dispensing a generic drug makes the brand-name manufacturer liable for injuries suffered by the generic-drug consumer is to "bootstrap" into existence a duty on the part of the brand-name manufacturer to that consumer;* the first inquiry must be whether the brand-name manufacturer had a duty to one who did not consume its product to publish adequate labeling. Apart from such bootstrapping, there is no basis to declare the existence of such a duty. See, e.g., *Mensing*, 588 F.3d at 613 ("Regardless of whether her doctor relied upon the Reglan label, Mensing must show that the name brand manufacturers owed *her* a duty of care.").[27]

The present case is not distinguishable from the above-discussed cases on the ground that the present case involves common-law claims of fraud in relation to deficient labeling. *Foster*, the Eighth Circuit Court of Appeals' *Mensing* case, Alabama federal district court decisions such as *Mosley*, and dozens of other well considered decisions cited above involve alleged defects in labeling. Indeed, many, if not most, of them involve common-law claims of misrepresentation of some sort. They consider, and often explain, the necessity of a duty arising from a relationship as no less applicable to claims of defects in the warnings that accompany a product than to defects in the pharmacology of the product.[28]

PLIVA

On June 23, 2011, the United States Supreme Court decided *PLIVA*.The Court held that state tort-law claims against manufacturers of generic drugs were preempted by the statutory and regulatory scheme that had been adopted by Congress and the FDA. 564 U.S. at ——, 131 S.Ct. at 2581–82. It is clear from the text of the *PLIVA* opinion itself that *PLIVA* did not undermine the rationale of the dozens of pre-*PLIVA decisions* discussed and cited above.

Foremost in this regard is the simple fact that the issue discussed in *PLIVA* was the effect of the federal law of preemption on the liability of *generic* manufacturers for their own drugs. Nothing in the Court's reasoning as to this issue has any bearing on the unrelated question under state law of relationship and duty of brand-name manufacturers with respect to drugs they do not manufacture.

***39** Second, the *PLIVA* Court includes statements in the opinion that contemplate that its ruling as to generic manufacturers does *not* mean that consumers injured by generic drugs will now be able to turn to manufacturers of brand-name drugs for compensation. The Supreme Court expressly recognizes the "unfortunate hand" that has been dealt to consumers of generic drugs given its decision:

> "We acknowledge the unfortunate hand that federal drug regulation has dealt Mensing, Demahy, and others similarly situated.
>
> "But 'it is not this Court's task to decide whether the

> statutory scheme established by Congress is unusual or even bizarre.'*Cuomo v. Clearing House Assn., L.L.C.*, 557 U.S. 519, 556 (2009) (THOMAS, J., concurring in part and dissenting in part) (internal quotation marks and brackets omitted)."

564 U.S. at ——, 131 S.Ct. at 2581–82. As Justice Sotomayor subsequently explained, under the majority decision, a consumer of a generic drug "now has no right to sue."564 U.S. at ——, 131 S.Ct. at 2592 (Sotomayor, J., dissenting).

Moreover, the Supreme Court expressed its understanding that the consumption of the brand-name manufacturer's drug remained a prerequisite to holding *that manufacturer* liable for a labeling deficiency: "Had Mensing and Demahy taken Reglan, the brand-name drug ..., *Wyeth [v. Levine*, 555 U.S. 555 (2009),[29]] would control and their lawsuits would not be pre-empted."564 U.S. at ——, 131 S.Ct. at 2581.

Cases Decided in the Wake of PLIVA

In the year and a half after *PLIVA* was decided, but before this Court issued its opinion on original submission in this case, 11 decisions applying the law of 10 states were reported. Every one of those decisions held that manufacturers of brand-name drugs had no duty or liability to the consumer of a generic drug manufactured and sold by another company.[30]Accordingly, there was (and, as will be seen, still is) unanimity among the courts that addressed the question in the wake of *PLIVA* that the holding of *PLIVA* as to the preemption of state-law claims against generic manufacturers does not undermine the rationale of the pre-*PLIVA* decisions discussed above or justify making brand-name manufacturers liable for a product they have not manufactured or sold. This includes each of the three United States Courts of Appeals to address the issue in the first year and a half following *PLIVA*—the Courts of Appeals for the Fifth, Sixth, and Eighth Circuits.

Perhaps the most noteworthy of the aforesaid three Court of Appeals' decisions was the short order issued on remand by the Eighth Circuit Court of Appeals in the *PLIVA* case itself. The same court whose judgment had just been reversed by the United States Supreme Court on the issue of preemption as to the liability of generic manufacturers evidently felt no compunction in deciding expressly to "reinstate Section III of [its original] opinion," the same section quoted at length above in which it had held that brand-name manufacturers were not liable for defects or deficiencies in the labeling of products manufactured and sold by others. *Mensing v. Wyeth, Inc.*, 658 F.3d 867 (8th Cir.2011).

***40** In *Smith v. Wyeth, Inc.*, 657 F.3d 420 (6th Cir.2011), the United States Court of Appeals for the Sixth Circuit also acknowledged, but was unaffected by, the holding in *PLIVA*.The court began by noting the applicability of the Kentucky Products Liability Act, which, it explained, was merely a codification of preexisting common-law principles, including common-law principles regarding the misrepresentation and "failure-to-warn" claims asserted against the manufacturers of brand-name drugs in that case. 657 F.3d at 423.[31]The court then proceeded, undeterred in any way by the *PLIVA* holding as to manufacturers of generic drugs, to explain its rejection of the misrepresentation claims against the brand-name manufacturer, Wyeth, as to the same drug that is at issue here:

> "*A threshold requirement of any products-liability claim is that the plaintiff assert that the defendant's product caused the plaintiff's injury.*See *Holbrook v. Rose*, 458 S.W.2d 155, 157 (Ky.1970). The plaintiffs in this case concede that they had consumed only generic versions of metoclopramide and not Reglan. As the district court observed, *adopting their theory of liability would require the court to attribute any deficiency in a name-brand manufacturer's labeling and marketing of its products to products manufactured by its generic competitors. Such a theory, however, fails to satisfy the threshold requirement of a products-liability action—that the defendant's product have injured the plaintiff.*As the district court stated, 'Just because a company is in the same business as a tortfeasor, the company is not automatically liable for the harm caused by the tortfeasor's product.'
>
> "*The plaintiffs' argument—that the name-brand defendants' liability stems from the fact that the regulatory structure governing name-brand and generic drugs makes it foreseeable that patients and their physicians will rely on the name-brand labels to use and prescribe generic drugs—has been rejected by all but one of the courts that have considered it.*The leading case is *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994), in which the court held that the manufacturer of a name-brand drug has no duty to patients who ingested only a generic version of the drug manufactured by the name-brand drug company's competitors....*As have the majority of courts to address this question, we reject the argument that a name-brand drug manufacturer owes a duty of care to individuals who have never taken the drug actually manufactured by that company.*"

657 F.3d at 423–24 (some emphasis added).

In the last of the aforesaid decisions by federal courts of appeals, the United States Court of Appeals for the Fifth Circuit explicitly held in *Demahy v. Schwarz Pharma, Inc.*, 702 F.3d 177, 184 (5th Cir.2012), that *PLIVA* changed nothing as to brand-name manufacturers:

> "We do not view [*PLIVA*] as overruling *Foster [v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994),] because *the court in*Foster*did not reach its holding by relying on the ability of a plaintiff to sue generic manufacturers.*Instead, the court's holding was based on its interpretation of Maryland law and the conclusion that *a name-brand manufacturer has no duty of care to consumers that are not using the manufacturer's product. Foster*, 29 F.3d at 171–72; see also *Smith v. Wyeth*, 657 F.3d 420, 423–24 (6th Cir.2011) (following *Foster's* conclusion that name-brand manufacturers have no duty to generic-brand consumers).*The* Foster *court's opinion in dicta on the viability of suits against generic manufacturers was proved wrong, but this fact does not impose on name-brand manufacturers a duty of care to customers using generic products.*"

***41** In *Phelps v. Wyeth, Inc.*, 857 F.Supp.2d 1114 (D.Or.2012), the federal district court for Oregon also explicitly rejected the notion that *PLIVA* changed anything as to brand-name manufacturers. In an opinion reflective of the other post-*PLIVA* decisions by federal district courts, it explained:

> "[W]hile [*PLIVA*] overrules *Foster [v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994),] with respect to a generic manufacturer's ability to alter labels, it does not overrule *Foster's* holding regarding the liability of name-brand manufacturers. Indeed, the *Foster* court's reluctance to hold name-brand defendants liable for generic drugs did not depend on a generic manufacturer's ability to alter the label, but rather on concepts of foreseeability *and duty.*Consequently, [*PLIVA*] does not overturn the central holding in *Foster.*"

857 F.Supp.2d at 1119 (emphasis added).

The Oregon court provided an instructive analysis as to the necessity of a relationship in order for there to exist a duty for purposes of a common-law claim based on deficient labeling of drugs:

> "It is undisputed that Mrs. Phelps never ingested metoclopramide manufactured by any of the name-brand defendants.... Under Oregon's product liability law, the name-brand defendants cannot be found liable for plaintiffs' injuries because *plaintiffs cannot show that their injuries resulted from the use of the name-brand manufacturers' product. See McEwen v. Ortho Pharma. Corp.*, 270 Or. 375, 407, 528 P.2d 522 (1974).*Nonetheless, plaintiffs request that the court apply common law principles of negligence, fraud, and misrepresentation* to extend liability to the name-brand defendants. They argue that regardless of whether Mrs. Phelps ingested the name-brand defendants' product, the name-brand defendants owed her a duty of care.
>
> "....
>
> "Plaintiffs cite neither Oregon nor federal law to support this proposition. Instead, plaintiffs argue that manufacturers owe a general duty to use care in connection with their conduct to all who may [be] injured by it, if such conduct is carried out in a negligent manner and *results in foreseeable injuries....* (citing *Palsgraf v. Long Island R.R. Co.*, 248 N.Y. 339, 162 N.E. 99 (1928)).*Plaintiffs assert that, based on federal regulations, name-brand defendants should have known that all generic manufacturers were required to duplicate the information on name-brand labels for generic drugs, and that generic manufacturers were prevented from including additional warnings or independently warning doctors of metoclopramide's risks.*Additionally, plaintiffs argue that name-brand defendants knew or should have known that their label did not adequately warn of the risks associated with metoclopramide. *Consequently, plaintiffs assert that the generics defendants' reliance on name-brand defendants' labels was a foreseeable cause of their injuries.*
>
> "... [In *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994),] [t]he plaintiffs brought suit

> against the name-brand manufacturer for negligent misrepresentation, but the Fourth Circuit ruled that Maryland law did not allow a manufacturer to be liable for an injury caused by a competitor's product. *Id.* at 171. While *Foster* recognized that reliance on the label was foreseeable, the court explained that *foreseeability alone does not create a duty of care*, and the court specifically rejected the plaintiffs' negligence claim. *Id*.... The *Foster* court found that there is '(n)o legal precedent for using a name brand manufacturer's statements about its own product as a basis for liability [for] injuries caused by other manufacturers' products, over whose production the name brand manufacturer had no control.'*Id.* at 170. Name-brand defendants cite *a plethora of courts which have followed* Foster *and concluded that name-brand defendants cannot be held liable for injuries caused by products produced by a generic manufacturer. See e.g. Smith v. Wyeth, Inc.*, 657 F.3d 420, 424 (6th Cir.2011); *Metz v. Wyeth LLC*, 830 F.Supp.2d 1291 (M.D.Fla.2011)."

***42** 857 F.Supp.2d at 1120–21 (emphasis added).

Finally, the Oregon court expressed the same understanding of the text of the *PLIVA* decision that is offered above:

> "*In fact, the Supreme Court [in*PLIVA*] acknowledged that the dual holdings of* Foster *and [* PLIVA*] left the plaintiff there with no remedy, as she could not successfully bring a claim against name-brand manufacturers under* Foster *and was barred on other grounds from suing the generic manufacturers.* [*PLIVA*], [564 U.S. at ——,] 131 S.Ct. at 2581 (acknowledging 'the unfortunate hand that federal drug regulation has dealt' plaintiff). The majority further stated that Congress or the FDA could change the law...."

857 F.Supp.2d at 1119–20 (emphasis added).

In an opinion issued not long after *PLIVA*, a federal district court applied the law of our neighboring state of Florida:

> "The vast majority of courts, in Florida and elsewhere, that have addressed the issue now before the Court have consistently held that consumers may not bring claims for negligence, fraud, strict liability, misrepresentation, or breach of warranty against a brand name pharmaceutical manufacturer when the consumers only ingested generic versions of the drug manufactured by third parties. [Numerous citations omitted.]
>
> "Plaintiffs attempt to overcome *the nearly unanimous adverse precedent* by arguing that the Supreme Court's decision in *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011), warrants a change in how Florida law is applied to producers of brand name pharmaceuticals. The thrust of Plaintiffs' argument is that the Fourth Circuit's holding in the seminal case of *Foster v. American Home Products Corp.*, 29 F.3d 165 (4th Cir.1994), was based on the proposition (discussed in *dicta*) that consumers could recover from generic manufacturers for misrepresentations relating to their products.*Id.* at 170. While it is true that this proposition was rejected by the Supreme Court in *[PLIVA]*, this proposition was by no means central to the ultimate holding in *Foster. The Fourth Circuit's holding in*Foster*was based on its interpretation of Maryland law and the general rule that one manufacturer cannot be held liable on a negligent misrepresentation theory for injuries caused by another manufacturer. Id. In fact, the* Foster *court held that, irrespective of whether consumers could recover from generic drug manufacturers, a brand name manufacturer simply had no duty of care to individual consumers that did not use the named brand manufacturer's product.Id.* at 171."

Metz v. Wyeth LLC, 830 F.Supp.2d 1291, 1293–94 (M.D.Fla.2011) (emphasis added).[32]

This Court's Opinion

In addition to dozens upon dozens of cases from other jurisdictions directly addressing the issue before us, Wyeth cites four Alabama cases for the proposition that a duty arising from a relationship or nexus between the parties is necessary: *Keck v. Dryvit Systems, Inc.*, 830 So.2d 1 (Ala.2002); *State Farm v. Owen*, 729 So.2d 834 (Ala.1998); *DiBiasi v. Joe Wheeler Electric Membership Corp.*, 988 So.2d 454 (Ala.2008); and *Thompson–Hayward Chemical Co. v. Childress*, 277 Ala. 285, 169 So.2d 305 (1964). The main opinion responds to these four cases by stating: "These cases are easily distinguishable from this case. Here, Wyeth authored the label with its warnings, and the generic manufacturers, as required by FDA regulations, copied that label verbatim." —— So.3d at ——. The fact that the generic manufacturer's label must contain the same information as the label published by Wyeth, the name-brand manufacturer, is true, but that fact does not make the present case distinguishable from the four cases cited.

***43** In each of those four cases, it was foreseeable that the

plaintiff would be injured by the tortious conduct of the defendant. *Despite this foreseeability, each of those cases was decided based on the fact that the alleged tortfeasor had no relationship or nexus with the plaintiff giving rise to a duty to the plaintiff.*

Likewise, and admittedly without question given the federal regulatory scheme for generic drugs, it was foreseeable that a generic drug might one day be produced and that, if it was, it would replicate any deficiency in Wyeth's brand-name drug, including its labeling, that might have been approved by the FDA. As was true in each of those other cases, however, such foreseeability, no matter how clear, simply is not all that is required. There was no liability in those four cases because the defendant did not have the requisite relationship or nexus with the injured party. Because the same is true here, those cases are not distinguishable, but instead support Wyeth's position.[33]

The main opinion concludes its analysis by quoting a passage from a 1998 opinion of the Court of Civil Appeals in *Carter v. Chrysler Corp.*, 743 So.2d 456 (Ala.Civ.App.1998), which, in turn, quotes a 1994 decision of the Alabama Supreme Court, *Hines v. Riverside Chevrolet–Olds, Inc.*, 655 So.2d 909, 919–20 (Ala.1994). As a threshold matter, I find the premise of the analysis quoted from *Hines* circular and confusing: " ' "*The extent of a legal duty* not to make a false representation or to suppress a material fact *informs our analysis* of whether two parties have a sufficient relationship *on which to base a duty* to disclose." ' " —— So.3d at —— (emphasis added). This passage essentially says that "the extent of a legal duty" will determine whether there is enough of a relationship on which "to base a duty."

Leaving aside the circularity of its premise, *Hines* does state that "the fact that two parties have had no contractual relationship or other dealings does not preclude the finding of a legal duty not to make a material misrepresentation or to suppress a material fact."655 So.2d at 920. It adds, however, that "whether a duty to disclose exists must be determined by examining the particular facts of each case."*Id.*

Hines did not involve an attempt to hold a manufacturer liable for injuries where the plaintiff has not used a product manufactured or sold by the defendant. Instead, *Hines* is a classic "privity" case. The question presented and addressed in *Hines* is whether the lack of a contract or other direct dealing between the plaintiff and the defendant—lack of privity—prevents the plaintiff from suing the defendant to recover for personal, or bodily, injuries. It is critical to a proper prospective of the *Hines* decision to note that the injury litigated in that case *resulted from the plaintiff's use of the defendant's product.*

Carter v. Chrysler and the cases cited in *Hines* address the same question as did *Hines*.[34]In accordance with the movement of American jurisprudence in the last century away from a privity-based model for recovery for personal injuries, *Hines* and those other cases found privity to be unnecessary for a claim based on personal injuries. The lack of privity in those cases does not mean, however, that there was not a "relationship," or nexus, between the plaintiff and the defendant arising out of the fact that the plaintiff was injured *by the defendant's product;* there was. There is not here.

***44** Ultimately, the main opinion is inextricably grounded on a single notion: The foreseeability of a deficiency in a brand-name drug, including its labeling, being replicated in a generic drug, including its labeling, is so great that we must recognize a duty owing from the brand-name manufacturer to whomever might be hurt by the deficiency in the generic drug. But the clear foreseeability upon which this notion is based has either been explicitly acknowledged or clearly understood by each of the scores of other federal and state courts that have addressed the issue we now address. Yet, essentially all of them reach a different conclusion than do we. They do so on the same ground that Professor Prosser implores us to remember: Foreseeability alone is not enough. See discussion, *infra*, citing W. Prosser, *Law of Torts*, 708 (4th ed.1971). In the words of the main opinion, therefore, I can reach no conclusion other than that the "ground" we plow today is "new." And we are the only court in the nation plowing it.[35]

A "Mountain of Authority" and an "Overwhelming National Consensus"

Aside from the discussion of the four cases and *Hines* reviewed above, the discussion and rationale offered by the main opinion today on application for rehearing are essentially unchanged from those offered in the opinion on original submission. Therefore, it is noteworthy that, since that original decision, there have been another dozen or more decisions on this issue by federal and state courts around the country, including decisions by four federal courts of appeals, two of them weighing in for the first time. In addition, the United States Supreme Court has now denied certiorari review in *Demahy v. Schwarz Pharma, Inc.*, 702 F.3d 177 (5th Cir.2012), cert. denied,

—— U.S. ——, 134 S.Ct. 57, 187 L.Ed.2d 25 (2013).[36] None of these courts have been persuaded by the rationale offered by this Court's original opinion.

Among the courts that have not been persuaded by our original decision is the Court of Appeals for the Fifth Circuit, which has decided two additional cases reaffirming the sound rationale it first embraced in *Demahy*.See *Lashley v. Pfizer, Inc.*, 750 F.3d 470 (5th Cir.2014); *Del Valle v. Teva Pharm. USA, Inc.*, 750 F.3d 470 (5th Cir.2014) (consolidated cases).

Likewise, the Court of Appeals for the Eighth Circuit has decided yet another case reaffirming its position. In *Bell v. Pfizer, Inc.*, 716 F.3d 1087 (8th Cir.2013), the Eighth Circuit held that, under Arkansas law, (i) the plaintiff's contention that "her injuries were foreseeable" was "insufficient" to impose a duty on the brand-name defendants; (ii) that the plaintiff had to "show that a product manufactured or distributed by the brand[-name] defendants caused her injuries"; and (iii) that because the plaintiff "never used Reglan the brand[-name] defendants manufactured, [she] could not hold them liable under Arkansas law." 716 F.3d at 1092–93. Further, the Eighth Circuit flatly rejected the plaintiff's suggestion that there was an "exception" to the "Arkansas product identification requirement" for "misrepresentation and fraud." *Id.*

***45** Recent appellate court decisions in Iowa are in accord. In *Huck v. Trimark Physicians Group*, 834 N.W.2d 82 (Iowa Ct.App.2013) (unpublished disposition), the Iowa Court of Appeals reaffirmed the settled, common-law rule that " 'a plaintiff in a products liability case must prove that the injury-causing product was a product manufactured or supplied by the defendant.'" (Quoting *Mulcahy v. Eli Lilly & Co.*, 386 N.W.2d 67, 76 (Iowa 1986).) Furthermore, much like decisions of this Court in the past, see, e.g., *Pfizer, Inc. v. Farsian*, 682 So.2d 405 (Ala.1996), the *Huck* court explained that plaintiffs who allege physical injuries caused by a product have, "regardless of the theory of liability" asserted, a products-liability claim that requires "product identification," a requirement that cannot be circumvented by pleading claims of "strict liability, negligence, misrepresentation, breach of warranties," and the like. See also note 31, *supra.*

Shortly before the release of the opinion in this case on rehearing, the Iowa Supreme Court vacated the decision of the Iowa Court of Appeals. It did so, however, in an opinion specifically rejecting this Court's opinion on original submission in the present case and agreeing with the Iowa Court of Appeals' position on the issue before us: "We adhere to [certain] bedrock principles ..., and join the multitude of courts that have concluded brand [-name] defendants owe no duty to consumers of generic drugs."*Huck v. Wyeth, Inc.*, 850 N.W.2d 353, 380 (Iowa 2014) (also declining, in its words, "to step onto the slippery slope" that could lead to brand-name-manufacturer liability for harm caused by copies of other types of products manufactured by competitors).

Three of the federal courts of appeals that have addressed the issue since our opinion on original submission specifically acknowledge our decision. All three of them, the United States Courts of Appeals for the Sixth, Tenth, and Eleventh Circuits, rejected our reasoning. See *Strayhorn v. Wyeth Pharm., Inc.*, 737 F.3d 378 (6th Cir.2013); *Schrock v. Wyeth, Inc.*, 727 F.3d 1273 (10th Cir.2013); and *Guarino v. Wyeth, LLC*, 719 F.3d 1245 (11th Cir.2013).[37] See also *Metz v. Wyeth, LLC*, 525 Fed.Appx. 893 (11th Cir.2013) (not published in F.3d). Two of those circuits, the Tenth Circuit and the Eleventh Circuit, have now weighed in for the first time.

Specifically, in *Schrock v. Wyeth*, the Court of Appeals for the Tenth Circuit joined all the other federal courts of appeals that have addressed the issue by declining to "impose a duty on drug manufacturers to warn of dangers in their competitors' products" because the brand-name defendants "d[id] not have any relationship with the [plaintiffs]."727 F.3d at 1283. And in *Guarino v. Wyeth, LLC*, the Eleventh Circuit explained in no uncertain terms that there simply can be "no liability when we know with certitude that a given manufacturer did not produce the allegedly dangerous product."719 F.3d at 1251.

***46** This Court continues to stand alone as the only appellate court in the country to hold that a brand-name manufacturer may be responsible for injuries caused to a party who ingests a generic drug that the brand-name manufacturer did not manufacture or sell. According to Wyeth, over 90 cases (a figure that includes trial courts) have now been decided in 25 states, including every state that borders Alabama, the federal circuit court that encompasses Alabama, and all six federal courts of appeals to have considered the issue. With the exception of two or three federal district court decisions already identified, all of them disagree with the position taken by this Court.

If the cases that decide the issue differently than we do were not logical and well reasoned, if they were not based on time-tested, bedrock legal principles, or if they did not resolve all the alleged distinctions between prescription-drug cases and other types of cases that have

been raised in the main opinion and in the special concurrence, then perhaps their sheer number would not matter. But they are all these things.

The Eleventh Circuit Court of Appeals has put it this way:

> "Our conclusion is fortified by the fact that the *overwhelming national consensus*—including the decisions of every court of appeal and the vast majority of district courts around the country to consider the question—is that a brand-name manufacturer cannot be liable for injuries caused by the ingestion of the generic form of a product. *See, e.g., Bell v. Pfizer, Inc.*, 716 F.3d 1087, No. 12–1674 (8th Cir. June 14, 2013) (rejecting negligence, *misrepresentation, and fraud claims* against the brand manufacturer of metoclopramide, and explaining that '[a]n overwhelming majority of courts considering this issue ... have rejected [plaintiff's] theory of liability' (internal quotation marks omitted)); *Demahy v. Schwarz Pharma, Inc.*, 702 F.3d 177, 182–83 (5th Cir.2012) (per curiam), *petition for cert. filed*,81 U.S.L.W. 3519 (U.S. Mar. 7, 2013) (No. 12–1093); *Smith [v. Wyeth, Inc.]*, 657 F.3d [420] at 423–24 [(6th Cir.2011)] ('*The plaintiffs' argument—that the name-brand defendants' liability stems from the fact that the regulatory structure governing name-brand and generic drugs makes it foreseeable that patients and their physicians will rely on the name-brand labels to use and prescribe generic drugs—has been rejected by all but one of the courts that have considered it.'*); *Mensing [v. Wyeth, Inc.]*, 658 F.3d [867] at 867 [(8th Cir.2011)] (expressly reinstating the portion of the opinion holding that brand-name manufacturers cannot be held liable under Minnesota law for damage caused by generic drugs); *Foster v. Am. Home Prods. Corp.*, 29 F.3d 165, 170–71 (4th Cir.1994); *Gardley–Starks v. Pfizer, Inc.*, 917 F.Supp.2d 597 (N.D.Miss. Jan. 10, 2013) ('The Court concludes that Mississippi law, consistent with the vast majority of courts to consider this issue, would not recognize a cause of action—*however styled*—against a brand manufacturer for injuries caused by use of its competitors' generic product.'); see also *id.* at [604] n. 4 (noting the defendants' citation to '*sixty-six decisions applying the law of twenty-three different jurisdictions* holding that brand-name manufacturers of a drug may not be held liable under *any theory* for injuries caused by the use of a generic manufacturer's product'). But see *Kellogg v. Wyeth*, 762 F.Supp.2d 694, 708–09 (D.Vt.2010); *Wyeth, Inc. v. Weeks*, No. 1101397 (Ala. Jan. 11, 2013), reh'g granted (June 13, 2013); *Conte v. Wyeth, Inc.*, 168 Cal.App.4th 89, 85 Cal.Rptr.3d 299, 310 (2008). Although only the law of Florida controls the outcome here, the cases denying recovery to plaintiffs bringing claims identical to those we confront in this case are *legion*, and this *mountain of authority* steels us in our determination that Florida law does not recognize a claim against the brand manufacturer of a prescription drug when the plaintiff is known to have consumed only the generic form."

***47** *Guarino*, 719 F.3d at 1252–53 (emphasis added).

The bedrock principles of tort law in this State are no different than the bedrock principles of tort law in every other state in this country, including the two dozen states whose laws have been considered in what the Eleventh Circuit call an "overwhelming national consensus." There is no reason for this State not to be part of that consensus.[38]

III.

One of the many amici curiae briefs supporting Wyeth asserts, with supporting authority:

> "Developing a prescription drug and taking it to market is a monumental undertaking. On average, it requires more than seven years and almost $2 billion to develop a single drug, obtain FDA approval for it, and bring it to market. 'Name brand manufacturers undertake the expense of developing pioneer drugs, performing the studies necessary to obtain premarketing approval, and formulating labeling information.'*Foster [v. American Home Products Corp.]*, 29 F.3d [165] at 170 [(4th Cir.1994)].
>
> "Brand-name manufacturers make research and development decisions against a particular legal backdrop. Under traditional tort principles, the brand-name manufacturer knows that it can be held responsible for injuries caused by its products under certain circumstances. See *Wyeth v. Levine*, 555 U.S. 555 (2009). The brand-name manufacturer also knows, however, that it will not be held liable for injuries caused by products that it neither made nor distributed. See, e.g., *Foster*, 29 F.3d at 168, 171.
>
> "....
>
> "... [T]he Plaintiffs' novel liability theory would retroactively frustrate legitimate investment-backed expectations. Decisions were made and capital invested decades ago to produce a drug for sale in a legal system that (as is traditional) allows recovery for injuries caused by the brand-name company's own product, but *not* for injuries caused by the products made by its

> competitors. The abrupt change that the Plaintiffs seek would wipe away that system and replace it with bet-the-company uncertainty.
>
> "[Looking forward], Plaintiffs' theory would destroy the predictability needed by brand-name manufacturers trying to decide whether to invest almost $2 billion and seven years of time to develop a new drug...."

Brief of amici curiae, The Chamber of Commerce of the United States of America and the Business Council of Alabama, at 20–24 (emphasis in original; some citations omitted).

Even proponents of the result urged by the plaintiffs admit that such a result is unfair to the brand-name manufacturers. See, e.g., Allen Rostron, *Prescription for Fairness: A New Approach to Tort Liability of Brand–Name and Generic Drug Manufacturers*, 60 Duke L.J. 1123, 1181 (Feb.2011) (admitting that "[u]nder the [approach of the California appeals court in] *Conte*[39] if a drug lacks adequate warnings, its brand-name manufacturer may wind up being liable for harm to those who took either the brand-name or the generic version of the drug, whereas the generic manufacturers likely will wind up not being liable to anyone. That asymmetry is particularly unfair given that the brand-name manufacturers make substantial investments in developing new drugs from which generic producers profit by copying."); Wesley E. Weeks, *Picking Up the Tab for Your Competitors: Innovator Liability After* PLIVA, Inc. v. Mensing, 19 Geo. Mason L.Rev. 1257, 1259 (Summer 2012) (conceding that holding brand-name manufacturers liable "is far from ideal. The brand-name manufacturer invests resources to produce helpful pharmaceuticals, and under innovator liability, it would be liable for harm caused by its competitors' drugs. As this reduces the profitability of creating new drugs, it could provide drug developers with a negative incentive, reducing the number of beneficial drugs developed in this country. Meanwhile, generic drug manufacturers are insulated from failure-to-warn lawsuits by the preemption recognized in *[PLIVA]*.").

***48** Another concern is insurability:

> "[G]iven the near impossibility of formulating bulletproof labeling, insurability represents a concern: cost spreading would further burden the shrinking share of customers for the brand-name drug (or else later patients taking unrelated drugs produced by that defendant) for the benefit of customers of the competitor's drug (who are already free riding on the original research and development efforts of the brand-name manufacturer). This threatens to chill therapeutic product innovation...."

Lars Noah, *Adding Insult to Injury: Paying for Harms Caused by a Competitor's Copycat Product*, 45 Tort Trial & Ins. Prac. L.J. 673, 695 n. 69 (2010).

All of these concerns are elevated by the realization that there will be no correlation between the brand-name manufacturer's continued participation in the marketplace with its own drug and its responsibility for generic drugs manufactured and sold by others. Under the rationale urged by the plaintiffs, and accepted by the majority of the Court today, a brand-name manufacturer's complete departure from the marketplace would offer no logical reason for terminating its responsibility for the deficiencies in the labeling associated with generic versions of its drugs that may be marketed indefinitely thereafter by its former competitors and perhaps even new entrants into the market.[40] At least one commentator has noted that this is a distinct possibility. See Noah, 45 Tort Trial & Ins. Prac. L.J. at 691–92 (noting as an example Hoffmann–La Roche's recent decision to withdraw its much litigated drug Accutane from the market and observing that, "[a]s a regulatory matter, so long as FDA does not withdraw the innovator's NDA [new drug approval] on safety or effectiveness grounds, existing (and the possibility for future) ANDAs [abbreviated new drug approvals] would remain unaffected").

Finally, and most troubling, I see no principled barrier to the extension of the "foreseeability" doctrine to deficient representations or design defects made by developers of other types of popular products copied by competitors. See, e.g., *Huck v. Wyeth*, *supra*.The line drawn today between the prescription-drug industry and all other industry exists only because we say it does; it will continue to exist only for so long as we say it does. There may be differences in the degree of foreseeability, but if foreseeability without relationship is to be the test, the line between the prescription-drug industry and other industry is arbitrary, and there is no principle to which this or other courts may anchor themselves in an effort to hold that line.[41]

Again, however, even if somehow this Court could guarantee that the "foreseeability" analysis embraced today never finds its way into cases involving other products or endeavors, either in this jurisdiction or in

others, the potential deleterious effect on the prescription-drug industry and those that depend upon it provide more than enough concern. In a 1977 case in which a federal court in New York explained that the fact that it was foreseeable that a statement might be relayed to and relied upon by a party with whom the maker had no relationship was not sufficient to create a duty to that party. In so doing, the court heeded the concerns of none other than Professor Prosser:

> ***49** "[W]here misstatements are claimed to be the cause of loss, even a 'reasonable anticipation that the statement will be communicated to others whose identity is unknown to the defendant, or even knowledge that the recipient intends to make some commercial use of it in dealing with unspecified third parties, is not sufficient to create a duty of care towards them.' W. Prosser, *Law of Torts*, 708 (4th ed.1971). The reason for such a rule is obvious. To quote Prosser again, it is required in order to avoid '[t]he spectre of unlimited liability, with claims devastating in number and amount crushing the defendant because of a momentary lapse from proper care....' *Id.*"

Demuth Dev. Corp. v. Merck & Co., 432 F.Supp. 990, 993–94 (E.D.N.Y.1977). We too should heed Professor Prosser's concerns.

The investment and innovation that over the past 50 years have resulted in the fastest pace of medical advances in human history have depended upon the incentives made available by America's free-market system. As they have for all types of products, the free-market system and the legal framework in which it has operated have coupled the risks and rewards of developing and distributing new medicines and, in so doing, have allowed entrepreneurs and innovators to assume both in corresponding measure. We now disrupt this critical dynamic.

Parallel Citations

Prod.Liab.Rep. (CCH) P 19,452

Footnotes

1 Although the style of the order certifying the question shows this entity as "Wyeth, Inc.," it is also referred to in the order, briefs, and other documents submitted to this Court as "Wyeth, LLC."

2 We have agreed to answer the certified question, which impacts only the narrow field of prescription drugs, which is subject to stringent Food and Drug Administration regulations and oversight. This opinion does not plow new ground, nor does it create a heretofore unknown field of tort law that has been referred to as "innovator liability," as discussed infra.Instead, this opinion answers the question whether the Weekses may bring a fraudulent-misrepresentation claim under Alabama law.

3 The Weekses also sued generic manufacturers of metoclopramide, Teva Pharmaceuticals USA and Actavis Elizabeth, LLC.

4 The clinical phase of testing on human subjects is divided into three phases: Phase one involves about 20 to 100 healthy, nominally paid volunteers and is designed to test for safety and tolerability (21 C.F.R. § 312.21(a)); phase two involves several hundred unpaid volunteers diagnosed with a particular condition and assesses the preliminary efficacy of the drug as well as safety and tolerability (21 C.F.R. § 312.21(b)); and phase three involves hundreds to several thousands of patients and is designed to evaluate the safety and efficacy of the drug on a larger segment of the population (21 C.F.R. § 312.21(c)). The FDA may require phase-four studies concurrent with market approval to conduct postmarketing reports in drugs intended to treat life-threatening and severely debilitating illnesses. 21 C.F.R § 312.95

5 The marketing of brand-name drugs also adds to the expense of the brand-name drugs. "The prescription drug industry is subject to extensive federal regulation, including the now familiar requirement that prescription drugs be dispensed only upon a physician's prescription. In light of this requirement, pharmaceutical companies have long focused their direct marketing efforts not on the retail pharmacies that dispense prescription drugs but on the medical practitioners who possess the authority to prescribe the drugs in the first place. Pharmaceutical companies promote their products to physicians through a process called 'detailing' whereby employees known as 'detailers' or 'pharmaceutical sales representatives' provide information to physicians in the hopes of persuading them to write prescriptions for the products in appropriate cases."*Christopher v. SmithKline Beecham Corp.*, —— U.S. ——, ——, 132 S.Ct. 2156, 2163, 183 L.Ed.2d 153 (2012) (footnote omitted).

6 It appears that this is the first time the highest court of a state has addressed the issue whether a manufacturer of a brand-name prescription drug may be held liable for the warning label on the drug when the plaintiff ingested a generic version of the brand-name drug. The numerous federal courts sitting in diversity have addressed this issue, predicting how the highest courts of those states would rule on the issue.*Erie R.R. v. Tompkins*, 304 U.S. 64, 58 S.Ct. 817, 82 L.Ed. 1188 (1938). But see *Huck v. Wyeth, Inc.*, 850 N.W.2d 353 (Iowa 2014) (disagreeing with this Court's holding on original submission in the present case, but expressly acknowledging that Iowa law differs from Alabama law in that Iowa law requires a plaintiff seeking recovery for the side effects of a prescription drug who sues a pharmaceutical company under any theory, including misrepresentation, to prove that he or she was injured by using the prescription drug manufactured or supplied by that pharmaceutical company).

7 See, e.g., *Baymiller v. Ranbaxy Pharm., Inc.*, 894 F.Supp.2d 1302 (D.Nev.2012); *Phelps v. Wyeth, Inc.*, 857 F.Supp.2d 1114 (D.Or.2012); *Fisher v. Pelstring* (No. 4:09–cv–00252–TLW, July 28, 2010) (D.S.C.2010) (not reported in F.Supp.2d)(collecting cases); *Swicegood v. PLIVA, Inc.*, 543 F.Supp.2d 1351, 1358 (N.D.Ga.2008); *Goldych v. Eli Lilly & Co.* (No. 5:04–CV–1477, July 19, 2006) (N.D.N.Y.2006) (not reported in F.Supp.2d); *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514, 538–43 (E.D.Pa.2006), aff'd in part and rev'd in part on other grounds, 521 F.3d 253 (3d Cir.2008), vacated, 556 U.S. 1101, 129 S.Ct. 1578, 173 L.Ed.2d 672 (2009); *Tarver v. Wyeth, Inc.* (No. Civ.A.3–04–2036, January 26, 2006) (W.D.La.2006) (not reported in F.Supp.2d); *Sharp v. Leichus* (2004–CA–0643, February 17, 2006)(Fla.Cir.Ct.2006); *Kelly v. Wyeth* (CIV. A. MICV 2003–03324B, May 6, 2005) (Super.Ct.Mass.2005); *Sheeks v. American Home Prods. Corp.* (No. 02CV337, October 15, 2004) (Colo.Dist.Ct.2004); *Doe v. Ortho–Clinical Diagnostics, Inc.*, 335 F.Supp.2d 614, 626–30 (M.D.N.C.2004); *Block v. Wyeth, Inc.* (No. Civ.A.3:02–CV–1077, January 28, 2003) (N.D.Tex.2003) (not reported in F.Supp.2d); and *Beutella v. A.H. Robins Co.* (No. 980502372, December 10, 2001) (Utah Dist.Ct.2001).

8 It is undisputed that Danny received metoclopramide through a prescription written by his physician.

9 To allow labels on generic versions of a brand-name drug to differ from the labels on the brand-name versions could not only insinuate that the generic versions were not the bioequivalent of the brand-name versions, but could also confuse physicians reviewing the different versions. The "FDA 'places a very high priority [on] assuring consistency in labeling,' so as 'to minimize any cause for confusion among health care professionals and consumers as well as to preclude a basis for lack of confidence in the equivalency of generic versus brand name products.'" Brief for the United States As Amicus Curiae Supporting Respondents, at 4, in *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567 (Nos. 09–993, 09–1039 and 09–1501) (alterations in original) (quoting Div. of Generic Drugs, FDA, Policy and Procedure Guide 37 (1989) (citing 57 Fed.Reg. 17,961 (1992))). Additionally, although both the brand-name manufacturer and the generic manufacturer have a continuing duty to report adverse reactions to the FDA, it may be that only the brand-name manufacturer has all the relevant data in light of trade-secrets concerns.

10 *Hines* was overruled on other grounds in *Owen.*The Court of Civil Appeals noted that "the discussion in *Hines* concerning the determination of whether a legal duty to disclose exists remains precedential."743 So.2d at 461.

11 It should also be noted that we are not deciding the merits of the underlying case. It may be that a jury finds that the warnings on the label were adequate or that it finds that Danny's physician did not rely on the warnings on the label authored by Wyeth when prescribing the generic version of Reglan to Danny.

12 Certain federal district court decisions cited in this Court's answer address the issue under the law that existed before the Supreme Court's decision in *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011), and are thus distinguishable. The numerous decisions from other jurisdictions that rely on principles rejected by *PLIVA* are similarly distinguishable.

13 Given that the federal district court has decided that the action is not an Alabama Extended Manufacturer's Liability Doctrine ("AEMLD")/defective-product action, I decline to accept the invitation of Wyeth to recharacterize the action under the anti-circumvention rule stated in *Pfizer, Inc. v. Farsian*, 682 So.2d 405 (Ala.1996), as one that is, in substance, alleging a defective-product claim and not a fraud claim. The application for rehearing takes this Court to task for failing to address this issue. However, as this Court's answer explains, citing *Tillman v. R.J. Reynolds Tobacco Co.*, 871 So.2d 28, 34–35 (Ala.2003), AEMLD claims and fraud claims are different. As cast by the district court in the question presented to us, this case presents a fraud action. I express no opinion as to whether it should be recharacterized. *Thompson–Hayward Chemical Co. v. Childress*, 277 Ala. 285, 169 So.2d 305 (1964), cited by Wyeth on rehearing, involves a negligence action, not a fraud action, and thus is inapplicable.

14 Danny's doctor wrote him a prescription for "Reglan" and directed its use; Danny's pharmacy filled the prescription with metoclopramide that was manufactured by someone other than Wyeth. It is the doctor's prescribed *use* of metoclopramide, which we must assume was based on what Wyeth told or failed to tell the doctor, that caused Danny's injury.

15 Thus, the numerous decisions of other jurisdictions that would hold that the injury that allegedly occurred in this case was not foreseeable are distinguishable. I would be hesitant to cite decisions rejecting foreseeability, as well as decisions that predate *PLIVA*, as calling into question the rationale of this Court's answer to the certified question.

16 Hines was overruled on other grounds by *State Farm Fire & Casualty Co. v. Owen*, 729 So.2d 834 (Ala.1998). See note 10, supra.

17 Pfizer, Inc., the third brand-name defendant, is the parent company of Wyeth. Brand-name defendants' brief on original submission, at 3 n. 2.

18 The Weekses allege that Danny first began ingesting metoclopramide, the generic name for Reglan, in 2007.

19 Other states, following the language in the Uniform Certification of Questions of Law Act (1967), permit certification of questions of law that "*may* be determinative of the cause then pending in the certifying court" or, following the 1995 version of that Act, that "*may* be determinative *of an issue* in pending litigation in the certifying court." (Emphasis added.) These broader formulations do not reflect the Alabama rule, which requires the presence of "questions or propositions of law of this State which *are* determinative of said cause."(Emphasis added.)

20 "[T]he concept of duty does not exist in a vacuum. It requires a relationship between two or more parties, a relationship that can be shown only through a history of contacts, conversations, and circumstances. Determining whether there is a duty necessarily requires analyzing the factual background of the case."729 So.2d at 839.

21 The Federalist No. 7, at 63 (Alexander Hamilton) (Clinton Rossiter ed., 1961).

22 There has been criticism of the notion that foreseeability should be understood as significant in determining duty. Some courts and commentators have attempted to explain that foreseeability that a given act will lead to a given harm goes only to the issue whether that act is unreasonable and thus falls short of the standard of care or to the issue whether the harm can be considered to have been proximately caused by the act. They view the existence vel non of a duty as a threshold issue determined solely by the relationship or nexus of the parties. See, e.g., *Gipson v. Kasey*, 214 Ariz. 141, 144, 150 P.3d 228, 231 (2007) ("[F]oreseeability often determines whether a defendant acted reasonably under the circumstances or proximately caused injury to a particular plaintiff.... Foreseeability, as this Court noted in *Martinez [v. Woodmar IV Condos. Homeowners Ass'n, Inc.*, 189 Ariz. 206, 211, 941 P.2d 218, 223 (1997)], is more properly applied to the factual determinations of breach and causation than to the legal determination of duty."); W. Jonathan Cardi, *Purging Foreseeability*, 58 Vand. L.Rev. 739 (April 2005).

It is not necessary here to grapple with this fundamental question. It is enough for present purposes to recognize that foreseeability alone is not enough to create a duty and that a relationship between the parties is essential.

23 My count might be low. An appendix to the appellants' application for rehearing lists more cases.

24 The following pre-*PLIVA* cases involve the same drug at issue in this case; many of them involve one or both of the same corporate defendants. In all of them, the court holds that the defendant brand-name manufacturer has no duty or liability with respect to generic metoclopramide not manufactured or sold by it: *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 612–14 (8th Cir.2009), rev'd in part on other grounds sub nom. *PLIVA, Inc. v. Mensing*, 564 U.S. ——, 131 S.Ct. 2567, 180 L.Ed.2d 580 (2011); *Bell v. Pfizer Inc.*, No. 5:10CV00101 BSM (E.D.Ark. Mar. 16, 2011) (not reported in F.Supp.2d); *Overton v. Wyeth, Inc.*, No. CA 10–0491–KD–C (S.D.Ala. Mar. 15, 2011) (not reported in F.Supp.2d), findings and recommendation adopted (S.D.Ala. Apr. 7, 2011) (not reported in F.Supp.2d); *Simpson v. Wyeth, Inc.*, No. 7:10–cv–01771–HGD (N.D.Ala. Dec. 9, 2010) (not reported in F.Supp.2d), report and recommendation adopted (N.D.Ala. Jan. 4, 2011) (not reported in F.Supp.2d); *Gross v. Pfizer, Inc.*, No. 10–CV–00110–AW (D.Md. Nov. 9, 2010) (not reported in F.Supp.2d); *Cooper v. Wyeth, Inc.*, No. 09–CV–929 (M.D.La. Oct. 26, 2010) (not reported in F.Supp.2d); *Fullington v. Pfizer, Inc.*, No. 4:10CV00236 JLH (E.D.Ark. Sept. 17, 2010) (not reported in F.Supp.2d); *Johnson v. Teva Pharm. USA, Inc.*, No. 2:10 CV 404 (W.D.La. Aug. 16, 2010) (not reported in F.Supp.2d); *Fisher v. Pelstring*, No. 4:09–cv–00252–TLW (D.S.C. July 28, 2010) (not reported in F.Supp.2d); *Neal v. Teva Pharm. USA, Inc.*, No. 09–CV–1027 (W.D.Ark. July 1, 2010) (not reported in F.Supp.2d); *Mosley v. Wyeth, Inc.*, 719 F.Supp.2d 1340 (S.D.Ala.2010); *Phelps v. Wyeth, Inc.*, No. 09–6168–TC (D.Or. May 28, 2010) (not reported in F.Supp.2d), findings and recommendation adopted (D. Or. June 21, 2010) (not reported in F.Supp.2d); *Craig v. Pfizer, Inc.*, No. 3:10–00227 (W.D.La. May 26, 2010) (not reported in F.Supp.2d); *Finnicum v. Wyeth, Inc.*, 708 F.Supp.2d 616, 619–21 (E.D.Tex.2010); *Howe v. Wyeth Inc.*, No. 8:09–CV–610–T–17 AEP (M.D.Fla. Apr.26, 2010) (not reported in F.Supp.2d); *Hardy v. Wyeth, Inc.*, No. 9:09CV152 (E.D.Tex. Mar. 8, 2010) (not reported in F.Supp.2d), report and recommendation adopted (E.D.Tex. Mar. 29, 2010) (not reported in F.Supp.2d); *Couick v. Wyeth, Inc.*, 691 F.Supp.2d 643, 645–46 (W.D.N.C.2010); *Levine v. Wyeth Inc.*, 684 F.Supp.2d 1338, 1344–48 (M.D.Fla.2010); *Washington v. Wyeth, Inc.*, No. 3:09–CV–01343 (W.D.La. Feb. 8, 2010) (not reported in F.Supp.2d); *Morris v. Wyeth, Inc.*, No. 09–0854 (W.D.La. Nov. 23, 2009) (not reported in F.Supp.2d); *Meade v. Parsley*, No. 2:09–cv–00388 (S.D.W.Va. Nov. 13, 2009) (not reported in F.Supp.2d); *Burke v. Wyeth, Inc.*, No. G–09–82 (S.D.Tex. Oct. 29, 2009) (not reported in F.Supp.2d); *Stoddard v. Wyeth, Inc.*, 630 F.Supp.2d 631, 633–34 (E.D.N.C.2009); *Fields v. Wyeth, Inc.*, 613 F.Supp.2d 1056, 1060–61 (W.D.Ark.2009); *Moretti v. Wyeth, Inc.*, No. 2:08–cv–00396–JCM–(GWF) (D.Nev. Mar. 20, 2009) (not reported in F.Supp.2d); *Schrock v. Wyeth,*

Inc., 601 F.Supp.2d 1262, 1266–67 (W.D.Okla.2009); *Cousins v. Wyeth Pharm., Inc.*, No. 3:08–CV–0310–N (N.D.Tex. Mar. 10, 2009) (not reported in F.Supp.2d); *Smith v. Wyeth, Inc.*, No. 5:07–CV–18–R (W.D. Ky. June 30, 2008) (not reported in F.Supp.2d), aff'd, 657 F.3d 420 (6th Cir.2011); *Wilson v. Wyeth, Inc.*, No. 3:07–CV–378–R (W.D. Ky. June 30, 2008) (not reported in F.Supp.2d), aff'd, 657 F.3d 420 (6th Cir.2011); *Morris v. Wyeth, Inc.*, No. 1:07–CV–176–R (W.D. Ky. June 30, 2008) (not reported in F.Supp.2d), aff'd, 657 F.3d 420 (6th Cir.2011); *Pustejovsky v. Wyeth, Inc.*, No. 4:07–CV–103–Y (N.D.Tex. Apr. 3, 2008) (not reported in F.Supp.2d); *Swicegood v. PLIVA, Inc.*, 543 F.Supp.2d 1351, 1358 (N.D.Ga.2008); *Tarver v. Wyeth, Inc.*, No. Civ.A.3–04–2036 (W.D.La. Jan. 26, 2006) (not reported in F.Supp.2d); *Tarver v. Wyeth, Inc.*, No. Civ.A.3–04–2036 (W.D. La. June 7, 2005) (not reported in F.Supp.2d); *Block v. Wyeth, Inc.*, No. Civ.A. 3:02–CV–1077 (N.D.Tex. Jan. 28, 2003) (not reported in F.Supp.2d); and *Sharp v. Leichus*, 952 So.2d 555 (Fla.Dist.Ct.App.2007).

In addition to *Foster*, the other pre-*PLIVA* cases holding that a manufacturer of a brand-name drug has no duty or liability to the consumer of a generic drug manufactured and sold by another company include *Barnhill v. Teva Pharmaceuticals USA, Inc.*, No. 06–0282–CB–M (S.D.Ala. Apr. 24, 2007) (not reported in F.Supp.2d); *Leblanc v. Wyeth, Inc.*, No. CIV A 04–0611 (W.D.La. Oct. 5, 2006) (not reported in F.Supp.2d); *Goldych v. Eli Lilly & Co.*, No. 5:04–CV–1477 (GLS/GJD) (N.D.N.Y. July 19, 2006) (not reported in F.Supp.2d); *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514, 540–41 (E.D.Pa.2006), rev'd on other grounds, 521 F.3d 253 (3d Cir.2008), vacated and remanded, 556 U.S. 1101, 129 S.Ct. 1578, 173 L.Ed.2d 672 (2009); *Possa v. Eli Lilly & Co.*, No. 05–1307–JJB–SCR (M.D.La. May 10, 2006) (not reported in F.Supp.2d); *Stanley v. Wyeth, Inc.*, 991 So.2d 31, 34–35 (La.Ct.App.2008); and *Flynn v. American Home Products Corp.*, 627 N.W.2d 342, 350 (Minn.Ct.App.2001).

In addition, according to briefs filed in this case, two Alabama circuit courts also have addressed the issue of liability for injuries allegedly caused by generic metoclopramide, both concluding that the brand-name manufacturer was *not liable* for injury caused by the generic drug manufactured and sold by another company. See *Buchanan v. Wyeth Pharm., Inc.*, No. CV–2007–900065, Oct. 20 2008; *Green v. Wyeth, Inc.*, No. CV–2006–3917, May 14, 2007.

25 See *Weeks v. Wyeth*, No. 1:10–cv–602–MEF (M.D.Ala. Mar. 31, 2011) (not reported in F.Supp.2d); *Conte v. Wyeth, Inc.*, 168 Cal.App.4th 89, 85 Cal.Rptr.3d 299, 315–18 (2008); and *Kellogg v. Wyeth*, 762 F.Supp.2d 694 (D.Vt.2010).

26 See also, e.g., *Tetuan v. A.H. Robins Co.*, 241 Kan. 441, 464, 738 P.2d 1210, 1228 (1987) ("[W]here a patient relies on a physician for treatment or advice ..., justifiable reliance by the physician on misrepresentations or concealment by the manufacturer of [a] device constitutes justifiable reliance by the patient."); *Reyes v. Wyeth Labs.*, 498 F.2d 1264, 1276 (5th Cir.1974) ("Pharmaceutical companies then, who must warn ultimate purchasers of dangers inherent in patent drugs sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as a 'learned intermediary' between manufacturer and consumer."); and *Lovejoy v. AT & T Corp.*, 92 Cal.App.4th 85, 95, 111 Cal.Rptr.2d 711, 718 (2001) ("Under the principle of indirect reliance, a fraudulent misrepresentation is actionable if it was communicated to an agent of the plaintiff and was acted upon by the agent to the plaintiff's damage. A classic example of indirect reliance would be a drug manufacturer's misrepresentation to physicians about the safety of its drug. A patient injured by the drug is permitted to sue the manufacturer for fraud without proof that his doctor repeated the falsehood to him, under the theory that the doctor was acting as plaintiff's agent.").

27 Of course, the corollary of this fact is that the generic manufacturer *does* have a duty to the consumer of its generic drug to publish a label upon which that consumer, through his or her physician or pharmacist, can rely. It does not change the lack of a duty by the brand-name manufacturer as to the manufacturer of the generic drug to say that the generic manufacturer must replicate for use with its own drug the wording of the dosing instructions and warnings approved by the FDA for use by the brand-name manufacturer. That fact, and whatever effect it may or may not have upon the generic manufacturer's liability to its consumer, is a matter between the generic manufacturer and the consumer, with "input" from Congress, the FDA, and the United States Supreme Court. The brand-name manufacturer plays no role in the generic manufacturer's decision to enter the market, and it is not responsible for crafting the regulatory and legal framework within which the generic manufacturer chooses to do so.

28 These cases take this approach because pharmacological defects and defective warnings are indistinguishable for purposes of considering liability associated with the consumption of a drug. As the United States Supreme Court recently explained in a non-drug case:

> "According to petitioners, these claims do not fall within the [Locomotive Inspection Act's] pre-empted field because '[t]he basis of liability for failure to warn ... is not the "design" or "manufacture" of a product,' but is instead 'the failure to provide adequate warnings regarding the product's risks.'...
>
> "We disagree. A failure-to-warn claim alleges that the product itself is unlawfully dangerous unless accompanied by sufficient warnings or instructions. *Restatement (Third) of Torts: Products Liability* § 2(c) (1997) (A failure-to-warn claim alleges that a product is defective 'when the foreseeable risks of harm posed by the product could have been reduced or avoided by the provision of reasonable instructions or warnings by the seller or other distributor, ... and *the omission of the instructions or warnings renders the product not reasonably safe*'); see also *id.*, Comment *1*, at 33 ('Reasonable designs and instructions or warnings both play important roles in the production and distribution of reasonably safe products').''

Kurns v. Railroad Friction Prods. Corp., —— U.S. ——, ——, 132 S.Ct. 1261, 1268, —— L.Ed.2d —— (2012) (emphasis added).

The indistinguishability of labeling and product is even clearer—and more tangible—in the case of prescription drugs. Prescription drugs are approved for sale by the FDA as safe and effective *only* for use as recommended in the approved labeling.

As an amicus brief in another case recently explained:

> "Attempts to selectively untether the design of a prescription drug from its labeling by allowing a claim that 'the drug's risks outweighed its benefits' making it unreasonably dangerous ignore one very salient fact: The FDA-approved 'benefit' is derived only by reference to the approved indications in the product labeling, and the source of the 'risks' to which the benefits are compared also is the FDA-approved labeling. In other words, *a pharmaceutical product cannot be divorced from its label as it is not possible to conduct a risk/benefit (i.e., design defect) evaluation without the product labeling.*"

Brief of the Generic Pharmaceutical Association as amicus curiae in support of the petitioner in *Mutual Pharm. Co. v. Bartlett*, No. 12–142, Jan. 22, 2013, p. 16 (appellate brief to United States Supreme Court 2013) (emphasis added). See also note 31, *infra*.Indeed, the United States Supreme Court in *PLIVA* itself treated the label and warnings that accompanied the drug as an integral part of the drug itself. Adequate warnings, or lack thereof, are an inseparable part of the product purchased and consumed by the plaintiff. (No one, for example, would contend that Tylenol brand acetaminophen sold to consumers as a pain remedy, but without any labels prescribing dosages or warning of the harmful side effects of taking more than the prescribed dosage would amount to the same product as Tylenol sold with a label prescribing a dosage of only two tablets every six hours and warning of harmful side effects if that dosage is exceeded.)

Even this Court has had occasion to express its understanding that the dosing instructions and the warnings of contraindications and side effects set out in a drug's label make the drug what it is. In *Stone v. Smith, Kline & French Lab.*, 447 So.2d 1301, 1304 (Ala.1984), this Court analyzed a "failure to warn" as an aspect of products-liability law, and explained that "the adequacy of the accompanying warning determines whether the drug, *as marketed*, is defective, or reasonably dangerous."

29 In *Wyeth v. Levine*, 555 U.S. 555, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009), the Supreme Court held that lawsuits against brand-name manufacturers of prescription drugs were not preempted by federal law.

30 See *Demahy v. Schwarz Pharma, Inc.*, 702 F.3d 177 (5th Cir.2012); *Smith v. Wyeth, Inc.*, 657 F.3d 420 (6th Cir.2011); *Mensing v. Wyeth, Inc.*, 658 F.3d 867 (8th Cir.2011); *Baymiller v. Ranbaxy Pharm., Inc.*, 894 F.Supp.2d 1302 (D.Nev.2012); *Strayhorn v. Wyeth Pharm., Inc.*, 882 F.Supp.2d 1020 (W.D.Tenn.2012); *Phelps v. Wyeth, Inc.*, 857 F.Supp.2d 1114 (D.Or.2012); *Metz v. Wyeth LLC*, 830 F.Supp.2d 1291 (M.D.Fla.2011); *Lashley v. Pfizer, Inc.*, 877 F.Supp.2d 466 (S.D.Miss.2012); *Guarino v. Wyeth LLC*, No. 8:10–cv–2885–T–30GTW (M.D.Fla. Apr. 3, 2012) (not reported in F.Supp.2d); *Gross v. Pfizer, Inc.*, No. 10–CV–00110–AW (D.Md. Sep. 7, 2011) (not reported in F.Supp.2d); and *Fullington v. PLIVA, Inc.*, No. 4:10CV00236JLH (E.D.Ark. Dec. 12, 2011) (not reported in F.Supp.2d). Some of these are cases in which a court that addressed the issue before *PLIVA* had an opportunity after *PLIVA* to revisit its previous ruling, only to reaffirm that previous ruling and implicitly or explicitly conclude that the Supreme Court's holding in *PLIVA* did not alter the court's pre-*PLIVA* analysis.

31 The court explained that the term "products liability action" was simply a reference to " 'any action brought for or on account of personal injury, death or property damage caused by or resulting from the manufacture, construction, design, formulation ... warning, instructing, marketing, advertising, packaging or labeling of any product.'" 657 F.3d at 423 (quoting Ky.Rev.Stat. § 411.300(1) (2010)).

Cases from jurisdictions decided under a legislatively, or in some cases judicially, crafted "products liability doctrine" that has supplanted or supplemented traditional common-law theories of recovery are entirely apposite to the question at hand. Such doctrines, as in Kentucky, invariably reflect common-law theories of recovery, including misrepresentation and suppression relating to labeling and warnings, and, like the common-law claims alleged here, also require the existence of a duty arising out of a sufficient nexus between the manufacturer and consumer in relation to the product consumed.

For the same reason, it is not necessary to address the issue whether the claims made by the plaintiffs in this case should be considered Alabama Extended Manufacturer's Liability Doctrine claims or may be considered conventional products-liability claims based on common-law theories of fraud and suppression. A duty arising from a relationship or nexus between the parties would be necessary in either case; none exists here.

32 The Florida federal district court went on to explain that "many of the pre-[*PLIVA*] decisions in Florida and elsewhere apparently assumed that consumers would have a remedy against generic drug manufacturers" but that this assumption was not the basis for those decisions. 830 F.Supp.2d at 1294.

As did the Oregon federal court in *Phelps v. Wyeth*, *supra*, the federal district court in *Metz* explained how the opinion in *PLIVA* itself reveals the Supreme Court's understanding that its decision in *PLIVA* changed nothing as to the lack of a duty on the part of brand-name manufacturers with respect to those injured as a result of deficient labeling of other manufacturers' products:

> "Tellingly, the Supreme Court in [*PLIVA*] appeared to contemplate that consumers of generic drugs may be without a remedy when it noted 'the unfortunate hand that federal drug regulation has dealt [consumers of generic drugs].' [564 U.S. at ——, 131 S.Ct.] at 2581; *see* [564 U.S. at ——, 131 S.Ct.] at 2592 (Sotomayor, J., dissenting)(noting that under the majority's decision, a consumer of a generic drug 'now has no right to sue')."

830 F.Supp.2d at 1294.

33 The problem in this case is that the relationship or nexus to which one would normally look as the basis for a duty exists between

the consumer and the generic manufacturer. As discussed, see note 27, *supra*, one therefore would expect that it would be the generic manufacturer that would bear responsibility for the plaintiffs' injuries. Nor would such an outcome be unfair. The generic manufacturer is not required to take on the manufacture or distribution of the generic drug. It does so freely, weighing the risks and rewards of manufacturing and selling a generic drug under whatever conditions are imposed by federal law. No one requires it to enter the market—not the federal government, and certainly not the brand-name manufacturer that developed the drug and that stands to lose market share and attendant profits if the generic manufacturer does enter the market. The generic manufacturer makes these decisions freely, knowing that when it seeks to profit from marketing a generic drug, certain risks come with that decision. It is not the fault of the brand-name manufacturer that the federal government has decided that the consumer of a competitor's product is to be blocked from imposing on that competitor the costs that would normally accompany the rewards attendant to the sale of that product.

34 "*Johnny Spradlin Auto Parts, Inc. v. Cochran*, 568 So.2d 738, 742–43 (Ala.1990); *Lawyers Title Ins. Corp. v. Vella*, 570 So.2d 578, 585 (Ala.1990); *Hopkins v. Lawyers Title Ins. Corp.*, 514 So.2d 786 (Ala.1986); *Mid–State Homes, Inc. v. Startley*, 366 So.2d 734 (Ala.Civ.App.1979); *Chandler v. Hunter*, 340 So.2d 818 (Ala.Civ.App.1976). Cf. *Sims v. Tigrett*, 229 Ala. 486, 158 So. 326 (1934)."*Carter v. Chrysler Corp.*, 743 So.2d at 461.

35 The special concurrence states that "[n]o decision of any other jurisdiction addresses the precise question of Alabama law discussed in our answer." —— So.3d at —— (Shaw, J., concurring specially). Beginning with *Foster*, however, there has been an almost endless stream of published opinions discussed hereinafter that address the exact issue we address here: a claim of "fraud," "suppression," or "misrepresentation" in connection with a generic manufacturer's use of deficient labeling in the "pervasively" regulated prescription-drug industry. And the fundamental legal principles employed in the analysis of this issue in these other cases are as elemental and imbedded in the law of this State as they are in the law of the other states discussed in those decisions.

36 The Supreme Court previously had denied certiorari review in *Smith v. Wyeth, Inc.*, 657 F.3d 420(6th Cir.2011), cert. denied, —— U.S. ——, 132 S.Ct. 2103, 182 L.Ed.2d 868 (2012).

37 In each of these three cases, the federal Court of Appeals refers to this Court's decision on original submission as being one of only two or three that have held as it did. See, e.g., *Guarino*, 719 F.3d at 1253, citing in juxtaposition to the "mountain" of cases to the contrary, this court's decision and the decisions of the Vermont district court in *Kellogg v. Wyeth*, 762 F.Supp.2d 694, 708–09 (D.Vt.2010), and the California district court in *Conte v. Wyeth, Inc.*, 168 Cal.App.4th 89, 85 Cal.Rptr.3d 299, 310 (2008).

38 The special concurrence characterizes the main opinion as simply applying "established Alabama decisions," "established Alabama tort law" and "existing law," concluding that the main opinion therefore "epitomizes ... judicial restraint." —— So.3d at —— (Shaw, J., concurring specially). For the reasons explained in this writing, however, existing Alabama precedents do not support the holding of this Court today. To the contrary, the decision of this Court today essentially stands alone against Alabama cases recognizing and applying the fundamental principles of relationship and duty discussed at length herein and against an unprecedented number (approaching 100 cases) from other jurisdictions applying the same fundamental principles specifically to the prescription-drug industry. As the Eleventh Circuit puts it, these latter cases do indeed constitute a "mountain of authority" representing an "overwhelming national consensus" to the contrary of the conclusion reached by this Court today.

> As for the persistent suggestion that this "mountain of authority" somehow addresses some issue or issues different than the issue this Court addresses today, I can do little more than once again point the reader to the discussion of and the quotations from so many of the cases that are part of that "mountain," as set out extensively on the several dozen pages that immediately precede this one. As already observed, beginning with *Foster*, most of this almost endless stream of precedents involves the exact issue addressed here, a claim of "fraud," "suppression," or "misrepresentation" in connection with a generic manufacturer's use of deficient labeling in the "pervasively" regulated prescription-drug industry. And, again, the fundamental legal principles employed in the analysis of this issue in these other cases are as elemental to the law of this State as they are to the law of the states discussed in those decisions.
>
> Finally, although I think it clear enough from the discussion that both precedes and follows this footnote, let me be explicit in stating that any discussion of economic or other practical concerns found herein is not offered out of a perceived need to supplant or to supplement the case authority cited. It is but to further explain the reason and soundness of that authority and, to that end, the ramifications generally and in regard to the prescription-drug industry in particular of an abandonment of the fundamental legal principles that inform that authority.

39 *Conte v. Wyeth, Inc.*, 168 Cal.App.4th 89, 85 Cal.Rptr.3d 299 (2008).

40 In fact, one of the defendants in the case before us today, Wyeth, Inc., ceased manufacturing Reglan or making any representations concerning it in about 2002; it sold its right to produce the drug to codefendant Schwarz Pharma, Inc.

41 Even the United States District Court for the Middle District of Alabama, in its order certifying to us the question at hand, agrees:

> "[T]he question's significance extends well beyond the Reglan litigation—and for that matter, even

> beyond pharmaceutical litigation. It is likely to recur any time a brand-name manufacturer (of any product) is sued on fraud, misrepresentation, and/or suppression theories by a plaintiff who claims to have been injured while using a generic-equivalent product."

See also Alissa J. Strong, "*But He Told Me It was Safe!": The Expanding Tort of Negligent Representation,* 40 U. Mem. L.Rev. 105, 142 (Fall 2009) (explaining that it is "not unreasonable to assume" that the *Conte* decision could be applied outside the drug context).

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131 S.Ct. 2567
Supreme Court of the United States

PLIVA, INC., et al., Petitioners,
v.
Gladys MENSING.
Actavis Elizabeth, LLC, Petitioner,
v.
Gladys Mensing.
Actavis, Inc., Petitioner,
v.
Julie Demahy.

Nos. 09–993, 09–1039, 09–1501. | Argued March 30, 2011. | Decided June 23, 2011.

Synopsis
Background: Consumer brought action in state court against generic drug manufacturer, alleging that long-term metoclopramide use caused her tardive dyskinesia and that the manufacturer was liable under the Louisiana Products Liability Act (LPLA). Following removal, the United States District Court for the Eastern District of Louisiana, Carl J. Barbier, J., 586 F.Supp.2d 642, granted in part and denied in part manufacturer's motion to dismiss. Manufacturer appealed. The United States Court of Appeals for the Fifth Circuit, Patrick E. Higginbotham, Circuit Judge, 593 F.3d 428, affirmed. In a separate suit, a second consumer brought action against generic drug manufacturers, alleging that long-term metoclopramide use caused her tardive dyskinesia and that the manufacturers were liable under Minnesota state tort law. The United States District Court for the District of Minnesota, 562 F.Supp.2d 1056, 2008 WL 4724286, entered summary judgment in favor of manufacturers. Consumer appealed. The United States Court of Appeals for the Eighth Circuit, Murphy, Circuit Judge, 588 F.3d 603, reversed in part. Certiorari was granted as to both cases, and the cases were consolidated.

[Holding:] The Supreme Court, Justice Thomas, held that federal law pre-empted state laws imposing the duty to change a drug's label upon generic drug manufacturers.

Reversed and remanded.

Justice Kennedy joined in part.

Justice Sotomayor, filed a dissenting opinion in which Justice Ginsburg, Justice Breyer, and Justice Kagan joined.

West Codenotes

Limited on Preemption Grounds
LSA–R.S. 9:2800.57

***2569 *Syllabus*[*]**

Five years after the Food and Drug Administration (FDA) first approved metoclopramide, a drug commonly used to treat digestive tract problems, under the brand name Reglan, generic manufacturers such as petitioners also began producing the drug. Because of accumulating evidence that long-term metoclopramide use can cause tardive dyskinesia, a severe neurological disorder, warning labels for the drug have been strengthened and clarified several times, most recently in 2009.

Respondents were prescribed Reglan in 2001 and 2002, but both received the generic drug from their pharmacists. After taking the drug as prescribed for several years, both developed tardive dyskinesia. In separate state-court tort actions, they sued petitioners, the generic drug manufacturers that produced the metoclopramide they took (Manufacturers). Each respondent alleged, *inter alia*, that long-term metoclopramide use caused her disorder and that the Manufacturers were liable under state tort law for failing to provide adequate warning labels. In both suits, the Manufacturers urged that federal statutes and FDA regulations pre-empted the state tort claims by requiring the same safety and efficacy labeling for generic metoclopramide as was mandated at the time for Reglan. The Fifth and Eighth Circuits rejected these arguments, holding that respondents' claims were not pre-empted.

Held: The judgment is reversed, and the cases are remanded.

588 F.3d 603 and 593 F.3d 428, reversed and remanded.

Justice THOMAS delivered the opinion of the Court with respect to all but Part III–B–2, concluding that federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, these state claims. Pp. 2573 – 2579, 2580 – 2582.

***2570** (a) Because pre-emption analysis requires a comparison between federal and state law, the Court begins by identifying the state tort duties and federal labeling requirements applicable to the Manufacturers. Pp. 2573 – 2577.

(1) State tort law requires a manufacturer that is, or should be, aware of its drug's danger to label it in a way that renders it reasonably safe. Respondents pleaded that the Manufacturers knew, or should have known, both that the long-term use of their products carried a high risk of tardive dyskinesia and that their labels did not adequately warn of that risk. Taking these allegations as true, the state-law duty required the Manufacturers to use a different, stronger label than the one they actually used. Pp. 2573 – 2574.

(2) On the other hand, federal drug regulations, as interpreted by the FDA, prevented the Manufacturers from independently changing their generic drugs' safety labels. A manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate. Although the same rules originally applied to all drugs, the 1984 law commonly called the Hatch–Waxman Amendments allows a generic drug manufacturer to gain FDA approval simply by showing that its drug is equivalent to an already-approved brand-name drug, and that the safety and efficacy labeling proposed for its drug is the same as that approved for the brand-name drug. Respondents contend that federal law nevertheless provides avenues through which the Manufacturers could have altered their metoclopramide labels in time to prevent the injuries here. These include: (1) the FDA's "changes-being-effected" (CBE) process, which permits drug manufacturers, without preapproval, to add or strengthen a warning label; and (2) sending "Dear Doctor" letters providing additional warnings to prescribing physicians and other healthcare professionals. However, the FDA denies that the Manufacturers could have used either of these processes to unilaterally strengthen their warning labels. The Court defers to the FDA's views because they are not plainly erroneous or inconsistent with the regulations, and there is no other reason to doubt that they reflect the FDA's fair and considered judgment. *Auer v. Robbins*, 519 U.S. 452, 461, 462, 117 S.Ct. 905, 137 L.Ed.2d 79. Assuming, without deciding, that the FDA is correct that federal law nevertheless required the Manufacturers to ask for the agency's assistance in convincing the brand-name manufacturer to adopt a stronger label, the Court turns to the pre-emption question. Pp. 2574 – 2577.

(b) Where state and federal law directly conflict, state law must give way. See, *e.g.*, *Wyeth v. Levine*, 555 U.S. 555, 583, 129 S.Ct. 1187, 173 L.Ed.2d 51. Such a conflict exists where it is "impossible for a private party to comply with both state and federal requirements." *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287, 115 S.Ct. 1483, 131 L.Ed.2d 385. Pp. 2577 – 2579, 2580 – 2582.

(1) The Court finds impossibility here. If the Manufacturers had independently changed their labels to satisfy their state-law duty to attach a safer label to their generic metoclopramide, they would have violated the federal requirement that generic drug labels be the same as the corresponding brand-name drug labels. Thus, it was impossible for them to comply with both state and federal law. And even if they had fulfilled their federal duty to ask for FDA help in strengthening the corresponding brand-name label, assuming such a duty exists, they would not have satisfied their state tort-law duty. State law demanded a safer label; it did not require ***2571** communication with the FDA about the possibility of a safer label. Pp. 2577 – 2578.

(2) The Court rejects the argument that the Manufacturers' pre-emption defense fails because they failed to ask the FDA for help in changing the corresponding brand-name label. The proper question for "impossibility" analysis is whether the private party could independently do under federal law what state law requires of it. See *Wyeth, supra*, at 573, 129 S.Ct. 1187. Accepting respondents' argument would render conflict pre-emption largely meaningless by making most conflicts between state and federal law illusory. In these cases, it is possible that, had the Manufacturers asked the FDA for help, they might have eventually been able to strengthen their warning label. But it is also *possible* that they could have convinced the FDA to reinterpret its regulations in a manner that would have opened the CBE process to them, persuaded the FDA to rewrite its generic drug regulations entirely, or talked Congress into amending the Hatch–Waxman Amendments. If these conjectures sufficed to prevent federal and state law from conflicting, it is unclear when, outside of express pre-emption, the Supremacy Clause would have any force. That Clause—which makes federal law "the supreme Law of the Land ... any Thing in the Constitution or Laws of any State to the Contrary notwithstanding," U.S. Const., Art. VI, cl. 2—cannot be read to permit an approach to pre-emption that renders conflict pre-emption all but meaningless. Here, it is enough to hold that when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes. Pp. 2578 – 2579, 2580 – 2581.

(3) *Wyeth* is not to the contrary. The Court there held that a state tort action against a brand-name drug manufacturer for failure to provide an adequate warning label was not pre-empted because it was possible for the manufacturer

to comply with both state and federal law under the FDA's CBE regulation. 555 U.S., at 572–573, 129 S.Ct. 1187. The federal statutes and regulations that apply to brand-name drug manufacturers differ, by Congress' design, from those applicable to generic drug manufacturers. And different federal statutes and regulations may, as here, lead to different pre-emption results. This Court will not distort the Supremacy Clause in order to create similar pre-emption across a dissimilar statutory scheme. Congress and the FDA retain authority to change the law and regulations if they so desire. Pp. 2580 – 2582.

THOMAS, J., delivered the opinion of the Court, except as to Part III–B–2. ROBERTS, C.J., and SCALIA and ALITO, JJ., joined that opinion in full, and KENNEDY, J., joined as to all but Part III–B–2. SOTOMAYOR, J., filed a dissenting opinion, in which GINSBURG, BREYER, and KAGAN, JJ., joined.

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Opinion

Justice THOMAS delivered the opinion of the Court, except as to Part III–B–2.[*]

These consolidated lawsuits involve state tort-law claims based on certain drug manufacturers' alleged failure to provide adequate warning labels for generic metoclopramide. The question presented is whether federal drug regulations applicable to generic drug manufacturers directly conflict with, and thus pre-empt, these state-law claims. We hold that they do.

I

Metoclopramide is a drug designed to speed the movement of food through the digestive system. The Food and Drug Administration (FDA) first approved metoclopramide tablets, under the brand name Reglan, in 1980. Five years later, generic manufacturers also began producing metoclopramide. The drug is commonly used to treat digestive tract problems such as diabetic gastroparesis and gastroesophageal reflux disorder.

Evidence has accumulated that long-term metoclopramide use can cause tardive dyskinesia, a severe neurological disorder. Studies have shown that up to 29% of patients who take metoclopramide for several years develop this condition. *McNeil v. Wyeth*, 462 F.3d 364, 370, n. 5 (C.A.5 2006); see also Shaffer, Butterfield, Pamer, & Mackey, Tardive Dyskinesia Risks and Metoclopramide Use Before and After U.S. Market Withdrawal of Cisapride, 44 J. Am. Pharmacists Assn. 661, 663 (2004) (noting 87 cases of metoclopramide-related tardive dyskinesia reported to the FDA's adverse event reporting system by mid–2003).

Accordingly, warning labels for the drug have been strengthened and clarified several times. In 1985, the label was modified to warn that "tardive dyskinesia ... may develop in patients treated with metoclopramide," and the drug's package insert added that "[t]herapy longer than 12 weeks has not been evaluated and cannot be recommended." Physician's Desk Reference 1635–1636 (41st ed.1987); see also Brief for Petitioner PLIVA et al. 21–22 (hereinafter PLIVA Brief). In 2004, the brand-name Reglan manufacturer requested, and the FDA approved, a label change to add that "[t]herapy should not

exceed 12 weeks in duration." Brief for United ***2573** States as *Amicus Curiae* 8 (hereinafter U.S. Brief). And in 2009, the FDA ordered a black box warning—its strongest—which states: "Treatment with metoclopramide can cause tardive dyskinesia, a serious movement disorder that is often irreversible .... Treatment with metoclopramide for longer than 12 weeks should be avoided in all but rare cases." See Physician's Desk Reference 2902 (65th ed.2011).

Gladys Mensing and Julie Demahy, the plaintiffs in these consolidated cases, were prescribed Reglan in 2001 and 2002, respectively. Both received generic metoclopramide from their pharmacists. After taking the drug as prescribed for several years, both women developed tardive dyskinesia.

In separate suits, Mensing and Demahy sued the generic drug manufacturers that produced the metoclopramide they took (Manufacturers). Each alleged, as relevant here, that long-term metoclopramide use caused her tardive dyskinesia and that the Manufacturers were liable under state tort law (specifically, that of Minnesota and Louisiana) for failing to provide adequate warning labels. They claimed that "despite mounting evidence that long term metoclopramide use carries a risk of tardive dyskinesia far greater than that indicated on the label," none of the Manufacturers had changed their labels to adequately warn of that danger. *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 605 (C.A.8 2009); see also *Demahy v. Actavis, Inc.*, 593 F.3d 428, 430 (C.A.5 2010).

In both suits, the Manufacturers urged that federal law pre-empted the state tort claims. According to the Manufacturers, federal statutes and FDA regulations required them to use the same safety and efficacy labeling as their brand-name counterparts. This means, they argued, that it was impossible to simultaneously comply with both federal law and any state tort-law duty that required them to use a different label.

The Courts of Appeals for the Fifth and Eighth Circuits rejected the Manufacturers' arguments and held that Mensing and Demahy's claims were not pre-empted. See 588 F.3d, at 614, 593 F.3d, at 449. We granted certiorari, 562 U.S. ——, 131 S.Ct. 817, 178 L.Ed.2d 550 (2010), consolidated the cases, and now reverse each.

II

Pre-emption analysis requires us to compare federal and state law. We therefore begin by identifying the state tort duties and federal labeling requirements applicable to the Manufacturers.

A

[1] [2] [3] It is undisputed that Minnesota and Louisiana tort law require a drug manufacturer that is or should be aware of its product's danger to label that product in a way that renders it reasonably safe. Under Minnesota law, which applies to Mensing's lawsuit, "where the manufacturer ... of a product has actual or constructive knowledge of danger to users, the ... manufacturer has a duty to give warning of such dangers." *Frey v. Montgomery Ward & Co.*, 258 N.W.2d 782, 788 (Minn.1977). Similarly, under Louisiana law applicable to Demahy's lawsuit, "a manufacturer's duty to warn includes a duty to provide adequate instructions for safe use of a product." *Stahl v. Novartis Pharmaceuticals Corp.*, 283 F.3d 254, 269–270 (C.A.5 2002); see also La.Rev.Stat. Ann. § 9:2800.57 (West 2009). In both States, a duty to warn falls specifically on the manufacturer. See *Marks v. OHMEDA, Inc.*, 2003–1446, pp. 8–9 (La.App.3/31/04), 871 So.2d 1148, 1155; *Gray v. Badger Min. Corp.*, 676 N.W.2d 268, 274 (Minn.2004).

***2574** Mensing and Demahy have pleaded that the Manufacturers knew or should have known of the high risk of tardive dyskinesia inherent in the long-term use of their product. They have also pleaded that the Manufacturers knew or should have known that their labels did not adequately warn of that risk. App. 437–438, 67–69, 94–96. The parties do not dispute that, if these allegations are true, state law required the Manufacturers to use a different, safer label.

B

Federal law imposes far more complex drug labeling requirements. We begin with what is not in dispute. Under the 1962 Drug Amendments to the Federal Food, Drug, and Cosmetic Act, 76 Stat. 780, 21 U.S.C. § 301 *et seq.*, a manufacturer seeking federal approval to market a new drug must prove that it is safe and effective and that the proposed label is accurate and adequate.[1] See, *e.g.*, 21 U.S.C. §§ 355(b)(1), (d); *Wyeth v. Levine*, 555 U.S. 555, 567, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009). Meeting those requirements involves costly and lengthy clinical testing. §§ 355(b)(1)(A), (d); see also D. Beers, Generic and Innovator Drugs: A Guide to FDA Approval

Requirements § 2.02[A] (7th ed.2008).

Originally, the same rules applied to all drugs. In 1984, however, Congress passed the Drug Price Competition and Patent Term Restoration Act, 98 Stat. 1585, commonly called the Hatch–Waxman Amendments. Under this law, "generic drugs" can gain FDA approval simply by showing equivalence to a reference listed drug that has already been approved by the FDA.[2] 21 U.S.C. § 355(j)(2)(A). This allows manufacturers to develop generic drugs inexpensively, without duplicating the clinical trials already performed on the equivalent brand-name drug. A generic drug application must also "show that the [safety and efficacy] labeling proposed ... is the same as the labeling approved for the [brand-name] drug." § 355(j)(2)(A)(v); see also § 355(j)(4)(G); Beers §§ 3.01, 3.03[A].

As a result, brand-name and generic drug manufacturers have different federal drug labeling duties. A brand-name manufacturer seeking new drug approval is responsible for the accuracy and adequacy of its label. See, *e.g.*, 21 U.S.C. §§ 355(b)(1), (d); *Wyeth, supra*, at 570–571, 129 S.Ct. 1187. A manufacturer seeking generic drug approval, on the other hand, is responsible for ensuring that its warning label is the same as the brand name's. See, *e.g.*, § 355(j)(2)(A)(v); § 355(j)(4)(G); 21 CFR §§ 314.94(a)(8), 314.127(a)(7).

[4] [5] The parties do not disagree. What is in dispute is whether, and to what extent, generic manufacturers may change their labels *after* initial FDA approval. Mensing and Demahy contend that federal law provided several avenues through which the Manufacturers could have altered their metoclopramide labels in time to prevent the injuries here. The FDA, however, tells us that it interprets its regulations to require that the warning labels ***2575** of a brand-name drug and its generic copy must always be the same—thus, generic drug manufacturers have an ongoing federal duty of "sameness." U.S. Brief 16; see also 57 Fed.Reg. 17961 (1992) ("[T]he [generic drug's] labeling must be the same as the listed drug product's labeling because the listed drug product is the basis for [generic drug] approval"). The FDA's views are "controlling unless plainly erroneous or inconsistent with the regulation[s]" or there is any other reason to doubt that they reflect the FDA's fair and considered judgment. *Auer v. Robbins*, 519 U.S. 452, 461, 462, 117 S.Ct. 905, 137 L.Ed.2d 79 (1997) (internal quotation marks omitted).[3]

1

[6] First, Mensing and Demahy urge that the FDA's "changes-being-effected" (CBE) process allowed the Manufacturers to change their labels when necessary. See Brief for Respondents 33–35; see also 593 F.3d, at 439–444; *Gaeta v. Perrigo Pharmaceuticals Co.*, 630 F.3d 1225, 1231 (C.A.9 2011); *Foster v. American Home Prods. Corp.*, 29 F.3d 165, 170 (C.A.4 1994). The CBE process permits drug manufacturers to "add or strengthen a contraindication, warning, [or] precaution," 21 CFR § 314.70(c)(6)(iii)(A) (2006), or to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product," § 314.70(c)(6)(iii)(C). When making labeling changes using the CBE process, drug manufacturers need not wait for preapproval by the FDA, which ordinarily is necessary to change a label. *Wyeth, supra*, at 568, 129 S.Ct. 1187. They need only simultaneously file a supplemental application with the FDA. 21 CFR § 314.70(c)(6).

The FDA denies that the Manufacturers could have used the CBE process to unilaterally strengthen their warning labels. The agency interprets the CBE regulation to allow changes to generic drug labels only when a generic drug manufacturer changes its label to match an updated brand-name label or to follow the FDA's instructions. U.S. Brief 15, 16, n. 7 (interpreting 21 CFR § 314.94(a)(8)(iv)); U.S. Brief 16, n. 8. The FDA argues that CBE changes unilaterally made to strengthen a generic drug's warning label would violate the statutes and regulations requiring a generic drug's label to match its brand-name counterpart's. *Id.*, at 15–16; see also 21 U.S.C. § 355(j)(4)(G); 21 CFR §§ 314.94(a)(8)(iii), 314.150(b)(10) (approval may be withdrawn if the generic drug's label "is no longer consistent with that for [the brand-name]").

We defer to the FDA's interpretation of its CBE and generic labeling regulations. Although Mensing and Demahy offer other ways to interpret the regulations, see Brief for Respondents 33–35, we do not find the agency's interpretation "plainly erroneous or inconsistent with the regulation." *Auer, supra*, at 461, 117 S.Ct. 905 (internal quotation marks omitted). Nor do Mensing and Demahy suggest there is any other reason to doubt the agency's reading. We therefore conclude that the CBE process was not open to the Manufacturers ***2576** for the sort of change required by state law.

2

Next, Mensing and Demahy contend that the Manufacturers could have used "Dear Doctor" letters to

send additional warnings to prescribing physicians and other healthcare professionals. See Brief for Respondents 36; 21 CFR § 200.5. Again, the FDA disagrees, and we defer to the agency's views.

[7] The FDA argues that Dear Doctor letters qualify as "labeling." U.S. Brief 18; see also 21 U.S.C. § 321(m); 21 CFR § 202.1(*l*)(2). Thus, any such letters must be "consistent with and not contrary to [the drug's] approved ... labeling." 21 CFR § 201.100(d)(1). A Dear Doctor letter that contained substantial new warning information would not be consistent with the drug's approved labeling. Moreover, if generic drug manufacturers, but not the brand-name manufacturer, sent such letters, that would inaccurately imply a therapeutic difference between the brand and generic drugs and thus could be impermissibly "misleading." U.S. Brief 19; see 21 CFR § 314.150(b)(3) (FDA may withdraw approval of a generic drug if "the labeling of the drug ... is false or misleading in any particular").

As with the CBE regulation, we defer to the FDA. Mensing and Demahy offer no argument that the FDA's interpretation is plainly erroneous. See *Auer*, 519 U.S., at 461, 117 S.Ct. 905. Accordingly, we conclude that federal law did not permit the Manufacturers to issue additional warnings through Dear Doctor letters.

3

Though the FDA denies that the Manufacturers could have used the CBE process or Dear Doctor letters to strengthen their warning labels, the agency asserts that a different avenue existed for changing generic drug labels. According to the FDA, the Manufacturers could have proposed—indeed, were required to propose—stronger warning labels to the agency if they believed such warnings were needed. U.S. Brief 20; 57 Fed.Reg. 17961. If the FDA had agreed that a label change was necessary, it would have worked with the brand-name manufacturer to create a new label for both the brand-name and generic drug. *Ibid.*

The agency traces this duty to 21 U.S.C. § 352(f)(2), which provides that a drug is "misbranded ... [u]nless its labeling bears ... adequate warnings against ... unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users." See U.S. Brief 12. By regulation, the FDA has interpreted that statute to require that "labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e).

According to the FDA, these requirements apply to generic drugs. As it explains, a " 'central premise of federal drug regulation is that the manufacturer bears responsibility for the content of its label at all times.' " U.S. Brief 12–13 (quoting *Wyeth*, 555 U.S., at 570–571, 129 S.Ct. 1187). The FDA reconciles this duty to have adequate and accurate labeling with the duty of sameness in the following way: Generic drug manufacturers that become aware of safety problems must ask the agency to work toward strengthening the label that applies to both the generic and brand-name equivalent drug. U.S. Brief 20.

The Manufacturers and the FDA disagree over whether this alleged duty to request a strengthened label actually existed. ***2577** The FDA argues that it explained this duty in the preamble to its 1992 regulations implementing the Hatch–Waxman Amendments. *Ibid.;* see 57 Fed.Reg. 17961 ("If a [generic drug manufacturer] believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised"). The Manufacturers claim that the FDA's 19–year–old statement did not create a duty, and that there is no evidence of any generic drug manufacturer ever acting pursuant to any such duty. See Tr. of Oral Arg. 19–24; Reply Brief for Petitioner PLIVA et al. 18–22. Because we ultimately find pre-emption even assuming such a duty existed, we do not resolve the matter.

C

To summarize, the relevant state and federal requirements are these: State tort law places a duty directly on all drug manufacturers to adequately and safely label their products. Taking Mensing and Demahy's allegations as true, this duty required the Manufacturers to use a different, stronger label than the label they actually used. Federal drug regulations, as interpreted by the FDA, prevented the Manufacturers from independently changing their generic drugs' safety labels. But, we assume, federal law also required the Manufacturers to ask for FDA assistance in convincing the brand-name manufacturer to adopt a stronger label, so that all corresponding generic drug manufacturers could do so as well. We turn now to the question of pre-emption.

III

[8] [9] [10] The Supremacy Clause establishes that federal law "shall be the supreme Law of the Land ... any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const., Art. VI, cl. 2. Where state and federal law "directly conflict," state law must give way. *Wyeth, supra,* at 583, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment); see also *Crosby v. National Foreign Trade Council,* 530 U.S. 363, 372, 120 S.Ct. 2288, 147 L.Ed.2d 352 (2000) ("[S]tate law is naturally preempted to the extent of any conflict with a federal statute"). We have held that state and federal law conflict where it is "impossible for a private party to comply with both state and federal requirements."[4] *Freightliner Corp. v. Myrick,* 514 U.S. 280, 287, 115 S.Ct. 1483, 131 L.Ed.2d 385 (1995) (internal quotation marks omitted).[5]

A

[11] We find impossibility here. It was not lawful under federal law for the Manufacturers to do what state law required of them. And even if they had fulfilled their federal duty to ask for FDA ***2578** assistance, they would not have satisfied the requirements of state law.

If the Manufacturers had independently changed their labels to satisfy their state-law duty, they would have violated federal law. Taking Mensing and Demahy's allegations as true, state law imposed on the Manufacturers a duty to attach a safer label to their generic metoclopramide. Federal law, however, demanded that generic drug labels be the same at all times as the corresponding brand-name drug labels. See, *e.g.*, 21 CFR § 314.150(b)(10). Thus, it was impossible for the Manufacturers to comply with both their state-law duty to change the label and their federal law duty to keep the label the same.

The federal duty to ask the FDA for help in strengthening the corresponding brand-name label, assuming such a duty exists, does not change this analysis. Although requesting FDA assistance would have satisfied the Manufacturers' federal duty, it would not have satisfied their state tort-law duty to provide adequate labeling. State law demanded a safer label; it did not instruct the Manufacturers to communicate with the FDA about the possibility of a safer label. Indeed, Mensing and Demahy deny that their state tort claims are based on the Manufacturers' alleged failure to ask the FDA for assistance in changing the labels. Brief for Respondents 53–54; cf. *Buckman Co. v. Plaintiffs' Legal Comm.,* 531 U.S. 341, 121 S.Ct. 1012, 148 L.Ed.2d 854 (2001) (holding that federal drug and medical device laws pre-empted a state tort-law claim based on failure to properly communicate with the FDA).

B

1

Mensing and Demahy contend that, while their state-law claims do not turn on whether the Manufacturers asked the FDA for assistance in changing their labels, the Manufacturers' federal affirmative defense of pre-emption does. Mensing and Demahy argue that if the Manufacturers had asked the FDA for help in changing the corresponding brand-name label, they might eventually have been able to accomplish under federal law what state law requires. That is true enough. The Manufacturers "freely concede" that they could have asked the FDA for help. PLIVA Brief 48. If they had done so, and if the FDA decided there was sufficient supporting information, and if the FDA undertook negotiations with the brand-name manufacturer, and if adequate label changes were decided on and implemented, then the Manufacturers would have started a Mouse Trap game that eventually led to a better label on generic metoclopramide.

This raises the novel question whether conflict pre-emption should take into account these possible actions by the FDA and the brand-name manufacturer. Here, what federal law permitted the Manufacturers to do could have changed, even absent a change in the law itself, depending on the actions of the FDA and the brand-name manufacturer. Federal law does not dictate the text of each generic drug's label, but rather ties those labels to their brand-name counterparts. Thus, federal law would permit the Manufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so.

Mensing and Demahy assert that when a private party's ability to comply with state law depends on approval and assistance from the FDA, proving pre-emption requires that party to demonstrate that the FDA would not have allowed compliance ***2579** with state law. Here, they argue, the Manufacturers cannot bear their burden of proving impossibility because they did not even *try* to start the process that might ultimately have allowed them

to use a safer label. Brief for Respondents 47. This is a fair argument, but we reject it.

The question for "impossibility" is whether the private party could independently do under federal law what state law requires of it. See *Wyeth*, 555 U.S., at 573, 129 S.Ct. 1187 (finding no pre-emption where the defendant could "unilaterally" do what state law required). Accepting Mensing and Demahy's argument would render conflict pre-emption largely meaningless because it would make most conflicts between state and federal law illusory. We can often imagine that a third party or the Federal Government *might* do something that makes it lawful for a private party to accomplish under federal law what state law requires of it. In these cases, it is certainly possible that, had the Manufacturers asked the FDA for help, they might have eventually been able to strengthen their warning label. Of course, it is also *possible* that the Manufacturers could have convinced the FDA to reinterpret its regulations in a manner that would have opened the CBE process to them. Following Mensing and Demahy's argument to its logical conclusion, it is also *possible* that, by asking, the Manufacturers could have persuaded the FDA to rewrite its generic drug regulations entirely or talked Congress into amending the Hatch–Waxman Amendments.

If these conjectures suffice to prevent federal and state law from conflicting for Supremacy Clause purposes, it is unclear when, outside of express pre-emption, the Supremacy Clause would have any force.[6] We do not read the Supremacy Clause to permit an approach to pre-emption that renders conflict pre-emption all but meaningless. The Supremacy Clause, on its face, makes federal law "the supreme Law of the Land" even absent an express statement by Congress. U.S. Const., Art. VI, cl. 2.

2

Moreover, the text of the Clause—that federal law shall be supreme, "any Thing in the Constitution or Laws of any State to the Contrary notwithstanding"—plainly contemplates conflict pre-emption by describing federal law as effectively repealing contrary state law. *Ibid.;* see Nelson, Preemption, 86 Va. L.Rev. 225, 234 (2000); *id.*, at 252–253 (describing discussion of the Supremacy Clause in state ratification debates as concerning whether federal law could repeal state law, or vice versa). The phrase "any [state law] to the Contrary notwithstanding" is a *non obstante* provision. *Id.*, at 238–240, nn. 43–45. Eighteenth-century legislatures used *non obstante* provisions to specify the degree to which a new statute was meant to repeal older, potentially conflicting statutes in the same field. *Id.*, at 238–240 (citing dozens of statutes from the 1770's and 1780's with similar provisions). A *non obstante* provision "in a new statute acknowledged that the statute might contradict prior law and instructed courts not to apply the general presumption against implied repeals." *Id.*, at 241–242; 4 M. Bacon, A New Abridgment of the Law 639 (4th ed. 1778) ("Although ***2580** two Acts of Parliament are *seemingly* repugnant, yet if there be no Clause of *non Obstante* in the latter, they shall if possible have such Construction, that the latter may not be a Repeal of the former by Implication"). The *non obstante* provision in the Supremacy Clause therefore suggests that federal law should be understood to impliedly repeal conflicting state law.

Further, the provision suggests that courts should not strain to find ways to reconcile federal law with seemingly conflicting state law. Traditionally, courts went to great lengths attempting to harmonize conflicting statutes, in order to avoid implied repeals. *Warder v. Arell*, 2 Va. 282, 296 (1796) (opinion of Roane, J.) ("[W]e ought to seek for such a construction as will reconcile [the statutes] together"); *Ludlow's Heirs v. Johnston*, 3 Ohio 553, 564 (1828) ("[I]f by any fair course of reasoning the two [statutes] can be reconciled, both shall stand"); *Doolittle v. Bryan*, 14 How. 563, 566, 14 L.Ed. 543 (1853) (requiring "the repugnance be quite plain" before finding implied repeal). A *non obstante* provision thus was a useful way for legislatures to specify that they did not want courts distorting the new law to accommodate the old. Nelson, *supra*, at 240–242; see also J. Sutherland, Statutes and Statutory Construction § 147, p. 199 (1891) ("[W]hen there is inserted in a statute a provision [of *non obstante*] .... It is to be supposed that courts will be less inclined against recognizing repugnancy in applying such statutes"); *Weston's Case*, 73 Eng. Rep. 780, 781 (K.B.1576) ("[W]hen there are two statutes, one in appearance crossing the other, and no clause of *non obstante* is contained in the second statute ... the exposition ought to be that both should stand in force"); G. Jacob, A New Law Dictionary (J. Morgan ed., 10th ed. 1782) (definition of "statute," ¶ 6: "[W]hen there is a seeming variance between two *statutes*, and no clause of *non obstante* in the latter, such construction shall be made that both may stand"). The *non obstante* provision of he Supremacy Clause indicates that a court need look no further than "the ordinary meanin[g]" of federal law, and should not distort federal law to accommodate conflicting state law. *Wyeth*, 555 U.S., at 588, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment) (internal quotation marks omitted).

To consider in our pre-emption analysis the contingencies inherent in these cases—in which the Manufacturers' ability to comply with state law depended on uncertain federal agency and third-party decisions—would be inconsistent with the *non obstante* provision of the Supremacy Clause. The Manufacturers would be required continually to prove the counterfactual conduct of the FDA and brand-name manufacturer in order to establish the supremacy of federal law. We do not think the Supremacy Clause contemplates that sort of contingent supremacy. The *non obstante* provision suggests that pre-emption analysis should not involve speculation about ways in which federal agency and third-party actions could potentially reconcile federal duties with conflicting state duties. When the "ordinary meaning" of federal law blocks a private party from independently accomplishing what state law requires, that party has established pre-emption.

3

[12] To be sure, whether a private party can act sufficiently independently under federal law to do what state law requires may sometimes be difficult to determine. But this is not such a case. Before the Manufacturers could satisfy state law, the FDA—a federal agency—had to undertake special effort permitting them to do so. To decide these cases, it is enough to hold ***2581** that when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for pre-emption purposes.

Here, state law imposed a duty on the Manufacturers to take a certain action, and federal law barred them from taking that action. The only action the Manufacturers could independently take—asking for the FDA's help—is not a matter of state-law concern. Mensing and Demahy's tort claims are pre-empted.

C

Wyeth is not to the contrary. In that case, as here, the plaintiff contended that a drug manufacturer had breached a state tort-law duty to provide an adequate warning label. 555 U.S., at 559–560, 129 S.Ct. 1187. The Court held that the lawsuit was not pre-empted because it was possible for Wyeth, a brand-name drug manufacturer, to comply with both state and federal law. *Id.*, at 572–573, 129 S.Ct. 1187.[7] Specifically, the CBE regulation, 21 CFR § 314.70(c)(6)(iii), permitted a brand-name drug manufacturer like Wyeth "to unilaterally strengthen its warning" without prior FDA approval. 555 U.S., at 573, 129 S.Ct. 1187; cf. *supra*, at 2575 – 2576. Thus, the federal regulations applicable to Wyeth allowed the company, of its own volition, to strengthen its label in compliance with its state tort duty.[8]

We recognize that from the perspective of Mensing and Demahy, finding pre-emption here but not in *Wyeth* makes little sense. Had Mensing and Demahy taken Reglan, the brand-name drug prescribed by their doctors, *Wyeth* would control and their lawsuits would not be pre-empted. But because pharmacists, acting in full accord with state law, substituted generic metoclopramide instead, federal law pre-empts these lawsuits. See, *e.g.*, Minn.Stat. § 151.21 (2010) (describing when pharmacists may substitute generic drugs); La.Rev.Stat. Ann. § 37:1241(A)(17) (West 2007) (same). We acknowledge the unfortunate hand that federal drug regulation has dealt Mensing, Demahy, and others similarly situated.[9]

***2582** But "it is not this Court's task to decide whether the statutory scheme established by Congress is unusual or even bizarre." *Cuomo v. Clearing House Assn., L.L. C.*, 557 U.S. 519, ——, 129 S.Ct. 2710, 2733, 174 L.Ed.2d 464 (2009) (THOMAS, J., concurring in part and dissenting in part) (internal quotation marks and brackets omitted). It is beyond dispute that the federal statutes and regulations that apply to brand-name drug manufacturers are meaningfully different than those that apply to generic drug manufacturers. Indeed, it is the special, and different, regulation of generic drugs that allowed the generic drug market to expand, bringing more drugs more quickly and cheaply to the public. But different federal statutes and regulations may, as here, lead to different pre-emption results. We will not distort the Supremacy Clause in order to create similar pre-emption across a dissimilar statutory scheme. As always, Congress and the FDA retain the authority to change the law and regulations if they so desire.

*** * ***

The judgments of the Fifth and Eighth Circuits are reversed, and the cases are remanded for further proceedings consistent with this opinion.

It is so ordered.

Justice SOTOMAYOR, with whom Justice GINSBURG, Justice BREYER, and Justice KAGAN join, dissenting.

The Court today invokes the doctrine of impossibility pre-emption to hold that federal law immunizes generic-drug manufacturers from all state-law failure-to-warn claims because they cannot unilaterally change their labels. I cannot agree. We have traditionally held defendants claiming impossibility to a demanding standard: Until today, the mere possibility of impossibility had not been enough to establish pre-emption.

The Food and Drug Administration (FDA) permits—and, the Court assumes, requires—generic-drug manufacturers to propose a label change to the FDA when they believe that their labels are inadequate. If it agrees that the labels are inadequate, the FDA can initiate a change to the brand-name label, triggering a corresponding change to the generic labels. Once that occurs, a generic manufacturer is in full compliance with both federal law and a state-law duty to warn. Although generic manufacturers may be able to show impossibility in some cases, petitioners, generic manufacturers of metoclopramide (Manufacturers), have shown only that they *might* have been unable to comply with both federal law and their state-law duties to warn respondents Gladys Mensing and Julie Demahy. This, I would hold, is insufficient to sustain their burden.

The Court strains to reach the opposite conclusion. It invents new principles of pre-emption law out of thin air to justify its dilution of the impossibility standard. It effectively rewrites our decision in *Wyeth v. Levine*, 555 U.S. 555, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009), which holds ***2583** that federal law does not pre-empt failure-to-warn claims against brand-name drug manufacturers. And a plurality of the Court tosses aside our repeated admonition that courts should hesitate to conclude that Congress intended to pre-empt state laws governing health and safety. As a result of today's decision, whether a consumer harmed by inadequate warnings can obtain relief turns solely on the happenstance of whether her pharmacist filled her prescription with a brand-name or generic drug. The Court gets one thing right: This outcome "makes little sense." *Ante*, at 2581.

I

A

Today's decision affects 75 percent of all prescription drugs dispensed in this country. The dominant position of generic drugs in the prescription drug market is the result of a series of legislative measures, both federal and state.

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, 98 Stat. 1585—commonly known as the Hatch–Waxman Amendments to the Federal Food, Drug, and Cosmetic Act (FDCA)—to "make available more low cost generic drugs by establishing a generic drug approval procedure," H.R.Rep. No. 98–857, pt. 1, p. 14 (1984). As the majority explains, to accomplish this goal the amendments establish an abbreviated application process for generic drugs. *Ante*, at 2574 – 2575; see also 21 U.S.C. § 355(j)(2)(A). The abbreviated approval process implements the amendments' core principle that generic and brand-name drugs must be the "same" in nearly all respects: To obtain FDA approval, a generic manufacturer must ordinarily show, among other things, that its product has the same active ingredients as an approved brand-name drug; that "the route of administration, the dosage form, and the strength of the new drug are the same" as the brand-name drug; and that its product is "bioequivalent" to the brand-name drug. §§ 355(j)(2)(A)(ii), (iii), (iv). By eliminating the need for generic manufacturers to prove their drugs' safety and efficacy independently, the Hatch–Waxman Amendments allow generic manufacturers to bring drugs to market much less expensively.

The States have also acted to expand consumption of low-cost generic drugs. In the years leading up to passage of the Hatch–Waxman Amendments, States enacted legislation authorizing pharmacists to substitute generic drugs when filling prescriptions for brand-name drugs. Christensen, Kirking, Ascione, Welage, & Gaither, Drug Product Selection: Legal Issues, 41 J. Am. Pharmaceutical Assn. 868, 869 (2001). Currently, all States have some form of generic substitution law. See *ibid.* Some States require generic substitution in certain circumstances. Dept. of Health and Human Servs., ASPE Issue Brief: Expanding the Use of Generic Drugs 7 (2010) (hereinafter Expanding the Use of Generic Drugs);[1] see, *e.g.*, N.Y. Educ. Law Ann. § 6816–a (West 2010). Others permit, but do not require, substitution. Expanding the Use of Generic Drugs 7; see, *e.g.*, Cal. Bus. & Prof.Code Ann. § 4073 (West Supp.2011). Some States require patient consent to substitution, and all States "allow the physician to specify that the brand name must be prescribed, although with different levels of effort from the physician." Expanding the

***2584** Use of Generic Drugs 7.[2]
These legislative efforts to expand production and consumption of generic drugs have proved wildly successful. It is estimated that in 1984, when the Hatch–Waxman Amendments were enacted, generic drugs constituted 19 percent of drugs sold in this country. Congressional Budget Office, How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry 27 (1998).[3] Today, they dominate the market. See Expanding the Use of Generic Drugs 2 (generic drugs constituted 75 percent of all dispensed prescription drugs in 2009). Ninety percent of drugs for which a generic version is available are now filled with generics. *Id.*, at 3–4. In many cases, once generic versions of a drug enter the market, the brand-name manufacturer stops selling the brand-name drug altogether. See Brief for Marc T. Law et al. as *Amici Curiae* 18 (citing studies showing that anywhere from one-third to one-half of generic drugs no longer have a marketed brand-name equivalent). Reflecting the success of their products, many generic manufacturers, including the Manufacturers and their *amici*, are huge, multinational companies. In total, generic drug manufacturers sold an estimated $66 billion of drugs in this country in 2009. See *id.*, at 15.

B

As noted, to obtain FDA approval a generic manufacturer must generally show that its drug is the same as an approved brand-name drug. It need not conduct clinical trials to prove the safety and efficacy of the drug. This does not mean, however, that a generic manufacturer has no duty under federal law to ensure the safety of its products. The FDA has limited resources to conduct postapproval monitoring of drug safety. See *Wyeth*, 555 U.S., at 578, 129 S.Ct. 1187. Manufacturers, we have recognized, "have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge." *Id.*, at 578–579, 129 S.Ct. 1187. Federal law thus obliges drug manufacturers—both brand-name and generic—to monitor the safety of their products.

Under federal law, generic manufacturers must "develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences" to the FDA.[4] 21 CFR § 314.80(b);[5] see also § 314.98 (making § 314.80 applicable to generic manufacturers); Brief for United States as *Amicus Curiae* 6, and n. 2 (hereinafter U.S. Brief). They must review all reports of adverse drug experiences received from "any source." § 314.80(b). If a manufacturer receives a report of a serious and unexpected ***2585** adverse drug experience, it must report the event to the FDA within 15 days and must "promptly investigate." §§ 314.80(c)(1)(i)-(ii); see also Tr. of Oral Arg. 8. Most other adverse drug experiences must be reported on a quarterly or yearly basis.[6] § 314.80(c)(2). Generic manufacturers must also submit to the FDA an annual report summarizing "significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product," including a "description of actions the [manufacturer] has taken or intends to take as a result of this new information." § 314.81(b)(2)(i); see also § 314.98(c).

Generic manufacturers, the majority assumes, also bear responsibility under federal law for monitoring the adequacy of their warnings. I agree with the majority's conclusion that generic manufacturers are not permitted unilaterally to change their labels through the "changes-being-effected" (CBE) process or to issue additional warnings through "Dear Doctor" letters. See *ante*, at 2574 – 2576. According to the FDA, however, that generic manufacturers cannot disseminate additional warnings on their own does not mean that federal law permits them to remain idle when they conclude that their labeling is inadequate. FDA regulations require that labeling "be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e) (2006), currently codified at 21 CFR § 201.80(e) (2010); see also *Wyeth*, 555 U.S., at 570–571, 129 S.Ct. 1187. The FDA construes this regulation to oblige generic manufacturers "to seek to revise their labeling and provide FDA with supporting information about risks" when they believe that additional warnings are necessary.[7] U.S. Brief 20.

***2586** The Manufacturers disagree. They read the FDA regulation to require them only to ensure that their labels match the brand-name labels. See Brief for Petitioner PLIVA et al. 38–41. I need not decide whether the regulation in fact obliges generic manufacturers to approach the FDA to propose a label change. The majority assumes that it does. And even if generic manufacturers do not have a duty to propose label changes, two points remain undisputed. First, they do have a duty under federal law to monitor the safety of their products. And, second, they may approach the FDA to propose a label change when they believe a change is required.

II

This brings me to the Manufacturers' pre-emption defense. State law obliged the Manufacturers to warn of dangers to users. See *Hines v. Remington Arms Co.*, 94–0455, p. 10 (La.12/8/94), 648 So.2d 331, 337; *Frey v. Montgomery Ward & Co.*, 258 N.W.2d 782, 788 (Minn.1977). The Manufacturers contend, and the majority agrees, that federal law pre-empts respondents' failure-to-warn claims because, under federal law, the Manufacturers could not have provided additional warnings to respondents without the exercise of judgment by the FDA. I cannot endorse this novel conception of impossibility pre-emption.

A

Two principles guide all pre-emption analysis. First, " 'the purpose of Congress is the ultimate touchstone in every pre-emption case.' " *Wyeth*, 555 U.S., at 565, 129 S.Ct. 1187 (quoting *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996)). Second, " '[i]n all pre-emption cases, and particularly in those in which Congress has legislated ... in a field which the States have traditionally occupied, ... we start with the assumption that the historic police powers of the States were not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.' " *Wyeth*, 555 U.S., at 565, 129 S.Ct. 1187 (quoting *Lohr*, 518 U.S., at 485, 116 S.Ct. 2240; some internal quotation marks omitted; alterations in original).

These principles find particular resonance in these cases. The States have traditionally regulated health and safety matters. See *id.*, at 485, 116 S.Ct. 2240. Notwithstanding Congress' "certain awareness of the prevalence of state tort litigation" against drug manufacturers, *Wyeth*, 555 U.S., at 575, 129 S.Ct. 1187, Congress has not expressly pre-empted state-law tort actions against prescription drug manufacturers, whether brand-name or generic. To the contrary, when Congress amended the FDCA in 1962 to "enlarg[e] the FDA's powers to 'protect the public health' and 'assure the safety, effectiveness, and reliability of drugs,' [it] took care to preserve state law." *Id.*, at 567, 129 S.Ct. 1187 (quoting 76 Stat. 780); see Pub.L. 87–781, § 202, 76 Stat. 793 ("Nothing in the amendments made by this Act to the [FDCA] shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law"). Notably, although Congress enacted an express pre-emption provision for medical devices in 1976, see Pub.L. 94–295, § 521, 90 Stat. 574, 21 U.S.C. § 360k(a), it included no such provision in the Hatch–Waxman Amendments eight years later. Cf. *Wyeth*, 555 U.S., at 567, 574–575, 129 S.Ct. 1187. Congress' "silence on the issue ... is powerful evidence that [it] did not intend FDA oversight to be the exclusive means ***2587** of ensuring drug safety and effectiveness." *Id.*, at 575, 129 S.Ct. 1187.

B

Federal law impliedly pre-empts state law when state and federal law "conflict"—*i.e.*, when "it is impossible for a private party to comply with both state and federal law" or when state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Crosby v. National Foreign Trade Council*, 530 U.S. 363, 372–373, 120 S.Ct. 2288, 147 L.Ed.2d 352 (2000) (internal quotation marks omitted). The Manufacturers rely solely on the former ground of pre-emption.

Impossibility pre-emption, we have emphasized, "is a demanding defense." *Wyeth*, 555 U.S., at 573, 129 S.Ct. 1187. Because pre-emption is an affirmative defense, a defendant seeking to set aside state law bears the burden to prove impossibility. See *ibid.*; *Silkwood v. Kerr–McGee Corp.*, 464 U.S. 238, 255, 104 S.Ct. 615, 78 L.Ed.2d 443 (1984). To prevail on this defense, a defendant must demonstrate that "compliance with both federal and state [law] is a physical impossibility." *Florida Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142–143, 83 S.Ct. 1210, 10 L.Ed.2d 248 (1963); see also *Wyeth*, 555 U.S., at 573, 129 S.Ct. 1187. In other words, there must be an "inevitable collision" between federal and state law. *Florida Lime*, 373 U.S., at 143, 83 S.Ct. 1210. "The existence of a hypothetical or potential conflict is insufficient to warrant" pre-emption of state law. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659, 102 S.Ct. 3294, 73 L.Ed.2d 1042 (1982); see also *Gade v. National Solid Wastes Management Assn.*, 505 U.S. 88, 110, 112 S.Ct. 2374, 120 L.Ed.2d 73 (1992) (KENNEDY, J., concurring in part and concurring in judgment). In other words, the mere possibility of impossibility is not enough.

The Manufacturers contend that it was impossible for them to provide additional warnings to respondents Mensing and Demahy because federal law prohibited them from changing their labels unilaterally.[8] They concede, however, that they could have asked the FDA to initiate a label change. If the FDA agreed that a label change was required, it could have asked, and indeed pressured, the brand-name manufacturer to change its

label, triggering a corresponding change to the Manufacturers' generic labels.[9] Thus, had the Manufacturers invoked the available mechanism for initiating label changes, they may well have been able to change their labels in sufficient time to warn respondents. ***2588** Having failed to do so, the Manufacturers cannot sustain their burden (at least not without further factual development) to demonstrate that it was impossible for them to comply with both federal and state law. At most, they have demonstrated only "a hypothetical or potential conflict." *Rice*, 458 U.S., at 659, 102 S.Ct. 3294.

Like the majority, the Manufacturers focus on the fact that they cannot change their labels unilaterally—which distinguishes them from the brand-name-manufacturer defendant in *Wyeth*. They correctly point out that in *Wyeth* we concluded that the FDA's CBE regulation authorized the defendant to strengthen its warnings before receiving agency approval of its supplemental application describing the label change. 555 U.S., at 568–571, 129 S.Ct. 1187; see also 21 CFR § 314.70(c)(6). But the defendant's label change was contingent on FDA acceptance, as the FDA retained "authority to reject labeling changes made pursuant to the CBE regulation." *Wyeth*, 555 U.S., at 571, 129 S.Ct. 1187. Thus, in the long run, a brand-name manufacturer's compliance with a state-law duty to warn required action by two actors: The brand-name manufacturer had to change the label and the FDA, upon reviewing the supplemental application, had to agree with the change.[10] The need for FDA approval of the label change did not make compliance with federal and state law impossible in every case. Instead, because the defendant bore the burden to show impossibility, we required it to produce "clear evidence that the FDA would not have approved a change to [the] label." *Ibid.*

I would apply the same approach in these cases. State law, respondents allege, required the Manufacturers to provide a strengthened warning about the dangers of long-term metoclopramide use.[11] Just like the brand-name manufacturer in *Wyeth*, the Manufacturers had available to them a mechanism for attempting to comply with their state-law duty to warn. Federal law thus "accommodated" the Manufacturers' state-law duties. See *ante*, at 2581, n. 8. It was not necessarily impossible for the Manufacturers to comply with both federal and state law because, had they approached the FDA, the FDA may well have agreed that a label change was necessary. Accordingly, as in *Wyeth*, I would require the Manufacturers to show that the FDA would not have approved a proposed label change. They have not made such a showing: They do "not argue that [they] attempted to give the kind of warning required by [state law] but [were] prohibited from doing so by the FDA." *Wyeth*, 555 U.S., at 572, 129 S.Ct. 1187.

This is not to say that generic manufacturers could never show impossibility. If a generic-manufacturer defendant proposed a label change to the FDA but the FDA rejected the proposal, it would be impossible for that defendant to comply with a state-law duty to warn. Likewise, impossibility would be established if the FDA had not yet responded to a generic manufacturer's request for a label change at the ***2589** time a plaintiff's injuries arose. A generic manufacturer might also show that the FDA had itself considered whether to request enhanced warnings in light of the evidence on which a plaintiff's claim rests but had decided to leave the warnings as is. (The Manufacturers make just such an argument in these cases. See, *e.g.*, Brief for Petitioner Actavis et al. 11.) But these are questions of fact to be established through discovery. Because the burden of proving impossibility falls on the defendant, I would hold that federal law does not render it impossible for generic manufacturers to comply with a state-law duty to warn as a categorical matter.

This conclusion flows naturally from the overarching principles governing our pre-emption doctrine. See *supra*, at 2586. Our "respect for the States as 'independent sovereigns in our federal system' leads us to assume that 'Congress does not cavalierly pre-empt state-law causes of action.' " *Wyeth*, 555 U.S., at 565–566, n. 3, 129 S.Ct. 1187 (quoting *Lohr*, 518 U.S., at 485, 116 S.Ct. 2240). It is for this reason that we hold defendants asserting impossibility to a "demanding" standard. *Wyeth*, 555 U.S., at 573, 129 S.Ct. 1187. This presumption against pre-emption has particular force when the Federal Government has afforded defendants a mechanism for complying with state law, even when that mechanism requires federal agency action. (The presumption has even greater force when federal law requires defendants to invoke that mechanism, as the majority assumes in these cases.) In such circumstances, I would hold, defendants will usually be unable to sustain their burden of showing impossibility if they have not even attempted to employ that mechanism. Any other approach threatens to infringe the States' authority over traditional matters of state interest—such as the failure-to-warn claims here—when Congress expressed no intent to pre-empt state law.

C

The majority concedes that the Manufacturers might have been able to accomplish under federal law what state law requires. *Ante*, at 2578 – 2579. To reach the conclusion that the Manufacturers have nonetheless satisfied their burden to show impossibility, the majority invents a new

pre-emption rule: "The question for 'impossibility' is whether the private party could *independently* do under federal law what state law requires of it." *Ante,* at 2579 (emphasis added). Because the Manufacturers could not have changed their labels without the exercise of judgment by the FDA, the majority holds, compliance with both state and federal law was impossible in these cases.[12]

The majority's new test has no basis in our precedents. The majority cites only *Wyeth* in support of its test. As discussed above, however, *Wyeth* does not stand for the proposition that it is impossible to comply with both federal and state law whenever federal agency approval is required. To the contrary, label changes by brand-name manufacturers such as Wyeth are subject to FDA review and acceptance. See *supra,* at 2588. And, even if *Wyeth* could be characterized as turning on the fact that the brand-name manufacturer could change its label unilaterally, the possibility ***2590** of unilateral action was, at most, a sufficient condition for rejecting the impossibility defense in that case. *Wyeth* did not hold that unilateral action is a necessary condition in every case.

With so little support in our case law, the majority understandably turns to other rationales. None of the rationales that it offers, however, makes any sense. First, it offers a *reductio ad absurdum:* If the possibility of FDA approval of a label change is sufficient to avoid conflict in these cases, it warns, as a "logical conclusion" so too would be the possibility that the FDA might rewrite its regulations or that Congress might amend the Hatch–Waxman Amendments. *Ante,* at 2581 – 2582. The logic of this conclusion escapes me. Conflict analysis necessarily turns on existing law. It thus would be ridiculous to conclude that federal and state law do not conflict on the ground that the defendant could have asked a federal agency or Congress to change the law. Here, by contrast, the Manufacturers' compliance with their state-law duty to warn did not require them to ask for a change in federal law, as the majority itself recognizes. See *ante,* at 2578 ("[F]ederal law would permit the Manufacturers to comply with the state labeling requirements if, and only if, the FDA and the brand-name manufacturer changed the brand-name label to do so"). The FDA already afforded them a mechanism for attempting to comply with their state-law duties. Indeed, the majority assumes that FDA regulations *required* the Manufacturers to request a label change when they had "reasonable evidence of an association of a serious hazard with a drug." 21 CFR § 201.57(e).

Second, the majority suggests that any other approach would render conflict pre-emption "illusory" and "meaningless." *Ante,* at 2579. It expresses concern that, without a robust view of what constitutes conflict, the Supremacy Clause would not have "any force" except in cases of express pre-emption. *Ibid.* To the extent the majority's purported concern is driven by its *reductio ad absurdum,* see *ante,* at 2579, n. 6, that concern is itself illusory, for the reasons just stated. To the extent the majority is concerned that our traditionally narrow view of what constitutes impossibility somehow renders conflict pre-emption as a whole meaningless, that concern simply makes no sense: We have repeatedly recognized that conflict pre-emption may be found, even absent impossibility, where state law "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Crosby,* 530 U.S., at 373, 120 S.Ct. 2288 (internal quotation marks omitted); see, *e.g., Geier v. American Honda Motor Co.,* 529 U.S. 861, 886, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000); *Barnett Bank of Marion Cty., N.A. v. Nelson,* 517 U.S. 25, 31, 116 S.Ct. 1103, 134 L.Ed.2d 237 (1996); *Hines v. Davidowitz,* 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941). The majority's expansive view of impossibility is thus unnecessary to prevent conflict pre-emption from losing all meaning.[13]

Third, a plurality of the Court adopts the novel theory that the Framers intended for the Supremacy Clause to operate as a so-called *non obstante* provision. See ***2591** *ante,* at 2579 – 2580 (citing Nelson, Preemption, 86 Va. L.Rev. 225 (2000)). According to the plurality, *non obstante* provisions in statutes "instruc[t] courts not to apply the general presumption against implied repeals." *Ante,* at 2579 (internal quotation marks omitted); see also *ante,* at 2580 (stating that when a statute contains a *non obstante* provision, " 'courts will be less inclined against recognizing repugnancy in applying such statutes' " (quoting J. Sutherland, Statutes and Statutory Construction § 147, p. 199 (1891)). From this understanding of the Supremacy Clause, the plurality extrapolates the principle that "courts should not strain to find ways to reconcile federal law with seemingly conflicting state law." *Ante,* at 2580.

This principle would have been news to the Congress that enacted the Hatch–Waxman Amendments in 1984: Our precedents hold just the opposite. For more than half a century, we have directed courts to presume that congressional action does *not* supersede "the historic police powers of the States ... unless that was the clear and manifest purpose of Congress." *Rice v. Santa Fe Elevator Corp.,* 331 U.S. 218, 230, 67 S.Ct. 1146, 91 L.Ed. 1447 (1947); see also *Gade,* 505 U.S., at 111–112, 112 S.Ct. 2374 (KENNEDY, J., concurring in part and concurring in judgment). We apply this presumption

against pre-emption both where Congress has spoken to the pre-emption question and where it has not. See *Wyeth*, 555 U.S., at 566, n. 3, 129 S.Ct. 1187. In the context of express pre-emption, we read federal statutes whenever possible not to pre-empt state law. See *Altria Group, Inc. v. Good*, 555 U.S. 70, 77, 129 S.Ct. 538, 172 L.Ed.2d 398 (2008) ("[W]hen the text of a pre-emption clause is susceptible of more than one plausible reading, courts ordinarily 'accept the reading that disfavors pre-emption' " (quoting *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005))); see also *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 518, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992). And, when the claim is that federal law impliedly pre-empts state law, we require a "strong" showing of a conflict "to overcome the presumption that state and local regulation ... can constitutionally coexist with federal regulation." *Hillsborough County v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 716, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985).

The plurality's new theory of the Supremacy Clause is a direct assault on these precedents.[14] Whereas we have long presumed that federal law does not pre-empt, or repeal, state law, the plurality today reads the Supremacy Clause to operate as a provision instructing courts "*not* to apply the general presumption against implied repeals." *Ante*, at 2579 (internal quotation marks omitted; emphasis added). And whereas we have long required evidence of a "clear and manifest" purpose to pre-empt, *Rice*, 331 U.S., at 230, 67 S.Ct. 1146, the plurality now instructs courts to "look no further than the ordinary meaning of federal law" before concluding that Congress must have intended to cast aside state law, *ante*, at 2580 (internal quotation marks and alteration omitted).

That the plurality finds it necessary to resort to this novel theory of the Supremacy Clause—a theory advocated by no party ***2592** or *amici* in these cases—is telling. Proper application of the longstanding presumption *against* pre-emption compels the conclusion that federal law does not render compliance with state law impossible merely because it requires an actor to seek federal agency approval. When federal law provides actors with a mechanism for attempting to comply with their state-law duties, "respect for the States as 'independent sovereigns in our federal system' " should require those actors to attempt to comply with state law before being heard to complain that compliance with both laws was impossible. *Wyeth*, 555 U.S., at 565–566, n. 3, 129 S.Ct. 1187 (quoting *Lohr*, 518 U.S., at 485, 116 S.Ct. 2240).

III

Today's decision leads to so many absurd consequences that I cannot fathom that Congress would have intended to pre-empt state law in these cases.

First, the majority's pre-emption analysis strips generic-drug consumers of compensation when they are injured by inadequate warnings. "If Congress had intended to deprive injured parties of [this] long available form of compensation, it surely would have expressed that intent more clearly." *Bates*, 544 U.S., at 449, 125 S.Ct. 1788. Given the longstanding existence of product liability actions, including for failure to warn, "[i]t is difficult to believe that Congress would, without comment, remove all means of judicial recourse for those injured by illegal conduct." *Silkwood*, 464 U.S., at 251, 104 S.Ct. 615; see also *Bruesewitz v. Wyeth LLC*, 562 U.S. ——, ——, 131 S.Ct. 1068, 1080, 179 L.Ed.2d 1 (2011) (noting our previously expressed "doubt that Congress would quietly preempt product-liability claims without providing a federal substitute"). In concluding that Congress silently immunized generic manufacturers from all failure-to-warn claims, the majority disregards our previous hesitance to infer congressional intent to effect such a sweeping change in traditional state-law remedies.

As the majority itself admits, a drug consumer's right to compensation for inadequate warnings now turns on the happenstance of whether her pharmacist filled her prescription with a brand-name drug or a generic. If a consumer takes a brand-name drug, she can sue the manufacturer for inadequate warnings under our opinion in *Wyeth*. If, however, she takes a generic drug, as occurs 75 percent of the time, she now has no right to sue. The majority offers no reason to think—apart from its new articulation of the impossibility standard—that Congress would have intended such an arbitrary distinction. In some States, pharmacists must dispense generic drugs absent instruction to the contrary from a consumer's physician. Even when consumers can request brand-name drugs, the price of the brand-name drug or the consumers' insurance plans may make it impossible to do so. As a result, in many cases, consumers will have no ability to preserve their state-law right to recover for injuries caused by inadequate warnings.

Second, the majority's decision creates a gap in the parallel federal-state regulatory scheme in a way that could have troubling consequences for drug safety. As we explained in *Wyeth*, "[s]tate tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly." 555 U.S., at 579, 129 S.Ct. 1187. Thus, we recognized, "state

law offers an additional, and important, layer of consumer protection that complements FDA regulation." *Ibid.* Today's decision eliminates the traditional state-law incentives for generic manufacturers to monitor and disclose safety risks. When a generic drug has a brand-name equivalent on the market, the brand-name ***2593** manufacturer will remain incentivized to uncover safety risks. But brand-name manufacturers often leave the market once generic versions are available, see *supra*, at 2573 – 2574, meaning that there will be no manufacturer subject to failure-to-warn liability. As to those generic drugs, there will be no "additional ... layer of consumer protection." *Wyeth*, 555 U.S., at 579, 129 S.Ct. 1187.

Finally, today's decision undoes the core principle of the Hatch–Waxman Amendments that generic and brand-name drugs are the "same" in nearly all respects.[15] See Brief for Rep. Henry A. Waxman as *Amicus Curiae* 9. The majority pins the expansion of the generic drug market on "the special, and different, regulation of generic drugs," which allows generic manufacturers to produce their drugs more cheaply. *Ante*, at 2582. This tells only half the story. The expansion of the market for generic drugs has also flowed from the increased acceptance of, and trust in, generic drugs by consumers, physicians, and state legislators alike.

Today's decision introduces a critical distinction between brand-name and generic drugs. Consumers of brand-name drugs can sue manufacturers for inadequate warnings; consumers of generic drugs cannot. These divergent liability rules threaten to reduce consumer demand for generics, at least among consumers who can afford brand-name drugs. They may pose "an ethical dilemma" for prescribing physicians. Brief for American Medical Association et al. as *Amici Curiae* 29. And they may well cause the States to rethink their longstanding efforts to promote generic use through generic substitution laws. See Brief for National Conference of State Legislators as *Amicus Curiae* 15 (state generic substitution laws "have proceeded on the premise that ... generic drugs are not, from citizens' perspective, materially different from brand ones, except for the lower price"). These consequences are directly at odds with the Hatch–Waxman Amendments' goal of increasing consumption of generic drugs.

Nothing in the Court's opinion convinces me that, in enacting the requirement that generic labels match their corresponding brand-name labels, Congress intended these absurd results. The Court certainly has not shown that such was the "*clear and manifest* purpose of Congress." *Wyeth*, 555 U.S., at 565, 129 S.Ct. 1187 (internal quotation marks omitted; emphasis added). To the contrary, because federal law affords generic manufacturers a mechanism for attempting to comply with their state-law duties to warn, I would hold that federal law does not categorically pre-empt state-law failure-to-warn claims against generic manufacturers. Especially in light of the presumption against pre-emption, the burden should fall on generic manufacturers to show that compliance was impossible on the particular facts of their case. By holding that the "possibility of *possibility* " is insufficient to "defea[t]" pre-emption in these cases, *ante*, at 2581, n. 8, the Court contorts our pre-emption doctrine and exempts defendants from their burden to establish impossibility. With respect, I dissent.

Parallel Citations

180 L.Ed.2d 580, 79 USLW 4606, Prod.Liab.Rep. (CCH) P 18,642, 11 Cal. Daily Op. Serv. 7694, 2011 Daily Journal D.A.R. 9237, 22 Fla. L. Weekly Fed. S 1222

Footnotes

* The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States v. Detroit Timber & Lumber Co.*, 200 U.S. 321, 337, 26 S.Ct. 282, 50 L.Ed. 499.

* Justice KENNEDY joins all but Part III–B–2 of this opinion.

1 All relevant events in these cases predate the Food and Drug Administration Amendments Act of 2007, 121 Stat. 823. We therefore refer exclusively to the pre–2007 statutes and regulations and express no view on the impact of the 2007 Act.

2 As we use it here, "generic drug" refers to a drug designed to be a copy of a reference listed drug (typically a brand-name drug), and thus identical in active ingredients, safety, and efficacy. See, *e.g.*, *United States v. Generix Drug Corp.*, 460 U.S. 453, 454–455, 103 S.Ct. 1298, 75 L.Ed.2d 198 (1983); 21 CFR § 314.3(b) (2006) (defining "reference listed drug").

3 The brief filed by the United States represents the views of the FDA. Cf. *Talk America, Inc. v. Michigan Bell Telephone Co.*, 564

U.S. ——, ——, n. 1, 131 S.Ct. 2254, 2257, n. 1, 180 L.Ed.2d 96, 2011 WL 2224429, at *3, n. 1 (2011); *Chase Bank USA, N.A. v. McCoy*, 562 U.S. ——, ——, 131 S.Ct. 871, 877–78, 178 L.Ed.2d 716 (2011). Although we defer to the agency's interpretation of its regulations, we do not defer to an agency's ultimate conclusion about whether state law should be pre-empted. *Wyeth v. Levine*, 555 U.S. 555, 576, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009).

4 We do not address whether state and federal law "directly conflict" in circumstances beyond "impossibility." See *Wyeth*, 555 U.S., at 582, 590–591, 129 S.Ct. 1187 (THOMAS, J., concurring in judgment) (suggesting that they might).

5 The Hatch–Waxman Amendments contain no provision expressly pre-empting state tort claims. See *post*, at 2586 – 2587, 2592 (SOTOMAYOR, J., dissenting). Nor do they contain any saving clause to expressly preserve state tort claims. Cf. *Williamson v. Mazda Motor of America, Inc.*, 562 U.S. ——, ——, 131 S.Ct. 1131, 1141–43, 179 L.Ed.2d 75 (2011) (THOMAS, J., concurring in judgment) (discussing the saving clause in the National Traffic and Motor Vehicle Safety Act of 1966, 49 U.S.C. § 30103(e)). Although an express statement on pre-emption is always preferable, the lack of such a statement does not end our inquiry. Contrary to the dissent's suggestion, the absence of express pre-emption is not a reason to find no *conflict* pre-emption. See *post*, at 2592.

6 The dissent asserts that we are forgetting "purposes-and-objectives" pre-emption. *Post*, at 2586 – 2587. But as the dissent acknowledges, purposes-and-objectives pre-emption is a form of conflict pre-emption. *Post*, at 2586 – 2587, 2590 – 2591. If conflict pre-emption analysis must take into account hypothetical federal action, including possible changes in Acts of Congress, then there is little reason to think that pre-emption based on the purposes and objectives of Congress would survive either.

7 Wyeth also urged that state tort law "creat[ed] an unacceptable 'obstacle to the accomplishment and execution of the full purposes and objectives of Congress.' " 555 U.S., at 563–564, 129 S.Ct. 1187 (quoting *Hines v. Davidowitz*, 312 U.S. 52, 67, 61 S.Ct. 399, 85 L.Ed. 581 (1941)). The Court rejected that argument, and that type of pre-emption is not argued here. Cf. *post*, at 2590, n. 13 (opinion of SOTOMAYOR, J.).

8 The FDA, however, retained the authority to eventually rescind Wyeth's unilateral CBE changes. Accordingly, the Court noted that Wyeth could have attempted to show, by "clear evidence," that the FDA would have rescinded any change in the label and thereby demonstrate that it would in fact have been impossible to do under federal law what state law required. *Wyeth, supra*, at 571, 129 S.Ct. 1187. Wyeth offered no such evidence.

That analysis is consistent with our holding today. The Court in *Wyeth* asked what the drug manufacturer could independently do under federal law, and in the absence of clear evidence that Wyeth could not have accomplished what state law required of it, found no pre-emption. The *Wyeth* Court held that, because federal law accommodated state law duties, "the possibility of impossibility" was "not enough." *Post*, at 2587; see also *Rice v. Norman Williams Co.*, 458 U.S. 654, 659, 102 S.Ct. 3294, 73 L.Ed.2d 1042 (1982) (rejecting "hypothetical" impossibility). But here, "existing" federal law directly conflicts with state law. *Post*, at 2590 ("Conflict analysis necessarily turns on existing law"). The question in these cases is not whether the possibility of *impossibility* establishes pre-emption, but rather whether the possibility of *possibility* defeats pre-emption. *Post*, at 2587.

9 That said, the dissent overstates what it characterizes as the "many absurd consequences" of our holding. *Post*, at 2592. First, the FDA informs us that "[a]s a practical matter, genuinely new information about drugs in long use (as generic drugs typically are) appears infrequently." U.S. Brief 34–35. That is because patent protections ordinarily prevent generic drugs from arriving on the market for a number of years after the brand-name drug appears. Indeed, situations like the one alleged here are apparently so rare that the FDA has no "formal regulation" establishing generic drug manufacturers' duty to initiate a label change, nor does it have any regulation setting out that label-change process. *Id.*, at 20–21. Second, the dissent admits that, even under its approach, generic drug manufacturers could establish pre-emption in a number of scenarios. *Post*, at 2588 – 2589.

1 Online at http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib. pdf (all Internet materials as visited June 17, 2011, and available in Clerk of Court's case file).

2 In addition, many insurance plans are structured to promote generic use. See Congressional Budget Office, Effects of Using Generic Drugs on Medicare's Prescription Drug Spending 9 (2010), online at http://www.cbo.gov/ftpdoc/118xx/doc11838/09–15–PrescriptionDrugs.pdf. State Medicaid programs similarly promote generic use. See Kaiser Comm'n on Medicaid and the Uninsured, State Medicaid Outpatient Prescription Drug Policies: Findings from a National Survey, 2005 Update 10 (2005), online at www.kff.org/medicaid/upload/state–medicaid–outpatient–prescription–drug–policies–findings–from–a–national–survey–2005–update–report.pdf.

3 Online at http://www.cbo.gov/ftpdocs/6xx/doc655/pharm.pdf.

4 An adverse drug experience is defined as "[a]ny adverse event associated with the use of a drug in humans, whether or not considered drug related." 21 CFR § 314.80(a) (2006).

5 Like the majority, I refer to the pre–2007 statutes and regulations. See *ante,* at 2574, n. 1.

6 At congressional hearings on the Hatch–Waxman Amendments, representatives of the generic drug manufacturers confirmed both their obligation and their ability to conduct postapproval investigation of adverse drug experiences. See Drug Legislation: Hearings on H.R. 1554 et al. before the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce, 98th Cong., 1st Sess., 45 (1983) (statement of Kenneth N. Larsen, chairman of the Generic Pharmaceutical Industry Association (GPhA)) (generic manufacturers "are sensitive to the importance of looking at adverse reactions"); *id.*, at 47–48 ("[W]e will do and provide whatever is required to be performed to meet the regulatory requirement to provide for the safety and well-being of those that are using the drug, this is our role and responsibility. This is an obligation to be in this business"); *id.*, at 50–51 (statement of Bill Haddad, executive officer and president of GPhA) ("Every single generic drug company that I know has a large research staff. It not only researches the drug that they are copying, or bringing into the market but it researches new drugs, researches adverse reaction[s]").

7 The FDA's construction of this regulation mirrors the guidance it provided to generic manufacturers nearly 20 years ago in announcing the final rule implementing the abbreviated application process for generic drugs:

> "If an ANDA [*i.e.*, application for approval of a generic drug] applicant believes new safety information should be added to a product's labeling, it should contact FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised. After approval of an ANDA, if an ANDA holder believes that new safety information should be added, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic and listed drugs should be revised." 57 Fed.Reg. 17961 (1992).
>
> FDA's internal procedures recognize that the Office of Generic Drugs will have to consult with other FDA components on "some labeling reviews." Manual of Policies and Procedures 5200.6, p. 1 (May 9, 2001). Consultations involving "possible serious safety concerns" receive the highest priority. *Id.*, at 3.

8 In its decision below, the Eighth Circuit suggested that the Manufacturers could not show impossibility because federal law merely permitted them to sell generic drugs; it did not require them to do so. See *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 611 (2009) ("The generic defendants were not compelled to market metoclopramide. If they realized their label was insufficient but did not believe they could even propose a label change, they could have simply stopped selling the product"); see also *Geier v. American Honda Motor Co.*, 529 U.S. 861, 873, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000) (describing "a case of impossibility" as one "in which state law penalizes what federal law *requires* " (emphasis added)). Respondents have not advanced this argument, and I find it unnecessary to consider.

9 At the time respondents' cause of action arose, the FDA did not have authority to require a brand-name manufacturer to change its label. (It received that authority in 2007. See Pub.L. 110–85, § 901, 121 Stat. 924–926, 21 U.S.C. § 355(*o*)(4) (2006 ed., Supp. III). It did, however, have the equally significant authority to withdraw the brand-name manufacturer's permission to market its drug if the manufacturer refused to make a requested labeling change. See 21 U.S.C. § 355(e) (2006 ed.); 21 CFR § 314.150(b)(3).

10 A brand-name manufacturer's ability to comply with a state-law duty to warn would depend on its own unilateral actions only during the period after it should have changed its label but before the FDA would have approved or disapproved the label change. The claim in *Wyeth* does not appear to have arisen during that period.

11 Respondents' state-law claim is not that the Manufacturers were required to ask the FDA for assistance in changing the labels; the role of the FDA arises only as a result of the Manufacturers' pre-emption defense.

12 These cases do not involve a situation where a brand-name manufacturer itself produces generic drugs. See Okie, Multinational Medicines—Ensuring Drug Quality in an Era of Global Manufacturing, 361 N. Eng. J. Med. 737, 738 (2009); see also GPhA, Frequently Asked Questions About Generics, http://www.gphaonline.org/about-gpha/about-generics/faq ("Brand-name companies make about half of generic drugs"). In that case, the manufacturer could independently change the brand-name label under the CBE regulation, triggering a corresponding change to its own generic label.

13 Justice THOMAS, the author of today's opinion, has previously expressed the view that obstacle pre-emption is inconsistent with the Constitution. See *Williamson v. Mazda Motor of America, Inc.*, 562 U.S. ——, ——, 131 S.Ct. 1131, 1141–43, 179 L.Ed.2d 75 (2011) (opinion concurring in judgment); *Wyeth v. Levine*, 555 U.S. 555, 604, 129 S.Ct. 1187, 173 L.Ed.2d 51 (2009) (opinion concurring in judgment). That position, however, has not been accepted by this Court, and it thus should not justify the majority's novel expansion of impossibility pre-emption.

14 The author of the law review article proposing this theory of the Supremacy Clause acknowledges as much. See Nelson, Preemption, 86 Va. L.Rev. 225, 304 (2000) ("The *non obstante* provision rejects an artificial presumption that Congress did not intend to contradict any state laws and that federal statutes must therefore be harmonized with state law"). The plurality, on the

other hand, carefully avoids discussing the ramifications of its new theory for the longstanding presumption against pre-emption.

15 According to the GPhA, both the FDA and the generic drug industry "spend millions of dollars each year ... seeking to reassure consumers that affordable generic drugs really are—as federal law compels them to be—*the same as* their pricier brand-name counterparts." Brief for GPhA as *Amicus Curiae* on Pet. for Cert. in Nos. 09–993, 09–1039, pp. 2–3.

128 S.Ct. 999
Supreme Court of the United States

Donna S. RIEGEL, individually and as administrator of the Estate of Charles R. Riegel, Petitioner,
v.
MEDTRONIC, INC.

No. 06–179. | Argued Dec. 4, 2007. | Decided Feb. 20, 2008.

Synopsis
Background: Cardiac patient sued manufacturer of balloon catheter used in his angioplasty, asserting state-law claims including strict liability, breach of implied warranty, and negligent design, testing, inspection, distribution, labeling, marketing, sale and manufacture. The United States District Court for the Northern District of New York, Lawrence E. Kahn, J., granted manufacturer's motions for summary judgment. Patient appealed. The United States Court of Appeals for the Second Circuit, 451 F.3d 104, affirmed. Certiorari was granted.

Holdings: The United States Supreme Court, Justice Scalia, held that:

[1] Food and Drug Administration's (FDA) premarket approval process established federal requirements, and

[2] patient's New York common-law claims of negligence, strict liability, and implied warranty against manufacturer were preempted.

Affirmed.

Justice Stevens filed an opinion concurring in part and concurring in the judgment.

Justice Ginsburg filed an opinion dissenting.

****1000 *Syllabus*[*]**
The Medical Device Amendments of 1976(MDA) created a scheme of federal ****1001** safety oversight for medical devices while sweeping back state oversight schemes. The statute provides that a State shall not "establish or continue in effect with respect to a device intended for human use any requirement—... (1) which is different from, or in addition to, any requirement applicable under [federal law] to the device, and ... (2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under" relevant federal law. 21 U.S.C. § 360k(a). The MDA calls for federal oversight of medical devices that varies with the type of device at issue. The most extensive oversight is reserved for Class III devices that undergo the premarket approval process. These devices may enter the market only if the Food and Drug Administration (FDA) reviews their design, labeling, and manufacturing specifications and determines that those specifications provide a reasonable assurance of safety and effectiveness. Manufacturers may not make changes to such devices that would affect safety or effectiveness unless they first seek and obtain permission from the FDA.

Charles Riegel and his wife, petitioner Donna Riegel, brought suit against respondent Medtronic after a Medtronic catheter ruptured in Charles Riegel's coronary artery during heart surgery. The catheter is a Class III device that received FDA premarket approval. The Riegels alleged that the device was designed, labeled, and manufactured in a manner that violated New York common law. The District Court held that the MDA pre-empted the Riegels' claims of strict liability; breach of implied warranty; and negligence in the design, testing, inspection, distribution, labeling, marketing, and sale of the catheter, and their claim of negligent manufacturing insofar as the claim was not premised on the theory that Medtronic had violated federal law. The Second Circuit affirmed.

Held: The MDA's pre-emption clause bars common-law claims challenging the safety or effectiveness of a medical device marketed in a form that received premarket approval from the FDA. Pp. 1006 – 1011.

(a) The Federal Government has established "requirement[s] applicable ... to" Medtronic's catheter within § 360k(a)(1)'s meaning. In *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 495, 500–501, 116 S.Ct. 2240, 135 L.Ed.2d 700, the Court interpreted the MDA's pre-emption provision in a manner "substantially informed" by an FDA regulation, 21 CFR § 808.1(d), which says that state requirements are pre-empted only when the FDA "has established specific counterpart regulations or there are other specific requirements applicable to a particular device" under federal law. Premarket approval imposes "specific requirements applicable to a particular device." The FDA requires that

a device that has received premarket approval be marketed without significant deviations from the specifications in the device's approval application, for the reason that the FDA has determined that those specifications provide a reasonable assurance of safety and effectiveness. Pp. 1006 – 1007.

(b) Petitioner's common-law claims are pre-empted because they are based upon New York "requirement[s]" with respect to Medtronic's catheter that are "different from, or in addition to," the federal ones, and that relate to safety and effectiveness, § 360k(a). Pp. 1007 – 1011.

(1) Common-law negligence and strict-liability claims impose "requirement[s]" ****1002** under the ordinary meaning of that term, see, *e.g.*, *Lohr, supra,* at 503–505, 512, 116 S.Ct. 2240; *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 521–523, 548–549, 112 S.Ct. 2608, 120 L.Ed.2d 407. There is nothing in the MDA that contradicts this normal meaning. Pp. 1007 – 1009.

(2) The Court rejects petitioner's contention that the duties underlying her state-law tort claims are not pre-empted because general common-law duties are not requirements maintained "with respect to devices." Petitioner's suit depends upon New York's "continu[ing] in effect" general tort duties "with respect to" Medtronic's catheter. Title 21 CFR § 808.1(d)(1)—which states that MDA pre-emption does not extend to "[s]tate or local requirements of general applicability [whose] purpose ... relates either to other products in addition to devices ... or to unfair trade practices in which the requirements are not limited to devices"—does not alter the Court's interpretation. Pp. 1009 – 1011.

(c) The Court declines to address in the first instance petitioner's argument that this lawsuit raises "parallel" claims that are not pre-empted by § 360k under *Lohr, supra,* at 495, 513, 116 S.Ct. 2240. P. 1011.

451 F.3d 104, affirmed.

SCALIA, J., delivered the opinion of the Court, in which ROBERTS, C. J., and KENNEDY, SOUTER, THOMAS, BREYER, and ALITO, JJ., joined, and in which STEVENS, J., joined except for Parts III–A and III–B. STEVENS, J., filed an opinion concurring in part and concurring in the judgment. GINSBURG, J., filed a dissenting opinion, *post,* 1013 – 1020.

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Opinion

Justice SCALIA delivered the opinion of the Court.

***315** We consider whether the pre-emption clause enacted in the Medical Device Amendments of 1976, 21 U.S.C. § 360k, bars common-law claims challenging the safety and effectiveness of a medical device given premarket approval by the Food and Drug Administration (FDA).

I

A

The Federal Food, Drug, and Cosmetic Act (FDCA), 52 Stat. 1040, as amended, 21 U.S.C. § 301 *et seq.*, has long required FDA approval for the introduction of new drugs into the market. Until the statutory enactment at issue here, however, the introduction of new medical devices was left largely for the States to supervise as they saw fit. See ****1003** *Medtronic, Inc. v. Lohr,* 518 U.S. 470, 475–476, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996).

The regulatory landscape changed in the 1960's and 1970's, as complex devices proliferated and some failed. Most notably, the Dalkon Shield intrauterine device, introduced in 1970, was linked to serious infections and several deaths, not to mention a large number of pregnancies. Thousands of tort claims followed. R. Bacigal, The Limits of Litigation: The Dalkon Shield Controversy 3 (1990). In the view of many, the Dalkon Shield failure and its aftermath demonstrated the inability

of the common-law tort system to manage the risks associated with dangerous devices. See, *e.g.*, S. Foote, Managing the Medical Arms Race 151–152 (1992). Several States adopted regulatory measures, including California, which in 1970 enacted a law requiring premarket approval of medical devices. 1970 Cal. Stats. ch. 1573, ***316** §§ 26670–26693; see also Leflar & Adler, The Preemption Pentad: Federal Preemption of Products Liability Claims After *Medtronic*, 64 Tenn. L.Rev. 691, 703, n. 66 (1997) (identifying 13 state statutes governing medical devices as of 1976).

Congress stepped in with passage of the Medical Device Amendments of 1976(MDA), 21 U.S.C. § 360c *et seq.*,[1] which swept back some state obligations and imposed a regime of detailed federal oversight. The MDA includes an express pre-emption provision that states:

> "Except as provided in subsection (b) of this section, no State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement—
>
> > "(1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and
> >
> > "(2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter." § 360k(a).
>
> The exception contained in subsection (b) permits the FDA to exempt some state and local requirements from pre-emption.

The new regulatory regime established various levels of oversight for medical devices, depending on the risks they present. Class I, which includes such devices as elastic bandages and examination gloves, is subject to the lowest level of oversight: "general controls," such as labeling requirements. § 360c(a)(1)(A); FDA, Device Advice: Device Classes, http://www.fda.gov/cdrh/devadvice/3132.html (all Internet materials as visited Feb. 14, 2008, and available in Clerk of Court's case file). Class II, which includes such devices as powered wheelchairs and surgical drapes, *ibid.*, ***317** is subject in addition to "special controls" such as performance standards and postmarket surveillance measures, § 360c(a)(1)(B).

The devices receiving the most federal oversight are those in Class III, which include replacement heart valves, implanted cerebella stimulators, and pacemaker pulse generators, FDA, Device Advice: Device Classes, *supra*. In general, a device is assigned to Class III if it cannot be established that a less stringent classification would provide reasonable assurance of safety and effectiveness, and the device is "purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health," or "presents a potential unreasonable risk of illness or injury." § 360c(a)(1)(C)(ii).

****1004** Although the MDA established a rigorous regime of premarket approval for new Class III devices, it grandfathered many that were already on the market. Devices sold before the MDA's effective date may remain on the market until the FDA promulgates, after notice and comment, a regulation requiring premarket approval. §§ 360c(f)(1), 360e(b)(1). A related provision seeks to limit the competitive advantage grandfathered devices receive. A new device need not undergo premarket approval if the FDA finds it is "substantially equivalent" to another device exempt from premarket approval. § 360c(f)(1)(A). The agency's review of devices for substantial equivalence is known as the § 510(k) process, named after the statutory provision describing the review. Most new Class III devices enter the market through § 510(k). In 2005, for example, the FDA authorized the marketing of 3,148 devices under § 510(k) and granted premarket approval to just 32 devices. P. Hutt, R. Merrill, & L. Grossman, Food and Drug Law 992 (3d ed.2007).

Premarket approval is a "rigorous" process. *Lohr*, *supra*, at 477, 116 S.Ct. 2240. A manufacturer must submit what is typically a multivolume application. FDA, Device Advice—Premarket ***318** Approval (PMA) 18, http://www.fda. gov/cdrh/devadvice/pma/printer.html. It includes, among other things, full reports of all studies and investigations of the device's safety and effectiveness that have been published or should reasonably be known to the applicant; a "full statement" of the device's "components, ingredients, and properties and of the principle or principles of operation"; "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device"; samples or device components required by the FDA; and a specimen of the proposed labeling. § 360e(c)(1). Before deciding whether to approve the application, the agency may refer it to a panel of outside experts, 21 CFR § 814.44(a)(2007), and may request additional data from the manufacturer, § 360e(c)(1)(G).

The FDA spends an average of 1,200 hours reviewing each application, *Lohr*, 518 U.S., at 477, 116 S.Ct. 2240, and grants premarket approval only if it finds there is a "reasonable assurance" of the device's "safety and

effectiveness," § 360e(d). The agency must "weig[h] any probable benefit to health from the use of the device against any probable risk of injury or illness from such use." § 360c(a)(2)(C). It may thus approve devices that present great risks if they nonetheless offer great benefits in light of available alternatives. It approved, for example, under its Humanitarian Device Exemption procedures, a ventricular assist device for children with failing hearts, even though the survival rate of children using the device was less than 50 percent. FDA, Center for Devices and Radiological Health, Debakey VAD Child Left Ventricular Assist System-H030003, Summary of Safety and Probable Benefit 20 (2004), http://www.fda.gov/cdrh/pdf3/H030003b.pdf.

The premarket approval process includes review of the device's proposed labeling. The FDA evaluates safety and effectiveness under the conditions of use set forth on the label, § 360c(a)(2)(B), and must determine that the proposed labeling is neither false nor misleading, § 360e(d)(1)(A).

***319** After completing its review, the FDA may grant or deny premarket approval. § 360e(d). It may also condition approval on adherence to performance standards, 21 CFR § 861.1(b)(3), restrictions upon sale or distribution, or compliance with other requirements, § 814.82. The agency is also ****1005** free to impose device-specific restrictions by regulation. § 360j(e)(1).

If the FDA is unable to approve a new device in its proposed form, it may send an "approvable letter" indicating that the device could be approved if the applicant submitted specified information or agreed to certain conditions or restrictions. 21 CFR § 814.44(e). Alternatively, the agency may send a "not approvable" letter, listing the grounds that justify denial and, where practical, measures that the applicant could undertake to make the device approvable. § 814.44(f).

Once a device has received premarket approval, the MDA forbids the manufacturer to make, without FDA permission, changes in design specifications, manufacturing processes, labeling, or any other attribute, that would affect safety or effectiveness. § 360e(d)(6)(A)(i). If the applicant wishes to make such a change, it must submit, and the FDA must approve, an application for supplemental premarket approval, to be evaluated under largely the same criteria as an initial application. § 360e(d)(6); 21 CFR § 814.39(c).

After premarket approval, the devices are subject to reporting requirements. § 360i. These include the obligation to inform the FDA of new clinical investigations or scientific studies concerning the device which the applicant knows of or reasonably should know of, 21 CFR § 814.84(b)(2), and to report incidents in which the device may have caused or contributed to death or serious injury, or malfunctioned in a manner that would likely cause or contribute to death or serious injury if it recurred, § 803.50(a). The FDA has the power to withdraw premarket approval based on newly reported data or existing information and must withdraw approval ***320** if it determines that a device is unsafe or ineffective under the conditions in its labeling. § 360e(e)(1); see also § 360h(e) (recall authority).

B

Except as otherwise indicated, the facts set forth in this section appear in the opinion of the Court of Appeals. The device at issue is an Evergreen Balloon Catheter marketed by defendant-respondent Medtronic, Inc. It is a Class III device that received premarket approval from the FDA in 1994; changes to its label received supplemental approvals in 1995 and 1996.

Charles Riegel underwent coronary angioplasty in 1996, shortly after suffering a myocardial infarction. App. to Pet. for Cert. 56a. His right coronary artery was diffusely diseased and heavily calcified. Riegel's doctor inserted the Evergreen Balloon Catheter into his patient's coronary artery in an attempt to dilate the artery, although the device's labeling stated that use was contraindicated for patients with diffuse or calcified stenoses. The label also warned that the catheter should not be inflated beyond its rated burst pressure of eight atmospheres. Riegel's doctor inflated the catheter five times, to a pressure of 10 atmospheres; on its fifth inflation, the catheter ruptured. Complaint 3. Riegel developed a heart block, was placed on life support, and underwent emergency coronary bypass surgery.

Riegel and his wife Donna brought this lawsuit in April 1999, in the United States District Court for the Northern District of New York. Their complaint alleged that Medtronic's catheter was designed, labeled, and manufactured in a manner that violated New York common law, and that these defects caused Riegel to suffer severe and permanent injuries. The complaint raised a number of common-law claims. The District Court held that the ****1006** MDA pre-empted Riegel's claims of strict liability; breach of implied warranty; and negligence in the design, testing, inspection, distribution, labeling, marketing, and sale of the catheter. App. to ***321** Pet. for Cert. 68a; Complaint 3–4. It also held that the

MDA pre-empted a negligent manufacturing claim insofar as it was not premised on the theory that Medtronic violated federal law. App. to Pet. for Cert. 71a. Finally, the court concluded that the MDA pre-empted Donna Riegel's claim for loss of consortium to the extent it was derivative of the pre-empted claims. *Id.*, at 68a; see also *id.*, at 75a.[2]

The United States Court of Appeals for the Second Circuit affirmed these dismissals. 451 F.3d 104 (2006). The court concluded that Medtronic was "clearly subject to the federal, device-specific requirement of adhering to the standards contained in its individual, federally approved" premarket approval application. *Id.*, at 118. The Riegels' claims were pre-empted because they "would, if successful, impose state requirements that differed from, or added to," the device-specific federal requirements. *Id.*, at 121. We granted certiorari.[3] 551 U.S. 1144, 127 S.Ct. 3000, 168 L.Ed.2d 725 (2007).

II

[1] Since the MDA expressly pre-empts only state requirements "different from, or in addition to, any requirement applicable ... to the device" under federal law, § 360k(a)(1), we must determine whether the Federal Government has established requirements applicable to Medtronic's catheter. If so, we must then determine whether the Riegels' ***322** common-law claims are based upon New York requirements with respect to the device that are "different from, or in addition to," the federal ones, and that relate to safety and effectiveness. § 360k(a).

We turn to the first question. In *Lohr*, a majority of this Court interpreted the MDA's pre-emption provision in a manner "substantially informed" by the FDA regulation set forth at 21 CFR § 808.1(d). 518 U.S., at 495, 116 S.Ct. 2240; see also *id.*, at 500–501, 116 S.Ct. 2240. That regulation says that state requirements are pre-empted "only when the Food and Drug Administration has established specific counterpart regulations or there are other specific requirements applicable to a particular device...." 21 CFR § 808.1(d). Informed by the regulation, we concluded that federal manufacturing and labeling requirements applicable across the board to almost all medical devices did not pre-empt the common-law claims of negligence and strict liability at issue in *Lohr*. The federal requirements, we said, were not requirements specific to the device in question—they reflected "entirely generic concerns about device regulation generally." 518 U.S., at 501, 116 S.Ct. 2240. While we disclaimed a conclusion that general federal requirements could never pre-empt, or general state duties never be pre-empted, ****1007** we held that no pre-emption occurred in the case at hand based on a careful comparison between the state and federal duties at issue. *Id.*, at 500–501, 116 S.Ct. 2240.

Even though substantial-equivalence review under § 510(k) is device specific, *Lohr* also rejected the manufacturer's contention that § 510(k) approval imposed device-specific "requirements." We regarded the fact that products entering the market through § 510(k) may be marketed only so long as they remain substantial equivalents of the relevant pre–1976 devices as a qualification for an exemption rather than a requirement. *Id.*, at 493–494, 116 S.Ct. 2240; see also *id.*, at 513, 116 S.Ct. 2240 (O'Connor, J., concurring in part and dissenting in part).

Premarket approval, in contrast, imposes "requirements" under the MDA as we interpreted it in *Lohr*. Unlike general ***323** labeling duties, premarket approval is specific to individual devices. And it is in no sense an exemption from federal safety review—it *is* federal safety review. Thus, the attributes that *Lohr* found lacking in § 510(k) review are present here. While § 510(k) is " 'focused on *equivalence*, not safety,' " *id.*, at 493, 116 S.Ct. 2240 (opinion of the Court), premarket approval is focused on safety, not equivalence. While devices that enter the market through § 510(k) have "never been formally reviewed under the MDA for safety or efficacy," *ibid.*, the FDA may grant premarket approval only after it determines that a device offers a reasonable assurance of safety and effectiveness, § 360e(d). And while the FDA does not " 'require' " that a device allowed to enter the market as a substantial equivalent "take any particular form for any particular reason," 518 U.S., at 493, 116 S.Ct. 2240, the FDA requires a device that has received premarket approval to be made with almost no deviations from the specifications in its approval application, for the reason that the FDA has determined that the approved form provides a reasonable assurance of safety and effectiveness.

III

[2] We turn, then, to the second question: whether the Riegels' common-law claims rely upon "any requirement" of New York law applicable to the catheter that is "different from, or in addition to," federal requirements and that "relates to the safety or effectiveness of the device or to any other matter included

in a requirement applicable to the device." § 360k(a). Safety and effectiveness are the very subjects of the Riegels' common-law claims, so the critical issue is whether New York's tort duties constitute "requirements" under the MDA.

A

In *Lohr,* five Justices concluded that common-law causes of action for negligence and strict liability do impose "requirement[s]" and would be pre-empted by federal requirements ***324** specific to a medical device. See 518 U.S., at 512, 116 S.Ct. 2240 (opinion of O'Connor, J., joined by Rehnquist, C. J., and SCALIA and THOMAS, JJ.); *id.,* at 503–505, 116 S.Ct. 2240 (BREYER, J., concurring in part and concurring in judgment). We adhere to that view. In interpreting two other statutes we have likewise held that a provision pre-empting state "requirements" pre-empted common-law duties. *Bates v. Dow Agrosciences LLC,* 544 U.S. 431, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005), found common-law actions to be pre-empted by a provision of the Federal Insecticide, Fungicide, and Rodenticide Act that said certain States " 'shall not impose or continue in effect *any requirements* for labeling or packaging in addition to or different from ****1008** those required under this subchapter.' " *Id.,* at 443, 125 S.Ct. 1788 (discussing 7 U.S.C. § 136v(b); emphasis added). *Cipollone v. Liggett Group, Inc.,* 505 U.S. 504, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992), held common-law actions pre-empted by a provision of the Public Health Cigarette Smoking Act of 1969, 15 U.S.C. § 1334(b), which said that "[n]o requirement or prohibition based on smoking and health shall be imposed under State law with respect to the advertising or promotion of any cigarettes" whose packages were labeled in accordance with federal law. See 505 U.S., at 523, 112 S.Ct. 2608 (plurality opinion); *id.,* at 548–549, 112 S.Ct. 2608 (SCALIA, J., concurring in judgment in part and dissenting in part).

Congress is entitled to know what meaning this Court will assign to terms regularly used in its enactments. Absent other indication, reference to a State's "requirements" includes its common-law duties. As the plurality opinion said in *Cipollone,* common-law liability is "premised on the existence of a legal duty," and a tort judgment therefore establishes that the defendant has violated a state-law obligation. *Id.,* at 522, 112 S.Ct. 2608. And while the common-law remedy is limited to damages, a liability award " 'can be, indeed is designed to be, a potent method of governing conduct and controlling policy.' " *Id.,* at 521, 112 S.Ct. 2608.

In the present case, there is nothing to contradict this normal meaning. To the contrary, in the context of this legislation ***325** excluding common-law duties from the scope of pre-emption would make little sense. State tort law that requires a manufacturer's catheters to be safer, but hence less effective, than the model the FDA has approved disrupts the federal scheme no less than state regulatory law to the same effect. Indeed, one would think that tort law, applied by juries under a negligence or strict-liability standard, is less deserving of preservation. A state statute, or a regulation adopted by a state agency, could at least be expected to apply cost-benefit analysis similar to that applied by the experts at the FDA: How many more lives will be saved by a device which, along with its greater effectiveness, brings a greater risk of harm? A jury, on the other hand, sees only the cost of a more dangerous design, and is not concerned with its benefits; the patients who reaped those benefits are not represented in court. As Justice BREYER explained in *Lohr,* it is implausible that the MDA was meant to "grant greater power (to set state standards 'different from, or in addition to,' federal standards) to a single state jury than to state officials acting through state administrative or legislative lawmaking processes." 518 U.S., at 504, 116 S.Ct. 2240. That perverse distinction is not required or even suggested by the broad language Congress chose in the MDA,[4] and we will not turn somersaults to create it.

***326 B**

The dissent would narrow the pre-emptive scope of the term "requirement" on ****1009** the grounds that it is "difficult to believe that Congress would, without comment, remove all means of judicial recourse" for consumers injured by FDA-approved devices. *Post,* at 1015 (opinion of GINSBURG, J.) (internal quotation marks omitted). But, as we have explained, this is exactly what a pre-emption clause for medical devices does by its terms. The operation of a law enacted by Congress need not be seconded by a committee report on pain of judicial nullification. See, *e.g., Connecticut Nat. Bank v. Germain,* 503 U.S. 249, 253–254, 112 S.Ct. 1146, 117 L.Ed.2d 391 (1992). It is not our job to speculate upon congressional motives. If we were to do so, however, the only indication available—the text of the statute—suggests that the solicitude for those injured by FDA-approved devices, which the dissent finds controlling, was overcome in Congress's estimation by solicitude for those who would suffer without new medical devices if juries were allowed to apply the tort law of 50 States to all innovations.[5]

In the case before us, the FDA has supported the position taken by our opinion with regard to the meaning of the statute. We have found it unnecessary to rely upon that agency view because we think the statute itself speaks clearly to the point at issue. If, however, we had found the statute ambiguous and had accorded the agency's current position deference, the dissent is correct, see *post*, at 1016, n. 8, that—inasmuch as mere *Skidmore* deference would seemingly be at issue—the degree of deference might be reduced by the fact that the agency's earlier position was different. See *Skidmore v. Swift & Co.*, 323 U.S. 134, 65 S.Ct. 161, 89 L.Ed. 124 (1944); *United States* ***327** *v. Mead Corp.*, 533 U.S. 218, 121 S.Ct. 2164, 150 L.Ed.2d 292 (2001); *Good Samaritan Hospital v. Shalala*, 508 U.S. 402, 417, 113 S.Ct. 2151, 124 L.Ed.2d 368 (1993). But of course the agency's earlier position (which the dissent describes at some length, *post*, at 1015 – 1016, and finds preferable) is even more compromised, indeed deprived of all claim to deference, by the fact that it is no longer the agency's position.

The dissent also describes at great length the experience under the FDCA with respect to drugs and food and color additives. *Post*, at 1016 – 1018. Two points render the conclusion the dissent seeks to draw from that experience—that the pre-emption clause permits tort suits—unreliable. (1) It has not been established (as the dissent assumes) that no tort lawsuits are pre-empted by drug or additive approval under the FDCA. (2) If, as the dissent believes, the pre-emption clause permits tort lawsuits for medical devices just as they are (by hypothesis) permitted for drugs and additives; and if, as the dissent believes, Congress wanted the two regimes to be alike; Congress could have applied the pre-emption clause to the entire FDCA. It did not do so, but instead wrote a pre-emption clause that applies only to medical devices.

C

The Riegels contend that the duties underlying negligence, strict-liability, and implied-warranty claims are not pre-empted even if they impose " 'requirements,' " because general common-law duties are not requirements maintained " 'with respect to devices.' " Brief for Petitioner 34–36. Again, a majority of this Court suggested otherwise in *Lohr*. See 518 U.S., at 504–505, 116 S.Ct. 2240 (opinion of BREYER, J.); *id.*, at 514, 116 S.Ct. 2240 (opinion of ****1010** O'Connor, J., joined by Rehnquist, C. J., and SCALIA and THOMAS, JJ.).[6] And with good reason. The ***328** language of the statute does not bear the Riegels' reading. The MDA provides that no State "may establish or continue in effect *with respect to a device ... any requirement*" relating to safety or effectiveness that is different from, or in addition to, federal requirements. § 360k(a) (emphasis added). The Riegels' suit depends upon New York's "continu[ing] in effect" general tort duties "with respect to" Medtronic's catheter. Nothing in the statutory text suggests that the pre-empted state requirement must apply *only* to the relevant device, or only to medical devices and not to all products and all actions in general.

[3] The Riegels' argument to the contrary rests on the text of an FDA regulation which states that the MDA's pre-emption clause does not extend to certain duties, including "[s]tate or local requirements of general applicability where the purpose of the requirement relates either to other products in addition to devices (e.g., requirements such as general electrical codes, and the Uniform Commercial Code (warranty of fitness)), or to unfair trade practices in which the requirements are not limited to devices." 21 CFR § 808.1(d)(1). Even assuming that this regulation could play a role in defining the MDA's pre-emptive scope, it does not provide unambiguous support for the Riegels' position. The agency's reading of its own rule is entitled to substantial deference, see *Auer v. Robbins*, 519 U.S. 452, 461, 117 S.Ct. 905, 137 L.Ed.2d 79 (1997), and the FDA's view put forward in this case is that the regulation does not refer to general tort duties of care, such as those underlying the claims in this case that a device was designed, labeled, or manufactured in an unsafe or ineffective manner, Brief for United States as *Amicus Curiae* 27–28. That is so, according to the FDA, because the regulation excludes from pre-emption requirements that relate only incidentally to medical devices, but not other requirements. General tort ***329** duties of care, unlike fire codes or restrictions on trade practices, "directly regulate" the device itself, including its design. *Id.*, at 28. We find the agency's explanation less than compelling, since the same could be said of general requirements imposed by electrical codes, the Uniform Commercial Code, or unfair-trade-practice law, which the regulation specifically excludes from pre-emption.

Other portions of 21 CFR § 808.1, however, support the agency's view that § 808.1(d)(1) has no application to this case (though still failing to explain why electrical codes, the Uniform Commercial Code, or unfair-trade-practice requirements are different). Section 808.1(b) states that the MDA sets forth a "general rule" pre-empting state duties "having the force and effect of law (whether established by statute, ordinance, regulation, *or court decision*)....." (Emphasis added.) This sentence is far more comprehensible under the FDA's view that § 808.1(d)(1)

has no application here than under the Riegels' view. We are aware of no duties established by court decision other than common-law duties, and we are aware of no common-law duties that relate solely to medical devices.

****1011** The Riegels' reading is also in tension with the regulation's statement that adulteration and misbranding claims are pre-empted when they "ha [ve] the effect of establishing a substantive requirement for a specific device, e.g., a specific labeling requirement" that is "different from, or in addition to," a federal requirement. § 808.1(d)(6)(ii). Surely this means that the MDA would pre-empt a jury determination that the FDA-approved labeling for a pacemaker violated a state common-law requirement for additional warnings. The Riegels' reading of § 808.1(d)(1), however, would allow a claim for tortious mislabeling to escape pre-emption so long as such a claim could also be brought against objects other than medical devices.

All in all, we think that § 808.1(d)(1) can add nothing to our analysis but confusion. Neither accepting nor rejecting the ***330** proposition that this regulation can properly be consulted to determine the statute's meaning; and neither accepting nor rejecting the FDA's distinction between general requirements that directly regulate and those that regulate only incidentally; the regulation fails to alter our interpretation of the text insofar as the outcome of this case is concerned.

IV

[4] [5] State requirements are pre-empted under the MDA only to the extent that they are "different from, or in addition to" the requirements imposed by federal law. § 360k(a)(1). Thus, § 360k does not prevent a State from providing a damages remedy for claims premised on a violation of FDA regulations; the state duties in such a case "parallel," rather than add to, federal requirements. *Lohr*, 518 U.S., at 495, 116 S.Ct. 2240; see also *id.*, at 513, 116 S.Ct. 2240 (O'Connor, J., concurring in part and dissenting in part). The District Court in this case recognized that parallel claims would not be pre-empted, see App. to Pet. for Cert. 70a–71a, but it interpreted the claims here to assert that Medtronic's device violated state tort law notwithstanding compliance with the relevant federal requirements, see *id.*, at 68a. Although the Riegels now argue that their lawsuit raises parallel claims, they made no such contention in their briefs before the Second Circuit, nor did they raise this argument in their petition for certiorari. We decline to address that argument in the first instance here.

* * *

For the foregoing reasons, the judgment of the Court of Appeals is

Affirmed.

Justice STEVENS, concurring in part and concurring in the judgment.

The significance of the pre-emption provision in the Medical Device Amendments of 1976(MDA), 21 U.S.C. § 360k, ***331** was not fully appreciated until many years after it was enacted. It is an example of a statute whose text and general objective cover territory not actually envisioned by its authors. In such cases we have frequently concluded that "it is ultimately the provisions of our laws rather than the principal concerns of our legislators by which we are governed." *Oncale v. Sundowner Offshore Services, Inc.*, 523 U.S. 75, 79–80, 118 S.Ct. 998, 140 L.Ed.2d 201 (1998). Accordingly, while I agree with Justice GINSBURG's description of the actual history and principal purpose of the pre-emption provision at issue in this case, *post*, at 1014 – 1018 (dissenting opinion), I am persuaded that its text does pre-empt state-law requirements that differ. I therefore write separately to add these few words about the MDA's history and the meaning of "requirements."

****1012** There is nothing in the preenactment history of the MDA suggesting that Congress thought state tort remedies had impeded the development of medical devices. Nor is there any evidence at all to suggest that Congress decided that the cost of injuries from Food and Drug Administration-approved medical devices was outweighed "by solicitude for those who would suffer without new medical devices if juries were allowed to apply the tort law of 50 States to all innovations." *Ante*, at 1009 (opinion of the Court). That is a policy argument advanced by the Court, not by Congress. As Justice GINSBURG persuasively explains, the overriding purpose of the legislation was to provide additional protection to consumers, not to withdraw existing protections. It was the then-recent development of state premarket regulatory regimes that explained the need for a provision pre-empting conflicting administrative rules. See *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 489, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996) (plurality opinion) ("[W]hen Congress enacted § 360k, it was primarily concerned with the problem of specific, conflicting state

statutes and regulations rather than the general duties enforced by common-law actions").

***332** But the language of the provision reaches beyond such regulatory regimes to encompass other types of "requirements." Because common-law rules administered by judges, like statutes and regulations, create and define legal obligations, some of them unquestionably qualify as "requirements."[1] See *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 522, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992) (plurality opinion) ("[C]ommon-law damages actions of the sort raised by petitioner are premised on the existence of a legal duty, and it is difficult to say that such actions do not impose 'requirements or prohibitions.'... [I]t is the essence of the common law to enforce duties that are either affirmative *requirements* or negative *prohibitions*"). And although not all common-law rules qualify as "requirements,"[2] the Court correctly points out that five Justices in *Lohr* concluded that the common-law causes of action for negligence and strict liability at issue in that case imposed "requirements" that were pre-empted by federal requirements ***333** specific to a medical device. Moreover, I agree with the Court's cogent explanation of why the Riegels' claims are predicated on New York common-law ****1013** duties that constitute requirements with respect to the device at issue that differ from federal requirements relating to safety and effectiveness. I therefore join the Court's judgment and all of its opinion except for Parts III–A and III–B.

Justice GINSBURG, dissenting.

The Medical Device Amendments of 1976 (MDA or Act), 90 Stat. 539, as construed by the Court, cut deeply into a domain historically occupied by state law. The MDA's preemption clause, 21 U.S.C. § 360k(a), the Court holds, spares medical device manufacturers from personal injury claims alleging flaws in a design or label once the application for the design or label has gained premarket approval from the Food and Drug Administration (FDA); a state damages remedy, the Court instructs, persists only for claims "premised on a violation of FDA regulations." *Ante*, at 1011.[1] I dissent from today's constriction of state authority. Congress, in my view, did not intend § 360k(a) to effect a radical curtailment of state common-law suits seeking compensation for injuries caused by defectively designed or labeled medical devices.

Congress' reason for enacting § 360k(a) is evident. Until 1976, the Federal Government did not engage in premarket regulation of medical devices. Some States acted to fill the void by adopting their own regulatory systems for medical devices. Section 360k(a) responded to that state regulation, and particularly to California's system of premarket approval for medical devices, by preempting State initiatives absent FDA permission. See § 360k(b).

***334 I**

The "purpose of Congress is the ultimate touchstone of pre-emption analysis." *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 516, 112 S.Ct. 2608, 120 L.Ed.2d 407 (1992) (internal quotation marks omitted). Courts have "long presumed that Congress does not cavalierly pre-empt state-law causes of action." *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996).[2] Preemption analysis starts with the assumption that "the historic police powers of the States [a]re not to be superseded ... unless that was the clear and manifest purpose of Congress." *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230, 67 S.Ct. 1146, 91 L.Ed. 1447 (1947). "This assumption provides assurance that 'the federal-state balance' will not be disturbed unintentionally by Congress or unnecessarily by the courts." *Jones v. Rath Packing Co.*, 430 U.S. 519, 525, 97 S.Ct. 1305, 51 L.Ed.2d 604 (1977) (citation omitted).

The presumption against preemption is heightened "where federal law is said to bar state action in fields of traditional state regulation." *New York State Conference of Blue Cross & Blue Shield Plans v. Travelers Ins. Co.*, 514 U.S. 645, 655, 115 S.Ct. 1671, 131 L.Ed.2d 695 (1995). Given the traditional "primacy of state regulation of matters of health and safety," *Lohr*, 518 U.S., at 485, 116 S.Ct. 2240, courts assume "that state and local regulation related to [those] matters ... can normally coexist with federal regulations," *Hillsborough County v. Automated Medical Laboratories*, ****1014** *Inc.*, 471 U.S. 707, 718, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985).

Federal laws containing a preemption clause do not automatically escape the presumption against preemption. See *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005); *Lohr*, 518 U.S., at 485, 116 S.Ct. 2240. A preemption clause tells us that Congress intended to supersede or modify state law to some extent. In the absence of legislative precision, however, courts may face the task of determining the substance ***335** and scope of Congress' displacement of state law. Where the text of a preemption clause is open to more than one plausible reading, courts ordinarily "accept the reading that disfavors pre-emption." *Bates*, 544 U.S., at 449, 125 S.Ct. 1788.

II

The MDA's preemption clause states:

> "[N]o State or political subdivision of a State may establish or continue in effect with respect to a device intended for human use any requirement—
>
> "(1) which is different from, or in addition to, any requirement applicable under this chapter to the device, and
>
> "(2) which relates to the safety or effectiveness of the device or to any other matter included in a requirement applicable to the device under this chapter." 21 U.S.C. § 360k(a).

"Absent other indication," the Court states, "reference to a State's 'requirements' includes its common-law duties." *Ante*, at 1008. Regarding the MDA, however, "other indication" is not "[a]bsent." Contextual examination of the Act convinces me that § 360k(a)'s inclusion of the term "requirement" should not prompt a sweeping preemption of mine-run claims for relief under state tort law.[3]

A

Congress enacted the MDA "to provide for the safety and effectiveness of medical devices intended for human use." ***336** 90 Stat. 539 (preamble).[4] A series of high-profile medical device failures that caused extensive injuries and loss of life propelled adoption of the MDA.[5] Conspicuous among these failures was the Dalkon Shield intrauterine device, used by approximately 2.2 ****1015** million women in the United States between 1970 and 1974. See *In re Northern Dist. of Cal., Dalkon Shield IUD Prods. Liability Litigation*, 693 F.2d 847, 848 (C.A.9 1982); *ante*, at 1002 – 1003. Aggressively promoted as a safe and effective form of birth control, the Dalkon Shield had been linked to 16 deaths and 25 miscarriages by the middle of 1975. H.R.Rep. No. 94–853, p. 8 (1976). By early 1976, "more than 500 lawsuits seeking compensatory and punitive damages totalling more than $400 million" had been filed. *Ibid.*[6] Given the publicity attending the Dalkon Shield litigation and Congress' awareness of the suits at the time the MDA was under consideration, I find informative ***337** the absence of any sign of a legislative design to preempt state common-law tort actions.[7]

The Court recognizes that "§ 360k does not prevent a State from providing a damages remedy for claims premised on a violation of FDA regulations." *Ante*, at 1011. That remedy, although important, does not help consumers injured by devices that receive FDA approval but nevertheless prove unsafe. The MDA's failure to create any federal compensatory remedy for such consumers further suggests that Congress did not intend broadly to preempt state common-law suits grounded on allegations independent of FDA requirements. It is "difficult to believe that Congress would, without comment, remove all means of judicial recourse" for large numbers of consumers injured by defective medical devices. *Silkwood v. Kerr–McGee Corp.*, 464 U.S. 238, 251, 104 S.Ct. 615, 78 L.Ed.2d 443 (1984).

The former chief counsel to the FDA explained:

> "FDA's view is that FDA product approval and state tort liability usually operate independently, each providing a significant, yet distinct, layer of consumer protection. FDA regulation of a device cannot anticipate and protect against all safety risks to individual consumers. Even the most thorough regulation of a product such as a critical medical device may fail to identify potential problems presented by the product. Regulation cannot ***338** protect against all possible injuries that might result from use of a device over time. Preemption of all such claims would result in the loss of a significant layer of consumer protection ...." Porter, The *Lohr* Decision: FDA Perspective and Position, 52 Food & Drug L.J. 7, 11 (1997).

Cf. Brief for United States as *Amicus Curiae* on Pet. for Cert. in *Smiths Industries Medical Systems, Inc. v. Kernats*, O.T.1997, No. 96–1405, pp. 17–18; Dept. of Health and Human Services, Public Health ****1016** Service, Advisory Opinion, Docket No. 83A–0140/AP, Letter from J. Hile, Associate Comm'r for Regulatory Affairs, to National Women's Health Network (Mar. 8, 1984).[8] The Court's construction of § 360k(a) has the "perverse effect" of granting broad immunity "to an entire industry that, in the judgment of Congress, needed more stringent regulation," *Lohr*, 518 U.S., at 487, 116 S.Ct. 2240 (plurality opinion), not exemption from liability in tort litigation.

The MDA does grant the FDA authority to order certain remedial action if, *inter alia*, it concludes that a device "presents ***339** an unreasonable risk of substantial harm to the public health" and that notice of the defect "would not by itself be sufficient to eliminate the unreasonable risk." 21 U.S.C. § 360h(b)(1)(A). Thus the FDA may order the manufacturer to repair the device, replace it, refund the

purchase price, cease distribution, or recall the device. § 360h(b)(2), (e). The prospect of ameliorative action by the FDA, however, lends no support to the conclusion that Congress intended largely to preempt state common-law suits. Quite the opposite: Section 360h(d) states that "[c]ompliance with an order issued under this section shall not relieve any person from liability under Federal or State law." That provision anticipates "[court-awarded] damages for economic loss" from which the value of any FDA-ordered remedy would be subtracted. *Ibid.*[9]

B

Congress enacted the MDA after decades of regulating drugs and food and color additives under the Federal Food, Drug, and Cosmetic Act (FDCA), 52 Stat. 1040, as amended, 21 U.S.C. § 301 *et seq*. The FDCA contains no preemption clause, and thus the Court's interpretation of § 360k(a) has no bearing on tort suits involving drugs and additives. But § 360k(a)'s confinement to medical devices hardly renders irrelevant to the proper construction of the MDA's preemption provision the long history of federal and state controls over drugs and additives in the interest of public health and welfare. Congress' experience regulating drugs and additives informed, and in part provided the model for, its regulation of medical ****1017** devices. I therefore turn to an examination of that experience.

***340** Starting in 1938, the FDCA required that new drugs undergo preclearance by the FDA before they could be marketed. See § 505, 52 Stat. 1052. Nothing in the FDCA's text or legislative history suggested that FDA preclearance would immunize drug manufacturers from common-law tort suits.[10]

By the time Congress enacted the MDA in 1976, state common-law claims for drug labeling and design defects had continued unabated despite nearly four decades of FDA regulation.[11] Congress' inclusion of a preemption clause in the MDA was not motivated by concern that similar state tort actions could be mounted regarding medical devices.[12] ***341** Rather, Congress included § 360k(a) and (b) to empower the FDA to exercise control over state premarket approval systems installed at a time when there was no preclearance at the federal level. See *supra*, at 1014, and n. 3; *infra*, at 1018, and n. 14.

Between 1938 and 1976, Congress enacted a series of premarket approval requirements, first for drugs, then for additives. Premarket control, as already noted, commenced with drugs in 1938. In 1958, Congress required premarket approval for food additives. Food Additives Amendment, § 4, 72 Stat. 1785, as amended, 21 U.S.C. § 348. In 1960, it required premarket approval for color additives. Color Additive Amendments, § 103(b), 74 Stat. 399, as amended, 21 U.S.C. § 379e. In 1962, it expanded the premarket approval process for new drugs to include review for effectiveness. Drug Amendments, ****1018** § 102, 76 Stat. 781, as amended, 21 U.S.C. §§ 321, 355. And in 1968, it required premarket approval for new animal drugs. Animal Drug Amendments, § 101(b), 82 Stat. 343, as amended, 21 U.S.C. § 360b. None of these Acts contained a preemption clause.

The measures just listed, like the MDA, were all enacted with common-law personal injury litigation over defective products a prominent part of the legal landscape.[13] At the ***342** time of each enactment, no state regulations required premarket approval of the drugs or additives in question, so no preemption clause was needed as a check against potentially conflicting state regulatory regimes. See Brief for Sen. Edward M. Kennedy et al. as *Amici Curiae* 10.

A different situation existed as to medical devices when Congress developed and passed the MDA. As the House Report observed:

> "In the absence of effective Federal regulation of medical devices, some States have established their own programs. The most comprehensive State regulation of which the Committee is aware is that of California, which in 1970 adopted the Sherman Food, Drug, and Cosmetic Law. This law requires premarket approval of all new medical devices, requires compliance of device manufacturers with good manufacturing practices and authorizes inspection of establishments which manufacture devices. Implementation of the Sherman Law has resulted in the *requirement* that intrauterine devices are subject to premarket clearance in California." H.R.Rep. No. 94–853, p. 45 (emphasis added).[14]

In sum, state premarket regulation of medical devices, not any design to suppress tort suits, accounts for Congress' inclusion of a preemption clause in the MDA; no such clause figures in earlier federal laws regulating drugs and additives, for States had not installed comparable control regimes in those areas.

***343 C**

Congress' experience regulating drugs also casts doubt on Medtronic's policy arguments for reading § 360k(a) to

preempt state tort claims. Section 360k(a) must preempt state common-law suits, Medtronic contends, because Congress would not have wanted state juries to second-guess the FDA's finding that a medical device is safe and effective when used as directed. Brief for Respondent 42–49. The Court is similarly minded. *Ante,* at 1008 – 1009.

But the process for approving new drugs is at least as rigorous as the premarket approval process for medical devices.[15] Courts that have considered the ****1019** question have overwhelmingly held that FDA approval of a new drug application does not preempt state tort suits.[16] Decades of drug ***344** regulation thus indicate, contrary to Medtronic's argument, that Congress did not regard FDA regulation and state tort claims as mutually exclusive.

III

Refusing to read § 360k(a) as an automatic bar to state common-law tort claims would hardly render the FDA's premarket approval of Medtronic's medical device application irrelevant to the instant suit. First, a "pre-emption provision, by itself, does not foreclose (through negative implication) any possibility of implied conflict preemption." *Geier v. American Honda Motor Co.*, 529 U.S. 861, 869, 120 S.Ct. 1913, 146 L.Ed.2d 914 (2000) (brackets and internal quotation marks omitted). See also *Freightliner Corp. v. Myrick*, 514 U.S. 280, 288–289, 115 S.Ct. 1483, 131 L.Ed.2d 385 (1995). Accordingly, a medical device manufacturer may have a dispositive ***345** defense if it can identify an actual conflict ****1020** between the plaintiff's theory of the case and the FDA's premarket approval of the device in question. As currently postured, this case presents no occasion to take up this issue for Medtronic relies exclusively on § 360k(a) and does not argue conflict preemption.

Second, a medical device manufacturer may be entitled to interpose a regulatory compliance defense based on the FDA's approval of the premarket application. Most States do not treat regulatory compliance as dispositive, but regard it as one factor to be taken into account by the jury. See Sharkey, Federalism in Action: FDA Regulatory Preemption in Pharmaceutical Cases in State Versus Federal Courts, 15 J. Law & Pol'y 1013, 1024 (2007). See also Restatement (Third) of Torts § 16(a) (Proposed Final Draft No. 1, Apr. 6, 2005). In those States, a manufacturer could present the FDA's approval of its medical device as evidence that it used due care in the design and labeling of the product.

The Court's broad reading of § 360k(a) saves the manufacturer from any need to urge these defenses. Instead, regardless of the strength of a plaintiff's case, suits will be barred *ab initio*. The constriction of state authority ordered today was not mandated by Congress and is at odds with the MDA's central purpose: to protect consumer safety.

* * *

For the reasons stated, I would hold that § 360k(a) does not preempt Riegel's suit. I would therefore reverse the judgment of the Court of Appeals in relevant part.

Parallel Citations

128 S.Ct. 999, 169 L.Ed.2d 892, 76 USLW 4087, Prod.Liab.Rep. (CCH) P 17,924, 08 Cal. Daily Op. Serv. 2105, 2008 Daily Journal D.A.R. 2524, 21 Fla. L. Weekly Fed. S 81

Footnotes

* The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States v. Detroit Timber & Lumber Co.*, 200 U.S. 321, 337, 26 S.Ct. 282, 50 L.Ed. 499.

1 Unqualified § 360 *et seq.* numbers hereinafter refer to sections of 21 U.S.C.

2 The District Court later granted summary judgment to Medtronic on those claims of Riegel it had found not pre-empted, viz., that Medtronic breached an express warranty and was negligent in manufacturing because it did not comply with federal standards. App. to Pet. for Cert. 90a. It consequently granted summary judgment as well on Donna Riegel's derivative consortium claim. *Ibid.* The Court of Appeals affirmed these determinations, and they are not before us.

[3] Charles Riegel having died, Donna Riegel is now petitioner on her own behalf and as administrator of her husband's estate. *Post*, p. 804. For simplicity's sake, the terminology of our opinion draws no distinction between Charles Riegel and the Estate of Charles Riegel and refers to the claims as belonging to the Riegels.

[4] The Riegels point to § 360k(b), which authorizes the FDA to exempt state "requirements" from pre-emption under circumstances that would rarely be met for common-law duties. But a law that permits an agency to exempt certain "requirements" from pre-emption does not suggest that no other "requirements" exist. The Riegels also invoke § 360h(d), which provides that compliance with certain FDA orders "shall not relieve any person from liability under Federal or State law." This indicates that some state-law claims are not pre-empted, as we held in *Lohr*. But it could not possibly mean that *all* state-law claims are not pre-empted, since that would deprive the MDA pre-emption clause of all content. And it provides no guidance as to which state-law claims are pre-empted and which are not.

[5] Contrary to Justice STEVENS' contention, *post*, at 1012 (opinion concurring in part and concurring in judgment), we do not "advanc[e]" this argument. We merely suggest that if one were to speculate upon congressional purposes, the best evidence for that would be found in the statute.

[6] The opinions joined by these five Justices dispose of the Riegels' assertion that *Lohr* held common-law duties were too general to qualify as duties "with respect to a device." The majority opinion in *Lohr* also disavowed this conclusion, for it stated that the Court did "not believe that [the MDA's] statutory and regulatory language necessarily precludes ... 'general' state requirements from ever being pre-empted...." 518 U.S., at 500, 116 S.Ct. 2240, 135 L.Ed.2d 700.

[1] The verdicts of juries who obey those rules, however, are not "requirements" of that kind. Juries apply rules, but do not make them. And while a jury's finding of liability may induce a defendant to alter its device or its label, this does not render the finding a "requirement" within the meaning of the MDA. "A requirement is a rule of law that must be obeyed; an event, such as a jury verdict, that merely motivates an optional decision is not a requirement." *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 445, 125 S.Ct. 1788, 161 L.Ed.2d 687 (2005). It is for that reason that the MDA does not grant " 'a single state jury' " any power whatsoever to set any standard that either conforms with or differs from a relevant federal standard. I do not agree with the colorful but inaccurate quotation in the Court's opinion, *ante*, at 1008.

[2] See *Cipollone*, 505 U.S., at 523, 112 S.Ct. 2608, 120 L.Ed.2d 407 (plurality opinion) (explaining that the fact that "the pre-emptive scope of § 5(b) cannot be limited to positive enactments does not mean that that section pre-empts all common-law claims" and proceeding to analyze "each of petitioner's common-law claims to determine whether it is in fact pre-empted"); *Bates*, 544 U.S., at 443–444, 125 S.Ct. 1788 (noting that a finding that "[7 U.S.C.] § 136v(b) may pre-empt judge-made rules, as well as statutes and regulations, says nothing about the *scope* of that pre-emption," and proceeding to determine whether the particular common-law rules at issue in that case satisfied the conditions of pre-emption).

[1] The Court's holding does not reach an important issue outside the bounds of this case: the preemptive effect of § 360k(a) where evidence of a medical device's defect comes to light only *after* the device receives premarket approval.

[2] In part, *Lohr* spoke for the Court, and in part, for a plurality. Unless otherwise indicated, citations in this opinion refer to portions of *Lohr* conveying the opinion of the Court.

[3] The very next provision, § 360k(b), allows States and their political subdivisions to apply for exemption from the requirements for medical devices set by the FDA when their own requirements are "more stringent" than federal standards or are necessitated by "compelling local conditions." This prescription indicates solicitude for state concerns, as embodied in legislation or regulation. But no more than § 360k(a) itself does § 360k(b) show that Congress homed in on state common-law suits and meant to deny injured parties recourse to them.

[4] Introducing the bill in the Senate, its sponsor explained: "The legislation is written so that the benefit of the doubt is always given to the consumer. After all it is the consumer who pays with his health and his life for medical device malfunctions." 121 Cong. Rec. 10688 (1975) (remarks of Sen. Kennedy).

[5] See, *e.g.*, H.R.Rep. No. 94–853, p. 8 (1976) ("Significant defects in cardiac pacemakers have necessitated 34 voluntary recalls of pacemakers, involving 23,000 units, since 1972."); S.Rep. No. 94–33, p. 6 (1975), U.S.Code Cong. & Admin.News 1976, pp. 1070, 1076 ("Some 10,000 injuries were recorded, of which 731 resulted in death. For example, 512 deaths and 300 injuries were attributed to heart valves; 89 deaths and 186 injuries to heart pacemakers; 10 deaths and 8,000 injuries to intrauterine devices."); 122 Cong. Rec. 5859 (1976) (remarks of Rep. Waxman) ("A 10–year FDA death-certificate search found over 850 deaths tied directly to medical devices."); 121 *id.*, at 10689–10690 (remarks of Sen. Nelson). See also *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 476, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996).

6 The Dalkon Shield was ultimately linked to "thousands of serious injuries to otherwise healthy women." Vladeck, Preemption and Regulatory Failure, 33 Pepperdine L.Rev. 95, 103 (2005). By October 1984, the manufacturer had settled or litigated approximately 7,700 Dalkon Shield cases. R. Sobol, Bending the Law: The Story of the Dalkon Shield Bankruptcy 23 (1991).

7 "[N]othing in the hearings, the Committee Reports, or the debates," the *Lohr* plurality noted, "suggest[ed] that any proponent of the legislation intended a sweeping pre-emption of traditional common-law remedies against manufacturers and distributors of defective devices. If Congress intended such a result, its failure even to hint at it is spectacularly odd, particularly since Members of both Houses were acutely aware of ongoing product liability litigation." 518 U.S., at 491, 116 S.Ct. 2240. See also Adler & Mann, Preemption and Medical Devices: The Courts Run Amok, 59 Mo. L.Rev. 895, 925 (1994) ("To the extent that Congress mentioned common law tort claims, it was not to criticize them or to suggest that they needed to be barred once a federal regulation was in place. Rather, it was to note how they demonstrated that *additional* protections for consumers were needed.").

8 The FDA recently announced a new position in an *amicus* brief. See Brief for United States as *Amicus Curiae* 16–24. An *amicus* brief interpreting a statute is entitled, at most, to deference under *Skidmore v. Swift & Co.*, 323 U.S. 134, 65 S.Ct. 161, 89 L.Ed. 124 (1944). See *United States v. Mead Corp.*, 533 U.S. 218, 229–233, 121 S.Ct. 2164, 150 L.Ed.2d 292 (2001). The weight accorded to an agency position under *Skidmore* "depend[s] upon the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control." 323 U.S., at 140, 65 S.Ct. 161. See also *Mead*, 533 U.S., at 228, 121 S.Ct. 2164 (courts consider, *inter alia*, the "consistency" and "persuasiveness" of an agency's position); *Good Samaritan Hospital v. Shalala*, 508 U.S. 402, 417, 113 S.Ct. 2151, 124 L.Ed.2d 368 (1993) ("[T]he consistency of an agency's position is a factor in assessing the weight that position is due."). Because the FDA's long-held view on the limited preemptive effect of § 360k(a) better comports with the presumption against preemption of state health and safety protections, as well as the purpose and history of the MDA, the FDA's new position is entitled to little weight.

9 The Court regards § 360h(d) as unenlightening because it "could not possibly mean that *all* state-law claims are not pre-empted" and "provides no guidance as to which state-law claims are pre-empted and which are not." *Ante*, at 1008, n. 4. Given the presumption against preemption operative even in construing a preemption clause, see *supra*, at 1003 – 1004, the perceived lack of "guidance" should cut against Medtronic, not in its favor.

10 To the contrary, the bill did not need to create a federal claim for damages, witnesses testified, because "[a] common-law right of action exist[ed]." Hearings on S.1944 before a Subcommittee of the Senate Committee on Commerce, 73d Cong., 2d Sess., 400 (1933) (statement of W.A. Hines). See also *id.*, at 403 (statement of J.A. Ladds) ("This act should not attempt to modify or restate the common law with respect to personal injuries.").

11 Most defendants, it appears, raised no preemption defense to state tort suits involving FDA-approved drugs. See, *e.g.*, *Salmon v. Parke, Davis & Co.*, 520 F.2d 1359 (C.A.4 1975) (North Carolina law); *Reyes v. Wyeth Labs.*, 498 F.2d 1264 (C.A.5 1974) (Texas law); *Hoffman v. Sterling Drug, Inc.*, 485 F.2d 132 (C.A.3 1973) (Pennsylvania law); *Singer v. Sterling Drug, Inc.*, 461 F.2d 288 (C.A.7 1972) (Indiana law); *McCue v. Norwich Pharmacal Co.*, 453 F.2d 1033 (C.A.1 1972) (New Hampshire law); *Basko v. Sterling Drug, Inc.*, 416 F.2d 417 (C.A.2 1969) (Connecticut law); *Parke–Davis & Co. v. Stromsodt*, 411 F.2d 1390 (C.A.8 1969) (North Dakota law); *Davis v. Wyeth Labs., Inc.*, 399 F.2d 121 (C.A.9 1968) (Montana law); *Roginsky v. Richardson–Merrell, Inc.*, 378 F.2d 832 (C.A.2 1967) (New York law); *Cunningham v. Charles Pfizer & Co.*, 532 P.2d 1377 (Okla.1974); *Stevens v. Parke, Davis & Co.*, 9 Cal.3d 51, 107 Cal.Rptr. 45, 507 P.2d 653 (1973); *Bine v. Sterling Drug, Inc.*, 422 S.W.2d 623 (Mo.1968) *(per curiam)*. In the few cases in which courts noted that defendants had interposed a preemption plea, the defense was unsuccessful. See, *e.g.*, *Herman v. Smith, Kline & French Labs.*, 286 F.Supp. 694 (E.D.Wis.1968). See also *infra*, at 1019, n. 16 (decisions after 1976).

12 See Leflar & Adler, The Preemption Pentad: Federal Preemption of Products Liability Claims After *Medtronic*, 64 Tenn. L.Rev. 691, 704, n. 71 (1997) ("Surely a furor would have been aroused by the very suggestion that ... medical devices should receive an exemption from products liability litigation while new drugs, subject to similar regulatory scrutiny from the same agency, should remain under the standard tort law regime."); Porter, The *Lohr* Decision: FDA Perspective and Position, 52 Food & Drug L.J. 7, 11 (1997) (With preemption, the "FDA's regulation of devices would have been accorded an entirely different weight in private tort litigation than its counterpart regulation of drugs and biologics. This disparity is neither justified nor appropriate, nor does the agency believe it was intended by Congress ....").

13 The Drug Amendments of 1962 reiterated Congress' intent not to preempt claims relying on state law: "Nothing in the amendments ... shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a direct and positive conflict between such amendments and such provision of State law." § 202, 76 Stat. 793.

14 Congress featured California's regulatory system in its discussion of § 360k(a), but it also identified California's system as a prime candidate for an exemption from preemption under § 360k(b). "[R]equirements imposed under the California statute," the House

Report noted, "serve as an example of requirements that the Secretary should authorize to be continued (provided any application submitted by a State meets requirements pursuant to the reported bill)." H.R.Rep. No. 94–853, p. 46. Thus Congress sought not to terminate all state premarket approval systems, but rather to place those systems under the controlling authority of the FDA.

15 The process for approving a new drug begins with preclinical laboratory and animal testing. The sponsor of the new drug then submits an investigational new drug application seeking FDA approval to test the drug on humans. See 21 U.S.C. § 355(i) (2000 ed. and Supp. V); 21 CFR § 312.1 *et seq.* (2007). Clinical trials generally proceed in three phases involving successively larger groups of patients: 20 to 80 subjects in phase I; no more than several hundred subjects in phase II; and several hundred to several thousand subjects in phase III. 21 CFR § 312.21. After completing the clinical trials, the sponsor files a new drug application containing, *inter alia*, "full reports of investigations" showing whether the "drug is safe for use and ... effective"; the drug's composition; a description of the drug's manufacturing, processing, and packaging; and the proposed labeling for the drug. 21 U.S.C. § 355(b)(1) (2000 ed., Supp. V).

16 See, *e.g.*, *Tobin v. Astra Pharmaceutical Prods., Inc.*, 993 F.2d 528, 537–538 (C.A.6 1993); *Hill v. Searle Labs., Div. of Searle Pharmaceuticals, Inc.*, 884 F.2d 1064, 1068 (C.A.8 1989); *In re Vioxx Prods. Liability Litigation*, 501 F.Supp.2d 776, 788–789 (E.D.La.2007); *In re Zyprexa Prods. Liability Litigation*, 489 F.Supp.2d 230, 275–278 (E.D.N.Y.2007); *Weiss v. Fujisawa Pharmaceutical Co.*, 464 F.Supp.2d 666, 676 (E.D.Ky.2006); *Perry v. Novartis Pharma. Corp.*, 456 F.Supp.2d 678, 685–687 (E.D.Pa.2006); *McNellis v. Pfizer, Inc.*, No. Civ. 05–1286(JBS), 2006 WL 2819046, *5 (D.N.J., Sept. 29, 2006); *Jackson v. Pfizer, Inc.*, 432 F.Supp.2d 964, 968 (D.Neb.2006); *Laisure–Radke v. Par Pharmaceutical, Inc.*, 426 F.Supp.2d 1163, 1169 (W.D.Wash.2006); *Witczak v. Pfizer, Inc.*, 377 F.Supp.2d 726, 732 (D.Minn.2005); *Zikis v. Pfizer, Inc.*, No. 04 C 8104, 2005 WL 1126909, *3 (N.D.Ill., May 9, 2005); *Cartwright v. Pfizer, Inc.*, 369 F.Supp.2d 876, 885–886 (E.D.Tex.2005); *Eve v. Sandoz Pharmaceutical Corp.*, No. IP 98–1429–C–Y/S, 2002 WL 181972, *1 (S.D.Ind., Jan.28, 2002); *Caraker v. Sandoz Pharmaceuticals Corp.*, 172 F.Supp.2d 1018, 1044 (S.D.Ill.2001); *Motus v. Pfizer, Inc.*, 127 F.Supp.2d 1085, 1087 (C.D.Cal.2000); *Kociemba v. G.D. Searle & Co.*, 680 F.Supp. 1293, 1299–1300 (D.Minn.1988). But see 71 Fed.Reg. 3933–3936 (2006) (preamble to labeling regulations discussing FDA's recently adopted view that federal drug labeling requirements preempt conflicting state laws); *In re Bextra & Celebrex Marketing Sales Practices & Prod. Liability Litigation*, No. M:05–1699 CRB, 2006 WL 2374742, *10 (N.D.Cal., Aug.16, 2006); *Colacicco v. Apotex, Inc.*, 432 F.Supp.2d 514, 537–538 (E.D.Pa.2006); *Needleman v. Pfizer Inc.*, No. Civ. A. 3:03–CV–3074–N, 2004 WL 1773697, *5 (N.D.Tex., Aug.6, 2004); *Dusek v. Pfizer Inc.*, No. Civ. A. H–02–3559, 2004 WL 2191804, *10 (S.D.Tex., Feb.20, 2004). But cf. 73 Fed.Reg. 2853 (2008) (preamble to proposed rule).

This Court will soon address the issue in *Levine v. Wyeth*, 183 Vt. 76, 944 A.2d 179 (2006), cert. granted, 552 U.S. 1161, 128 S.Ct. 1118, 169 L.Ed.2d 845 (2008). The question presented in that case is: "Whether the prescription drug labeling judgments imposed on manufacturers by the Food and Drug Administration ('FDA') pursuant to FDA's comprehensive safety and efficacy authority under the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq.*, preempt state law product liability claims premised on the theory that different labeling judgments were necessary to make drugs reasonably safe for use." Pet. for Cert. in *Wyeth v. Levine*, O.T.2007, No. 06–1249, p. i.

End of Document

COMMODITY FUTURES TRADING COMMISSION

17 CFR Part 170

RIN 3038–AE09

Membership in a Registered Futures Association

Correction

In proposed rule document 13–26790 beginning on page 67078 in the issue of Friday, November 8, 2013, make the following correction:

On page 67078, in the third column, under **DATES**, in the last line ''January 17, 2014'' should read ''January 7, 2014''.

[FR Doc. C1–2013–26790 Filed 11–12–13; 8:45 am]

BILLING CODE 1505–01–D

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 314 and 601

[Docket No. FDA–2013–N–0500]

RIN 0910–AG94

Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is proposing to amend its regulations to revise and clarify procedures for application holders of an approved drug or biological product to change the product labeling to reflect certain types of newly acquired information in advance of FDA's review of the change. The proposed rule would create parity among application holders with respect to such labeling changes by permitting holders of abbreviated new drug applications (ANDAs) to distribute revised product labeling that differs in certain respects, on a temporary basis, from the labeling of its reference listed drug (RLD) upon submission to FDA of a ''changes being effected'' (CBE–0) supplement. The proposed rule describes the process by which information regarding a CBE–0 labeling supplement submitted by a new drug application (NDA) holder, an ANDA holder, or a biologics license application (BLA) holder would be made publicly available during FDA's review of the labeling change and clarifies requirements for all ANDA holders to submit conforming labeling revisions after FDA has taken an action on the NDA or ANDA holder's CBE–0 labeling supplement. The proposed rule also would amend the regulations to allow submission of a CBE–0 labeling supplement for certain changes to the ''Highlights of Prescribing Information'' for drug products with labeling in the ''Physician Labeling Rule'' (PLR) format.

DATES: Submit either electronic or written comments on the proposed rule by January 13, 2014. See section VII for the proposed effective date of a final rule based on this proposed rule. Submit comments on information collection issues under the Paperwork Reduction Act of 1995 (the PRA) by December 13, 2013, (see the ''Paperwork Reduction Act of 1995'' section of this document).

ADDRESSES: You may submit comments, identified by Docket No. FDA–2013–N–0500 and/or Regulatory Information Number (RIN) 0910–AG94, by any of the following methods, except that comments on information collection issues under the PRA must be submitted to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB) (see the ''Paperwork Reduction Act of 1995'' section of this document).

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: *http://www.regulations.gov.* Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- Mail/Hand delivery/Courier (for paper or CD–ROM submissions): Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the Agency name and Docket No. FDA–2013–N–0500 and RIN 0910–AG94 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided. For additional information on submitting comments, see the ''Comments'' heading of the **SUPPLEMENTARY INFORMATION** section.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov* and insert the docket number(s), found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Janice L. Weiner, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6304, Silver Spring, MD 20993–0002, 301–796–3601.

SUPPLEMENTARY INFORMATION:

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Executive Summary

Purpose of the Regulatory Action

The Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 301 et seq.) and the Public Health Service Act (the PHS Act) (42 U.S.C. 201 et seq.) provide FDA with authority over the labeling for drugs and biological products, and authorize the Agency to enact regulations to facilitate FDA's review and approval of applications regarding the labeling for those products. FDA is proposing to amend its regulations to revise and clarify procedures for application holders to change the labeling of an approved drug or biological product to reflect certain types of newly acquired information in advance of FDA's review of the change through a CBE–0 supplement. The proposed rule would create parity among application holders with respect to these safety-related labeling changes by permitting ANDA holders to distribute revised generic drug labeling that differs in certain respects, on a temporary basis, from the RLD labeling upon submission to FDA of a CBE–0 supplement.

Summary of the Major Provisions of the Regulatory Action

The proposed rule would enable ANDA holders to update product labeling promptly to reflect certain types of newly acquired information related to drug safety, irrespective of whether the revised labeling differs from that of the RLD. An ANDA holder would be required to send notice of the labeling change proposed in the CBE–0 supplement, including a copy of the information supporting the change, to the NDA holder for the RLD at the same time that the supplement to the ANDA is submitted to FDA, unless approval of the NDA has been withdrawn. This proposal would ensure that the NDA holder for the RLD is promptly advised of the newly acquired information that was considered to warrant the labeling change proposed for the drug in the CBE–0 supplement.

If approval of the NDA for the RLD has been withdrawn (for reasons other than safety or effectiveness), FDA's evaluation of the labeling change proposed by the ANDA holder would consider any submissions related to the proposed labeling change from any other application holder for drug products containing the same active ingredient.

To make the safety-related changes to drug labeling described in a CBE–0 supplement readily available to prescribing health care providers and the public while FDA is reviewing the supplement, FDA proposes to establish a dedicated Web page (or, alternatively, to modify an existing FDA Web page) on which FDA would promptly post information regarding the labeling changes proposed in a CBE–0 supplement.

A supplement to an approved ANDA for a safety-related labeling change that is submitted in a prior approval supplement or in a CBE–0 supplement would be approved upon approval of the same labeling change for the RLD. The proposed rule would establish a 30-day timeframe in which all ANDA holders would be required to submit a CBE–0 supplement with conforming labeling changes after FDA approval of a revision to the labeling for the RLD.

The proposed rule also would amend the regulations to allow submission of a CBE–0 labeling supplement for certain changes to the ''Highlights of Prescribing Information'' for drug products with labeling in the PLR format. This is intended to remove an unnecessary impediment to prompt communication of the most important safety-related labeling changes (e.g., boxed warnings and contraindications) for drug products with labeling in the PLR format.

Finally, FDA regulations provide that FDA may take steps to withdraw approval of an ANDA if the generic drug labeling is no longer consistent with the labeling for the RLD, subject to certain exceptions specified in the regulations. The proposed rule would amend the regulations to add a new exception for generic drug labeling that is temporarily inconsistent with the labeling for the RLD due to safety-related labeling changes submitted by the ANDA holder in a CBE–0 supplement.

Costs and Benefits

The economic benefits to the public health from adoption of the proposed rule are not quantified. By allowing all application holders to update labeling based on newly acquired information that meets the criteria for a CBE–0 supplement, communication of important drug safety information to prescribing health care providers and the public could be improved. The primary estimate of the costs of the proposed rule includes costs to ANDA and NDA holders for submitting and reviewing CBE–0 supplements. The Agency estimates the net annual social costs to be between $4,237 and $25,852. The present discounted value over 20 years would be in the range of $63,040 to $384,616 at a 3 percent discount rate, and in the range of $44,890 to $273,879 at a 7 percent discount rate.

I. Background

A. Drug Labeling

Under the FD&C Act, the PHS Act, and FDA regulations, the Agency makes decisions regarding the approval of marketing applications, including supplemental applications, based on a comprehensive analysis of the product's risks and benefits under the conditions of use prescribed, recommended, or suggested in the labeling (see 21 U.S.C. 355(d); 42 U.S.C. 262).

FDA-approved drug labeling summarizes the essential information needed for the safe and effective use of the drug,[1] and reflects FDA's finding regarding the safety and effectiveness of the drug under the labeled conditions of use. The primary purpose of labeling (commonly referred to as the ''package insert'' or ''prescribing information'') for prescription drugs is to provide health care practitioners with the essential scientific information needed to facilitate prescribing decisions, thereby enhancing the safe and effective use of prescription drug products and reducing the likelihood of medication errors. Prescription drug labeling is directed to health care practitioners, but may include FDA-approved patient labeling (see § 201.57(c)(18) (21 CFR 201.57(c)(18)) and 21 CFR 201.80(f)(2)). The over-the-counter (OTC) *Drug Facts* labeling is directed to consumers and conveys information in a clear, standardized format to enable patient self-selection of an appropriate drug and enhance the safe and effective use of the drug (see 21 CFR 201.66).

All drugs have risks, and health care practitioners and patients must balance the risks and benefits of a drug when making decisions about medical therapy. As a drug is used more widely or under diverse conditions, new information regarding the risks and benefits of a drug may become available. This may include new risks or new information about known risks. Accordingly, all holders of NDAs, ANDAs, and BLAs are required to develop written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA (see §§ 314.80(b), 314.98(a), and 600.80(b) (21 CFR 314.80(b), 314.98(a), and 600.80(b)). Application holders must promptly review all adverse drug experience information obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiological/surveillance studies, reports in the scientific literature, and unpublished scientific papers, and comply with applicable reporting and recordkeeping requirements (see §§ 314.80(b), 314.98(a), and 600.80(b)). Application holders also must comply with requirements for other postmarketing reports under § 314.81 (21 CFR 314.81) and 21 CFR 600.81 and section 505(k) of the FD&C Act (21 U.S.C. 355(k)). These requirements include submission of an annual report (including a brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product, and a description of actions the applicant has taken or intends to take as a result of this new information) and, if appropriate, proposed revisions to product labeling (see § 314.81).

When new information becomes available that causes information in labeling to be inaccurate, the

[1] For the purposes of this document, unless otherwise specified, references to ''drugs'' or ''drug products'' include drugs approved under the FD&C Act and biological products licensed under the PHS Act, other than biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)).

application holder must take steps to change the content of its labeling, in accordance with §§ 314.70, 314.97, and 601.12 (21 CFR 314.70, 314.97, and 601.12). All holders of marketing applications for drug products have an ongoing obligation to ensure their labeling is accurate and up-to-date. A drug is misbranded in violation of the FD&C Act when its labeling is false or misleading, or does not provide adequate directions for use and adequate warnings (see 21 U.S.C. 331(a) and (b) and 352(a), (f), and (j)).

B. Current Requirements Related to Changes to Approved Drug Labeling

For most substantive changes to product labeling, an application holder is required to submit a prior approval supplement and receive FDA approval for the change (see §§ 314.70(b) and 601.12(f)(1)). However, in the interest of public health, the regulations permit certain labeling changes based on newly acquired information about an approved drug to be implemented upon receipt by the Agency of a supplemental application that includes the change. These supplements are commonly referred to as ''changes being effected supplements'' or ''CBE–0 supplements'' (see §§ 314.70(c)(6)(iii) and 601.12(f)(2)).

The current regulations provide that application holders may submit CBE–0 supplements for the following types of changes to product labeling:

- To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c);
- To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage;
- To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product;
- To delete false, misleading, or unsupported indications for use or claims for effectiveness; or
- Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that FDA specifically requests be submitted under this provision.

The CBE–0 supplement procedures originated from a 1965 policy based on FDA's enforcement discretion regarding certain labeling changes that should be placed into effect ''at the earliest possible time'' (see ''Supplemental New-Drug Applications,'' 30 FR 993, January 30, 1965). Over the years, FDA has clarified the types of labeling changes that may be made by a CBE–0 supplement through a series of rulemakings.

In 1985, FDA updated its procedures for CBE–0 supplements and emphasized that CBE–0 supplements were intended as a narrow exception to the general rule that labeling changes require FDA's prior approval (see ''New Drug and Antibiotic Regulations''; final rule, 50 FR 7452 at 7470, February 22, 1985).

In 2006, FDA amended its regulations governing the content and format of prescription drug labeling to require, among other things, that the labeling of new and recently approved products include introductory prescribing information titled ''Highlights of Prescribing Information'' (see 21 CFR 201.57(a); see also ''Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products''; final rule, 71 FR 3922, January 24, 2006). The ''Highlights of Prescribing Information'' (Highlights) is intended to summarize the information that is most important for prescribing the drug safely and effectively, and to organize the information into logical groups to enhance accessibility, retention, and access to the more detailed information (see 71 FR 3922 at 3931). As part of this rulemaking, FDA amended the CBE–0 labeling supplement provisions to exclude most changes to the information required in the Highlights, which must be made by a prior approval supplement unless FDA specifically requests that the labeling change be submitted in a CBE–0 supplement or FDA grants a waiver request under § 314.90 (21 CFR 314.90).

In 2008, FDA amended the regulations governing CBE–0 supplements to codify the Agency's view that a CBE–0 labeling supplement is appropriate only to reflect newly acquired information and to clarify that a CBE–0 supplement may be used to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is sufficient evidence of a causal association with the approved product. FDA explained that these requirements are intended to help ensure that scientifically accurate information appears in the approved labeling for such products (''Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices''; final rule, 73 FR 49603 at 49604, August 22, 2008).

FDA carefully reviews any labeling change proposed in a CBE–0 supplement, as well as the underlying information or data supporting the change. FDA has the authority to accept, reject, or request modifications to the proposed changes as the Agency deems appropriate, and has the authority to bring an enforcement action if the added information makes the labeling false or misleading (see 21 U.S.C. 352(a)). If the newly acquired information changes the benefit/risk balance for the drug, such that the product no longer meets FDA's standard for approval, then FDA will take appropriate action (see 21 U.S.C. 355(e) and 355–1).

The CBE–0 supplement regulations allow application holders to comply with the requirement to update labeling promptly to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug (§ 201.57(c)(6)), and other risk information as required by the regulations (§§ 201.57(c) and 201.100(d)(3)).

C. Specific Labeling Requirements Related to Generic Drugs

The FD&C Act describes different routes for obtaining approval of two broad categories of drug applications: An NDA containing full reports of investigations of safety and effectiveness, for which the requirements are set out in section 505(b) and (c) of the FD&C Act, and an ANDA, for which the requirements are set out in section 505(j).

The ANDA category can be further subdivided into an ANDA and a ''petitioned ANDA.'' An ANDA must contain information to show that the proposed drug product is the same as a drug previously approved under section 505(c) of the FD&C Act (the RLD) with respect to active ingredient(s), dosage form, route of administration, strength, labeling, and conditions of use, among other characteristics, and is bioequivalent to the RLD. An applicant that can meet the requirements under section 505(j) of the FD&C Act for approval may rely upon the Agency's finding of safety and effectiveness for the RLD and need not repeat the extensive nonclinical and clinical investigations required for approval of an NDA submitted under section 505(b)(1) of the FD&C Act. A ''petitioned ANDA'' is a type of ANDA for a drug that differs from a previously approved drug product in dosage form, route of administration, strength, or active ingredient (in a product with more than one active ingredient), for which FDA has determined, in response to a suitability petition submitted under section 505(j)(2)(C) of the FD&C Act, that clinical studies are not necessary to demonstrate safety and effectiveness.

A generic drug is classified as therapeutically equivalent to the RLD if it is a pharmaceutical equivalent and has demonstrated bioequivalence (see

''Approved Drug Products With Therapeutic Equivalence Evaluations'' (the Orange Book), 33rd ed., 2013, p. vii). The generic drug program is based on the principle that ''products classified as therapeutically equivalent can be substituted with the full expectation that the substituted product will produce the same clinical effect and safety profile as the prescribed product'' (Orange Book, 33rd ed., 2013, p. vii). Currently, approximately 80 percent of all drugs dispensed are generic drugs (Ref. 1). After the introduction of a generic drug, the market share of the ''brand name'' drug (i.e., the drug approved in an NDA under section 505(c) of the FD&C Act) may drop substantially. Among drugs for which a generic version is available, approximately 94 percent are dispensed as a generic (Ref. 1). For any given brand name drug, there may be multiple approved generic drugs, and the prescribing health care provider ordinarily would not know which generic drug may be substituted for the prescribed product under applicable State law.

A generic drug is required to have the same labeling as the RLD at the time of approval, except for changes required because of differences approved under a suitability petition (see section 505(j)(2)(C) of the FD&C Act and 21 CFR 314.93) or because the drug product and the RLD are produced or distributed by different manufacturers (see section 505(j)(2)(A)(v) of the FD&C Act). FDA has described those differences in § 314.94(a)(8)(iv) (21 CFR 314.94(a)(8)(iv)) as including, for example, differences in formulation, bioavailability, or pharmacokinetics; labeling revisions made to comply with current FDA labeling guidelines or other guidance; or omission of an indication or other aspect of labeling protected by patent or exclusivity. FDA has generally taken the position that a generic drug must maintain the same labeling as the RLD throughout the lifecycle of the generic drug product (see § 314.150(b)(10) (21 CFR 314.150(b)(10)). Thus, if an ANDA holder believes that newly acquired safety information should be added to its product labeling, it should provide adequate supporting information to FDA, and FDA will determine whether the labeling for the generic drug(s) and the RLD should be revised (see 57 FR 17950 at 17961; April 28, 1992).

Although FDA has expressed differing views on this issue over the years, FDA generally has advised that an ANDA holder may use the CBE–0 supplement process only to update its product labeling to conform with approved labeling for the RLD or to respond to FDA's specific request to submit a labeling change under this provision, and may not unilaterally change ANDA labeling in a manner that differs from the RLD (see § 314.150(b)(10); see also 57 FR 17950 at 17961, and ''Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices''; proposed rule, 73 FR 2848 at 2849; footnote 1; January 16, 2008).

At the time of FDA's adoption of the generic drug regulations in 1992, FDA believed it was important that product labeling for the RLD and any generic drugs be the same to assure physicians and patients that generic drugs were, indeed, equivalent to their RLD. However, as the generic drug industry has matured and captured an increasing share of the market, tension has grown between the requirement that a generic drug have the same labeling as its RLD, which facilitates substitution of a generic drug for the prescribed product, and the need for an ANDA holder to be able to independently update its labeling as part of its independent responsibility to ensure that the labeling is accurate and up-to-date. In the current marketplace, in which approximately 80 percent of drugs dispensed are generic and, as we have learned, brand name drug manufacturers may discontinue marketing after generic drug entry, FDA believes it is time to provide ANDA holders with the means to update product labeling to reflect data obtained through postmarketing surveillance, even though this will result in temporary labeling differences among products. In a study of FDA safety-related drug labeling changes made in 2010, FDA found that the median time from initial approval of the drug product to the time of making the safety-related labeling change was 11 years, which confirms that data supporting labeling changes may become available after approval of generic versions of the drug product (see Ref. 2). FDA found that ''[t]he most critical safety-related label changes, boxed warnings and contraindications, occurred a median 10 and 13 years after drug approval (and the range spanned from 2 to 63 years after approval), underscoring the importance of persistent and vigilant postmarket drug safety surveillance'' (Ref. 2).

D. Recent Court Decisions

In two recent cases, the United States Supreme Court considered the issue of whether Federal law preempts State law tort claims against pharmaceutical manufacturers for failing to provide adequate warnings in drug product labeling (''failure-to-warn claims'') (see *Pliva, Inc.* v. *Mensing,* 131 S.Ct. 2567 (2011) and *Wyeth* v. *Levine,* 555 U.S. 555 (2009)). In *Pliva* v. *Mensing,* the Court held that the difference between NDA and ANDA holders' ability to independently change product labeling through CBE–0 supplements leads to different outcomes on whether Federal labeling requirements preempt State law failure-to-warn claims. In *Wyeth* v. *Levine,* the Court decided that Federal law does not preempt a State law failure-to-warn claim that a brand name drug's labeling did not contain an adequate warning. The Court found that the drug manufacturer could have unilaterally added a stronger warning to product labeling under the CBE–0 regulation as applied to NDAs, and absent clear evidence that FDA would not have approved such a labeling change, it was not impossible for the manufacturer to comply with both Federal and State requirements. The Court reaffirmed that ''through many amendments to the [FD&C Act] and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times'' (555 U.S. at 570–571).

Two years later, in *Pliva* v. *Mensing,* the Court decided that Federal law does preempt a State law failure-to-warn claim that a generic drug's labeling did not contain an adequate warning. The Court deferred to FDA's interpretation of its CBE–0 supplement and labeling regulations for ANDAs, and found that Federal law did not permit a generic drug manufacturer to use the CBE–0 supplement process to unilaterally strengthen warnings in its labeling or to issue additional warnings through ''Dear Health Care Professional'' letters, which FDA ''argues . . . qualify as 'labeling' '' (131 S.Ct. at 2576). The Court found that, under the current regulatory scheme, it was impossible for a generic drug manufacturer to comply with its Federal law duty to have the same labeling as the RLD and satisfy its State law duty to provide adequate labeling (131 S.Ct. at 2578). In September 2011, Public Citizen petitioned the Agency to revise its regulations in response to the *Mensing* decision (see Docket No. FDA–2011–P–0675).

As a result of the decisions in *Wyeth* v. *Levine* and *Pliva* v. *Mensing,* an individual can bring a product liability action for failure to warn against an NDA holder, but generally not an ANDA holder, and thus access to the courts is dependent on whether an individual is dispensed a brand name or generic drug. The *Mensing* decision alters the

incentives for generic drug manufacturers to comply with current requirements to conduct robust postmarketing surveillance, evaluation, and reporting, and to ensure that the labeling for their drugs is accurate and up-to-date.

We are proposing to change our regulations to expressly provide that ANDA holders may distribute revised labeling that differs from the RLD upon submission of a CBE–0 supplement to FDA. FDA's proposed revisions to its regulations would create parity between NDA holders and ANDA holders with respect to submission of CBE–0 supplements for safety-related labeling changes based on newly acquired information. This proposal is also intended to ensure that generic drug companies actively participate with FDA in ensuring the timeliness, accuracy, and completeness of drug safety labeling in accordance with current regulatory requirements. If this proposed regulatory change is adopted, it may eliminate the preemption of certain failure-to-warn claims with respect to generic drugs.

II. Description of the Proposed Rule

A. Supplement Submission for Safety-Related Labeling ''Changes Being Effected'' (Proposed §§ 314.70(b)(2), (c)(6), and (c)(8) and 601.12(f)(2))

1. Equal Applicability to NDA Holders and ANDA Holders (Proposed § 314.70(c)(8))

We are proposing to add § 314.70(c)(8) to enable ANDA holders to submit a CBE–0 supplement for generic drug labeling that differs from the labeling of the RLD and to establish that § 314.70(c)(6)(iii) applies equally to the holder of an approved NDA or ANDA. Proposed § 314.70(c)(8) states that an application holder may submit to its approved NDA or ANDA a supplement described by § 314.70(c)(6)(iii).

If an NDA holder or ANDA holder obtains or otherwise receives newly acquired information that should be reflected in product labeling to accomplish any of the objectives specifically described in § 314.70(c)(6)(iii)(A) through (c)(6)(iii)(D), the NDA holder or ANDA holder must submit a CBE–0 supplement (see § 314.70(c)(6)(iii); see also 21 CFR 314.3(b) (defining ''newly acquired information'')). As discussed in section I.A, all application holders, including ANDA holders, are required to conduct surveillance, evaluation, and reporting of postmarketing adverse drug experiences and, if warranted, to propose revisions to product labeling. Proposed § 314.70(c)(8) would expressly permit ANDA holders to update product labeling promptly to reflect newly acquired information that meets the criteria described in § 314.70(c)(6)(iii)(A) through (c)(6)(iii)(D) irrespective of whether the revised labeling differs from that of the RLD. In addition, if an ANDA holder submits a CBE–0 supplement for a labeling change that meets the criteria described in § 314.70(c)(6)(iii)(A) through (c)(6)(iii)(E), the ANDA holder may distribute a ''Dear Health Care Provider'' letter (which also meets the statutory definition of ''labeling'') regarding this labeling change in the same manner as an NDA holder or BLA holder, and be subject to the same statutory prohibition against marketing a misbranded product (see 21 U.S.C. 321(m), 331(a) and (b), and 352, and 21 CFR 201.100(d)(1) and 202.1(*l*)(2)). A ''Dear Health Care Provider'' letter may be used to disseminate the important new drug safety information that warranted the CBE–0 supplement, for example, a significant hazard to health or other important change in product labeling (see 21 CFR 200.5). FDA will continue to undertake any communication plans to health care providers (including distribution of ''Dear Health Care Provider'' letters) that are part of Risk Evaluation and Mitigation Strategies (REMS) that include one or more generic drugs (see 21 U.S.C. 355–1(i)(2)).

The obligation to ensure that labeling is accurate and up-to-date applies equally to all ANDA holders. In certain circumstances, if the RLD approved under section 505(c) of the FD&C Act has been withdrawn from the market, FDA may select a drug product approved in an ANDA (including a petitioned ANDA) to be the ''reference standard'' that an applicant seeking approval of an ANDA that relies upon the withdrawn RLD must use in conducting an in vivo bioequivalence study required for approval (see 57 FR 17950 at 17954). However, the duty to maintain accurate product labeling does not differ between an ANDA designated as the reference standard for bioequivalence studies and other approved ANDAs.

FDA acknowledges that there may be concerns about temporary differences in safety-related labeling for drugs that FDA has determined to be therapeutically equivalent, especially if multiple ANDA holders submit CBE–0 supplements with labeling changes that differ from each other and from the RLD. FDA also recognizes that health care practitioners are unlikely to review product labeling for each of the generic drugs that may be substituted for the prescribed product when making treatment decisions with their patients based on the balance of potential benefits and risks of the drug product for that patient. To address these concerns, FDA proposes to establish a dedicated Web page (or, alternatively, to modify an existing FDA Web page) on which FDA would promptly post information regarding the labeling changes proposed in a CBE–0 supplement while FDA is reviewing the supplement (see proposed §§ 314.70(c)(8) and 601.12(f)(2)(iii)). The public may subscribe to FDA's free email subscription service to receive an email message each time there is an update to this proposed FDA Web page.

The FDA Web page would provide information about pending CBE–0 supplements for safety-related labeling changes, including but not limited to: The active ingredient, the trade name (if any), the application holder, the date on which the supplement was submitted, a description of the proposed labeling change and source of the information supporting the proposed labeling change (e.g., spontaneous adverse event reports, published literature, clinical trial, epidemiologic study), a link to the current labeling for the drug product containing the changes being effected, and the status of the pending CBE–0 supplement (e.g., whether FDA is reviewing the proposed labeling change, has taken an action on the CBE–0 supplement, or has determined that the supplement does not meet the criteria for a CBE–0 supplement). It is expected that a valid safety concern regarding a generic drug product also would generally warrant submission of a supplement for a change to the labeling by the NDA holder for the RLD, as well as other ANDA holders. The CBE–0 supplements would remain posted on FDA's Web page until FDA has completed its review and issued an action letter. If the CBE–0 supplement is approved, the final approved labeling will be made available on the proposed FDA Web page through a link to FDA's online labeling repository at *http://labels.fda.gov.* After an adequate time period to communicate FDA's decision regarding approval of the CBE–0 labeling supplements and to facilitate submission of conforming CBE–0 supplements by other application holders, as appropriate, the original entry on FDA's Web page would be archived. Approved labeling would continue to be available at *http://labels.fda.gov.* As discussed in section II.B, a prior approval supplement or CBE–0 supplement submitted by an ANDA holder will be approved upon

the approval of the same safety-related labeling change for the RLD approved in an NDA under section 505(c) of the FD&C Act, except that if approval of the NDA for the RLD has been withdrawn under § 314.150, FDA may approve an ANDA holder's prior approval supplement or CBE–0 supplement (see section 505(j)(2)(A)(v) of the FD&C Act and proposed § 314.97(b); see also section II.A.1.b and d). Upon FDA approval of revised labeling, other ANDA holders will be required to submit a CBE–0 supplement with conforming revisions. We invite comment on this approach.

Proposed §§ 314.70(c)(8) and 601.12(f)(2)(iii) state that FDA will promptly post on its Web site information regarding labeling changes proposed in a CBE–0 supplement to an NDA, ANDA, or BLA. This proposal is intended to enhance transparency and facilitate access by health care providers and the public to labeling containing newly acquired information about important drug safety issues so that such information may be used to inform treatment decisions. We also invite comment on whether the benefits of a dedicated FDA Web page for CBE–0 supplements could be realized through modification of FDA's existing online labeling repository (*http://labels.fda.gov*). For example, the online labeling repository could be modified to enable a separate listing of pending CBE–0 supplements, thereby improving existing resources and consolidating labeling information on a single FDA Web page.

Current §§ 314.70(c)(6) and 601.12(f)(2) state that the application holder may distribute the drug accompanied by the revised labeling upon submission to FDA of a CBE–0 supplement. However, FDA expects that if an application holder acquires important new safety-related information that warrants submission of a CBE–0 supplement under §§ 314.70(c)(6) or 601.12(f)(2), the application holder will use available means (e.g., distribution of revised labeling in electronic format to the public) to distribute the revised labeling at the time of submission of the CBE–0 supplement to FDA (compare section II.A.1.d). Indeed, the need to promptly communicate certain safety-related labeling changes based on newly acquired information is the basis for this exception to the general requirement for FDA approval of revised labeling prior to distribution (see section I.B). Accordingly, we are proposing to expressly require that applicants submit final printed labeling in structured product labeling (SPL) format at the time of submission of the CBE–0 supplement so that the revised labeling can be made publicly available on FDA's Web site and in other databases (e.g., DailyMed, a Web site provided by the National Library of Medicine that includes drug labeling submitted to FDA) promptly after submission. This proposed change would make the regulations consistent with FDA's previous announcement that ''the Agency will make the revised labeling proposed in a CBE supplement publicly available on its Web site and through the DailyMed shortly after the CBE supplement is received and before FDA has necessarily reviewed or approved it'' (draft guidance for industry on ''Public Availability of Labeling Changes in 'Changes Being Effected' Supplements'' (2006)).[2] We note that the technical means by which the CBE–0 supplements are made publicly available through the FDA Web site may change with evolving technology and Agency practices.

Proposed §§ 314.70(c)(8) and 601.12(f)(2)(iii) would require the applicant to verify that the correct information regarding the labeling changes proposed in its CBE–0 supplement appears on FDA's Web page. If the information is incorrect, then the applicant must contact FDA within 5 business days of posting on the FDA Web page. The applicant may determine that information regarding the labeling changes proposed in its CBE–0 supplement has been posted on the FDA Web page by monitoring the FDA Web page after submission of a CBE–0 supplement or subscribing to FDA's Web page to receive an email notification. FDA intends to identify the FDA contact person(s) who should receive any corrections to such information for NDAs, ANDAs, and BLAs on the proposed FDA Web page. We invite comment on whether this is a sufficient amount of time for an applicant to check the accuracy and completeness of the posted information regarding the CBE–0 supplement and the link to current labeling.

a. *Contents of supplement.* We are proposing to add § 314.70(c)(8)(i) to clarify FDA's expectations regarding the contents of a CBE–0 supplement submitted under § 314.70(c)(6)(iii), and to facilitate publication of information regarding the CBE–0 supplement on FDA's Web page. Current § 314.70(c)(4) requires that a CBE supplement include information listed in § 314.70(b)(3)(i) through (b)(3)(vii), which describes information that must be included in a CBE supplement for a manufacturing change. To clarify FDA's expectations for the contents of a CBE–0 labeling supplement and to facilitate listing information on FDA's proposed Web page, we are proposing to require that a CBE–0 supplement submitted under § 314.70(c)(6)(iii) contain the following information:

i. *The application number(s) of the drug product(s) involved.* If a CBE–0 supplement is being submitted by an NDA or ANDA holder to multiple applications for a drug product or product class, the application holder should identify the application number of each application to which the CBE–0 supplement is being submitted.

ii. *A description of the labeling change proposed in the CBE–0 supplement.* The applicant should submit a proposed narrative description of the proposed labeling change in the CBE–0 supplement for posting on the FDA Web page. This brief narrative description should include the affected section(s) of labeling, the labeling change, and the source of the data (e.g., spontaneous adverse event reports, published literature, clinical trial, epidemiologic study). For example, ''Revised contraindication: Drug X is contraindicated in patients with diabetes. Source: Published literature, epidemiologic study.''

iii. *The basis for the labeling change proposed in the CBE–0 supplement.* The basis for the labeling change proposed in the CBE–0 supplement should include available data supporting the change (e.g., spontaneous adverse event reports, published literature, clinical trial, epidemiologic study). If the supplement has been submitted in response to FDA's specific request to submit a CBE–0 supplement for the labeling change (see § 314.70(c)(6)(iii)(E)), the applicant should describe the specific change requested by FDA and reference the FDA communication containing the request.

iv. *A copy of the product labeling proposed in the CBE–0 supplement.* A copy of the final printed labeling containing the changes being effected should be provided in SPL format for posting on FDA's Web site and distribution to DailyMed. The application holder also should submit a copy of the current product labeling annotated with the labeling change proposed in the CBE–0 supplement (e.g., use of underscoring and/or strikethrough text to show the changes being effected in the product labeling

[2] When final, this guidance will represent FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance Web page at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*.

proposed in the CBE–0 supplement as compared to the approved labeling).

v. *Confirmation that notice has been sent to the NDA holder for the RLD.* If the changes being effected supplement is submitted by an ANDA holder and approval of the NDA for the RLD has not been withdrawn under § 314.150, the ANDA holder must include in its submission a statement confirming that the notice described in proposed § 314.70(c)(8)(ii) has been sent to the NDA holder for the RLD.

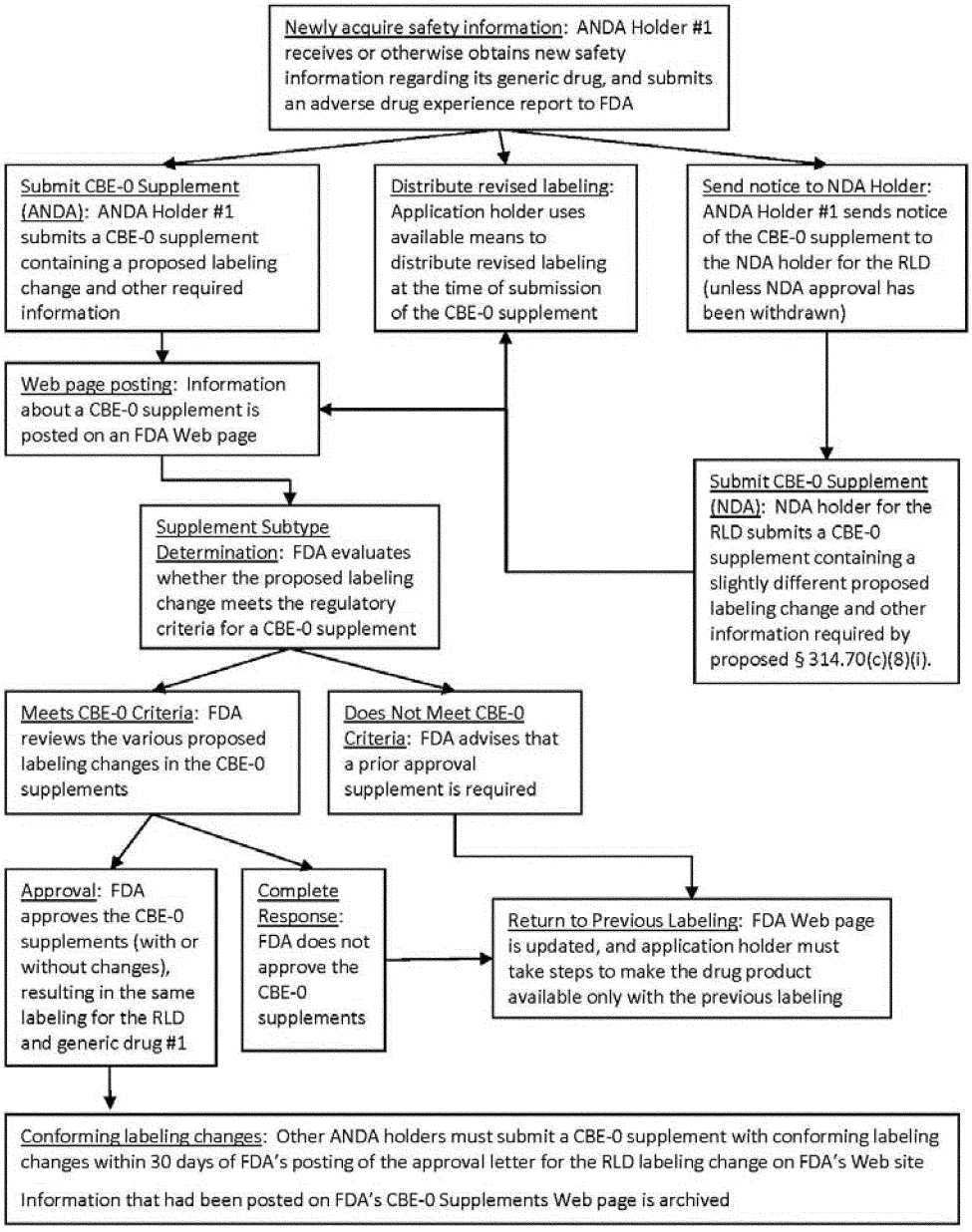
b. *Notice of labeling changes being effected.* We are proposing to add § 314.70(c)(8)(ii) to require an ANDA holder to send notice of the labeling change proposed in the CBE–0 supplement, including a copy of the information supporting the change (with any personally identifiable information redacted), to the NDA holder for the RLD at the same time that the supplement to the ANDA is submitted to FDA, unless approval of the NDA has been withdrawn under § 314.150. This proposal would ensure that the NDA holder for the RLD is promptly advised of the newly acquired information that was considered to warrant the labeling change proposed for the drug in the CBE–0 supplement.

The ANDA holder would be required to send a copy of the information (e.g., published literature, spontaneous adverse event reports) supporting the labeling change described in the CBE–0 supplement to the NDA holder for the RLD so that the NDA holder may consider this information as part of its review and evaluation of postmarketing data under § 314.80(b). If the information supporting the ANDA holder's labeling change described in the CBE–0 supplement contains personally identifiable information (e.g., spontaneous adverse event reports), the ANDA holder should redact that information prior to sending a copy of the information to the NDA holder for the RLD, in accordance with 21 CFR 20.63(f). The NDA holder has full access to the data upon which the RLD was approved and, in most cases, has substantial knowledge about the postmarketing experience for the drug product. FDA's analysis of whether the labeling change proposed by an ANDA holder in a CBE–0 supplement should be approved (and required for inclusion in the labeling of all versions of the drug) would benefit from the views of the NDA holder for the listed drug that was the basis for ANDA submission. Other holders of NDAs or ANDAs for drug products containing the same active ingredient may learn of pending CBE–0 supplements by subscribing to FDA's proposed Web page, and also may submit CBE–0 supplements or provide comments to FDA regarding a pending CBE–0 supplement. This approach to considering information from other application holders is intended to mitigate concerns that a single ANDA holder may not possess sufficient data to perform an adequate assessment of the potential new safety concern raised by the newly acquired information.

It should be emphasized that interpretation of postmarketing safety data is complex, involving analysis of postapproval clinical data, detailed review of adverse drug experience reports in the context of relevant clinical studies, estimates of drug usage and adverse drug experience reporting rates, estimates of background rates of the adverse event, and other relevant information. FDA recognizes that decisions about how to address a safety concern often are a matter of judgment, about which reasonable persons with relevant expertise may disagree, and this may be reflected in different approaches to proposed labeling changes based on newly acquired safety information (see Guidance on ''Drug Safety Information—FDA's Communication to the Public'' (2007)). Figure 1 illustrates one of the possible scenarios involving submission of CBE–0 supplements by multiple application holders.

BILLING CODE 4160–01–P

Figure 1. Example of Process for Submission of CBE-0 Supplements by ANDA Holder and NDA Holder



BILLING CODE 4160–01–C

Proposed § 314.70(c)(8)(ii) would provide that an NDA holder or any ANDA holder may submit (on its own initiative or in response to a request from FDA) a labeling supplement or correspondence to its NDA or ANDA, as applicable, regarding the labeling changes proposed in a CBE–0 supplement. It is expected that a valid safety concern regarding a generic drug product also would generally warrant a change to the labeling through a CBE–0 supplement by the NDA holder for the RLD and, as a consequence, other generic drug products that reference the RLD. In the event that the NDA holder for the RLD does not submit a supplement seeking approval for a related or conforming labeling change, FDA may send a supplement request letter to the NDA holder or, if appropriate, notify the responsible person of new safety information under section 505(o)(4) of the FD&C Act (see 21 U.S.C. 355(o)(2)(A) defining ''responsible person''). In situations in which the safety information prompting the submission of the CBE–0 supplement would require a label change for other drugs containing the same active ingredient, even if approved under a different NDA, FDA also may send a supplement request letter to the persons responsible for those other drugs.

We recognize that the authority to order safety labeling changes under section 505(o)(4) of the FD&C Act for new safety information about a risk of a serious adverse drug experience will not apply to all potential safety-related labeling changes (see 21 U.S.C. 355–1(b) defining ''new safety information'' and ''serious adverse drug experience''). Based on our experience, we expect that NDA holders will implement safety-related labeling changes requested by FDA even if not required under section 505(o)(4) of the FD&C Act. In circumstances in which section 505(o)(4) of the FD&C Act does not apply, if the NDA holder declined to submit a supplement to make the

change that FDA has concluded is appropriate, FDA would consider whether the NDA holder's failure to update its labeling would warrant the initiation of proceedings to withdraw approval of the NDA (see section 505(e) of the FD&C Act).

It should be noted that if an NDA holder has discontinued marketing a drug product, but approval of the NDA has not been withdrawn under § 314.150, the NDA holder still must comply with applicable statutory and regulatory requirements. These requirements include, for example, postmarketing reporting of adverse drug experiences, submission of an annual report (including a brief summary of significant new information from the previous year that might affect the safety, effectiveness, or labeling of the drug product, and a description of actions the applicant has taken or intends to take as a result of this new information) and, if appropriate, proposed revisions to product labeling. If approval of the NDA for the RLD is withdrawn under § 314.150 for reasons other than safety or effectiveness, any generic versions that remain on the market will be expected to contain the same essential labeling.

c. *Distribution of revised labeling.* We are proposing to add § 314.70(c)(8)(iii) and revise § 601.12(f)(2)(ii) to expressly describe our longstanding practice with respect to labeling supplements that have been submitted as CBE–0 supplements, but that do not meet the regulatory criteria for CBE–0 supplements, and thus do not fall within this narrow exception to the general requirement for FDA approval of revised labeling prior to distribution. Proposed §§ 314.70(c)(8)(iii) and 601.12(f)(2)(ii) explain that if FDA determines during its review period that the supplement does not meet the criteria described in § 314.70(c)(6)(iii) or § 601.12(f)(2)(i), as applicable, the supplement will be converted to a prior approval supplement, and the manufacturer must cease distribution of the drug product(s) accompanied by the revised labeling. In this scenario, the manufacturer must take steps to make the drug product available only with the previous version of the label. This may include, for example, replacing the CBE–0 labeling with the previous labeling on the manufacturer's Web site, requesting replacement of the CBE–0 labeling with the previous labeling on *http://labels.fda.gov,* and attaching the previous package insert to the drug product as soon as feasible thereafter or at the time of next printing of the product labeling for packaging.

This approach is consistent with our clarifying revision in proposed § 314.70(c)(7), which explains that if the Agency does not approve the supplemental application, the manufacturer must cease distribution of the drug product(s) accompanied by the revised labeling. The current text of § 314.70(c)(7) describes the implications of a complete response letter to the applicant for a CBE supplement for manufacturing changes, and does not expressly address CBE–0 labeling supplements. For consistency with § 314.110 (21 CFR 314.110), we are proposing to replace the word ''disapproves'' in § 314.70(c)(7) with the phrase ''issues a complete response letter'' and to make other editorial changes for clarity.

d. *Conforming labeling requirements.* Proposed § 314.70(c)(8)(iv) would establish a 30-day timeframe in which ANDA holders are required to submit a CBE–0 supplement under § 314.70(c)(6)(iii)(E) with conforming labeling after FDA approval of a revision to the labeling for the RLD. Currently, FDA advises ANDA holders to revise product labeling to conform to the labeling of the RLD ''at the very earliest time possible'' (see guidance for industry on ''Revising ANDA Labeling Following Revision of the RLD Labeling'' (2000)). In light of the range of timeframes in which ANDA holders currently submit such labeling supplements, we are proposing to revise these regulations to clarify FDA's expectations regarding the timeframe for submission of conforming labeling changes.

Proposed § 314.70(c)(8)(iv) states that upon FDA approval of changes to the labeling of the RLD, or if approval of the NDA for the RLD has been withdrawn under § 314.150, upon FDA approval of changes to the labeling of an ANDA that relied on the RLD, any other ANDA holder that relied upon the RLD must submit a CBE–0 supplement with conforming labeling revisions within 30 days of FDA's posting of the approval letter for the labeling change on FDA's Web site, unless FDA requires the ANDA holder's labeling revisions at a different time in accordance with sections 505(o)(4) or 505–1 of the FD&C Act, or other applicable authority. The ANDA holder would be expected to submit updated labeling for posting on *http://labels.fda.gov* and DailyMed at the time of submission of the CBE–0 supplement. However, we recognize that distribution of drug products accompanied by an updated package insert may take additional time, depending on how often the drug is packaged, the size of manufacturer inventories, and other factors. Accordingly, proposed § 314.70(c)(8)(iv) is directed to prompt distribution of revised labeling in electronic format, and timely distribution of drug product accompanied by an updated package insert as soon as feasible thereafter or at the time of next printing of the product labeling for packaging.

FDA may require an ANDA holder to submit revised product labeling at a different time for safety labeling changes required under section 505(o)(4) of the FD&C Act or for REMS under section 505–1 of the FD&C Act. This may occur, for example, in the context of approval of modifications to a single, shared system REMS that are made to conform to safety labeling changes (see section 505–1(i)(1)(B) of the FD&C Act).

2. Changes to Highlights of Prescribing Information (Proposed §§ 314.70(c)(6) and 601.12(f)(1) and (f)(2))

We are proposing to revise §§ 314.70(c)(6) and 601.12(f)(1) and (f)(2) to remove the limitation on submission of CBE–0 supplements for changes to the Highlights of drug labeling in the PLR format.

Current §§ 314.70(c)(6) and 601.12(f)(1) and (f)(2) exclude most changes to the information required in the Highlights, which are classified as a ''major change'' that must be made by a prior approval supplement, unless FDA specifically requests that the labeling change be submitted in a CBE–0 supplement or FDA grants a waiver request under § 314.90. This exception reflected the Agency's earlier view that FDA review and approval of most proposed changes to the information in the Highlights of labeling was necessary because of the difficulty involved in summarizing the complex information presented in the full prescribing information (see ''Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products,'' 71 FR 3922 at 3932, January 24, 2006).

Based on our experience implementing the PLR, we have found this restriction on CBE–0 supplements to be unnecessary in practice. In response to an applicant's inquiry about submission of a CBE–0 supplement for a change that would affect the Highlights of drug labeling, FDA typically waives this limitation under § 314.90 or specifically requests that the applicant proceed with a CBE–0 supplement under § 314.70(c)(6)(iii)(E) or § 601.12(f)(2)(i)(E).

The Highlights of drug labeling is intended to summarize the information that is most important for prescribing the drug safely and effectively. The

types of newly acquired information that would otherwise meet the criteria for submission of a CBE–0 supplement include the critical safety information that is presented in the Highlights. Accordingly, we believe that limiting the availability of CBE–0 supplements for changes to the Highlights of drug labeling in the PLR format may pose an unnecessary impediment to prompt communication of the most important safety-related labeling changes (e.g., boxed warnings and contraindications). Compare 50 FR 7452 at 7470, February 22, 1985 (stating that substantive changes in labeling are appropriately approved by FDA in advance, ''unless they relate to important safety information, like a new contraindication or warning, that should be immediately conveyed to the user'').

Our proposal to remove the limitation on submission of CBE–0 supplements for changes to the Highlights also would create parity between application holders for drugs with labeling in the older format and application holders for drugs with PLR labeling. For example, this proposal would eliminate differences in the ability of application holders to submit CBE–0 supplements for a new or substantively revised contraindication based solely on whether current labeling appeared in the older format or PLR format.

We also are proposing to make conforming revisions to § 314.70(b)(2)(v)(C) to clarify that a prior approval supplement is required for any changes to the Highlights of drug labeling other than changes under § 314.70(c)(6)(iii), except for the specified changes that may be reported in an annual report.

3. Clarifying Revisions and Editorial Changes

We are proposing to revise the title to § 314.70(c) to refer to CBE–0 supplements to clarify the scope of paragraph (c). As revised, § 314.70(c) would describe changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (CBE–30 supplements) and certain changes being effected pending supplement approval (CBE–0 supplements). We also are proposing to add titles to paragraphs (c)(1) through (c)(7) of § 314.70 for clarity.

We are proposing to revise § 314.70(c)(1) to clarify that submission of a CBE–0 supplement is required for any change in the labeling to reflect newly acquired information of the type described in § 314.70(c)(6)(iii). The current text of § 314.70(c)(1) is directed only to submission of supplements for certain manufacturing changes and does not fully describe the range of supplements for moderate changes that are described by this paragraph.

We are proposing to move the statement regarding the contents of a CBE supplement for certain manufacturing changes from existing § 314.70(c)(4) to § 314.70(c)(3) without changes.

We are proposing to revise § 314.70(c)(6)(iii) to clarify that an NDA holder or ANDA holder may distribute the drug product with revised labeling upon ''submission'' to FDA of the CBE–0 supplement for the labeling change, rather than upon FDA's ''receipt'' of the change. For ANDAs, section 744B(a)(5) of the FD&C Act (21 U.S.C. 379j–42(a)(5)) clarifies the time when a supplement is ''submitted'' to FDA, whereas the term ''received'' has a specific meaning that generally refers to FDA's determination that a submitted application has met certain criteria for completeness (see 21 CFR 314.101). This proposed revision is intended to avoid potential confusion, and more clearly establish the date on which distribution of revised labeling may occur.

B. Approval of Supplements to an Approved ANDA for a Labeling Change (Proposed § 314.97(b))

We are proposing to revise § 314.97 by designating the current text as paragraph (a) and by adding proposed paragraph (b) to clarify the process for approval of a supplement to an approved ANDA for a labeling change. Proposed § 314.97(b) explains that a supplement to an approved ANDA for a safety-related labeling change that is submitted in a prior approval supplement under § 314.70(b) or in a CBE–0 supplement under § 314.70(c)(6) will be approved upon approval of the same labeling change for the RLD, except that if approval of the NDA for the RLD has been withdrawn under § 314.150, FDA may approve an ANDA holder's prior approval supplement or CBE–0 supplement.

It has been FDA's longstanding position that an ANDA holder may submit a prior approval supplement to request a change to product labeling, and ''FDA will determine whether the labeling for the generic and [reference] listed drugs should be revised'' (57 FR 17950 at 17961, April 28, 1992; see also 57 FR 17950 at 17965 (describing requirement for ''ANDA applicants to submit a periodic report of adverse drug experiences even if the ANDA applicant has not received any adverse drug experience reports *or initiated any labeling changes''*) (emphasis added)). Proposed § 314.97(b) would expressly state that a prior approval supplement to an ANDA for a safety-related change in product labeling will be approved upon approval of the same labeling for the RLD. This approach ensures that the approved labeling for a generic drug continues to be the same as the approved labeling of its RLD (see section 505(j)(2)(A)(v) of the FD&C Act). If approval of the NDA for the RLD has been withdrawn under § 314.150, FDA may approve an ANDA holder's prior approval supplement for a safety-related labeling change (see § 314.105; see also proposed § 314.70(c)(8)(iv)).

Similarly, FDA would approve a CBE–0 labeling supplement to an ANDA upon the approval of the same labeling change for the RLD (see section 505(j)(2)(A)(v) of the FD&C Act), except that if approval of the NDA for the RLD has been withdrawn under § 314.150, FDA may approve an ANDA holder's CBE–0 supplement (see § 314.105; see also proposed § 314.70(c)(8)(iv)). As explained in section I.B, FDA may accept, reject, or request modifications to the labeling changes proposed in the CBE–0 supplement. FDA's evaluation of the labeling change proposed by the ANDA holder would consider any submissions related to the proposed labeling change from the NDA holder for the RLD and from any other NDA or ANDA holders for drug products containing the same active ingredient. The Agency intends to act expeditiously, taking into account the reliability of the data, the magnitude and seriousness of the risk, and number of CBE–0 supplements, and reach a decision on the approvability of labeling proposed by ANDA and NDA holders regarding the safety issue at the same time. After approval of a labeling change, other ANDA holders would be required to submit any necessary conforming labeling changes in accordance with proposed § 314.70(c)(8)(iv).

C. Exception for ANDA Labeling Differences Resulting From ''Changes Being Effected'' Supplement (Proposed § 314.150(b)(10)(iii))

We are proposing to revise § 314.150(b)(10) to provide an additional exception regarding circumstances in which FDA may seek to withdraw approval of an ANDA based on generic drug labeling that is no longer consistent with the labeling for the RLD. Proposed § 314.150(b)(10)(iii) would include, as a permissible difference, changes to generic drug labeling under a CBE–0 supplement, with the understanding that such differences generally will be temporary.

This proposed exception reflects the Agency's judgment that concerns related to temporary differences in labeling between generic drugs and their RLDs are outweighed by the benefit to the public health that would result from all application holders having the ability to independently update drug product labeling to reflect newly acquired information regarding important drug safety issues through CBE–0 labeling supplements (compare section 505(j)(10) of the FD&C Act).

III. Legal Authority

FDA's legal authority to modify §§ 314.70, 314.97, 314.150, and 601.12 arises from the same authority under which FDA initially issued these regulations. The FD&C Act (21 U.S.C. 301 et seq.) and the PHS Act (42 U.S.C. 201 et seq.) provide FDA with authority over the labeling for drugs and biological products, and authorize the Agency to enact regulations to facilitate FDA's review and approval of applications regarding the labeling for those products. Section 502 of the FD&C Act (21 U.S.C. 352) provides that a drug or biological product will be considered misbranded if, among other things, the labeling for the product is false or misleading in any particular (21 U.S.C. 352(a); see also 42 U.S.C. 262(j)). Under section 502(f) of the FD&C Act, a product is misbranded unless its labeling bears adequate directions for use, including adequate warnings against, among other things, unsafe dosage or methods or duration of administration or application. Moreover, under section 502(j) of the FD&C Act, a product is misbranded if it is dangerous to health when used in the manner prescribed, recommended, or suggested in its labeling.

In addition to the misbranding provisions, the premarket approval provisions of the FD&C Act authorize FDA to require that product labeling provide adequate information to permit safe and effective use of the product. Under section 505(c) of the FD&C Act (21 U.S.C. 355), FDA will approve an NDA only if the drug is shown to be both safe and effective for its intended use under the conditions set forth in the drug's labeling. Under section 505(j) of the FD&C Act, FDA will approve an ANDA only if the drug is, with limited exceptions, the same as a drug previously approved under section 505(c) of the FD&C Act with respect to active ingredient(s), dosage form, route of administration, strength, labeling, and conditions of use, among other characteristics, and is bioequivalent to the RLD.

Section 351 of the PHS Act (42 U.S.C. 262) provides additional legal authority for the Agency to regulate the labeling of biological products. Licenses for biological products are to be issued only upon a showing that the biological product is safe, pure, and potent (42 U.S.C. 262(a)). Section 351(b) of the PHS Act prohibits any person from falsely labeling any package or container of a biological product. FDA's regulations in 21 CFR part 201 apply to all prescription drug products, including biological products.

In addition, section 701(a) of the FD&C Act (21 U.S.C. 371(a)) authorizes FDA to issue regulations for the efficient enforcement of the FD&C Act. FDA's regulations relating to CBE–0 supplements are supported by this provision. In 1965, FDA determined that, in the interest of drug safety, manufacturers should make certain safety-related changes to their product labeling at the earliest possible time (see 30 FR 993, January 30, 1965). Thus, for nearly 50 years, FDA, as the Agency entrusted with administration and enforcement of the FD&C Act and the protection and promotion of the public health, has required NDA holders, and subsequently BLA holders, to update drug product labeling with important, newly acquired safety information through submission of a CBE–0 supplement.

FDA's authority to extend the CBE–0 supplement process for safety-related labeling changes to ANDA holders arises from the same authority under which our regulations relating to NDA holders and BLA holders were issued. Nothing in the Hatch-Waxman Amendments or subsequent amendments to the FD&C Act limits the Agency's authority to revise the CBE–0 supplement regulations to apply to ANDA holders to help ensure that generic drugs remain safe and effective under the conditions of use prescribed, recommended, or suggested in the labeling throughout the life cycle of the generic drug product.

In *Pliva* v. *Mensing,* the Supreme Court recognized that ''Congress and the FDA retain the authority to change the law and regulations if they so desire'' (131 S. Ct. 2567, 2582). Recently, in *Mutual Pharmaceutical Co., Inc.* v. *Bartlett,* 133 S. Ct. 2466 (2013), the Court indicated that ''Congress' decision to regulate the manufacture and sale of generic drugs in a way that reduces their cost to patients but leaves generic drug manufacturers incapable of modifying either the drugs' compositions or their warnings'' contributed to the outcome in that case (preemption of the tort claim against the generic manufacturer). We do not read this language to suggest that the Agency would not have authority to extend the CBE–0 supplement process to ANDA holders. The changes proposed in this rulemaking are authorized under the FD&C Act, which provides authority for FDA to permit NDA holders and BLA holders to change their product labeling to include certain newly acquired safety-related information through submission of a CBE–0 supplement.

IV. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Pub. L.104–4). Executive Orders 12866 and 13563 direct Agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The Agency believes that this proposed rule would not be an economically significant regulatory action as defined by Executive Order 12866.

If a rule has a significant economic impact on a substantial number of small businesses, the Regulatory Flexibility Act requires Agencies to analyze regulatory alternatives that would minimize any significant impact of a rule on small entities. FDA has determined that this proposed rule would not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that Agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $141 million, using the most current (2012) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

The public health benefits from adoption of the proposed rule are not quantified. By allowing all application holders to update labeling based on newly acquired information that meets

the criteria for a CBE–0 supplement, communication of important drug safety information to prescribing health care providers and the public could be improved. The proposed rule may reduce the time in which ANDA holders make safety-related labeling changes for generic drugs for which approval of the NDA for the RLD has been withdrawn. In addition, the proposed rule generally would reduce the time in which all ANDA holders make safety-related labeling changes, by requiring such ANDA holders to submit conforming labeling changes within 30 days of FDA's posting of the approval letter for the RLD's labeling change on its Web site. The primary estimate of the costs of the proposed rule includes costs to ANDA and NDA holders for submitting and reviewing CBE–0 supplements. We assume that the proposed rule will have no effect on the number of CBE–0 supplements submitted by BLA holders.

The proposed rule is expected to generate little cost. The Agency estimates the net annual social costs to be between $4,237 and $25,852. The present discounted value over 20 years would be in the range of $63,040 to $384,616 at a 3 percent discount rate, and in the range of $44,890 to $273,879 at a 7 percent discount rate.

FDA has examined the economic implications of the final rule as required by the Regulatory Flexibility Act. This proposed rule would only impose new burdens on small generic drug manufacturers who submit CBE–0 supplements for safety-related labeling changes. Given the small cost per submission and the uncertainty in the estimated number of CBE–0 labeling supplements for safety-related labeling changes that may be submitted by an ANDA holder, we do not expect this proposed rule to impose a significant impact on a substantial number of small entities. We therefore propose to certify that that this proposed rule would not have a significant economic impact on a substantial number of small entities.

V. Paperwork Reduction Act of 1995

This proposed rule contains collections of information that are subject to review by the Office of Management and Budget (OMB) under the PRA (44 U.S.C. 3501–3520). A description of these provisions is given in this document with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information.

FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products

Description: The proposed rule would permit ANDA holders to submit a CBE–0 supplement for certain types of labeling changes based on newly acquired information. At the time of submission, the ANDA holder would be required to send notice of the labeling change proposed in the CBE–0 supplement, including a copy of the information supporting the change, to the NDA holder for the RLD, unless the NDA for the RLD has been withdrawn.

Description of Respondents: Respondents to this collection of information are NDA holders, ANDA holders, and BLA holders.

Burden Estimates: FDA regulations at §§ 314.70 and 314.97 set forth the requirements for submitting supplements to FDA for certain changes to an approved NDA or ANDA. These regulations specify the submission of supplements at different times, depending on the change to the approved application. Under § 314.70(c)(6), an applicant may commence distribution of a drug product upon receipt by FDA of a supplement for a change to the applicant's approved application (a CBE–0 supplement). The changes for which a CBE–0 supplement may be submitted include, among other things, changes in the labeling (§ 314.70(c)(6)(iii)) to reflect newly acquired information, for example, to add or strengthen a contraindication, warning, precaution, or adverse reaction for which there is reasonable evidence of a causal association.

FDA currently has OMB approval (OMB control number 0910–0001) for the submission of supplements to FDA for changes to an approved NDA or ANDA under §§ 314.70 (including § 314.70(c)(6)(iii)) and 314.97.

Under the proposed rule, ANDA holders would be permitted to submit a supplement to FDA for certain types of labeling changes based on newly acquired information. This collection of information is not currently approved under OMB control number 0910–0001. Under proposed § 314.70(c)(8), if an NDA holder or ANDA holder obtains or otherwise receives newly acquired information that should be reflected in product labeling to accomplish any of the objectives specifically described in § 314.70(c)(6)(iii), the NDA holder or ANDA holder should submit a CBE–0 supplement to FDA. Proposed § 314.70(c)(8) is intended to permit ANDA holders to update product labeling promptly, without FDA's special permission and assistance, to reflect newly acquired information that meets the criteria described in § 314.70(c)(6)(iii) irrespective of whether the revised labeling differs from that of the RLD.

To minimize confusion and make safety-related changes to generic drug labeling readily available to prescribing health care providers and the public while FDA is reviewing a CBE–0 supplement, FDA would establish, under proposed § 314.70(c)(8), a dedicated Web page (or, alternatively, a modification of an existing FDA Web page) on which FDA would promptly post information regarding the labeling changes proposed in a CBE–0 supplement. ANDA holders would be required to verify that the correct information regarding the labeling changes proposed in their CBE–0 supplement appears on the FDA Web page. If the information is incorrect, the ANDA holder must contact the appropriate FDA review division within 2 business days of posting on the FDA Web page.

At the time of submission of the CBE–0 labeling supplement to FDA, proposed § 314.70(c)(8)(ii) would require the ANDA holder to send notice of the labeling change proposed in the supplement, including a copy of the information supporting the change, to the NDA holder for the RLD, unless the NDA for the RLD has been withdrawn.

Based on the data summarized in section IV (Analysis of Impacts), we estimate that a total of approximately 15 ANDA holders (''number of respondents'' in table 1) would submit to us annually a total of approximately 20 CBE–0 labeling supplements under proposed § 314.70(c)(8), if this rule is finalized (''total annual responses'' in table 1). We also estimate that preparing and submitting each CBE–0 labeling supplement under proposed § 314.70(c)(8) will take approximately 12 hours per ANDA holder (''hours per response'' in table 1). This burden hour estimate includes the time needed by an

ANDA holder to verify, as required under proposed § 314.70(c)(8), that the correct information regarding the labeling change proposed in its CBE–0 supplement appears on the FDA Web page, and the time needed to contact FDA if the information is incorrect.

In addition, we estimate that a total of approximately 15 ANDA holders would send notice of the labeling change proposed in each of the 20 CBE–0 labeling supplements, including a copy of the information supporting the change, to the NDA holder for the RLD, as required under proposed § 314.70(c)(8)(ii). We also estimate that preparing and sending each notice would take approximately 3 hours per ANDA holder.

FDA estimates the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

21 CFR Section	Number of respondents	Number of responses per respondent	Total annual responses	Hours per response	Total hours
CBE–0 supplement submission by ANDA holders (314.70(c)(8))	15	1.34	20	12	240
ANDA holder notice to NDA holder (314.70(c)(8)(ii))	15	1.34	20	3	60
Total					300

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202–395–7245, or emailed to *oira_submission@omb.eop.gov*. All comments should be identified with the title, ''Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products.''

In compliance with the PRA (44 U.S.C. 3407(d)), the Agency has submitted the information collection provisions of this proposed rule to OMB for review. These requirements will not be effective until FDA obtains OMB approval. FDA will publish a notice concerning OMB approval of these requirements in the **Federal Register**.

VI. Environmental Impact

The Agency has determined under 21 CFR 25.30(h) and 25.31(a) and (g) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Effective Date

FDA proposes that any final rule based on this proposal become effective 30 days after the date of its publication in the **Federal Register**.

We intend to apply this rule, if finalized, to any submission received by FDA on or after the effective date. This proposed rule provides sufficient notice to all interested parties, including NDA holders, ANDA holders, and BLA holders, to adjust their submissions and actions by the time we issue any final rule. However, we invite comments on how a final rule should be implemented.

VIII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule, if finalized, would not contain policies that would have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the Agency tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

IX. Request for Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov*.

X. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday, and are available electronically at *http://www.regulations.gov*. (FDA has verified the Web site address in this reference section, but we are not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

1. IMS Institute for Healthcare Informatics, ''The Use of Medicines in the United States: Review of 2011,'' April 2012 (available at *http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_Medicines_in_U.S_Report_2011.pdf*).

2. Lester J., G. A. Neyarapally, E. Lipowski, et al., ''Evaluation of FDA Safety-Related Drug Label Changes in 2010,'' *Pharmacoepidemiology Drug Safety,* vol. 22, pp. 302–305, 2013.

List of Subjects

21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

21 CFR Part 601

Administrative practice and procedure, Biologics, Confidential business information.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, FDA proposes to amend 21 CFR parts 314 and 601 as follows:

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

■ 1. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 356a, 356b, 356c, 371, 374, 379e.

§ 314.70 [Amended]

■ 2. Amend § 314.70 as follows:
■ a. Revise paragraph (b)(2)(v)(C) introductory text;
■ b. Revise the paragraph (c) heading;
■ c. Add headings to paragraphs (c)(1) through (c)(7);
■ d. Revise paragraphs (c)(1), (c)(3), (c)(4), (c)(6) introductory text, (c)(6)(iii) introductory text, and (c)(7); and
■ e. Add new paragraph (c)(8).

§ 314.70 Supplements and other changes to an approved application.

* * * * *

(b) * * *

(2) * * *

(v) * * *

(C) Any change to the information required by § 201.57(a) of this chapter other than changes under paragraph (c)(6)(iii) of this section, with the following exceptions that may be reported in an annual report under paragraph (d)(2)(x) of this section:

* * * * *

(c) *Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change and certain changes being effected pending supplement approval (moderate changes).*

(1) *Types of changes for which a supplement is required.* A supplement must be submitted for any change in the drug substance, drug product, production process, quality controls, equipment, or facilities that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product. A supplement also must be submitted for any change in the labeling to reflect newly acquired information of the type described in paragraph (c)(6)(iii) of this section. If the supplement provides for a labeling change under paragraph (c)(6)(iii) of this section, 12 copies of the final printed labeling must be included.

(2) *Changes requiring supplement submission at least 30 days prior to distribution of the drug product made using the change (changes being effected in 30 days).* * * *

* * * * *

(3) *Explanation of basis for the change and supplement identifier.* A supplement submitted under paragraph (c)(1) of this section is required to give a full explanation of the basis for the change and identify the date on which the change is to be made. The supplement must be labeled ''Supplement—Changes Being Effected in 30 Days'' or, if applicable under paragraph (c)(6) of this section, ''Supplement—Changes Being Effected.'' The information listed in paragraphs (b)(3)(i) through (b)(3)(vii) of this section must be contained in the supplement.

(4) *Distribution of drug product pending supplement approval (for changes being effected in 30 days).* Pending approval of the supplement by FDA, except as provided in paragraph (c)(6) of this section, distribution of the drug product made using the change may begin not less than 30 days after receipt of the supplement by FDA.

(5) *Limitations on distribution of drug product pending supplement approval (for changes being effected in 30 days).* * * *

* * * * *

(6) *Changes requiring supplement submission prior to distribution of the drug product made using the change (changes being effected).* The agency may designate a category of changes for the purpose of providing that, in the case of a change in such category, the holder of an approved application may commence distribution of the drug product involved upon submission to the agency of a supplement for the change. These changes include, but are not limited to:

(i) * * *

(ii) * * *

(iii) Changes in the labeling to reflect newly acquired information to accomplish any of the following:

* * * * *

(7) *Effect of complete response letter for changes being effected supplement.* If the agency issues a complete response letter to the supplemental application, the manufacturer may be ordered to cease distribution of the drug product(s) made with the manufacturing change or, if the supplemental application was submitted for a labeling change under paragraph (c)(6) of this section, the manufacturer must cease distribution of the drug product(s) accompanied by the revised labeling.

(8) *Equal applicability to application holders and abbreviated application holders.* An application holder may submit to its approved application or abbreviated application a supplement described by paragraph (c)(6)(iii) of this section. FDA will promptly post on its Web site information regarding the labeling changes proposed in the changes being effected supplement. The applicant must verify that the correct information regarding the labeling changes proposed in the changes being effected supplement appears on FDA's Web site and must contact FDA within 5 business days of posting if the information is incorrect.

(i) *Contents of supplement.* A supplement to an approved application or abbreviated application described by paragraph (c)(6)(iii) of this section must contain the following information:

(A) The application number(s) of the drug product(s) involved;

(B) A description of the labeling change proposed in the changes being effected supplement;

(C) The basis for the labeling change proposed in the changes being effected supplement, including the data supporting the change or, if submitted under paragraph (c)(6)(iii)(E), the specific change requested by FDA;

(D) A copy of the final printed labeling and current product labeling annotated with the labeling change proposed in the changes being effected supplement;

(E) If the changes being effected supplement is submitted by an abbreviated application holder and approval of the application for the reference listed drug has not been withdrawn under § 314.150 of this chapter, a statement confirming that the notice described in paragraph (c)(8)(ii) of this section has been sent to the application holder for the reference listed drug.

(ii) *Notice of labeling changes being effected.* An abbreviated application holder must send notice of the labeling change proposed in the changes being effected supplement, including a copy of the information supporting the change (with any personally identifiable information redacted), to the application holder for the reference listed drug at the same time that the supplement to the abbreviated application is submitted to FDA, unless approval of the application has been withdrawn under § 314.150 of this chapter. An application holder or any abbreviated application holder may submit (on its own initiative or in response to a request from FDA) a labeling supplement or correspondence to its application or abbreviated application, as applicable, regarding the proposed labeling changes.

(iii) *Distribution of revised labeling.* Pending approval of the supplement by FDA, distribution of the drug product with the revised labeling may be made by an application holder or abbreviated application holder upon submission to FDA of the supplement, except that if FDA determines during its review period that the supplement does not meet the criteria described in paragraph (c)(6)(iii) of this section, the supplement will be converted to a prior approval supplement, and the manufacturer must cease distribution of the drug product(s) accompanied by the revised labeling.

(iv) *Conforming labeling requirements.* Upon FDA approval of changes to the labeling of the reference listed drug or, if the application for the reference listed drug has been withdrawn, upon FDA approval of changes to the labeling of an abbreviated application that relied on the reference listed drug, any other abbreviated application holder that relied upon the reference listed drug must submit a supplement under paragraph (c)(6)(iii)(E) of this section with conforming labeling revisions within 30 days of FDA's posting of the approval letter on its Web site, unless FDA requires the abbreviated application holder's labeling revisions at a different time in accordance with sections 505(o)(4) or 505–1 of the Federal Food, Drug, and Cosmetic Act.

* * * * *

§ 314.97 [Amended]

■ 3. Revise § 314.97 to read as follows:

§ 314.97 Supplements and other changes to an approved abbreviated application.

(a) The applicant must comply with the requirements of §§ 314.70 and 314.71 regarding the submission of supplemental applications and other changes to an approved abbreviated application.

(b) A supplement to an approved abbreviated application for a safety-related change in the labeling that is submitted under § 314.70(b) or (c)(6) will be approved upon approval of the same labeling change for the reference listed drug, except that if approval of the application for the reference listed drug has been withdrawn under § 314.150, FDA may approve such a supplement to an approved abbreviated application.

§ 314.150 [Amended]

■ 4. Amend § 314.150 as follows:

■ a. In paragraph (b)(10)(i), remove the word ''or'';

■ b. In paragraph (b)(10)(ii), remove the period and replace with a semicolon followed by the word ''or''; and

■ c. Add paragraph (b)(10)(iii).

§ 314.150 Withdrawal of approval of an application or abbreviated application.

* * * * *

(b) * * *

(10) * * *

(iii) Changes to the labeling for the drug product that is the subject of the abbreviated application under § 314.70(c)(6)(iii) of this chapter.

* * * * *

PART 601—LICENSING

■ 5. The authority citation for 21 CFR part 601 continues to read as follows:

Authority: 15 U.S.C. 1451–1561; 21 U.S.C. 321, 351, 352, 353, 355, 356b, 360, 360c–360f, 360h–360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263, 264; sec 122, Pub. L. 105–115, 111 Stat. 2322 (21 U.S.C. 355 note).

■ 6. Amend § 601.12 by revising paragraphs (f)(1), (f)(2)(i) introductory paragraph, and (f)(2)(ii); and by adding new paragraph (f)(2)(iii) to read as follows:

§ 601.12 Changes to an approved application.

* * * * *

(f) * * * (1) *Labeling changes requiring supplement submission—FDA approval must be obtained before distribution of the product with the labeling change.* Except as described in paragraphs (f)(2) and (f)(3) of this section, an applicant shall submit a supplement describing a proposed change in the package insert, package label, container label, or, if applicable, a Medication Guide required under part 208 of this chapter, and include the information necessary to support the proposed change. The supplement shall clearly highlight the proposed change in the labeling. An applicant may report the minor changes to the information specified in paragraph (f)(3)(i)(D) of this section in an annual report. The applicant shall obtain approval from FDA prior to distribution of the product with the labeling change.

(2) *Labeling changes requiring supplement submission—product with a labeling change that may be distributed before FDA approval.* (i) An applicant shall submit, at the time such change is made, a supplement for any change in the package insert, package label, or container label to reflect newly acquired information to accomplish any of the following:

* * * * *

(ii) Pending approval of the supplement by FDA, the applicant may distribute a product with a package insert, package label, or container label bearing such change at the time the supplement is submitted, except that if FDA determines during its review period that the supplement does not meet the criteria described in paragraph (f)(2)(i) of this section, the supplement will be converted to a prior approval supplement, and the manufacturer must cease distribution of the drug product(s) accompanied by the revised labeling. The supplement shall clearly identify the change being made and include necessary supporting data. The supplement and its mailing cover shall be plainly marked: ''Special Labeling Supplement—Changes Being Effected.''

(iii) FDA will promptly post on its Web site information regarding the labeling changes proposed in the changes being effected supplement. The applicant must verify that the correct information regarding the labeling changes proposed in the changes being effected supplement appears on FDA's Web site and must contact FDA within 5 business days of posting if the information is incorrect.

* * * * *

Dated: November 5, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–26799 Filed 11–8–13; 11:15 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2013–0319]

RIN 1625–AA09

Drawbridge Operation Regulation; Gulf Intracoastal Waterway, Treasure Island, FL

AGENCY: Coast Guard, DHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Coast Guard proposes to change the operating schedule that governs the Treasure Island Causeway Bridge, mile 119.0, Treasure Island, Florida. The Treasure Island Bridge is a double-leaf bascule bridge that provides a vertical clearance of 21 feet in the closed position. The Treasure Island Bridge crosses the Gulf Intracoastal Waterway at mile 119.0, Treasure Island, Pinellas County, Florida. Changing the schedule from on signal to three times an hour during the week and twice an hour on the weekends and Federal holidays between the hours of 7 a.m. and 7 p.m. will reduce vehicle traffic issues caused by the bridge openings. Between 7 p.m. and 7 a.m. the bridge will continue to open only on signal.

DATES: Comments and related material must reach the Coast Guard on or before February 11, 2014.

ADDRESSES: You may submit comments identified by docket number USCG–2013–0319 using any one of the following methods:

(1) *Federal Rulemaking Portal: http://www.regulations.gov.*

Escherichia coli O157:H7,'' *Journal of Food Protection*, 65:1388–1393, 2002.

*53. Niemira, B.A., ''Radiation Sensitivity and Recoverability of *Listeria monocytogenes* and Salmonella on 4 Lettuce Types,'' *Journal of Food Science*, 68: 2784–2787, 2003.

*54. Niemira, B.A., ''Relative Efficacy of Sodium Hypochlorite Wash Versus Irradiation to Inactivate *Escherichia coli* O157:H7 Internalized in Leaves of Romaine Lettuce and Baby Spinach,'' *Journal of Food Protection*, 70:2526–2532, 2007.

*55. Zhang, L., Z. Lu, and H. Wang, ''Effect of Gamma Irradiation on Microbial Growth and Sensory Quality of Fresh-Cut Lettuce,'' *International Journal of Food Microbiology*, 106:348–351, 2006.

*56. Zhang, L., Z. Lu, F. Lu, and X. Bie, ''Effect of Gamma Irradiation on Quality Maintaining of Fresh-Cut Lettuce,'' *Food Control*, 17:225–228, 2006.

*57. Fan, X. and K.J. Sokorai, ''Sensorial and Chemical Quality of Gamma-Irradiated Fresh-Cut Iceberg Lettuce in Modified Atmosphere Packages,'' *Journal of Food Protection*, 65:1760–1765, 2002.

*58. Fan, X. and K.J. Sokorai, ''Assessment of Radiation Sensitivity of Fresh-Cut Vegetables Using Electrolyte Leakage Measurement,'' *Postharvest Biology and Technology*, 36:191–197, 2005.

*59. Fan, X., B.A. Niemira, and K.J. Sokorai, ''Use of Ionizing Radiation to Improve Sensory and Microbial Quality of Fresh-cut Green Onion Leaves,'' *Journal of Food Science*, 68:1478–1483, 2003.

*60. Petran, R.L., W.H. Sperber, and A.B. Davis, ''*Clostridium botulinum* Toxin Formation in Romaine Lettuce and Shredded Cabbage: Effect of Storage and Packaging Conditions,'' *Journal of Food Protection*, 58, 624–627, 1995.

*61. Renner, H. W., U. Graf, F.E. Wurgler, H. Altmann, J.C. Asquith, and P.S. Elias, ''An Investigation of the Genetic Toxicology of Irradiated Foodstuffs Using Short-Term Test Systems, III—in vivo Tests in Small Rodents and in Drosophila melangaster,'' *Food Chemistry and Toxicology*, 30:867–878, 1982.

List of Subjects in 21 CFR Part 179

Food additives, Food labeling, Food packaging, Radiation protection, Reporting and record keeping requirements, Signs and symbols.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 179 is amended as follows:

PART 179—IRRADIATION IN THE PRODUCTION, PROCESSING AND HANDLING OF FOOD

■ 1. The authority citation for 21 CFR part 179 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 343, 348, 373, 374.

■ 2. Section 179.26 is amended in the table in paragraph (b) by adding a new item ''12.'' under the headings ''Use'' and ''Limitations'' to read as follows:

§ 179.26 Ionizing radiation for the treatment of food.

* * * * *

(b) * * *

Use	Limitations
* * * * * * *	
12. For control of food-borne pathogens and extension of shelf-life in fresh iceberg lettuce and fresh spinach.	Not to exceed 4.0 kGy.

* * * * *

Dated: August 19, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–19573 Filed 8–21–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 314, 601, and 814

[Docket No. FDA–2008–N–0032] (formerly Docket No. 2008N–0021)

RIN 0910–ZA32

Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations regarding changes to an approved new drug application (NDA), biologics license application (BLA), or medical device premarket approval application (PMA). This final rule provides that a supplemental application submitted under certain FDA regulations is appropriate to amend the labeling for an approved product to reflect newly acquired information and to add or strengthen a contraindication, warning, precaution, or adverse reaction if there is sufficient evidence of a causal association with the drug, biologic, or device, as defined in other FDA regulations and guidance documents.

DATES: This rule is effective September 22, 2008.

FOR FURTHER INFORMATION CONTACT:

For information regarding devices: Nicole Wolanski, Center for Devices and Radiological Health (HFZ–402), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 240–276–4010.

For information regarding biologics: Christopher Joneckis, Center for Biologics Evaluation and Research (HFM–1), Food and Drug Administration, 1401 Rockville Pike, Rockville MD 20852, 301–827–0373.

For information regarding drugs: Laurie Burke, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6462, Silver Spring, MD 20933, 301–796–0900.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of January 16, 2008 (73 FR 2848), FDA proposed amending its regulations regarding changes to an NDA, BLA, or PMA to codify the agency's longstanding view concerning when a change to the labeling of an approved drug, biologic, or medical device may be made in advance of the agency's review and approval of such change (the January 2008 proposed rule). With respect to drugs, § 314.70(c)(6)(iii) (21 CFR 314.70(c)(6)(iii)) provides that certain labeling changes related to an approved drug may be implemented upon receipt by the agency of a supplemental new drug application (sNDA) that includes the change. The corresponding regulation for biological products, § 601.12(f)(2) (21 CFR 601.12(f)(2)), provides that products with certain labeling changes may be distributed before FDA approval. Similarly, with respect to devices, § 814.39(d) (21 CFR 814.39(d)) provides that certain labeling changes may be placed into effect upon submission of a PMA supplement, but prior to the sponsor's receipt of a written FDA order approving the supplement. The supplements described by §§ 314.70(c), 601.12(f)(2), and 814.39(d) are commonly referred to as ''changes being effected supplements''

or ''CBE supplements.''[1] FDA proposed amending these provisions to affirm that a CBE supplement is appropriate to amend the labeling for an approved product only to reflect newly acquired information and to make it clear that a CBE supplement may be used to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is sufficient evidence of a causal association with the drug, biologic, or medical device. The phrase ''sufficient evidence of a causal association'' refers to the standards for drugs and biologics described in § 201.57(c)(6) (21 CFR 201.57(c)(6)) (for Warnings and Precautions—''reasonable evidence''), and in § 201.57(c)(7) (21 CFR 201.57(c)(7)) (for Adverse Reactions—''some basis to believe'') and to the standard for devices in the Device Labeling Guidance, General Program Memorandum G91–1 (March 8, 1991) (*http://www.fda.gov/cdrh/g91-1.html*) (''reasonable evidence'') for the level of evidence needed to support a causal association with these medical products.

As described in the January 2008 proposed rule, FDA believes that amending FDA's CBE regulations is consistent with the agency's role in protecting the public health. Before approving an NDA, BLA, or PMA, FDA undertakes a detailed review of the proposed labeling, allowing only information for which there is a scientific basis to be included in the FDA-approved labeling. Under the Federal Food, Drug, and Cosmetic Act (the act), the Public Health Service Act (the PHS Act), and FDA regulations, the agency makes approval decisions, including the approval of supplemental applications, based on a comprehensive scientific evaluation of the product's risks and benefits under the conditions of use prescribed, recommended, or suggested in the labeling. See, e.g., 21 U.S.C. 355(d); 42 U.S.C. 262; 21 U.S.C. 360e(d)(2). FDA's comprehensive scientific evaluation is embodied in the labeling for the product which reflects thorough FDA review of the pertinent scientific evidence and communicates to health care practitioners the agency's formal, authoritative conclusions regarding the conditions under which the product can be used safely and effectively. Expressly requiring that a CBE supplement reflect newly acquired information and be based on sufficient evidence of a causal association will help to ensure that scientifically accurate information appears in the approved labeling for such products.

II. Changes to the January 2008 Proposed Rule

FDA has made the following changes to the January 2008 proposed rule:

The definition of ''newly acquired information'' has been revised to clarify that data, whether derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) needs to be of a ''different type or greater severity or frequency than previously included in submissions to FDA''. The codified section of the January 2008 proposed rule suggested that this limitation applied only to data derived from reports of adverse events. Instead, it applies to data derived from new clinical studies, reports of adverse events, and new analyses of previously submitted data.

In addition, FDA has made one technical correction to the January 2008 proposed rule. The technical correction is in § 601.12, where an amendment was proposed adding paragraph (f)(5), containing the definition of ''newly acquired information.'' In fact, the amendment should have proposed adding this definition to paragraph (f)(6) of § 601.12 rather than to paragraph (f)(5) of § 601.12.

III. Comments

FDA received approximately 20 comments to the January 2008 proposed rule. The comments were submitted by consumer advocacy groups, individuals, law firms, law professors, pharmaceutical companies, trade associations, and Members of Congress.

(Comment 1) Several comments stated that this proposed amendment would make it more difficult for sponsors to warn about new risks. Most of these comments were focused on the aspect of the rule that imposed a requirement that sponsors have a sufficient amount of causal evidence before a CBE should be used.

In addition, comments argued that FDA should distinguish between situations when sponsors are obligated to warn of a new risk, and situations when the sponsor is permitted to warn. For example, some comments stated that the requirement in § 201.57(c)(6) that there be some evidence of a causal relationship should apply to situations when a manufacturer must warn, but should not apply to when manufacturers may warn. These comments argue that public policy should not discourage sponsors from warning, even when the regulations do not require it.

Similarly, one comment argued that causation is not a binary issue (i.e., causation is either present or not). Rather, the causal relationship between a product and an adverse effect is often difficult to establish and may require large trials, often specifically designed to assess the risk. One comment argued that because of this difficulty, drug and device sponsors may delay warning and delay making labeling changes by asserting that the CBE regulation (if finalized as proposed) would not permit them to amend their labeling.

FDA does not agree that this rule will make it more difficult to provide appropriate warnings regarding hazards associated with medical products. This rule is intended to describe FDA's existing labeling standards and policies, but does not amend the standards under which sponsors must provide warnings regarding risks (§ 201.57(c)(6)). Nor is the rule intended to suggest that there is a mathematically precise distinction between whether there is, or is not, sufficient evidence of a causal relation between a drug and an adverse effect to support its inclusion in the labeling. The rule is, nevertheless, sufficiently clear and objective to allow sponsors to determine whether a medical product's labeling should be amended. If new safety information meets the requirements of § 201.57(c)(6), it is appropriate for inclusion in the labeling of a drug or biologic and a sponsor must update its labeling ''as soon as'' such information becomes available. That section states that causation need not have been ''definitely established'' for a warning to be required to appear in labeling, but rather that there need only be ''reasonable'' evidence of a causal association with the drug, a standard that could be met by a wide range of evidence. A CBE submission may be made when the evidence meets the standard set forth in this rule, even if that evidence would not also support a higher evidentiary standard, such as a finding that there is a ''preponderance'' of evidence that a product actually causes a particular kind of adverse event. A sponsor's submission or FDA's acceptance of a CBE supplement does not necessarily mean that a drug product actually has caused any particular adverse event or type of adverse event.

Through § 201.57 (and the predecessor regulation, now codified at § 201.80 (21 CFR 201.80)), the agency set uniform standards for drug labeling, seeking to ensure that scientifically sound information is provided in the labeling of the drug. There is no reason the standard for adding new information to labeling should be different from the

[1] For devices, such supplements are also referred to as Special PMA Supplements. This document will use the term ''CBE supplement.''

standard for the initial labeling. If new information about a drug comes to light, a sponsor must make a decision as to whether the requirements of § 201.57 are met, and whether to submit a CBE supplement or other type of supplemental application. Failure to update labeling as required could result in regulatory actions or criminal penalties. If there is doubt as to whether the standard of § 201.57(c)(6) has been met, a sponsor should confer with FDA. The agency has clarified by regulation and guidance the types of supplements that should be filed to satisfy a sponsor's obligations to change a drug's labeling, and sponsors can consult with FDA on that question as well. *See* 21 CFR 314.70; Guidance for Industry: Changes to an Approved NDA or ANDA (November 1999) (*http://www.fda.gov/cder/guidance/2766fnl.pdf*).

This rule does not undermine a sponsor's responsibility to maintain its label—rather, it clarifies FDA's longstanding practice of requiring that sponsors must have sufficient evidence that the standards are met (§ 201.57(c) and Device Labeling Guidance).

With respect to comments suggesting that § 201.57 sets the standard for when sponsors must warn, but that a lower standard should be used under § 314.70(c)(6) for when a sponsor may warn, FDA has previously stated and reiterates here that it ''interprets the Act to establish both a 'floor' and a 'ceiling', such that additional disclosures of risk information can expose a manufacturer to liability under the act if the additional statement is unsubstantiated or otherwise false or misleading'' (71 FR 3922 at 3935, January 24, 2006) (the 2006 Physician Labeling Rule). FDA, therefore, declines to set different standards for when a sponsor must warn, as opposed to when it may warn of a particular risk or adverse event.

(Comment 2) Several comments stated that the rule would conflict with the intent of Congress. FDA in no way believes that this rule conflicts with Congressional intent. Another, comment stated that Congress did not intend for the act to preempt State law because there is no express preemption provision with respect to drugs. Several comments referred to the recently enacted Food and Drug Administration Amendments Act of 2007 (FDAAA) in support of this position. These comments suggest that for FDA to change the circumstances when sponsors could update their labeling by a CBE would conflict with congressional intent. FDAAA provided additional authority for FDA to require sponsors to make safety related changes to their labeling. The statute also included a rule of construction as part of a paragraph providing new authority to the Secretary to require labeling changes for drug products: ''This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under section 505(j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).'' (Section 505(o)(4)(I) of the act (21 U.S.C. 355(o)(4)(I))).

FDA does not believe that the absence of an express preemption provision with respect to drugs affects the application of the doctrine of implied preemption. Furthermore, FDA does not agree that the rule of construction affects FDA's ability to finalize the January 2008 proposed rule for several, independent reasons.[2] The January 2008 proposed regulation is consistent with the rule of construction. First, the rule of construction, by its terms, contemplates amendments to applicable regulations by its reference to ''successor regulations'' governing a sponsor's obligation to change product labeling. Congress, therefore, expressly acknowledged that FDA's regulations are not static and may be subsequently amended by the agency, as FDA is doing here. Second, the rule of construction operates to preserve Federal labeling obligations only in the face of an argument that ''this paragraph''—21 U.S.C. 355(o)(4), the new statutory provision permitting the Secretary of Health and Human Services (the Secretary) to impose labeling changes after meeting certain procedural requirements—''affects'' those responsibilities. Third, the rule of construction refers to, and therefore preserves only a sponsor's Federal-law (as opposed to State-law) ''responsibility[ies] * * * to maintain its label.'' As was noted in the U.S. Government's amicus brief at the merits stage in *Wyeth* v. *Levine*, No. 06–1249 (June 2008) (*http://www.justice.gov/osg/briefs/2007/3mer/1ami/2006-1249.mer.ami.pdf*), the rule of construction ''simply means that the relevant amendments do not affect obligations under other *federal* laws. It does not manifest any intent to depart from the application of ordinary principles governing the preemption of conflicting *state* laws. * * * [T]he text of the rule of construction that Congress actually enacted, which is limited to the effect of Section 901, itself preserves *complementary federal* requirements without evincing any intent to protect *conflicting state* laws.'' *Id.* at 32 (emphases in original).

(FDA has verified the Web site addresses in this document, but FDA is not responsible for subsequent changes after this document publishes in the **Federal Register**).

In other words, the rule of construction makes it clear that a sponsor cannot contend that, because the Secretary has the power to order new labeling changes, the sponsor no longer has an obligation to monitor post-marketing experiences and maintain its labeling under applicable Federal regulations. Indeed, it can maintain its labeling by using all existing tools, including through prior approval supplements, CBE-30 day supplements (§§ 314.70(c), 601.12(c) and 814.39(e)), and CBE supplements, along with other changes that may be reported in an annual report. Under both the rule of construction and this final rule, a sponsor still must update its labeling under Federal law ''to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug'' (§ 201.57(c)(6)), and add other risk information as required by the regulations (§ 201.57(c)).

If FDA were to interpret section 505(o)(4) of the act as eliminating the ability or obligation under Federal law of a sponsor to ''maintain'' its label, this would conflict with the rule of construction. But this final rule does not take away a sponsor's obligation to maintain its labeling under Federal law under appropriate circumstances. FDA is amending the text of the rules at issue here not because of the new powers in section 505(o)(4) of the act, but to clarify a sponsor's responsibilities and to make the text of the regulations match FDA's practice regarding CBE labeling changes, which predate FDAAA. Manufacturers continue to have a responsibility under Federal law, including the amended regulations under this rulemaking, to maintain their labeling and update the labeling with new safety information.

(Comment 3) One comment asserted that this rule could undermine consumer confidence in medical products and FDA. Consumer confidence in medical products and in FDA itself is critically important. This amendment is intended to clarify FDA's existing policies and is intended to ensure that scientifically valid and appropriately worded warnings will be provided in the approved labeling for medical products, and to prevent overwarning, which may deter

[2] FDA notes that the rule of construction in 21 U.S.C. 355(o)(4) on its face does not relate to medical devices.

appropriate use of medical products, or overshadow more important warnings. Accordingly, FDA does not agree that the rule will undermine confidence in medical products or the agency.

(Comment 4) One comment stated that the January 2008 proposed rule's reference to ''newly acquired information'' might undermine warnings in situations where a sponsor warns about a particular risk, but then later information demonstrates that the warning was insufficient.

FDA believes that the final rule addresses this concern. First, if later data or analyses demonstrate that prior warnings were insufficient, such data would clearly qualify as newly acquired information under the rule. Indeed, the rule expressly provides that new analyses of previously submitted information are considered new information that could be submitted by a CBE supplement (provided that other requirements for a CBE supplement are met). Therefore, if a sponsor determined that existing warnings were insufficient based on newly acquired information such as a new analysis of previously submitted data, the sponsor could still submit a CBE based on its new analysis of the previous data, provided the other requirements of the rule are met. Moreover, FDA now has new tools to address this situation, including its authority to require labeling changes under section 505(o) of the act.

(Comment 5) Several comments asserted that sponsors, not FDA, have the most information about their products and should have authority to revise their labeling as soon as new information comes to light.

Sponsors are still required to act promptly to add risk information to labeling (§ 201.57(c)(6)). This rule describes the standard for one type of change to the labeling. It is intended to clarify the circumstances in which sponsors are required to update labeling, not to undermine or remove a sponsor's obligation to modify labeling to reflect appropriate new information. Under FDA's regulations and this final rule, sponsors are required to warn as soon as appropriate new information comes to light (§ 201.57(c)(6)).

(Comment 6) Several comments stated that FDA did not have sufficient resources to review all potential warnings before labeling may be updated. As stated in the January 2008 proposed rule, FDA does not consider this amendment to substantively change the standards for submission of CBE or prior review supplements. The agency does not expect that it will increase the number of prior approval supplements or otherwise increase agency workloads.

(Comment 7) One comment requested that FDA clarify the relationship between the January 2008 proposed rule and statements made by FDA in the preamble to the 2006 Physician Labeling Rule (71 FR 3922). The comment inquired whether these changes ''supersede'' certain statements in the preamble to the 2006 Physician Labeling Rule. The agency believes that these amendments are consistent with prior statements by FDA, including those in the 2006 Physician Labeling Rule. The preamble to the 2006 Physician Labeling Rule set forth a number of principles regarding FDA's regulation of drug labeling. See, e.g. 71 FR 3922 at 3935 (''FDA interprets the act to establish both a 'floor' and a 'ceiling,' such that additional disclosures of risk information can expose a manufacturer to liability under the act'' * * *); ibid. (''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 * * *''). That preamble also set forth some non-exclusive examples of instances of preemption. Id. at 3935–3936 (stating that ''at least'' the enumerated cases are preempted). In a proposed rule that published in the **Federal Register** of May 29, 2008 (73 FR 30831 at 30861), FDA reiterated its support for the general principles underlying preemption set forth in the 2006 Physician Labeling Rule. In briefs recently filed in the Supreme Court of the United States and in testimony before Congress, FDA has also stated a more generally applicable rule that is consistent with the examples of preempted cases and the principles set forth in the preamble to the 2006 Physician Labeling Rule that: (1) The labeling requirements are not a mere minimum safety standard, but rather strike a balance between risks and benefits, and (2) FDA's regulations permit changes in labeling without prior approval only in narrow circumstances. Specifically, FDA has explained that State law claims that ''challenge labeling that FDA approved after being informed of the relevant risk'' are preempted. Brief of the United States as Amicus Curiae Supporting Petitioner, *Wyeth* v. *Levine*, No. 06–1249; Testimony of Deputy FDA Commissioner Randall Lutter before The House Committee on Oversight and Government Reform 5 (2008) *http://oversight.house.gov/documents/20080514142253.pdf* (''* * * State law claims are preempted if they challenge a design or labeling that FDA approved, after being informed of the relevant health risk * * *''). FDA reiterates and reaffirms here the positions set forth in those documents. FDA further notes that FDA there explained the interplay between this CBE regulation and preemption. FDA believes that this explanation sufficiently describes the relationship between this CBE regulation and the 2006 Physician Labeling Rule preamble.

(Comment 8) One comment requested that FDA make it clear that information previously known to the manufacturer, but not submitted to FDA, can be eligible for inclusion in a CBE amendment.

The term ''newly acquired information'' is defined in the final rule as ''information not previously submitted to FDA * * *.'' Accordingly, if information was previously known to the manufacturer, but not submitted to FDA, it would be ''newly acquired information'' that may qualify for inclusion in a CBE supplement (provided other requirements for a CBE supplement have been met).

(Comment 9) Several comments requested that FDA clarify the effect of this amendment on State tort liability and preemption, and one comment stated that this rule lacked a sufficient statement of irreconcilable conflict to justify the agency's assertion of implied preemption of ''all [S]tate law''. This rule does not preempt all State tort law and, furthermore, an ''irreconcilable conflict'' (i.e., an impossibility of compliance with both Federal and State law) is not the only basis for preemption of State law. Under implied preemption principles, if a State law frustrates Federal objectives, the State law is preempted. As a result, FDA's views on preemption, as explained elsewhere in this preamble, are amply justified by well-established principles of preemption. See *Geier* v. *American Honda Co.*, 529 U.S. 861 (2000); *English* v. *General Electric Co.*, 496 U.S. 72, 79 (1990); *Florida Lime & Avocado Growers, Inc.*, 373 U.S. 132, 142–43 (1963); *Hines* v. *Davidowitz*, 312 U.S. 52, 67 (1941). Moreover, liability imposed under State tort law constitutes a State ''requirement'' within the meaning of 21 U.S.C. 360k(a). See *Reigel* v. *Medtronic*, 128 S.Ct. 999, 1008–09 (2008). For further discussion of the scope of preemption, see the response to comment 7 of this document and section VIII. Federalism of this document.

(Comment 10) One comment requested that FDA develop an alternative mechanism to address proposed labeling changes. FDA believes that its regulations (as modified

in this final rule) provide appropriate and adequate regulatory pathways for updating and modifying labeling of drugs, biological products, and medical devices. See § 314.70(c) (for drugs), § 601.12(f)(2) (for biological products) and § 814.39(d) (for medical devices).

(Comment 11) One comment requested that FDA clarify the degree of certainty that is required for demonstrating causation under FDA's regulations. FDA does not believe that additional clarification of its labeling rules is necessary. The regulations set forth in § 201.57 provide relevant standards for when information is appropriate for inclusion in labeling, including causation standards. FDA believes that standard is sufficiently clear and objective.

(Comment 12) One comment noted that the preamble to the January 2008 proposed rule stated that ''FDA intends to consider information 'newly acquired' if it consists of data, analyses, or other information not previously submitted to the agency, *or submitted within a reasonable time period prior to the CBE supplement* * * *.'' (73 FR 2848 at 2850) (emphasis added). The comment requested that FDA clarify the temporal relationship between the submission of new information to FDA and a subsequent CBE supplement. FDA agrees that this issue should be clarified here so as to provide greater guidance to sponsors in determining their regulatory obligations. Newly acquired information includes information not previously submitted to FDA. If a sponsor submits data or analysis to FDA as part of a discussion of the kind of labeling change that would be appropriate and decides as a result of that discussion to prepare and submit a CBE supplement, then the supporting data or analysis will not be considered ''previously submitted to FDA''—even if it was not first submitted on the same day as the CBE supplement. This allows for a labeling change when a sponsor submits data or analysis to FDA before the sponsor has completed its CBE supplement, and is also designed so as not to deter the sponsor from submitting the information for fear that such a submission would preclude the sponsor from making a CBE change. This clarification is designed to address the situation where a sponsor submits data or analyses to FDA as part of the process of determining what labeling change is appropriate, and then diligently and promptly prepares a CBE supplement.

Moreover, FDA also notes that the definition of ''newly acquired information'' includes ''new analyses'' of previously submitted information. If a sponsor submits information to FDA, then later conducts a new analysis that demonstrates that labeling should be revised to account for that information, a CBE would be appropriate. For example, if the sponsor submits adverse event information to FDA, and then later conducts a new analysis of data showing risks of a different type or of greater severity or frequency than did reports previously submitted to FDA, the sponsor meets the requirement for ''newly acquired information''.

(Comment 13) One comment requested that FDA clarify the relationship between the CBE regulations and risk evaluation and mitigation strategies (REMS) for drugs and biological products.

Under the new authority provided in FDAAA, FDA may require the submission of a proposed REMS if FDA believes that such a strategy is necessary to ensure that the benefits of the drug outweigh its risks. A REMS must be approved by FDA (21 U.S.C. 355–1(h)), as must proposed modifications to a REMS (21 U.S.C. 355–1(g)). Accordingly, if the labeling for a drug describes an element of an approved REMS, the sponsor must receive prior approval of any labeling changes that would necessitate a change to the sponsor's REMS. For example, if a REMS included elements to assure safe use under section 505–1(f) of the act, some of those elements might be described in the approved labeling for the drug or biologic. If the sponsor became aware of newly acquired safety information that would otherwise be appropriate for a CBE, but would require the sponsor to modify an element to assure safe use that is required under a REMS, the sponsor would need to receive prior approval of the labeling change. However, if the newly acquired information is related to the concern leading to a REMS but the proposed change to labeling could be made without requiring a modification of the REMS, the approved labeling for the product could be strengthened without prior approval. For example, if a REMS was imposed requiring periodic monitoring of liver enzymes to ensure the risk of liver toxicity for a drug was outweighed by the benefits of the drug, strengthening warnings related to that risk may be made by a CBE supplement (provided that other requirements for a CBE supplement are met and that the change can be made without modifying the REMS).

(Comment 14) One comment requested that FDA clarify that any change to the Highlights section of the labeling of a drug or biologic must be made by a prior approval supplement.

The agency agrees that this issue should be clarified, but does not agree that changes to Highlights can never be accomplished by a CBE supplement. Under existing regulations, changes to the Highlights are classified as a ''major change,'' requiring a prior approval supplement (§ 314.70(b)(2)(v)(C)). Accordingly, in most cases, changes to Highlights will require a prior approval supplement. However, in the preamble to the January 2008 proposed rule, we noted that FDA could waive this limitation under § 314.90 or request that a sponsor make a change to Highlights under § 314.70(c)(6)(iii)(E) or § 601.12(f)(2)(E). These provisions authorize FDA to waive the Highlights limitation or otherwise ask the sponsor to submit a CBE supplement in appropriate circumstances.

(Comment 15) One comment requested that FDA clarify that sponsors may not use the CBE process to submit labeling changes for drugs or biological products under section 505(o) of the act.

FDA disagrees with this comment. Under section 505(o) of the act, FDA must notify the sponsor if the agency becomes aware of new safety information that should be included in the labeling for a particular drug or biologic. Following that notification, the sponsor must submit a ''supplement'' proposing changes to the labeling or submit a statement explaining the reasons why the sponsor believes the labeling change is not warranted. Nothing in section 505(o) limits this ''supplement'' to a prior approval supplement. In fact, to effect the change most rapidly, FDA may request that the sponsor file a CBE supplement under these circumstances.

(Comment 16) One comment requested that FDA provide a comprehensive, written response to every CBE supplement submitted to the agency by a sponsor, describing FDA's grounds for approval, disapproval, or, as the case may be, request for modification to the submitted CBE supplement. FDA disagrees with this comment. The comment failed to provide a compelling justification for this proposal.

(Comment 17) One comment asserted that if FDA finalizes this rule, it will create a disincentive for sponsors to conduct additional trials of their products because the sponsors would have to provide additional warnings if causation is shown. Under current regulations, sponsors must warn about risks of approved products if the requirements for updating labeling are triggered. This rule does not change those standards. FDA therefore does not believe that it will change the incentives

for sponsors to conduct new clinical trials.

(Comment 18) One comment stated that the rule would unjustifiably impose an added regulatory burden. FDA disagrees with this comment, as this rule does not add to the existing regulatory burden. Rather, as previously stated, the rule simply affirms that a CBE supplement is appropriate to amend the labeling for an approved product only to reflect newly acquired information and makes it clear that a CBE supplement may be used to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is sufficient evidence of a causal association with the drug, biologic, or medical device. For further discussion of the regulatory burden, see sections V. Analysis of Impacts and VI. Paperwork Reduction Act of this document.

IV. Legal Authority

As explained in the January 2008 proposed rule, FDA's legal authority to modify §§ 314.70, 601.12, and 814.39 arises from the same authority under which FDA initially issued these regulations. The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 *et seq.*) and the Public Health Service Act (42 U.S.C. 201 *et seq.*) provide FDA with authority over the labeling for drugs, biological products, and medical devices, and authorize the agency to enact regulations to facilitate FDA's review and approval of applications regarding the labeling for such products.

Section 502 of the act (21 U.S.C. 352) provides that a drug, biologic,[3] or medical device will be considered misbranded if, among other things, the labeling for the product is false or misleading in any particular (21 U.S.C. 352(a)). Under section 502(f) of the act, a product is misbranded unless its labeling bears adequate directions for use, including adequate warnings against, among other things, unsafe dosage or methods or duration of administration or application. Moreover, under section 502(j) of the act, a product is misbranded if it is dangerous to health when used in the manner prescribed, recommended, or suggested in its labeling.

In addition to the misbranding provisions, the premarket approval provisions of the act authorize FDA to require that product labeling provide adequate information to permit safe and effective use of the product. Under section 505 of the act (21 U.S.C. 355), FDA will approve an NDA only if the drug is shown to be both safe and effective for its intended use under the conditions set forth in the drug's labeling. Similarly, under section 515(d)(2) of the act (21 U.S.C. 360e(d)(2)), FDA must assess whether to approve a PMA according to the ''conditions of use prescribed, recommended, or suggested in the proposed labeling'' of the device. Section 701(a) of the act (21 U.S.C. 371(a)) authorizes FDA to issue regulations for the efficient enforcement of the act.

Section 351 of the PHS Act (42 U.S.C. 262) provides additional legal authority for the agency to regulate the labeling of biological products. Licenses for biological products are to be issued only upon a showing that the biological product is safe, pure, and potent (42 U.S.C. 262(a)). Section 351(b) of the PHS Act (42 U.S.C. 262(b)) prohibits any person from falsely labeling any package or container of a biological product. FDA's regulations in part 201 apply to all prescription drug products, including biological products.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because these amendments to existing regulations are intended only to codify the agency's interpretation of current policy, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $127 million, using the most current (2006) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

The objective of the final rule is to make explicit the agency's view of when a change to the labeling of an approved drug, biologic, or medical device may be made in advance of the agency's review of the change. More specifically, the purpose of the final rule is to clarify that a CBE supplement is appropriate to amend the labeling for an approved product only to reflect newly acquired information, and to clarify that a CBE supplement may be used to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is reasonable evidence of a causal association with the approved drug, biologic, or medical device. FDA does not consider this to be a substantive policy change, and it does not alter the agency's current practices with respect to accepting or rejecting labeling changes proposed by a CBE supplement.

Because this final rule does not establish any new regulatory or recordkeeping requirements, the agency does not expect that there will be any associated compliance costs. The final rule simply clarifies the agency's interpretation of when sponsors are allowed to add information regarding the risks associated with a product to the labeling without prior approval from FDA. It is expected that these clarifications will promote more effective and safe use of approved drug, biologic, and medical device products. The agency believes that any potential impacts of these amendments to existing regulations will be minimal because this action does not represent a substantive change from current policy. We did not receive any comments on the January 2008 proposed rule that would cause us to reconsider these determinations.

VI. Paperwork Reduction Act of 1995

This final rule refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 35013520). The collections of information in 21 CFR part 314 have been approved under OMB Control No. 0910–0001 (expires May 31, 2011); 21 CFR part 601 have been approved under OMB Control No. 0910–0338 (expires June 30, 2010); and 21 CFR part 814 have been approved under OMB Control No. 0910–0231 (expires November 30, 2010). Therefore,

[3] Although the language of section 502 of the act refers only to drugs and devices, it is also applicable to biologics. (See 42 U.S.C. 262(j)).

clearance by OMB under the PRA is not required.

VII. Environmental Impact

The agency has determined under 21 CFR 25.31(a) and 25.34(e) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VIII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. Section 4(a) of the Executive order requires agencies to ''construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Like any Federal requirement, if a State law requirement makes compliance with both Federal law and State law impossible, or would frustrate Federal objectives, the State requirement would be preempted. See *Geier* v. *American Honda Co.*, 529 U.S. 861 (2000); *English* v. *General Electric Co.*, 496 U.S. 72, 79 (1990); *Florida Lime & Avocado Growers, Inc.*, 373 U.S. 132, 142–43 (1963); *Hines* v. *Davidowitz*, 312 U.S. 52, 67 (1941). Moreover, if a State requirement constitutes a requirement that is different from, or in addition to, a Federal requirement applicable to a medical device, and which relates to the safety or effectiveness of the device, the State law requirement is preempted. See 21 U.S.C. 360k(a), *Reigel* v. *Medtronic*, 128 S.Ct. 999 (2008). In addition to the discussion above in response to comment 7 of this document, FDA notes that, at least when a sponsor did not meet the standard to change its labeling through a CBE supplement under this rule to include the warning a plaintiff alleges should have been added to labeling, State law liability that is premised on a failure to warn is preempted.

FDA has provided the States with an opportunity to comment on the January 2008 proposed rule. Specifically, following publication of the January 2008 proposed rule in the **Federal Register**, FDA issued a ''Dear Colleague'' letter on January 17, 2008. The purpose of this letter was to alert officials in various organizations within the 50 States about the rulemaking, including officials with State pharmacy boards, State medical boards, health commissioners, and drug program directors. The letter briefly explained what the rulemaking would do when it became final and it encouraged the officials to review the January 2008 proposed rule and provide FDA with any comments they may have concerning the impact this rule may have on the following: (1) On the States, (2) on the relationship between the national government and the States, or (3) on the distribution of power and responsibilities among the various levels of government. FDA received one comment that appears to be in response to this ''Dear Colleague'' letter. This comment is addressed in the final rule.

List of Subjects

21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

21 CFR Part 601

Administrative practice and procedure, Biologics, Confidential business information.

21 CFR Part 814

Administrative practice and procedure, Confidential business information, Medical devices, Medical research, Reporting and recordkeeping requirements.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR parts 314, 601, and 814 are amended as follows:

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

■ 1. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 356a, 356b, 356c, 371, 374, 379e.

■ 2. Section 314.3 is amended in paragraph (b) by alphabetically adding the definition for ''newly acquired information'' to read as follows:

§ 314.3 Definitions.

* * * * *

(b) * * *

Newly acquired information means data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

* * * * *

■ 3. Section 314.70 is amended by revising paragraphs (c)(6)(iii) introductory text and (c)(6)(iii)(A) to read as follows:

§ 314.70 Supplements and other changes to an approved application.

* * * * *

(c) * * *

(6) * * *

(iii) Changes in the labeling to reflect newly acquired information, except for changes to the information required in § 201.57(a) of this chapter (which must be made under paragraph (b)(2)(v)(C) of this section), to accomplish any of the following:

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

* * * * *

PART 601—LICENSING

■ 4. The authority citation for 21 CFR part 601 continues to read as follows:

Authority: 15 U.S.C. 1451–1561; 21 U.S.C. 321, 351, 352, 353, 355, 356b, 360, 360c–360f, 360h–360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263, 264; sec 122, Pub. L. 105–115, 111 Stat. 2322 (21 U.S.C. 355 note).

■ 5. Section 601.12 is amended by revising paragraphs (f)(2)(i) introductory text and (f)(2)(i)(A), and by adding paragraph (f)(6) to read as follows:

§ 601.12 Changes to an approved application.

* * * * *

(f) * * *

(2) *Labeling changes requiring supplement submission—product with a labeling change that may be distributed before FDA approval.* (i) An applicant shall submit, at the time such change is made, a supplement for any change in the package insert, package label, or container label to reflect newly acquired information, except for changes to the package insert required in § 201.57(a) of this chapter (which must be made under paragraph (f)(1) of this section), to accomplish any of the following:

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

* * * * *

(6) For purposes of paragraph (f)(2) of this section, information will be considered newly acquired if it consists of data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

* * * * *

PART 814—PREMARKET APPROVAL OF MEDICAL DEVICES

■ 6. The authority citation for 21 CFR part 814 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 353, 360, 360c–360j, 371, 372, 373, 374, 375, 379, 379e, 381.

■ 7. Section 814.3 is amended by adding paragraph (o) to read as follows:

§ 814.3 Definitions.

* * * * *

(o) *Newly acquired information* means data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

■ 8. Section 814.39 is amended by revising paragraphs (d)(1) introductory text and (d)(2)(i) to read as follows:

§ 814.39 PMA supplements.

* * * * *

(d)(1) After FDA approves a PMA, any change described in paragraph (d)(2) of this section to reflect newly acquired information that enhances the safety of the device or the safety in the use of the device may be placed into effect by the applicant prior to the receipt under § 814.17 of a written FDA order approving the PMA supplement provided that:

* * * * *

(2) * * *

(i) Labeling changes that add or strengthen a contraindication, warning, precaution, or information about an adverse reaction for which there is reasonable evidence of a causal association.

* * * * *

Dated: August 19, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–19572 Filed 8–21–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 100

[Docket No. USCG–2008–0424]

Special Local Regulation; U.S. Nationals Waterski Racing Championship; Mission Bay, San Diego, CA

AGENCY: Coast Guard, DHS.

ACTION: Notice of enforcement of regulation.

SUMMARY: The Coast Guard will enforce the U.S. Nationals Waterski Racing Championship special local regulation on Mission Bay from 8 a.m. on October 10, 2008 through 5 p.m. on October 12, 2008. This action is necessary to provide for the safety of the participants, crew, spectators, participating vessels, and other vessels and users of the waterway. During the enforcement period, no person or vessel may enter the special local regulation without permission of the Captain of the Port.

DATES: The regulations in 33 CFR 100.1101 will be enforced from 8 a.m. on October 10, 2008 through 5 p.m. on October 12, 2008.

FOR FURTHER INFORMATION CONTACT: Petty Officer Kristen Beer, USCG, Waterways Management, U.S. Coast Guard Sector San Diego at (619) 278–7233.

SUPPLEMENTARY INFORMATION: The Coast Guard will enforce the special local regulation for the U.S. Nationals Waterski Racing Championship in 33 CFR 100.1101 on October 10, 2008, from 8 a.m. to 7 p.m., October 11, 2008, from 8 a.m. to 7 p.m., and October 12, 2008, from 8 a.m. to 7 p.m.

Under the provisions of 33 CFR 100.1101, a vessel may not enter the regulated area, unless it receives permission from the COTP. Spectator vessels may safely transit outside the regulated area but may not anchor, block, loiter in, or impede the transit of participants or official patrol vessels. The Coast Guard may be assisted by other Federal, State, or local law enforcement agencies in enforcing this regulation.

This notice is issued under authority of 33 CFR 100.1101(a) and 5 U.S.C. 552(a). In addition to this notice in the **Federal Register**, the Coast Guard will provide the maritime community with extensive advance notification of this enforcement period via the Local Notice to Mariners, marine information broadcasts, local radio stations and area newspapers. If the COTP or his designated representative determines that the regulated area need not be enforced for the full duration stated in this notice, he or she may use a Broadcast Notice to Mariners to grant general permission to enter the regulated area.

Dated: August 8, 2008.

T.H. Farris,

Captain, U.S. Coast Guard, Captain of the Port Sector San Diego.

[FR Doc. E8–19532 Filed 8–21–08; 8:45 am]

BILLING CODE 4910–15–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 165

[Docket Number USCG–2008–0769]

Oregon Symphony Celebration Fireworks Display, Portland, OR

AGENCY: Coast Guard, DHS.

ACTION: Notice of enforcement of regulation.

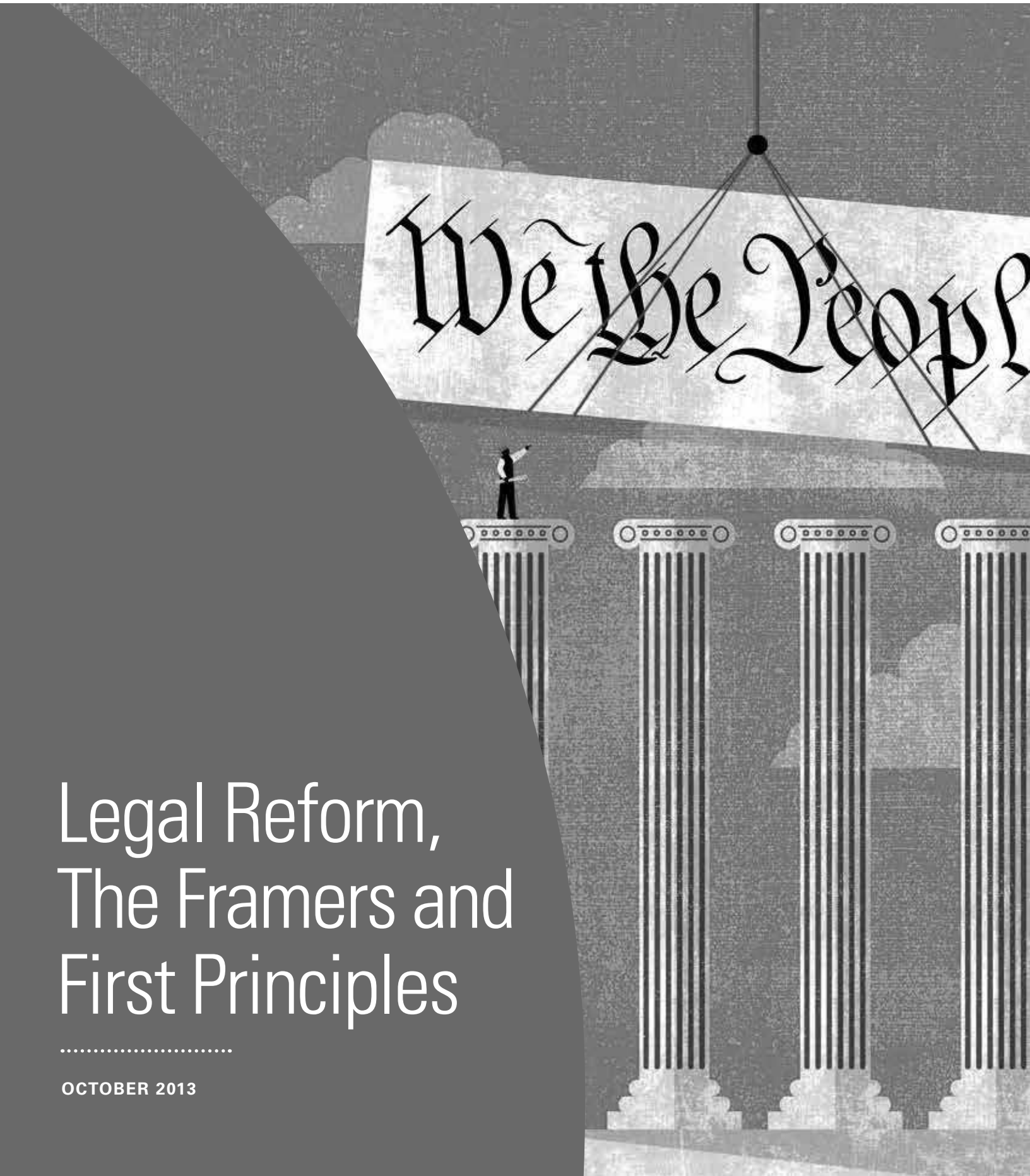
SUMMARY: The Coast Guard will enforce the ''Oregon Symphony Celebration Fireworks Display safety zone on the Willamette River''; from 8:30 p.m. through 11:30 p.m. on August 28, 2008. This action is necessary to provide a safe display for the public and to keep them clear of the fall out area of the fireworks. During the enforcement period, no person or vessel may enter the safety zone without permission of the Captain of the Port Portland or his designated representative.

DATES: The regulations in 33 CFR 165.1315(a)(7) will be enforced from 8:30 p.m. through 11:30 p.m. on August 28, 2008.

FOR FURTHER INFORMATION CONTACT: BM2 Joshua Lehner, Sector Portland Waterways Management at (503) 247–4015.

SUPPLEMENTARY INFORMATION: The Coast Guard will enforce the safety zone for the Oregon Symphony Celebration Fireworks Display in 33 CFR 165.1315(a)(7) on August 28, 2008 from 8:30 p.m. to 11:30 p.m.

U.S. CHAMBER
Institute for Legal Reform



Legal Reform, The Framers and First Principles

OCTOBER 2013

U.S. CHAMBER
Institute for Legal Reform

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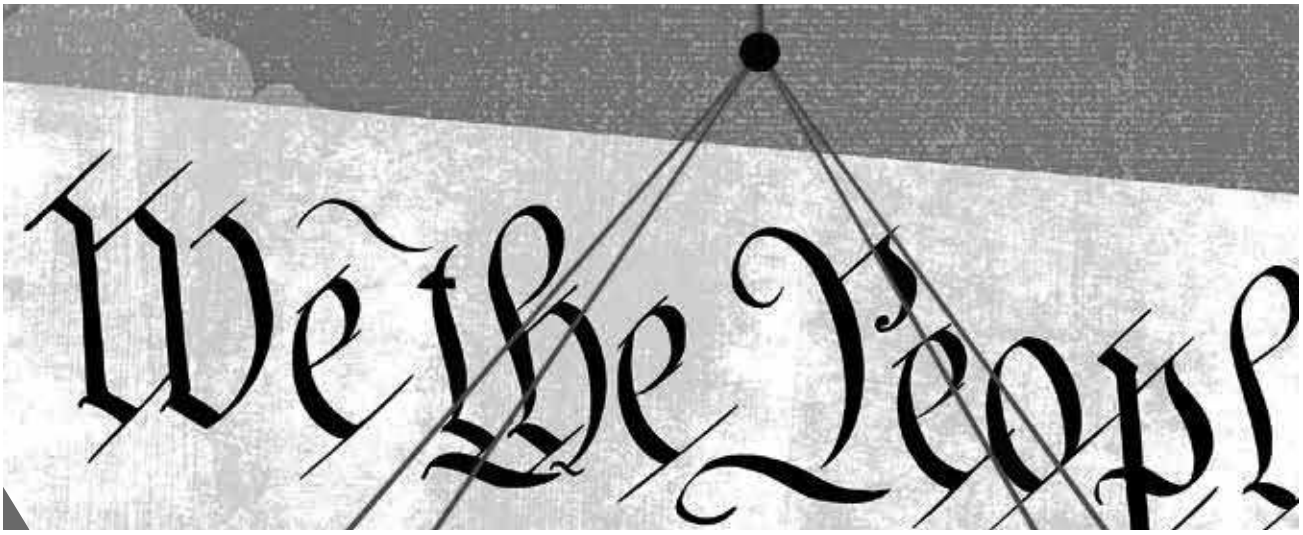
Executive Summary

The validity of legal reform efforts is a hotly debated topic in legislatures and courts across the country. All too often, this discussion overlooks the views of the Framers, which can helpfully inform policy views on both sides of the debate. This paper attempts to return the discussion to first principles by evaluating how the Framers' views on separation of powers, constitutional values, and federalism can help inform the national dialogue on legal reform.

As explained in the discussion that follows, the Framers' views on the separation of powers would cause them to view state legislatures as the central actor in legal reform efforts and would make them highly skeptical of state judicial actions invalidating legislatively-enacted legal reforms. At the same time, the Constitution generally, and the first ten amendments in particular, reflect a dedication to the rule of law that should inform the debate over legal reform. Finally, the Framers' innovative system of federalism counsels in favor of, not against, legal reform efforts at the state level.



Legal Reform and the Separation of Powers

Any discussion of the Constitution and the Framers' views should begin with the structural provisions of the Constitution. While much modern discussion and litigation focuses on the amendments to the Constitution, many of which expressly protect individual rights, the Framers were focused first and foremost on establishing a workable structure for the new federal government.

Indeed, the Federalist Papers, widely considered the definitive source for the views of the Framers, were aimed exclusively at securing the ratification of the unamended Constitution. And as the Supreme Court has emphasized in recent years, those structural protections exist not primarily to protect the prerogatives of any one part of the government, but to "protect[] individual liberty."[1]

The separation of powers was the animating principle for the structure of the new federal government under the Constitution. It is no accident that the Constitution was divided into articles, and the first three articles addressed the powers of the Congress, the President, and the Judiciary respectively. "The structure of our Government as conceived by the Framers of our Constitution disperses the federal power among the three branches—the Legislative, the Executive, and the Judicial."[2] The Framers "viewed the principle of separation of powers as the absolutely central guarantee of a just Government" and "essential to the preservation of liberty."[3] As James Madison observed in Federalist No. 47, "[n]o political truth is certainly of greater intrinsic value, or is stamped with the authority of more enlightened patrons of liberty."[4] "Without a secure structure of separated powers, our Bill of Rights would be worthless, as are the bills of rights of many nations of the world that have adopted, or even improved upon, the mere words of ours."[5]

A central tenant of the Framers' belief in divided government is what has been loosely described as a system of "checks and balances." Each branch is vested with core powers—legislative, executive, and judicial respectively—which are to

be exercised exclusively by that branch. Thus, for example, the Framers allocated to Congress—and Congress alone—the ability to make laws. Article I, § 1, cl.1, states unequivocally that "[a]ll legislative Powers herein granted shall be vested" in Congress. But at the same time the Constitution grants all the legislative power to Congress and all the executive power to the executive, it also puts a check on the tendencies of any one branch toward self-aggrandizement by giving each branch a "'partial agency'" in the affairs of the others.[6] The Constitution does this not by dividing powers such that the judiciary exercises a little of the legislative power, but by granting each branch the authority to exercise its own power to check the authority of the other branches. Thus, for example, the President wields the executive power of the veto and the judiciary reviews the constitutionality of acts of Congress, both of which place a check on Congress' ability to exercise "[a]ll legislative Powers herein granted."

Another example is Congress' authority to pass legislation that shapes the way the executive and judicial branches discharge their core functions. Article I, § 8, cl. 18, makes plain that the legislative power includes the power "[t]o make all Laws which shall be necessary and proper for carrying into Execution the foregoing powers, and all other Powers vested by this Constitution in the Government of the United States . . . ." This "necessary and proper" clause is expressly not limited to augmenting Congress' own authority, but also clearly extends to enacting laws necessary and proper to carry out the powers vested in the other branches of the "Government of the United States."

Congress' power to enact laws that impact the way the Article III courts discharge their judicial function is particularly clear in the Constitution. In addition to the necessary and proper clause, Article III, § 1, provides that "[t]he judicial Power of the United States, shall be vested in one Supreme Court, and in such inferior Courts as the Congress may from time to time ordain and establish." As Justice Samuel Chase noted just before the close of the 18th century, "the truth is, that the disposal of the judicial power (except in a few specified instances) belongs to congress. If congress has given the power to this court, we possess it, not otherwise . . . ."[7] That is because, "[i]n republican government, the legislative authority necessarily predominates."[8]

The Judiciary Act of 1789, adopted during Congress' first session, provides a particularly good window into the Framers' views on the nature and extent of legislative powers vis-à-vis the operation of the judiciary. That Act addressed everything from the fundamental—such as setting up the Supreme Court—to the smallest details—such as where, when, and how the courts would operate—and everything in between, including the scope of the courts' jurisdiction and powers.[9] The Act even addressed the process for selecting juries.[10] And the example set by the first Congress is still followed today. Congress regularly passes laws, such as the Class Action Fairness Act and even the Federal Rules of Evidence, that govern the details of how courts resolve legal disputes.

To be sure, the Framers' views regarding the critical importance of the separation of powers and the interaction between the legislature and the judiciary were directed at the newly-formed federal

government, and they do not directly govern the separation of powers applicable in state systems. For example, no one thinks Nebraska violates the federal Constitution by having a unicameral legislature. Nonetheless, much of the Framers' wisdom about the separation of powers generally and the division of authority between the legislative and judicial branches in particular applies with equal force to state governments. Thus, even though the federal Constitution does not directly regulate the separation of powers within states, the Framers' views should still inform the policy debate about the proper role for state legislatures in legal reform efforts at the state level. The Framers who granted Congress the power to establish inferior courts, determine their jurisdiction, and enact rules necessary and proper for the exercise of that jurisdiction would clearly envision state legislatures as having the primary role in legal reform efforts. The members of the Framing generation who sat in the first Congress and enacted laws dictating the details of how federal juries would be selected would certainly be puzzled by state court interference with legal reform efforts, such as the Oklahoma Supreme Court's invalidation of legislation reforming the State's civil justice system.[11] That comprehensive reform package, which was enacted by an overwhelming majority of elected lawmakers, is exactly the sort of thing that the Framers would have thought should be left to the discretion of the legislature.

"The Framers who granted Congress the power to establish inferior courts, determine their jurisdiction, and enact rules necessary and proper for the exercise of that jurisdiction would clearly envision state legislatures as having the primary role in legal reform efforts."

Legal Reform and the Rule of Law

The Framers likely would have viewed legal reform efforts as well within the heartland of legislative powers. The Framers likewise would have assumed that the legislative branches—both state and federal—would have substantial discretion to adopt rules for ensuring the fair conduct of litigation in the courts.

In extreme cases, some litigation excesses and some legislative responses could implicate the constitutional limits on legislative power. But even where those constitutional limits are not actually violated, the principles they reflect can inform the policy debate over legal reform. First and foremost, legal reform efforts should take account of due process principles, and legislatures should ensure their reforms are consistent with the letter and spirit of those principles. Seventh Amendment values are also implicated by state legal reform efforts and should be respected, although that Amendment still grants state legislatures considerable latitude in deciding which questions should go to the jury. Moreover, other constitutional constraints against taking of property, bills of attainder, and denials of equal protection can influence the debate.

The Due Process Clause

The Due Process Clause prohibits the deprivation "of life, liberty, or property, without due process of law."[12] The values embodied in the Due Process Clause were of paramount importance to the Framers and should play an important part in the debate surrounding legal reform. The Due Process Clause reflects the Framers' dedication to the rule of law and aversion to arbitrary action. "The touchstone of due process is protection of the individual against arbitrary action of government."[13] One critical component of the due process guarantee is the concept of "fair notice"—that litigants have clear expectations about whether conduct is illegal and the consequences of any illegality.[14] Indeed, "notice and opportunity to be heard" are the basic building blocks of modern due process jurisprudence and protect against arbitrary deprivations of life, liberty, and property.[15] Thus, legal reform proposals that make state court litigation more predictable and less arbitrary promote the rule of law and due process values. Reasonable people can differ as to which rules are superior in guaranteeing uniform, predictable, and just results. But a policy debate that proceeds on the basis of those values is one the Framers would clearly understand.

The modern Supreme Court has developed and applied these due process principles in the punitive damages context. The Supreme Court has repeatedly "recognized that the Constitution imposes a substantive limit on the size of punitive damages awards."[16] As the Court stated in *BMW of N. America v. Gore*, 517 U.S. 559 (1996), "[t]he Due Process Clause of the Fourteenth Amendment prohibits a State from imposing a 'grossly excessive' punishment on a tortfeasor," and mandates that punitive damages "bear a 'reasonable relationship' to compensatory damages."[17] Not surprisingly, the Court has grounded this jurisprudence in principles of notice. "Elementary notions of fairness enshrined in our constitutional jurisprudence dictate that a person receive fair notice not only of the conduct that will subject him to punishment, but also of the severity of the penalty that a State may impose."[18] But notice is not an end in itself; it is a critical means to avoid the arbitrary deprivation of property. "To the extent an award is grossly excessive, it furthers no legitimate purpose and constitutes an arbitrary deprivation of property" in violation of the Due Process Clause.[19] While the most extreme punitive damages awards actually violate the constitutional due process limits articulated by the Supreme Court, those same constitutional principles can inform the debate over legal reform proposals that can operate prophylactically to prevent due process violations from happening and to promote results that are predictable and fair, rather than arbitrary.[20]

The Supreme Court's punitive damages jurisprudence also underscores the importance of appellate review to prevent arbitrary and unpredictable results. Indeed, the first of the Court's modern punitive damages cases to find a constitutional violation, *Honda v. Oberg*, 512 U.S. 415 (1994), focused on the need for judicial review. In *Oberg*, the Court observed that "[j]udicial review of the size of punitive damages awards has been a safeguard against excessive verdicts for as long as punitive damages have been awarded."[21] The Court emphasized that such review provides much-needed "protection against arbitrary deprivations of property" and ensures that fundamental notions of justice and fair play are observed.[22] Thus, the failure of the Oregon courts to provide meaningful judicial review of punitive damages awards violated the Due Process Clause. Notably, even Justices Scalia and Thomas, who have been skeptical of the Court's later punitive damages cases, agreed that Oregon violated procedural due process by not providing judicial review.

While the Court has developed these due process principles with greater clarity in the punitive damages context, they are by no means limited to that context. The same basic principles extend to other departures from fair adjudication. For example, a party that "receive[s] neither notice of, nor sufficient representation in," litigation is not bound by the outcome of that litigation as a matter of federal due process.[23] Finally, it should be underscored that while the Due Process Clause puts outer limits on truly arbitrary results (like the award struck down in *Gore*) or anomalous state rules (like the absence of judicial review in *Oberg*), the Constitution generally leaves substantial latitude for state legislative efforts, especially those that promote due process values. For that reason, the Due Process Clause is not an obstacle to legal

reform proposals that promote predictability and fair notice. The Supreme Court has noted that "it is not at all clear that the Due Process Clause in fact requires that a legislatively enacted compensation scheme either duplicate the recovery at common law or provide a reasonable substitute remedy."[24] It is well established that "[a] person has no property, no vested interest, in any rule at common law."[25] The "Constitution does not forbid the creation of new rights, or the abolition of old ones recognized by the common law, to attain a permissible legislative object," "despite the fact that 'otherwise settled expectations' may be upset thereby."[26] And, in all events, due process is not offended in this context so long as a law "provide[s] a reasonably just substitute for the common-law or state tort law remedies it replaces."[27]

Legislatures should ensure that their legal reform efforts not only avoid actual constitutional violations, but further the rule of law values that underscore the Framers' concern with due process. As examples, rules that promote predictability, limit arbitrariness, provide notice and ensure meaningful judicial review—such as expert evidence reforms and laws that increase transparency in tort litigation—are consistent not just with the minimal requirements of due process, but with the broader values the constitutional protection promotes.

The Seventh Amendment

The Seventh Amendment provides that "[i]n Suits at common law, where the value in controversy shall exceed twenty dollars, the right to trial by jury shall be preserved . . . ."[28] The Seventh Amendment, unlike virtually every other provision of the Bill of Rights, has not been treated as incorporated into the Fourteenth Amendment and thus does not apply to the states.[29] Indeed, the Framers' decision not to address the availability of jury trials in state courts was a deliberate accommodation of the variety of approaches employed by different states. As soon-to-be-Justice James Iredell explained in 1788: "[t]he States in these particulars differ very much in their practice from each other."[30] Thus, a uniform federal rule applicable to state courts was not practical; "if they had pleased some States they must have displeased others."[31] Alexander Hamilton made a similar point in Federalist No. 83, and elaborated on "[t]he great difference between the limits of the jury trial in different states," and thus "no general rule could have been fixed upon."[32] But, as with other constitutional provisions not directly applicable to the states, the values that underlie the Seventh Amendment should inform the policy debate about legal reform at the state level.

The Seventh Amendment reflects the Framers' "concern[] with preserving the right of trial by jury in civil cases where it

existed at common law."[33] While some commenters have contended that legal reform and Seventh Amendment values are incompatible, that is simply not the case. To be sure, a wholesale legislative effort (as opposed to private agreement) to take away damages issues from a jury and give them to a judge when a statutory or common law cause of action is at issue may raise questions with Seventh Amendment principles that would need to be addressed. As the Supreme Court recognized in *Feltner v. Columbia Pictures Television, Inc.*, 523 U.S. 340 (1998), "[i]t has long been recognized that 'by the law the jury are the judges of damages.'"[34] "'[T]he common law rule as it existed at the time of the adoption of the Constitution' was that 'in cases where the amount of damages was uncertain[,] their assessment was a matter so peculiarly within the province of the jury that the Court should not alter it.'"[35]

That said, any argument that Seventh Amendment values reflected in cases like *Feltner* conflict with legal reform efforts cannot survive a careful reading of *Feltner* itself. *Feltner* found only that a plaintiff bringing an infringement suit under the Copyright Act was entitled to have a jury determine the amount of his or her statutory damages, not that a plaintiff had a right to have a jury exceed the limits set by Congress on such damages. The Copyright Act authorizes damages either "in a sum of not less than $500 or more than $20,000," or "a sum of not more than $100,000," depending on the circumstances.[36] There was no hint in *Feltner* that the statutory damages cap imposed by the Copyright Act was in any way constitutionally problematic. To the contrary, the Court emphasized the long historical compatibility of statutory damage limits, including a specified liquidated damage amount per page copied, and the jury's role in adjudicating the facts necessary to apply the legislatively-chosen damages provision.

In short, the legislature retains substantial discretion to enact laws that determine what facts are legally relevant. The fact that a legislative initiative may make a particular factual inquiry—for example, the amount of non-economic damages above a cap—legally irrelevant does not intrude on the jury's role, as long as the jury determines the facts that remain legally relevant. This is underscored by a review of jury practice during the Framers' time. As Justice James Iredell observed in 1788: "[i]n respect to the trial by jury in civil cases, it must be observed that it is a mistake to suppose that such a trial takes place in all civil cases now. Even in the common law courts, such a trial is only had where facts are disputed between the parties, and there are even some facts triable by other methods."[37] At the Founding, the jury's role was defined

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by three procedures: the "case stated," the "demurrer to the evidence," and the "special verdict."[38] Most relevant for present purposes, "[t]he 'case stated' procedure was a trial device employed to bypass the jury when only undisputed facts remained in a case. When this occurred, the jury's role was reduced to a mere formality."[39] The jury remained on hand to resolve fact issues in case they arose, but was otherwise uninvolved in the proceedings.[40] "The 'case stated' procedure, therefore, demonstrates that, at the time the Constitution was adopted, the jury's sole function was to resolve disputed facts."[41]

Accordingly, to the extent that legal reform is structured so as to retain the jury's role in assessing the facts that remain relevant, state legislators can determine which facts remain relevant while fully respecting Seventh Amendment values. For example, allowing a jury to determine the amount of damages suffered by a plaintiff, but then allowing a court to ascertain the legal consequences of that assessment, including the application of any statutory cap, would not implicate the values underlying the Seventh Amendment. A judge who "merely implement[s] a policy decision of the legislature in applying the law enacted by the legislature when it predetermined the extent and amount of damages that it, the legislature, would allow in a malpractice action" does not "reexamin[e] a 'fact tried by a jury"' within the meaning of the Seventh Amendment.[42]

Other Constitutional Provisions

Beyond the Due Process Clause and the Seventh Amendment, other provisions in the Constitution also reflect concerns of the Framers that remain relevant to contemporary debates about legal reform. For example, the Taking Clause reflects the Framers' concerns about using the machinery of government to take property in an arbitrary manner. Likewise, the prohibitions on bills of attainder in the unamended Constitution reflect a concern against singling out unpopular entities for especially disfavored treatment. And, the Commerce Clause and the constitutional grant of diversity jurisdiction both demonstrate the Framers' concern that states not discriminate against out-of-state entities. All of these concerns can appropriately inform a debate about legal reform and the optimal rules for adjudicating disputes with fairness and predictability. Some commentators have argued that legal reforms aimed at capping damages violate the Equal Protection Clause by

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impermissibly creating two classes of plaintiffs—a class of "less seriously injured" plaintiffs "who are entitled to keep everything which the jury awards," and a class of "more seriously injured" plaintiffs whose damages are capped.[43] These arguments are essentially a non-starter under modern equal protection analysis. Such "classifications" would—at most—be subjected to rational basis. Under the rational basis test, courts will not invalidate a law "'unless the varying treatment of different groups or persons is so unrelated to the achievement of any combination of legitimate purposes that [the court] can only conclude that [the governmental] actions were irrational.'"[44] Several courts have rejected efforts to characterize legal reforms as irrational, and thus problematic under the Equal Protection Clause.[45] These courts have concluded that the Equal Protection Clause does not pose an obstacle to the legislature's responsibility to "strike[] a balance between a tort victim's right to recover noneconomic damages and society's interest in preserving the availability of affordable liability insurance."[46]

Legal Reform and Federalism

The Framers thought that the vertical division of authority between the federal and state governments, much like the horizontal separation of powers in the new federal government, was a critical aspect of the Constitution. In fact, "federalism was the unique contribution of the Framers to political science and political theory."[47] And, as with the separation of powers, the Framers viewed this structural aspect of the Constitution as critical to protecting individual rights and individual liberties.[48]

Numerous provisions of the Constitution reflect the Framers' view that the new federal government in no way eliminated the sovereignty or critical role of the states. As the Supreme Court has underscored, under the Constitution the states "'retain a residuary and inviolable sovereignty'"—"[t]hey are not relegated to the role of mere provinces or political corporations, but retain the dignity, though not the full authority, of" sovereigns.[49] One way in which the Constitution reflects the continuing sovereignty and vitality of states is by granting the federal Congress only limited and enumerated powers, while recognizing that only states exercise plenary authority, or what is sometimes referred to as the "general police power."[50]

This division of authority does not mean that the federal government has no role in legal reform. As discussed in "Federalism, The Framers, And Legal Reform" (Sept. 27, 2012), the federal government can address such issues when exercising powers granted to it by the Constitution, whether via the Commerce Clause, the Bankruptcy Clause or other grants of power. Indeed, even the Constitution itself reflects a degree of federal "legal reform" by establishing the diversity jurisdiction of federal courts and granting Congress the power to establish the metes and bounds of that jurisdiction. "Congress has wide latitude to address and remove obstacles to interstate commerce whether they arise from state positive law, state common law or even state procedural rules," and federal legal reform would be a valid exercise of Congress' power under the Commerce Clause.[51] Moreover, "Congress is not limited to its commerce power in

addressing distortions created by state law; exercises of narrower federal powers under such provisions as the spending power, Necessary and Proper Clause, and Bankruptcy Clause also provide Congress with the authority to override state law."[52]

At the same time, the ability of the federal government to take action to effect legal reform when it implicates one of the enumerated powers granted to the federal government in no way detracts from the ability of states to use their plenary power to address legal reform issues. Of course, if Congress exercises one of its enumerated powers in a manner that preempts state law, the state laws must give way under the Supremacy Clause.[53] But absent the relatively rare instance in which Congress not only addresses a legal reform issue, but does so with preemptive effect, the states retain the full authority to address such issues for themselves. In fact, the Framers would undoubtedly have viewed the states as having principle responsibility for advancing legal reform. Although the Framers would have recognized a role for the federal government to address state laws that create an affirmative obstacle to the free flow of interstate commerce, they would have hoped that states would craft sensible laws that prevent such obstacles from arising in the first place. That would clearly have been the case for state courts and state tort systems, which the Framers would have recognized as the principal responsibility of the states, with the federal government playing a complementary role only when uniquely federal interests are implicated, as illustrated by the grant of diversity jurisdiction.

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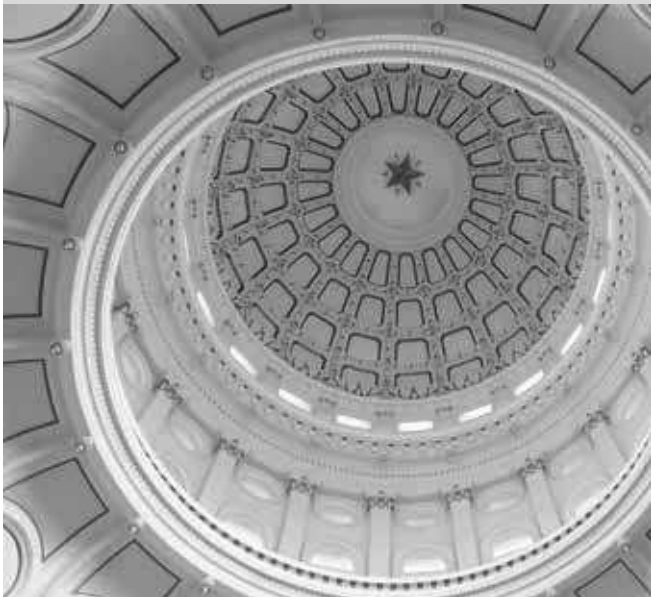

Conclusion

In sum, numerous aspects of the Constitution reinforce the critical role state legislatures play in considering legal reform, and a number of constitutional values are relevant to the policy debates over legal reform. The Framers viewed separation of powers as critical and envisioned a significant role for the legislature in determining the rules applicable in adjudicating cases.

The first Congress, populated by many of the signers of the Constitution, enacted the Judiciary Act of 1789, which reflects a robust role for the legislature on procedural matters both big and small. While the Framers' views on such matters do not directly constrain the states, they certainly can inform a discussion of the proper role of state legislatures. The Constitution also includes a number of provisions that reflect the Framers' dedication to the rule of law and abhorrence for arbitrary results. In extreme cases, constitutional provisions, such as the Due Process Clause, may render a particular application of state law unconstitutional, and the role of such constitutional provisions in not so limited. Judges applying federal constitutional rules can serve as the ultimate backstop to prevent the most arbitrary results, but states retain the primary role in designing a system that is both informed by constitutional values and avoids unconstitutional results. In a similar fashion, the federal Congress retains a role when state rules, including those created by judges or labeled procedural, implicate some uniquely federal interest. But the role of federal actors remains a backstop for relatively extreme and unusual circumstances. It is the states and state legislatures in particular who are on the front lines of the policy debates over the best rules to foster predictability and avoid arbitrary results. The views of the Framers on everything from separation of powers to due process to the role of judicial review and juries retain considerable relevance to these contemporary debates.

Endnotes

1 *Bond v. United States*, 131 S. Ct. 2355, 2365 (2011) (it is the "structure of our Government that protects individual liberty"); *Loving v. United States*, 517 U.S. 748, 756 (1996) (the "separation of powers" is a "defense against tyranny").

2 *Metro. Washington Airports Auth. v. Citizens for Abatement of Aircraft Noise, Inc.*, 501 U.S. 252, 272 (1991).

3 *Morrison v. Olson*, 487 U.S. 654, 697 (1988) (Scalia, J., dissenting); *Mistretta v. United States*, 488 U.S. 361, 380 (1989).

4 The Federalist No. 47, at 301 (C. Rossiter ed. 1961).

5 *Morrison*, 487 U.S. at 697.

6 *Clinton v. Jones*, 520 U.S. 681, 703 (1997) (quoting Federalist No. 47, at 325).

7 *Turner v. Bank of North America*, 4 Dall. 8, 10 n.1 (1799); *see United States v. Hudson*, 11 U.S. 32, 33 (1812) ("Courts created by the general Government possess no jurisdiction but what is given them by the power that creates them, and can be vested with none but what the power ceded to the general Government will authorize them to confer."). The Federalist No. 51, at 322 (James Madison) (C. Rossiter ed. 1961)

8 The Federalist No. 51, at 322 (James Madison) (C. Rossiter ed. 1961).

9 *See, e.g.*, 1 Stat. 73, § 9 ("the district courts shall have . . . cognizance of all crimes and offences . . . committed within their respective districts"); *id.* § 11 ("the circuit courts shall have original cognizance . . . of all suits of a civil nature at common law or in equity"); *id.* § 14 ("the before-mentioned courts . . . shall have the power to issue writs of scire facias, habeas corpus, and all other writs").

10 *See id.* § 29 ("jurors in all cases to serve in the courts of the United States shall be designated by lot").

11 *See Douglas v. Cox Retirement Properties, Inc.*, 302 P.3d 789 (Okla. 2013).

12 U.S. Const. amend. V; U.S. Const. amend. XIV.

13 *Meachum v. Fano*, 427 U.S. 215, 226 (1976) (internal quotation marks omitted); *see Wolff v. McDonnell*, 418 U.S. 539, 558 (1974); *County of Sacramento v. Lewis*, 523 U.S. 833, 845-46 (1998).

14 *See, e.g., F.C.C. v. Fox Television Stations, Inc.*, 132 S. Ct. 2307, 2317 (2012) ("A fundamental principle in our legal system is that laws which regulate persons or entities must give fair notice of conduct that is forbidden or required.").

15 *See, e.g., Joint Anti-Fascist Refugee Comm. v. McGrath*, 341 U.S. 123, 178 (1951) ("Notice and opportunity to be heard are fundamental to due process of law.").

16 *Honda Motor Co., Ltd. v. Oberg*, 512 U.S. 415, 418 (1994) (citing *Pacific Mut. Life Ins. Co. v. Haslip*, 499 U.S. 1 (1991)).

17 *BMW of N. America v. Gore*, 517 U.S. 559, 562, 580 (1996) (quoting *TXO Production Corp. v. Alliance Resources Corp.*, 509 U.S. 443, 454 (1993)).

18 *Id.* at 574; *accord State Farm Mut. Auto. Ins. Co. v. Campbell*, 538 U.S. 408, 416-17 (2003).

19 *Id.*; *see Haslip*, 438 U.S. at 42 (O'Connor, J., dissenting) ("Punitive damages are a powerful weapon. Imposed wisely and with restraint, they have the potential to advance legitimate state interests. Imposed indiscriminately, however, they have a devastating potential for harm. Regrettably, common-law procedures for awarding punitive damages fall into the latter category.").

20 Justice Scalia and Justice Thomas have both expressed the view that "the Constitution does not constrain the size of punitive damages awards." *State Farm Mut. Auto. Ins. Co. v. Campbell*, 538 U.S. 408, 429 (2003) (Thomas, J., dissenting); *see id.* at 429 ("the Due Process Clause provides no substantive protections against 'excessive' or 'unreasonable' awards of punitive damages") (Scalia, J., dissenting).

21 *Oberg*, 512 U.S. at 421.

22 *Id.* at 430.

23 *See, e.g., Richards v. Jefferson County*, 517 U.S. 793, 805 (1996); *see Hansberry v. Lee*, 311 U.S. 32, 37 (1940) (it would violate due process to bind litigants to a judgment rendered in an earlier litigation to which they were not parties and in which they were not adequately represented).

24 *Duke Power Co. v. Carolina Environmental Study Group, Inc.*, 438 U.S. 59, 88 (1978).

25 *Second Employers' Liability Cases*, 223 U.S. 1, 50 (1912).

26 *Silver v. Silver*, 280 U.S. 117, 122 (1929); *Duke Power*, 438 U.S. at 88 n.32 (quoting *Usery v. Turner Elkhorn Mining Co.*, 428 U.S. 1, 16 (1976)).

27 *Duke Power*, 438 U.S. at 88 (citing *New York Central R. Co. v. White*, 243 U.S. 188 (1917); *Crowell v. Benson*, 285 U.S. 22 (1932)).

28 U.S. Const. amend. VII.

29 *See Dohany v. Rogers*, 281 U.S. 362, 369 (1930); *Walker v. Sauvinet*, 92 U.S. 90, 92 (1875).

30 James Iredell, Answers to Mr. Mason's Objections to the New Constitution (1788), reprinted in 5 The Founders' Constitution 357.

31 *Id.*

32 Federalist No. 83, at 336 (C. Rossiter ed. 1961).

33 *Colgrove v. Battin*, 413 U.S. 149, 155 (1973).

34 523 U.S. 340, 353 (quoting *Lord Townshend v. Hughes*, 2 Mod. 150, 151, 86 Eng. Rep. 994, 994-95 (C.P. 1677)).

35 *Id.* (quoting *Dimick v. Schiedt*, 293 U.S. 474, 480 (1935)).

36 17 U.S.C. § 504(c)(1)-(2).

37 Iredell, *supra*, at 357.

38 Edith G. Henderson, *The Background of the Seventh Amendment*, 80 Harv. L. Rev. 289, 319 (1966).

39 *Etheridge v. Medical Center Hospitals*, 237 Va. 87 (1989) (rejecting challenge to statute capping recovery in medical malpractice actions).

40 *See* Henderson, *supra*, at 305-06.

41 *Etheridge*, 237 Va. at 95.

42 *Davis v. Omitowoju*, 883 F.2d 1155, 1162 (3d Cir. 1989); *see Boyd v. Bulala*, 877 F.2d 1191, 1196 (4th Cir. 1989) ("[I]t is not the role of the jury to determine the legal consequences of its factual findings. . . . That is a matter for the legislature.").

43 *Murphy v. Edmonds*, 323 Md. 342, 355 (1992) (rejecting challenge to cap on noneconomic damages in personal injury actions).

44 *Gregory v. Ashcroft*, 501 U.S. 452, 471 (1991) (quoting *Vance v. Bradley*, 440 U.S. 93, 97 (1979)).

45 *See, e.g., Omitowoju*, 883 F.2d at 1159; *Bulala*, 877 F.2d at 1196-97.

46 *Patton v. TIC United Corp.*, 77 F.3d 1235, 1247 (10th Cir. 1996).

47 *United States v. Lopez*, 514 U.S. 549, 575 (1995) (Kennedy, J., concurring).

48 *Bond*, 131 S. Ct. at 2365 (it is the "structure of our Government that protects individual liberty").

49 *Alden v. Maine*, 527 U.S. 706, 715 (1999) (quoting The Federalist No. 39, at 245 (James Madison) (C. Rossiter ed. 1961)).

50 *See, e.g.*, *United States v. Morrison*, 529 U.S. 598, 618 n.6 (2000) (discussing states' "general police powers").

51 Federalism, The Framers, And Legal Reform 1 (Sept. 27, 2012).

52 *Id.*

53 *See, e.g.*, *Gade v. Nat'l Solid Wastes Mgmt. Ass'n*, 505 U.S. 88, 108 (1992).

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