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THOUGHTS ON PREEMPTION IN THE WAKE OF THE *LEVINE* DECISION

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ABSTRACT

On November 16, 2009, one of the authors participated in a panel at the University of Maryland School of Law on the prospects for preemption doctrine in the wake of the Supreme Court's decision in *Wyeth v. Levine*.¹ This Article repeats and expands on the views she presented during the panel. Part I describes the *Levine* decision. Part II examines the majority's holding as it relates to impossibility preemption and considers the future of the doctrine in failure-to-warn suits after *Levine*. We argue that the announced standard for impossibility preemption—the *clear evidence* standard—should be interpreted reasonably and not in a manner that effectively eviscerates the doctrine. We also describe other instances of impossibility in the food and drug regulatory context that were not presented to the Court. Part III considers *Levine*'s obstacle preemption analysis and its implications for future pharmaceutical tort litigation. We conclude that the future for obstacle preemption is uncertain, unless FDA conducts rulemaking on the issue or the Court reconsiders the substantial evidence that state tort litigation impedes FDA's proper functioning.

I. BACKGROUND: THE *LEVINE* DECISION

Plaintiff Diana Levine brought failure-to-warn claims against Wyeth for injuries she suffered after receiving a direct intravenous injection, known as an "IV-push," of Wyeth's drug Phenergan.² The IV-push inadvertently injected Phenergan into an artery, causing gangrene and eventually requiring amputation of Levine's hand and forearm.³ Levine sued Wyeth, alleging that the company had

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1. 129 S. Ct. 1187 (2009).

2. *Id.* at 1191–92.

3. *Id.* at 1191.

inadequately warned of the risk that an improper IV-push could cause injuries like those she suffered.⁴ Wyeth argued that Levine's failure-to-warn claims were preempted by federal law because FDA had specifically approved Phenergan for direct IV injection and had approved labeling that warned of its risks.⁵ The jury found for Levine, and she received a damages award of \$6.7 million.⁶ Over the dissent of its Chief Justice, the Vermont Supreme Court affirmed the jury's verdict.⁷

The Supreme Court ruled, with three justices dissenting,⁸ that federal law did not preempt Levine's failure-to-warn claim.⁹ The majority opinion, authored by Justice Stevens and joined by four others, rejected two preemption arguments.¹⁰ First, the majority rejected the argument that Levine's state law claims were preempted because it would be impossible for Wyeth to comply with the state law requirement in question, FDA's decisions regarding its labeling, and the agency's rules governing labeling changes ("impossibility" preemption).¹¹ Second, the majority rejected the argument that requiring Wyeth to comply with the state law requirement in question would interfere with congressional entrustment of new drug labeling decisions to FDA and, in particular, would stand as an obstacle to FDA's achievement of its statutory objectives ("obstacle" preemption).¹² We discuss the majority's reasoning in more detail below.¹³

II. LEVINE ON IMPOSSIBILITY PREEMPTION

A. The Doctrine

It is well-settled doctrine that, under the Supremacy Clause of the Constitution,¹⁴ state law is preempted "where compliance with both federal and

4. *Id.* at 1191–92.

5. *See id.* at 1192–93 (discussing FDA's approval process with regard to Phenergan and its labeling).

6. *Levine v. Wyeth*, 944 A.2d 179, 182–83 (Vt. 2006).

7. *Id.* at 197.

8. *Levine*, 129 S. Ct. at 1217. Justice Alito dissented and was joined by Chief Justice Roberts and Justice Scalia. *Id.*

9. *Id.* at 1204.

10. *Id.* at 1190, 1193, 1199. Justice Stevens' opinion was joined by Justices Kennedy, Souter, Ginsburg, and Breyer. *Id.* at 1190. Justice Thomas concurred only in the judgment. *Id.*

11. *Id.* at 1196, 1199.

12. *Id.* at 1199.

13. *See infra* Part II.B.

14. U.S. CONST. art. VI, cl. 2. The Supremacy Clause states:

This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby; any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.

Id.

state regulations is a physical impossibility”¹⁵ The doctrine of *impossibility preemption* is more often described than applied, however, as the courts have found that very few factual situations satisfy the standard.¹⁶ It is not enough that state law prohibits something that federal law permits,¹⁷ or vice versa.¹⁸ In each of these scenarios, a party could still comply with both laws by refraining from the conduct in question. In order for a court to find that it is genuinely impossible to comply with both state and federal law, one body of law must require something that the other prohibits.¹⁹

FDA has long taken the view that its determinations must preempt state requirements when compliance with both state and federal requirements is impossible. In the preamble to its 2006 physician labeling rule, which is discussed in more detail below, the agency identified scenarios in which it would be “impossible” for drug companies to comply with both FDA requirements and state law.²⁰ For example, “when [state laws] purport to compel a firm to include in labeling or advertising a statement that FDA has considered and found scientifically unsubstantiated,” compliance with such laws “would render the drug misbranded under the act.”²¹ Likewise, when state law “purports to preclude a firm from including in labeling or advertising a statement that is included in prescription drug labeling,” compliance with the state law would constitute misbranding.²²

15. *Fla. Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 142–43 (1963). *See also* *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995) (noting preemption “where it is ‘impossible for a private party to comply with both state and federal requirements’” (quoting *English v. Gen. Elec. Co.*, 496 U.S. 72, 79 (1990))); *Pac. Gas & Elec. Co. v. State Energy Res. Conservation & Dev. Comm’n*, 461 U.S. 190, 204 (1983) (citing *Fla. Lime & Avocado Growers, Inc.*, 373 U.S. at 142–43); *Fid. Fed. Sav. & Loan Ass’n v. De La Cuesta*, 458 U.S. 141, 153 (1982) (same).

16. Mary J. Davis, *Unmasking the Presumption in Favor of Preemption*, 53 S.C. L. REV. 967, 984 n.96 (2002) (“The impossibility standard of implied preemption is often mentioned but rarely applied.”); Caleb Nelson, *Preemption*, 86 VA. L. REV. 225, 228 (2000) (calling the impossibility standard “vanishingly narrow”); Christopher H. Schroeder, *Supreme Court Preemption Doctrine*, in *PREEMPTION CHOICE: THE THEORY, LAW, AND REALITY OF FEDERALISM’S CORE QUESTION* 119, 131 (William W. Buzbee ed., 2009) (“There are very few actual case law examples of physical impossibility.”).

17. *See, e.g.*, *Barnett Bank of Marion County, N.A. v. Nelson*, 517 U.S. 25, 31 (1996) (finding no impossibility even where “the Federal Statute authorizes national banks to engage in activities that the State Statute expressly forbids”); *Columbia Plaza Ltd. P’ship v. Cowles*, 403 F. Supp. 1337, 1343 (D.D.C. 1975) (holding no impossibility because federal standard is permissive, rather than mandatory).

18. *See, e.g.*, *Mich. Cannery & Freezers Ass’n v. Agric. Mktg. & Bargaining Bd.*, 467 U.S. 461, 477–78 (1984). The Court in *Mich. Cannery & Freezers Ass’n* considered a Michigan law that “empower[ed] producers’ associations to do precisely what the federal Act forbid[] them to do.” *Id.* The Court noted that “[b]ecause the Michigan Act is cast in permissive rather than mandatory terms . . . this is not a case in which it is impossible for an individual to comply with both state and federal law.” *Id.* at 478 n.21.

19. *See, e.g.*, *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 873 (2000) (describing a case of impossibility as “a case in which state law penalizes what federal law requires”).

20. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3935 (Jan. 24, 2006).

21. *Id.*

22. *Id.*

Since the 1970s, the Department of Justice has submitted amicus briefs on behalf of FDA in cases before the federal courts, where the agency concluded on impossibility grounds that a particular state requirement must give way to conflicting FDA requirements.²³

The courts have largely supported FDA's position. Despite the overall scarcity of impossibility preemption rulings, there are some findings of impossibility preemption in the context of food and drug regulation, particularly

23. See, e.g., Brief for United States as Amicus Curiae at 12–13, *Jones v. Rath Packing Co.*, 430 U.S. 519 (1977) (No. 75-1053), 1976 WL 194685 [hereinafter Brief for United States as Amicus Curiae, *Jones v. Rath Packing Co.*] (arguing that California's flour labeling regulations must give way to federal requirements, where compliance with both is impossible). The Department of Justice also asserted impossibility preemption in a 1985 Second Circuit case involving cheese labeling requirements. Memorandum of United States FDA and USDA at 23, *Grocery Mfrs. of Am., Inc. v. Gerace*, 755 F.2d 993 (2d Cir. 1985) (No. 83 Civ. 8629) (“New York’s *per se* rule applies to all cheese substitutes notwithstanding FDA’s determination that it may actually be misleading to label a nutritious alternative food an ‘imitation.’ Any state law [that] requires a manufacturer or distributor to engage in conduct violative of Federal law must be deemed preempted.” (citations omitted)). And in a 2000 case in the Southern District of New York involving the labeling of the drug Cardura, the government again asserted impossibility preemption. Statement of Interest of United States at 11, *Bernhardt v. Pfizer, Inc.*, 2000 WL 1738645 (S.D.N.Y. Nov. 22, 2000) (No. 00 Civ. 4042) [hereinafter Statement of Interest of United States] (“[W]ere the Court to grant plaintiffs’ request that changes be made to Cardura’s label and packaging, this would create a direct conflict by requiring a labeling change at odds with the specific product labeling that was approved by the FDA, even though changes to labels and packaging must be specifically approved by the FDA.”); see also Brief of United States as Amicus Curiae in Support of Defendants-Appellees at 19–20, *Colacicco v. Apotex, Inc.*, 521 F.3d 253 (3d Cir. 2008) (No. 06-3107) [hereinafter Brief of United States as Amicus in Support of Apotex] (“Mr. Colacicco seeks to impose liability under state tort law for defendants’ alleged failure to provide a warning that had been specifically rejected by FDA as of October 2003, and accordingly would have constituted unlawful misbranding had it been included on the labeling for the defendants’ drugs. In such circumstances, the Supremacy Clause bars the imposition of liability under state law.”); Amicus Brief for United States in Support of the Defendant-Appellee and Cross-Appellant, and in Favor of Reversal of District Court’s Order Denying Partial Summary Judgment to Defendant-Appellee and Cross-Appellant at 16, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004) (No. 02-55372) [hereinafter Amicus Brief for United States in Support of Defendant, *Motus v. Pfizer*] (“[S]tate law may not require the manufacturer of a drug to warn of a specific danger that FDA, based on scientific analysis, concludes does not exist. Such a warning label, one not based on reliable scientific evidence of known risks, would be ‘false or misleading’, and thus would misbrand the drug. It is a violation of the [Food, Drug, and Cosmetic Act (FDCA)] to market a misbranded product.” (citations omitted)); Amicus Curiae Brief of United States in Support of Defendants/Respondents SmithKline Beecham Consumer Healthcare LP, et al. at 27, *Dowhal v. SmithKline Beecham Consumer Health Care LP*, 88 P.3d 1 (Cal. 2004) (No. S109306) [hereinafter Amicus Brief of United States in Support of SmithKline] (“Accordingly, if Proposition 65 required [d]efendants to use Dowhal’s warning labeling, that state law would conflict with . . . and must yield to federal law under the doctrine of conflict preemption.”); Corrected Amicus Brief for United States at 25, *Kallas v. Pfizer, Inc.*, 2005 WL 2559710 (D. Utah Sept. 15, 2005) (No. 2:04CV00998) [hereinafter Amicus Brief for United States, *Kallas v. Pfizer*] (“Under the Supremacy Clause, a state may not cause a drug manufacturer to choose either to avoid state tort liability or comply with federal law. Thus, state law may not validly require the manufacturer of a drug to warn of a specific danger that FDA, based on the agency’s scientific analysis, did not believe to be sufficiently supported to warrant such a warning.” (citations omitted)).

with respect to labeling.²⁴ For example, the California Supreme Court applied the doctrine in a case in which FDA and the State of California had mandated different warnings for a smoking cessation product.²⁵ California state law required all nicotine delivery products to bear a warning indicating that they contained “a chemical known to the state of California to cause reproductive harm”²⁶ But FDA “never permitted defendants to use the [state law] warning.”²⁷ Instead, after an eight-year deliberation about the appropriate pregnancy-related warning for smoking cessation products, including several exchanges with the defendant manufacturers, the agency mandated that the products bear a warning that read:

If you are pregnant or breast-feeding, only use this medicine on the advice of your health care provider. Smoking can seriously harm your child. Try to stop smoking without using any nicotine replacement medicine. This medicine is believed to be safer than smoking. However, the risks to your child from this medicine are not fully known.²⁸

The California Supreme Court found the state warning to be preempted on the grounds that “[i]f a defendant were to add a warning to its label advising that nicotine can cause fetal harm, it would violate the FDA’s determination and would risk legal sanctions.”²⁹

B. The Levine Majority’s Reasoning

The majority in *Levine* rejected the legal argument that Wyeth could not unilaterally add a warning without violating federal law governing misbranding and unauthorized distribution of unapproved drugs.³⁰ We believe this did not adequately take into account how FDA actually operates. Under the rules and

24. See, e.g., *McDermott v. Wisconsin*, 228 U.S. 115, 133–34 (1913) (holding that a state food labeling statute was preempted because it required a food vendor to remove a label, the removal of which would render the product misbranded under federal food labeling law); *Hurley v. Lederle Labs. Div. of Am. Cyanamid Co.*, 863 F.2d 1173, 1179 (5th Cir. 1989) (holding that if a company has provided all of the requisite information to FDA, the agency’s labeling determination would preempt any conflicting state requirements); *Grocery Mfrs. of Am., Inc. v. Gerace*, 755 F.2d 993, 1001 (2d Cir. 1985), *aff’d*, 474 U.S. 801 (1985) (holding that New York’s requirements for labeling of imitation cheese were preempted because “[c]ompliance with both the state and federal requirements [wa]s impossible”); *Lever Bros. Co. v. Maurer*, 712 F. Supp. 645, 651 (S.D. Ohio 1989) (invalidating an Ohio statute prohibiting the use of “butter” in labeling on the grounds that it conflicted with a federal requirement that ingredients be listed on food labels). See also Mary J. Davis, *The Battle Over Implied Preemption: Products Liability and the FDA*, 48 B.C. L. REV. 1089, 1113 (2007) (noting that, in *McDermott*, “[t]he impossibility of dual compliance required defeat of the state law”).

25. *Dowhal*, 88 P.3d at 4, 9–11.

26. *Id.* at 4.

27. *Id.*

28. *Id.*

29. *Id.* at 9–11. The court found preemption even though the federal law “contain[s] a savings clause designed specifically to preserve” California’s power to impose a requirement that is “different from or in addition to, or that is otherwise not identical with, a requirement under” the statute. *Id.* at 4.

30. *Wyeth v. Levine*, 129 S. Ct. 1187, 1197 (2009).

norms that govern the industry in its dealings with FDA, it is not realistically possible for a company to change its package insert without first seeking the consent of the review division at FDA responsible for approval of the drug in question.

FDA's oversight of a new drug revolves around that drug's labeling.³¹ No new drug may be marketed without approval of a new drug application (NDA) or abbreviated NDA.³² In addition to preclinical data, clinical data, and information on chemical composition and manufacturing methods, among other things, the NDA must contain proposed labeling.³³ This labeling is the focal point of the submission because the statute requires the applicant to show that the drug is "safe for use under the conditions prescribed, recommended, or suggested *in the proposed labeling*" and that there is "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 . . .*"³⁴ The exact phrasing of the labeling evolves during the NDA review and approval process, as the agency and applicant work together to ensure that the data and labeling align, so that—as required by statute—the drug, when approved, is both safe and effective when used as described in the labeling, and the labeling is neither false nor misleading.³⁵

Agency regulations require NDA holders to revise their product labeling "when new information becomes available that causes the labeling to become inaccurate, false, or misleading."³⁶ Every holder of an approved NDA must,

31. The statute defines *labeling* as "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) (2006). The Supreme Court has construed *labeling* broadly to include both documents that are physically attached to the product and those that are not physically attached but nevertheless "supplements or explains" the product. *E.g.*, *Kordel v. United States*, 335 U.S. 345, 349–50 (1948). It therefore reaches both the professional labeling (package insert), which is submitted in and approved as part of a new drug application (NDA), and promotional labeling, which by regulation must be consistent with and not contrary to the approved professional labeling. 21 C.F.R. § 201.100(d)(1) (2009).

32. 21 U.S.C. § 355(a)–(b), (j).

33. *Id.* § 355(b)(1); 21 C.F.R. § 314.50.

34. 21 U.S.C. § 355(d) (emphasis added).

35. *Id.*; see 21 C.F.R. § 314.105(b) (stating that approval of an NDA is "conditioned upon the applicant incorporating the specified labeling changes exactly as directed").

36. 21 C.F.R. § 201.56(a)(2). FDA can also initiate labeling changes itself. Prior to 2007, the agency largely relied on section 505(e) of the statute. This provision authorizes FDA to initiate proceedings to withdraw marketing approval for a drug if new evidence shows that the drug is not safe for use under the conditions of use for which it was approved or if its labeling is false or misleading in any particular way and was not corrected within a reasonable time. 21 U.S.C. § 355(e). The agency has sometimes also taken the position that an applicant's failure to amend labeling to take account of new safety information is an act of misbranding under sections 502(a) and 201(n). This is the position the agency took in the Selacryn and Oralflex prosecutions in the 1980s. See *Factual Basis for the Pleas at 14–17, United States v. Eli Lilly & Co.*, Nos. IP85 53 CR, IP85 54 CR (S.D. Ind., Aug. 21, 1985); *Information, passim, United States v. SmithKline Beckman Corp.*, No. 84-00227 (E.D. Pa. June 1, 1981). FDA has also taken this position in the Federal Register notices calling for changes in the labeling of approved drugs. *E.g.*, *Labeling for Oral Hypoglycemic Drugs of the Sulfonylurea Class*, 49

however, notify FDA about, and in most cases seek approval of, any change in a condition established in the approved application, beyond those already provided for in the application.³⁷ Changes fall into three categories: major changes, which require prior approval; moderate changes, which must be approved by FDA but may be implemented before the agency has rendered a decision; and minor changes, which must be reported on an annual basis.³⁸

FDA regulations establish a default requirement of prior approval for a labeling change.³⁹ Certain editorial changes can be made and described to the agency in an annual report to the NDA file.⁴⁰ In addition, certain safety-related changes can be described in a supplement submitted to the agency contemporaneously with, or in some cases thirty days prior to, use of the new labeling.⁴¹ Such a “changes being effected” (CBE) supplement is permitted only when the changes reflect newly acquired information⁴² and where there is sufficient evidence of causation.⁴³

Fed. Reg. 14,303, 14,306–07 (April 11, 1984). Distribution of a misbranded drug can lead to product seizure, an injunction, and even criminal penalties. *Id.* §§ 332, 333, 334, 352. Section 505(o)(4) of the FDCA, added in 2007, gave FDA significant new authority to require labeling changes. *Id.* § 355(o) (West Supp. 2009). Violation of a labeling change order issued pursuant to section 505(o)(4) is a federal crime and can lead to substantial civil money penalties. *Id.* § 333 (2006).

37. 21 C.F.R. § 314.70(a)(1).

38. *Id.* § 314.70(b)–(d). These rules govern any changes to the conditions established in an approved application, not just changes to the approved labeling. *Id.*

39. *See id.* § 314.70(b)(2)(v) (requiring prior approval for labeling changes, with three exceptions, found in 21 C.F.R. §§ 314.70(c)(6)(iii), (d)(2)(ix), and (d)(2)(x)).

40. *E.g., id.* § 314.70(d)(2)(ix)–(x).

41. *Id.* § 314.70(c)(6)(iii). The regulation permitting changes to the labeling of a new drug to be made without prior approval by the agency does not have a corresponding statutory provision. *Cf.* 21 U.S.C. § 356a(d)(3)(B)(ii) (authorizing FDA to designate a category of non-major manufacturing changes for which distribution of the drug may commence upon submission of a supplemental application). It is the descendant of a 1965 policy in which FDA announced it would “take no action” against a company if certain safety-related labeling changes were implemented prior to receipt of formal FDA approval. Supplemental New-Drug Applications, 30 Fed. Reg. 993, 994 (Jan. 30, 1965); *see also* New Drug and Antibiotic Regulations, 50 Fed. Reg. 7452, 7454 (Feb. 22, 1985) (reasserting the rule that some labeling changes may be implemented without prior FDA approval).

42. 21 C.F.R. § 314.70(c)(6)(iii); *see also id.* § 314.3(b) (defining *newly acquired information* as “data, analyses, or other information not previously submitted to the agency”); New Drug and Antibiotic Regulations, 47 Fed. Reg. 46,622, 46,623 (Oct. 19, 1982) (stating that the regulation only applies “to correct concerns about newly discovered risks from the use of a drug”).

43. *See* Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 2,848, 2,848 (Jan. 16, 2008) (to be codified at 21 C.F.R. pts. 314, 601, and 814) (“[FDA’s] longstanding position [is] that a supplemental application . . . is appropriate to amend the labeling . . . to add or strengthen a contraindication, warning, precaution, or adverse reaction only if there is sufficient evidence of a causal association with the drug”); Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, 49,603, 49,608 (Aug. 22, 2008) (to be codified at 21 C.F.R. pts. 314, 601, and 814) (“[A] supplemental application . . . is appropriate to amend the labeling . . . to add or strengthen a contraindication, warning, precaution, or adverse reaction if there is sufficient evidence of a causal association FDA does not consider this to be a substantive policy change, and it does not alter the

The *Levine* majority made short shrift of Wyeth's impossibility argument on the ground that the CBE regulation would have allowed it to make the change sought by Levine without prior FDA approval. Although the decision called Wyeth's reading of the regulation "cramped,"⁴⁴ the majority itself took a cramped and unrealistic view of the legal and practical situation facing regulated industry. Regardless of the mechanism used, the process is the same. Following a manufacturer's submission of a supplement proposing a labeling change, FDA evaluates the scientific evidence pertaining to the proposed change and determines for itself "whether the proposed labeling change is appropriate based on such factors as the frequency of the risk of a side-effect/adverse outcome, the severity of the potential risks, and the potential benefits and risks associated with the proposed warning."⁴⁵ "If the agency disapproves the proposed change[], the manufacturer may not use the unapproved labeling."⁴⁶ Indeed, if the company marketed the product using the disapproved labeling, it would violate the prohibition against marketing an unapproved new drug and/or against marketing a misbranded drug.⁴⁷ Accordingly, while the CBE process provides a theoretical means by which manufacturers are permitted to add warnings to their labeling without prior "approval" from FDA, a company typically seeks consent from the relevant review division prior to submission of the formal CBE supplement. This practice is industry-wide and explicitly acknowledged by FDA.⁴⁸ The fact that it is not

agency's current practices with respect to accepting or rejecting labeling changes proposed by a CBE supplement.").

44. *Wyeth v. Levine*, 129 S. Ct. 1187, 1197 (2009).

45. Amicus Brief of United States in Support of SmithKline, *supra* note 23, at 10.

46. Amicus Brief for United States, *Kallas v. Pfizer*, *supra* note 23, at 9.

47. 21 U.S.C. §§ 352(a), 352(f), 355(a)–(b) (2006 & West Supp. 2009); *see also* Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3935 (Jan. 24, 2006) (to be codified at 21 C.F.R. pts. 201, 314, and 601) (noting that inclusion of "a statement that FDA has considered and found [to be] scientifically unsubstantiated . . . would render the drug misbranded"); Brief for Respondent at 35–36, *Levine*, 129 S. Ct. 1187 (No. 06-1249), 2008 WL 3285388 (acknowledging that certain changes to the labeling would render a product a "new drug"); Amicus Brief for United States in Support of Defendant, *Motus v. Pfizer*, *supra* note 23, at 17 (noting that a proposed warning "would have misbranded the product because the warning would not have been supported by science"); Statement of Interest of United States, *supra* note 23, at 14 (warning that, if the court were to mandate labeling changes that FDA determined were not supported by the evidence, the drug would be deemed misbranded).

48. FDA has stated that:

While a sponsor is permitted to add risk information to the [full package insert] without first obtaining FDA approval via a CBE supplement, FDA reviews all such submissions and may later deny approval of the supplement, and the labeling remains subject to enforcement action if the added information makes the labeling false or misleading under section 502(a) of the act. Thus, in practice, manufacturers typically consult with FDA prior to adding risk information to labeling.

Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3934 (citations omitted). As explained twenty years earlier by a former Chief Counsel of the agency, because manufacturers must obtain FDA's approval after the fact, "the actual

embodied in the Federal Food, Drug, and Cosmetic Act (FDCA) or an FDA regulation does not make it any less of a “rule” from a real world perspective, and it should have been treated as such by the *Levine* majority.

After rejecting Wyeth’s argument that it was not legally possible to change its labeling unilaterally, the majority looked for “clear evidence” in the record that FDA would not have approved a change to Phenergan’s package insert.⁴⁹ Its judgment that there was no such evidence must be understood within the confines of its description of the factual record. According to the majority, in the seventeen years after Wyeth submitted a supplemental NDA regarding the risks of IV-push, the company and FDA corresponded only “intermittently” about the labeling.⁵⁰ It did acknowledge that, in 1987 and 1988, “FDA suggested different warnings about” the risk of IV-push, Wyeth submitted labeling incorporating the proposed changes, and FDA failed to respond to the proposal.⁵¹ But it disregarded that exchange because Wyeth’s proposed changes “did not differ in any material respect from the FDA-approved warning,” and “FDA viewed the change as non-substantive”⁵² Apart from this single exchange, the only facts cited by the majority were that Wyeth did not propose the warning deemed appropriate by the Vermont jury,⁵³ and that Wyeth did not supply FDA with “an evaluation or analysis concerning the specific dangers posed by the IV-push method.”⁵⁴ The majority appears to have ignored many facts that the dissent regarded as relevant to the issue of whether FDA would have approved a labeling change,⁵⁵ relying instead on the factual determinations of the lower courts.⁵⁶

C. Impossibility Preemption After *Levine*

There are two open issues with respect to impossibility preemption in the new drug labeling context: the application of the *clear evidence* standard,⁵⁷ and the operation of the impossibility doctrine when a CBE supplement is not legally permitted.⁵⁸

freedom of manufacturers unilaterally to change the package insert is minimal.” Richard M. Cooper, *Drug Labeling and Products Liability: The Role of the Food and Drug Administration*, 41 FOOD DRUG COSM. L.J. 233, 236 (1986).

49. *Levine*, 129 S. Ct. at 1198.

50. *Id.* at 1192.

51. *Id.*

52. *Id.* at 1198 n.5.

53. *Id.* at 1198.

54. *Id.* at 1199.

55. *See id.* at 1222–26 (Alito, J., dissenting).

56. *Id.* at 1198–99 (majority opinion).

57. *See infra* Part II.C.1.

58. *See infra* Part II.C.2.

1. *The Clear Evidence Standard*

Although the *Levine* decision requires “clear evidence that the FDA would not have approved a change” as a prerequisite to a finding of impossibility preemption,⁵⁹ it specifies only one set of circumstances that does not constitute *clear evidence*. What satisfies the standard must now be fleshed out in the lower courts. Important policy considerations support a reasonable interpretation of *clear evidence* in the context of FDA’s review of prescription drug labeling. For example, it would be impossible for a defendant to show that FDA actually rejected the precise language proposed by the plaintiff on the basis of precisely the same information and arguments as opposed to, for example, a single subsequent postmarket safety report or a new meta-analysis of previously submitted data.⁶⁰ The *Levine* decision cannot be read to require a showing that is impossible to make. Nor, as a policy matter, should it be read to require industry to inundate the agency with labeling change submissions, which a “precise wording” or an “actual rejection” approach could prompt. In fact, the decision itself suggests a more reasonable approach. The standard is not that FDA *did not* approve *the* change; it is that FDA *would not have* approved *a* change. Under this standard, it might be relevant, or even sufficient, that the agency considered and rejected (whether proposed by the manufacturer or on its own initiative) inclusion of the relevant risk information—with any wording—in the package insert. It might also be relevant, or even sufficient, that the agency did not require a safety labeling change, for example under section 505(o)(4) of the FDCA, when faced with evidence that is not qualitatively different from the evidence on which the plaintiff relies.⁶¹

Two interesting test cases for the *clear evidence* standard are currently pending before district courts in the Tenth Circuit.⁶² The plaintiffs in the cases have argued that the labeling of two antidepressants, Paxil and Effexor, should have

59. *Levine*, 129 S. Ct. at 1198.

60. This would require manufacturers to imagine and propose every conceivable variation in wording when submitting labeling changes. Moreover, safety reports are submitted to the agency on a rolling basis, and stakeholders (companies, the agency, insurers, and the scientific community) analyze and reanalyze safety information continually. See generally Jill D. Jacobson & David Feigal, *Red Sky in the Morning: Modifying Prescription Drug Labels as a Result of Postmarket Surveillance*, 62 FOOD & DRUG L.J. 529, 531–32 (2007) (outlining the postmarket safety reporting procedures and FDA’s evaluation of those reports). Thus, it will always be possible to point to some subsequent “information” that was not before the agency decisionmaker when it considered the precise wording that plaintiffs demand.

61. 21 U.S.C. § 355(o)(4) (West Supp. 2009) (requiring the agency to initiate a safety labeling change when it becomes aware of new safety information on the basis of which it believes a change should be made).

62. *Dobbs v. Wyeth Pharm.*, No. 08-6018, 2010 WL 2179290, at *1 (10th Cir. June 2, 2010), *vacating and remanding* *Dobbs v. Wyeth Pharm.*, 530 F. Supp. 2d 1275 (W.D. Okla. 2008); *Miller v. SmithKline Beecham Corp.*, Nos. 08-5042, 08-5050, 2010 WL 2180615, at *1 (10th Cir. June 2, 2010), *vacating and remanding* *Miller v. SmithKline Beecham Corp.*, No. 03-CV-393-GKF-FHM, 2008 WL 510449 (N.D. Okla. Feb. 15, 2008).

included warnings about suicidality in adults in 1998 and 2002, respectively.⁶³ Before *Levine*, both district courts held that the plaintiffs' claims were preempted, but *Levine* was handed down while the appeals were pending, prompting the Tenth Circuit to remand the cases for reconsideration in light of the new *clear evidence* standard.⁶⁴

The facts in these cases appear to provide compelling support for satisfaction of the *clear evidence* standard. As the defendants have pointed out, FDA has been examining the issue of suicidality and antidepressants for nearly two decades and has consistently rejected the argument that antidepressants should bear a warning about adult suicidality.⁶⁵ In addition to the safety information that the agency collected pursuant to its clinical trial safety reporting, postmarket reporting, and annual report regulations⁶⁶ and the voluminous scientific literature addressing the issue,⁶⁷ FDA also received a number of citizen petitions asserting that labeling changes or product withdrawal were necessary on account of suicide risk.⁶⁸

63. *E.g.*, Complaint at 3, *Miller*, 2008 WL 510449 (No. 03-CV-393-GKF-FHM), 2003 WL 24063926; Complaint at 5–6, *Dobbs*, 530 F. Supp. 2d 1275 (No. CIV-04-1762-D), 2004 WL 3139491.

64. *See Dobbs*, 530 F. Supp. 2d at 1291 (holding that the plaintiff's "claims are preempted by the applicable FDA regulations governing labeling of prescription drugs"), *vacated and remanded by Dobbs*, 2010 WL 2179290, at *1; *Miller*, 2008 WL 510449, at 1 (granting summary judgment on grounds of conflict preemption), *vacated and remanded by Miller*, 2010 WL 2180615, at *1.

65. *See* Brief of Defendant-Appellee/Cross-Appellant at 41–45, *Miller v. SmithKline Beecham Corp.*, Nos. 08-5042, 08-5050 (10th Cir. Sept. 1, 2009); Brief for Defendant-Appellee Wyeth at 54–60, *Dobbs v. Wyeth Pharm.*, No. 08-6018 (10th Cir. July 16, 2009); *see also infra* notes 66–77 and accompanying text. *But see* *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 396 (7th Cir. 2010) (holding that the regulatory history did not constitute *clear evidence* as to young adult suicidality).

66. *See* 21 C.F.R. §§ 312.32(c), 314.80(c), 314.81(b) (2009) (requiring the submission of safety information and reports).

67. *E.g.*, W. Creaney et al., *Antidepressant Induced Suicidal Ideation*, 6 HUM. PSYCHOPHARMACOLOGY 329, 329–31 (1991) (outlining a study of two patients on antidepressants and concluding that "the emergence of suicidal ideation on antidepressants cannot always be attributed to a lifting of psychomotor retardation but rather that the ideas may in some instances be produced by antidepressants"); Robert A. King et al., *Emergence of Self-Destructive Phenomena in Children and Adolescents During Fluoxetine Treatment*, 30 J. AM. ACAD. CHILD & ADOLESCENT PSYCHIATRY 179, 183 (1991) (describing how a sample of children and adolescents developed self-injurious behavior during fluoxetine treatment); Prakash Masand et al., Letter to the Editor, *Suicidal Ideation Related to Fluoxetine Treatment*, 324 NEW ENG. J. MED. 420, 420 (1991) (reporting two cases in which a strong association between suicidal ideation and fluoxetine treatment existed); Anthony J. Rothschild & Carol A. Locke, *Reexposure to Fluoxetine After Serious Suicide Attempts by Three Patients: The Role of Akathisia*, 52 J. CLINICAL PSYCHIATRY 491, 491–92 (1991) (outlining a study where patients were re-exposed to fluoxetine and developed severe akathisia, and stating that a previous suicide attempt while on fluoxetine was also precipitated by akathisia); Martin H. Teicher et al., *Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment*, 147 AM. J. PSYCHIATRY 207, 207–09 (1990) (presenting several case studies in which patients felt "intense self-destructive thoughts" as a result of fluoxetine treatment).

68. *See* Citizen Petition of Sidney M. Wolfe & Ida Hellander, Health Research Group, Public Citizen, FDA Dkt. No. 91P-0203 (May 23, 1991) (providing extensive documentation in support of a boxed warning on suicidality in Prozac labeling); Citizen Petition of Sanford Block, Citizens Comm'r on Human Rights, FDA Dkt. No. 90P-0342 (Oct. 11, 1990) (requesting that the agency withdraw its

Moreover, the agency requested supplemental reports from the manufacturers,⁶⁹ and on at least six different occasions between 1990 and 2006 it convened advisory committees to review questions relating to modern antidepressant safety.⁷⁰ Having thus examined the potential link between suicide and antidepressants, both individually and as a class, the agency has never judged adult suicide warnings to be appropriate. To this day it has not adopted a suicide warning for adults over the age of 25.⁷¹ Instead, FDA has denied the citizen petitions requesting withdrawal or labeling changes based on suicidality.⁷² It has directed the manufacturers to avoid labeling changes and to use class (rather than product-specific) labeling.⁷³ Furthermore, the agency has repeatedly communicated its views on modern

approval of Prozac); Citizen Petition of Rosellen Meysenburg, FDA Dkt. No. 97P-0010 (Jan. 2, 1997) (requesting revision of the Prozac labeling to include a specific warning concerning suicide).

69. *See, e.g.*, Brief of the Pharmaceutical Research and Manufacturers of America as Amicus Curiae in Support of Appellee at 17, *Dobbs v. Wyeth Pharm.*, No. 08-6018, 2009 WL 2429125 (10th Cir. July 24, 2009) (“FDA has also asked Wyeth to provide a report on its data, which FDA has then independently analyzed in conjunction with data from other . . . manufacturers [of similar drugs].”) (citing Letter from FDA to Wyeth (July 22, 2003)).

70. Transcript of Psychopharmacological Drugs Advisory Committee at 30 (Nov. 19, 1990); Transcript of Psychopharmacological Drugs Advisory Committee at 12 (Sept. 20, 1991), *available at* <http://www.fda.gov/OHRMS/DOCKETS/AC/prozac/2443T1.PDF>; Transcript of Psychopharmacological Drugs Advisory Committee at 51 (Apr. 30, 1993); Transcript of Psychopharmacologic Drugs Advisory Committee with the Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committee at 12–14 (Feb. 2, 2004), *available at* <http://www.fda.gov/ohrms/dockets/ac/04/transcripts/4006T1.pdf>; Transcript of Joint Meeting of the CDER Psychopharmacologic Drugs Advisory Committee and the FDA Pediatric Advisory Committee at 6, 16 (Sept. 13, 2004), *available at* <http://www.fda.gov/ohrms/dockets/ac/04/transcripts/2004-4065T1.pdf>; Transcript of Psychopharmacologic Drugs Advisory Committee at 7 (Dec. 13, 2006), *available at* <http://www.fda.gov/ohrms/dockets/ac/06/transcripts/2006-4272t1-part1.pdf>.

71. In 2007, FDA adopted a warning about suicide risk for *young* adults, age 24 and younger, adding that the data did not show an increased risk in adults older than 24. Food & Drug Admin., *New Warnings Proposed for Antidepressants* (May 3, 2007), <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm048950.htm>.

72. *See* Response to Citizen Petition of Sanford Block, Citizens Comm’r on Human Rights, FDA Dkt. No. 90P-0342 (July 26, 1991) (denying request that the agency withdraw its approval of Prozac and reviewing the scientific basis for the decision); Response to Citizen Petition of Sidney M. Wolfe & Ida Hellander, Health Research Group, Public Citizen, FDA Dkt. No. 91P-0203 (June 3, 1992) (denying request that FDA revise Prozac’s labeling to include a boxed warning related to its association with suicidality and citing the unanimous conclusion of the Psychopharmacological Drugs Advisory Committee that “the evidence was not sufficient to show that antidepressants in general, or Prozac in particular, cause the emergence and/or intensification of suicidality and/or other violent behavior”); Response to Citizen Petition of Rosellen Meysenburg, FDA Dkt. No. 97P-0010 (June 25, 1997) (enclosing the response to the citizen petition from Public Citizen).

73. *See, e.g.*, Letter from Russell Katz, Dir., Div. of Neuropharmacological Drug Prods., Ctr. for Drug Evaluation & Research, Food & Drug Admin., to Kenneth Bonk, Dir., Worldwide Regulatory Affairs, Wyeth Pharm., Inc. (May 13, 2004), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2004/20151slr028,030,032,20699slr041,048,052ltr.pdf (noting an agreement to not change the label and to maintain current warning language).

antidepressants and suicide risk to the public through a *Talk Paper*⁷⁴ and at least five Public Health Advisories.⁷⁵ Thus, the defendants appear to have a strong argument that FDA has judged adult suicide warnings to be scientifically unfounded and would therefore have rejected them in 1998 and 2002.

Still, it is possible that even such an extensive and well-documented history of agency consideration will fail to constitute *clear evidence* under certain interpretations of *Levine*. In fact, the Seventh Circuit recently held that the agency's history of studying the issue of suicidality and antidepressants does not constitute *clear evidence* that it would have rejected a warning related to suicidality in young adults.⁷⁶ It remains to be seen whether the Tenth Circuit will draw the same conclusion with respect to suicidality in adults.⁷⁷

74. Food & Drug Admin., FDA Talk Paper: FDA Statement Regarding the Anti-Depressant Paxil for Pediatric Population (June 19, 2003), <http://web.archive.org/web/20031003215653/www.fda.gov/bbs/topics/ANSWERS/2003/ANS01230.html>.

75. Press Release, Food & Drug Admin., FDA Proposes New Warnings About Suicidal Thinking, Behavior in Young Adults Who Take Antidepressant Medications (May 2, 2007), <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2007/ucm108905.htm>; Food & Drug Admin., Public Health Advisory: Suicidality in Adults Being Treated with Antidepressant Medications (June 3, 2005), <http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm053169.htm>; Food & Drug Admin., Reports of Suicidality in Pediatric Patients Being Treated with Antidepressant Medications for Major Depressive Disorder (MDD) (Oct. 27, 2003), <http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm168828.htm>; Food & Drug Admin., Suicidality in Children and Adolescents Being Treated with Antidepressant Medications (Oct. 15, 2004), <http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm161679.htm>; Food & Drug Admin., Worsening Depression and Suicidality in Patients Being Treated with Antidepressants (Mar. 22, 2004), <http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm161696.htm>.

76. See *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 396 (7th Cir. 2010) (holding that plaintiffs' claims are not preempted because the defendant "did not meet its burden of demonstrating by clear evidence that the FDA would have rejected a label change warning about the risk of suicide by young adults").

77. There is one—arguably significant—difference between the facts in *Mason* and those in the Tenth Circuit cases: FDA eventually required drugs such as Prozac (generally known as selective serotonin reuptake inhibitors or SSRIs) to bear a warning related to suicidality in young adults, whereas it still has not required any such warning as to adult suicidality. See *supra* note 71. In *Mason*, the court noted that:

[I]n May of 2007, the FDA ordered all antidepressant manufacturers to include an additional warning about the increased likelihood of suicidality in young adults under the age of 24. . . . Since these events occurred well after [plaintiff]'s suicide [in 2003], they are not persuasive in determining whether there was clear evidence that the FDA would have rejected the proposed warning at the time of . . . death. *To the extent these subsequent events have any sway, however, they clearly cut towards making it less likely that the FDA would have rejected the plaintiffs' proposed warning in 2003.*

Mason, 596 F.3d at 395–96 (emphasis added). Thus, the Tenth Circuit could judge that there is stronger evidence—namely, the agency's continued refusal to require such a warning, even after doing so for other patient populations—that FDA would have rejected an adult suicide warning. At least one of the lower courts appears to have given weight to that fact. See *Dobbs v. Wyeth Pharm.*, 530 F. Supp. 2d 1275, 1289–90 & n.6 (W.D. Okla. 2008) (noting that FDA had not only considered and rejected an adult suicidality warning at the time of the plaintiff's suicide, but that it still had not required such a warning at the time of the decision). Because the significance of such subsequent regulatory developments is

2. Limited Use of the CBE Supplement

Even if the CBE mechanism was theoretically available in the *Levine* case, there are situations in which a CBE supplement is not legally permitted. Each of these situations should give rise to impossibility preemption. To begin with, some safety-related changes to the labeling do not qualify for use of the CBE mechanism by the plain terms of 21 C.F.R. § 314.70 because the evidence is not newly acquired or because there is insufficient evidence of causation.⁷⁸ FDA's regulatory scheme precludes use of the CBE in other situations as well. For example, FDA regulations require submission of a prior approval supplement for any change to the *Highlights* information, except for certain minor changes.⁷⁹ Important safety changes to prescribing information—for example, substantive changes to the boxed warnings, contraindications, or warnings and precautions sections of the package insert—must also be reflected in the *Highlights* section.⁸⁰ Thus, for those drugs to which the new rules apply,⁸¹ the addition of major new safety information will require prior approval, since the corresponding changes to the *Highlights* section cannot legally take the form of a CBE supplement. Changes to an approved Medication Guide (MedGuide) also require prior approval, and any MedGuide must be consistent with the approved professional labeling.⁸² Where the addition of

debatable, if the Tenth Circuit decision does find *clear evidence* that FDA would have rejected an adult suicide warning, where the Seventh Circuit did not find *clear evidence* as to young adult suicidality, the circuit split could provide an opportunity for the Supreme Court to revisit and elucidate *Levine's clear evidence* standard.

78. See 21 C.F.R. § 314.70(c)(6)(iii) (2009) (outlining the circumstances in which a CBE supplement may be used).

79. *Id.* §§ 314.70(b)(2)(v)(C), (c)(6)(iii), 601.12(f)(1), (f)(2)(i). Given the importance of the *Highlights* section and the difficulty in summarizing the information in the *Full Prescribing Information*, the agency concluded that it was “essential for FDA to review and approve most proposed changes to the information in *Highlights*.” Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3932 (Jan. 24, 2006). FDA has authority to waive the prior approval requirement under 21 C.F.R. § 314.90.

80. 21 C.F.R. § 201.57(a)(5). The changes that must be included in *Highlights* are “those changes that are significant to the clinical use of the drug and, therefore, have significant clinical implications for practitioners (i.e., substantive changes).” Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3938. As one FDA official has explained, this requirement means that “probably all important safety changes will now result in a change to *Highlights*.” Brian Marson, *Labeling Rule Requires Sponsors to Start Safety Discussions with FDA Earlier*, THE PINK SHEET, Oct. 29, 2007, at 26 (quoting Laurie Burke, CDER study endpoints and labeling team leader, during a Drug Information Association call).

81. The new labeling regulations apply only to prescription drug products for which an NDA, biologics license application (BLA), or efficacy supplement was approved after June 30, 2001. 21 C.F.R. § 201.56(b)(1). The manufacturers of these products must modify the drug's labeling to meet the requirements of new regulations, which are phased in through 2013 based on the approval date of the application. *Id.* § 201.56(c). Manufacturers of other products may voluntarily adopt the new labeling requirements at any time. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3928.

82. 21 C.F.R. § 208.20(a)(2). A MedGuide is required for any drug products “that the [agency] determines pose a serious and significant public health concern requiring distribution of FDA-approved

significant new safety information to the professional labeling of a product requires a corresponding change to its MedGuide, the change to the professional labeling will effectively be subject to prior approval.⁸³

Another series of cases has raised a novel variation on the impossibility question in *Levine*. The question presented is whether state failure-to-warn claims against generic manufacturers are preempted because of the federal statutory requirement that the labeling of a generic drug be identical to that of the reference listed product on which it is based.⁸⁴ FDA has taken the position that impossibility preemption applies, because generic manufacturers may not revise their labeling unilaterally.⁸⁵ The agency's own statement that generic manufacturers may not revise their labeling to vary from that of the innovator⁸⁶ strikes us as "clear evidence" that FDA would reject the labeling changes demanded by the plaintiffs. But the lower court rulings are mixed, with a (slight) majority rejecting

patient information." *Id.* § 208.1(a). The agency requires a MedGuide when it determines that the MedGuide is necessary to permit patients to use the drug product safely and effectively. *Id.* § 208.1(b); *see also id.* § 208.1(c) (requiring a MedGuide when (1) a MedGuide "could help prevent serious adverse effects;" (2) the drug has serious risks that "could affect patients' decision to use . . . the product;" or (3) "adherence to directions for use is crucial to the drug's effectiveness"). FDA approves the content of all MedGuides.

83. *Id.* § 314.70(b)(v)(B). Similar reasoning applies with respect to the labeling of a drug with an approved Risk Evaluation and Mitigation Strategy (REMS). By statute, changes to the REMS require prior approval. 21 U.S.C. § 355-1(h)(3), (h)(5)(H) (West Supp. 2009). Some elements of a REMS constitute labeling and must therefore, under FDA regulations, be consistent with and not contrary to the approved professional labeling. Some safety-related labeling changes will require coordinated changes to the REMS on account of the consistency rule. These labeling changes will therefore require prior approval. *See* Supplemental Applications Proposing Labeling Changes for Approved Drugs, Biologics, and Medical Devices, 73 Fed. Reg. 49,603, 49,607 (Aug. 22, 2008) ("[I]f the labeling for a drug describes an element of an approved REMS, the sponsor must receive prior approval of any labeling change that would necessitate a change to the sponsor's REMS.").

84. *See, e.g.,* Bartlett v. Mut. Pharm. Co., 659 F. Supp. 2d 279, 281 (D. N.H. 2009) (stating the question presented as "whether state-law tort claims alleging the defective labeling of generic drugs are preempted by federal law"); Kellogg v. Wyeth, 612 F. Supp. 2d 437, 438-39, 442 (D. Vt. 2009) (considering the question of whether generic manufacturers are subject to *Levine* for the purposes of an interlocutory appeal and motion to stay proceedings against the generic manufacturers).

85. Brief of United States as Amicus in Support of Apotex, *supra* note 23, at 7-8 & n.4 (arguing that the manufacturer of generic paroxetine hydrochloride should not be liable for failure to warn because generic drug manufacturers are required to maintain the same labeling as their name brand counterparts; may not make labeling changes without getting prior FDA approval; and, in particular, are not eligible to use the CBE process). The Third Circuit found preemption in *Colacicco v. Apotex, Inc.*, 521 F.3d 253, 271 (3d Cir. 2008), but the decision was vacated and remanded for further consideration in light of *Levine*. *Colacicco v. Apotex, Inc.*, 129 S. Ct. 1578, 1578-79 (2009). FDA then withdrew as an amicus, declining to take a position on reconsideration because it had not yet adequately examined the implications of *Levine*. Letter from Sharon Swingle, Attorney, Civil Div., U.S. Dep't of Justice, to Marcia M. Waldron, Clerk, U.S. Court of Appeals for the Third Circuit (Apr. 28, 2009).

86. *See* 21 U.S.C. § 355(j)(4)(G) (2006) (showing that an abbreviated new drug application (ANDA) may not be approved if the labeling is different, with certain narrow exceptions not including safety information); 21 C.F.R. § 314.94(a)(8)(iv) (listing variations permitted in generic drug labeling); *id.* § 314.127(a)(7) (describing labeling differences that require disapproval of ANDA).

impossibility preemption.⁸⁷ Only two circuit courts have rendered decisions, both holding that the state law was not preempted by FDA regulations.⁸⁸

III. LEVINE ON OBSTACLE PREEMPTION

A. The Doctrine

The doctrine of “obstacle preemption” is usually attributed to *Hines v. Davidovitz*,⁸⁹ in which the Supreme Court considered whether Pennsylvania’s alien registration requirements were preempted by a recently enacted national scheme.⁹⁰ Although there was no express preemption provision in the federal statute and compliance with the two regimes was not impossible, the Court nevertheless found the Pennsylvania requirements preempted on the grounds that they would “stand[] as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress.”⁹¹

The *Hines* Court observed that “there can be no one crystal clear distinctly marked formula” for this kind of preemption.⁹² The Court rested its conclusion that Pennsylvania’s requirements posed an obstacle to the federal regime on the traditional role of the federal government in matters of foreign affairs,⁹³ the breadth and comprehensiveness of Congress’s plan,⁹⁴ and evidence in the legislative history that Congress had sought to “steer a middle path” between security and personal

87. *Compare, e.g.*, *Dorsett v. Sandoz Inc.*, 2010 WL 1174204 at *19 (C.D. Cal. Mar. 26, 2010) (declining to find preemption); *Bartlett*, 659 F. Supp. 2d at 308 (same); *Kellogg*, 612 F. Supp. 2d at 442 (same); *Stacel v. Teva Pharm., USA*, 620 F. Supp. 2d 899, 907 (N.D. Ill. 2009) (same); *Schrock v. Wyeth, Inc.*, 601 F. Supp. 2d 1262, 1265 (W.D. Okla. 2009) (same), *with Gaeta v. Perrigo Pharm. Co.*, No. C 05-04115 JW, 2009 WL 4250690, at *5 (N.D. Cal. Nov. 24, 2009) (denying plaintiffs’ motion for reconsideration on preemption); *Masterson v. Apotex, Corp.*, No. 07-61665-CIV, 2008 WL 3262690, at *5 (S.D. Fla. Aug. 7, 2008) (finding preemption); *Morris v. Wyeth*, No. 1:07-CV-176-R, 2009 WL 736200, at *1 (W.D. Ky. Mar. 4, 2009), *aff’g* 582 F. Supp. 2d 861, 868 (W.D. Ky. 2008) (same); *Smith v. Wyeth, Inc.*, No. 5:07-CV-18-R, 2009 WL 736208, at *1 (W.D. Ky. Mar. 4, 2009), *aff’g* 2009 WL 425032, at *4, *7 (W.D. Ky. Feb. 20, 2009) (same); *Wilson v. Wyeth, Inc.*, No. 3:07-CV-00378-R, 2009 WL 736198, at *1 (W.D. Ky. Mar. 4, 2009), *aff’g* 2008 WL 4696995, at *6 (W.D. Ky. Oct. 24, 2008) (same).

88. *Mensing v. Wyeth, Inc.*, 588 F.3d 603, 608 (8th Cir. 2009); *Demahy v. Actavis, Inc.*, 593 F.3d 428, 449 (5th Cir. 2010). At this writing, appeals on the issue are pending before the Sixth Circuit. *See* Appellant Lala Smith’s Opening Brief at 1, *Smith v. Wyeth, Inc.*, No. 09-5460 (6th Cir. Dec. 1, 2009), 2009 WL 4611244 (presenting the question “[w]hether the district court erred in holding that the FDCA preempts . . . claims for personal injuries caused by generic a [sic] drug manufacturer failure to warn” on appeal to the Sixth Circuit); Appellant Alice Wilson’s Opening Brief at 1, *Wilson v. Pliva, Inc.*, No. 09-5466 (6th Cir. Dec. 1, 2009), 2009 WL 4611245 (same); Appellant Dennis Morris’s Opening Brief at 1, *Morris v. Wyeth, Inc.*, No. 09-5509 (6th Cir. Dec. 1, 2009), 2009 WL 4611243 (same).

89. 312 U.S. 52 (1941).

90. *Id.* at 59–60.

91. *Id.* at 67, 74.

92. *Id.* at 67.

93. *Id.* at 62–63.

94. *Id.* at 69.

liberty.⁹⁵ Subsequent courts have invoked similar themes in their obstacle preemption analyses by focusing on the character of the subject matter (i.e., whether it is traditionally a federal matter or particularly requires uniformity),⁹⁶ the purposes of the federal law,⁹⁷ and whether the federal scheme effects a balance or compromise between competing objectives.⁹⁸

FDA has repeatedly pointed to the relevance of these considerations in the drug regulatory context. In briefs filed by the government on FDA's behalf in *Levine* and many other cases over the last three decades, the agency has emphasized that regulating prescription drugs is a federal responsibility, requiring the agency to exercise exclusive control in order to provide uniform information to the public.⁹⁹ The agency has also repeatedly invoked the purposes of the FDCA, such as to provide for complex regulatory decisions to be made by experts based on a wide range of viewpoints.¹⁰⁰ In addition, the agency has consistently described its

95. *Id.* at 73–74.

96. *See, e.g.,* *United States v. Locke*, 529 U.S. 89, 108 (2000) (declining to apply a presumption against preemption of state law “when the State regulates in an area where there has been a history of significant federal presence” and observing that the federal statutory scheme “has as one of its objectives a uniformity of regulation for maritime commerce”); *Boyle v. United Techs. Corp.*, 487 U.S. 500, 504 (1988) (noting that in areas involving “unique federal interests,” the Court is more likely to find that a state law is preempted); *Fla. Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 143–44 (1963) (considering whether “the nature of the subject matter” requires that the state law give way to the federal by examining whether it is a “subject by its very nature admitting only of national supervision” or a “subject demanding exclusive federal regulation in order to achieve uniformity vital to national interests”).

97. *See, e.g.,* *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 374–77 (2000) (examining Congress's objectives in enacting the federal statute granting the President control over diplomatic relations with Burma); *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 875–81 (2000) (enumerating various purposes served by a passive restraint regulation).

98. *See, e.g.,* *Int'l Paper Co. v. Ouellette*, 479 U.S. 481, 494–97 (1987) (finding preemption of a state law that “upset[] the balance of public and private interests so carefully addressed” by the federal statute and thereby potentially undermined “Congress' considered judgment as to the best method of serving the public interest and reconciling . . . often competing concerns”); *Cipollone v. Liggett Group, Inc.*, 789 F.2d 181, 187 (3d Cir. 1986) (finding obstacle preemption when the federal statute represented “a carefully drawn balance between the purposes of warning the public of the hazards of cigarette smoking and protecting the interests of national economy”).

99. Brief for United States as Amicus Curiae Supporting Petitioner at 9, 11, 13–14, *Wyeth v. Levine*, 129 S. Ct. 1187 (2009) (No. 06-1249), 2008 WL 2308908 [hereinafter *Amicus Brief Supporting Wyeth*] (describing FDA's expertise and authority in providing uniform information to the public); *see also* Brief for United States as Amicus Curiae Supporting Petitioner at 18, *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001) (No. 98-1768), 2000 WL 1364441 [hereinafter *Amicus Brief Supporting Buckman Co.*] (“[T]he field involving an individual's obligation to provide accurate information to a federal regulatory agency is one in which there is an overriding and longstanding federal interest.”); Statement of Interest of United States at 1–2, 5, *Bernhardt v. Pfizer, Inc.*, 2000 WL 1738645 (S.D.N.Y. 2000) (No. 00 Civ. 4042) (observing that “the Federal Government, through the FDA, is responsible for regulating prescription drugs,” and stressing that the success of the agency's mission to protect the public health depends on its ability to exercise “exclusive control over . . . drug labeling” and thereby “ensure that the public receives uniform, consistent information”).

100. *See, e.g.,* *Amicus Brief Supporting Buckman Co.*, *supra* note 99, at 21 (“The FDCA establishes a comprehensive scheme to regulate the information that an entity must submit to FDA . . .”); Brief of

mandate as one of careful balancing of the competing considerations of promoting safety while not discouraging beneficial use.¹⁰¹ On these grounds, FDA has argued that permitting state juries to impose alternative requirements on drug companies would undermine Congress' objectives in establishing the agency and "frustrate the agency's implementation of its statutory mandate."¹⁰² Among other concerns, the agency has pointed out that the prospect of such liability encourages drug manufacturers to include warnings about "speculative risks" (i.e., to

United States at 6, *In re Paxil Litigation*, 2002 U.S. Dist. LEXIS 24621 (C.D. Cal. Sept. 5, 2002) (No. CV 01-07937), 2002 U.S. Dist. Ct. Motions LEXIS 10378 ("In enacting the FDCA, Congress clearly desired that the full range of scientific and medical opinion be brought to bear on the question of publicly available prescription drug information." (citing 21 U.S.C. § 393(b)(4) (2006))); Statement of Interest of United States, *supra* note 99, at 10 ("Consultation with a full range of experts, as well as cooperation with all those affected, is what the FDA does and is precisely what Congress desired." (citing 21 U.S.C. § 393(b)(4))); Amicus Brief of United States in Support of SmithKline, *supra* note 23, at 31 ("[B]y enacting the FDCA, Congress established a comprehensive regulatory plan designed to ensure the safety and effectiveness of drugs. Congress gave FDA plenary authority to regulate the labeling of drug products.").

101. See, e.g., Amicus Brief Supporting Wyeth, *supra* note 99, at 10–11 (explaining that "labeling must strike a balance between notifying users of potential dangers and not unnecessarily deterring beneficial uses" through overwarning); Statement Regarding the Demonstrations of Effectiveness of Human Drug Products and Devices, 60 Fed. Reg. 39,180, 39,180 (Aug. 1, 1995) ("In evaluating the safety of a new drug or medical device, FDA weighs the product's demonstrated effectiveness against its risks to determine whether the benefits outweigh the risks. This weighing process also takes into account information such as the seriousness and outcome of the disease, the presence and adequacy of existing treatments, and adverse reaction and other safety data."); Prescription Drug Products; Revocation of Patient Package Insert Requirements, 47 Fed. Reg. 39,147, 39,149 (Sep. 7, 1982) ("[A]s part of the approval process to which virtually all prescription drugs are subject, risks are weighed against potential benefits, and not considered as absolutes. Patient information that is heavily 'warning' oriented, therefore, might undermine the more balanced approach to informing patients about drug therapy . . .").

102. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006); see also 150 CONG. REC. S8657 (daily ed. July 22, 2004) (Letter from Peter Barton Hutt et al., former Chief Counsels of FDA, to The Honorable Judd Gregg, Chairman of the Health, Education, Labor & Pensions Comm., U.S. Senate) ("If every state judge and jury could fashion their own labeling requirements for drugs and medical devices, there would be regulatory chaos for these two industries that are so vital to the public health, and FDA's ability to advance the public health by allocating scarce space in product labeling to the most important information would be seriously eroded.").

“overwarn”),¹⁰³ which can diminish the effectiveness of FDA-mandated warnings and deter use of beneficial treatments.¹⁰⁴

Courts have agreed that certain state requirements pose obstacles to the accomplishment of the federal government’s food and drug regulatory objectives.¹⁰⁵ Indeed, in 2001, the Supreme Court invalidated state “fraud-on-the-FDA” claims on the grounds that they posed just such an obstacle in *Buckman Co. v. Plaintiffs’ Legal Committee*.¹⁰⁶ Echoing most of the major obstacle preemption themes from *Hines*, the *Buckman* Court noted that the subject of the case was “federal in character,”¹⁰⁷ that it involved a comprehensive federal scheme,¹⁰⁸ and

103. See Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3935 (“[T]he threat of significant damage awards . . . creates pressure on manufacturers to attempt to add warnings that FDA has neither approved nor found to be scientifically required.”); Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81,082, 81,083 (Dec. 22, 2000) (“[T]he use of labeling in product liability and medical malpractice lawsuits, together with increasing litigation costs, has caused manufacturers to become more cautious and include virtually all known adverse event information, regardless of its importance or its plausible relationship to the drug.”); Letter Brief from Peter D. Keisler et al. at 26, *Hom v. Thoratec Corp.*, 376 F.3d 163 (3d Cir. 2004) (No. 02-4597), 2004 WL 1143720 (noting in the device context that the threat of tort litigation can cause inappropriate warnings or unnecessary withdrawals of FDA-approved products).

104. See Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3935 (“[D]efensive labeling’ . . . could result in scientifically unsubstantiated warnings and underutilization of beneficial treatments.”); Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,447 (June 26, 1979) (“[I]ncluding theoretical hazards as contraindications in drug labeling would cause that very important section of the labeling to lose its significance.”); *id.* at 37,448 (“[T]o ensure the significance of boxed warnings in drug labeling, they are permitted in labeling only when specifically required by FDA.”); CTR. FOR DEVICES & RADIOLOGICAL HEALTH, U.S. FOOD & DRUG ADMIN., WRITE IT RIGHT: RECOMMENDATIONS FOR DEVELOPING USER INSTRUCTION MANUALS FOR MEDICAL DEVICES USED IN HOME HEALTH CARE 7 (1993) (“Overwarning has the effect of not warning at all. The reader stops paying attention to excess warnings.”); W. Kip Viscusi, *Individual Rationality, Hazard Warnings, and the Foundations of Tort Law*, 48 RUTGERS L. REV. 625, 665–66 (1996) (“Excessive warnings are not innocuous. . . . [I]f warnings are included for inconsequential risks, they will serve to further dilute the warnings for the real hazards that should be identified to consumers.”).

105. See *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 348–53 (2001) (finding preemption of state fraud-on-the-FDA tort on the grounds that it conflicted with FDA’s authority to police fraud according to its own “delicate balance of statutory objectives”); *Jones v. Rath Packing Co.*, 430 U.S. 519, 540–43 (1977) (finding a California flour packaging statute preempted on the grounds that, by permitting variations from the stated weight, it posed an obstacle to a federal statute that aimed at facilitating comparisons among products); *Cosmetic, Toiletry & Fragrance Ass’n v. Minnesota*, 440 F. Supp. 1216, 1224 (D. Minn. 1977), *aff’d*, 575 F.2d 1256 (8th Cir. 1978) (holding that a Minnesota cosmetic labeling requirement was “an obstacle to full effectuation of the federal purpose,” even though it was possible to comply with both requirements, because the state scheme “would require more time and expense and thus cause more disruption”); *Dowhal v. SmithKline Beecham Consumer Healthcare*, 88 P.3d 1, 15 (Cal. 2004) (finding preemption of California’s warning because the state’s policy goal conflicts with FDA’s “nuanced goal—to inform pregnant women of the risks of [nicotine replacement therapy] products, but in a way that will not lead some women, overly concerned about those risks, to continue smoking”).

106. *Buckman*, 531 U.S. at 347–50.

107. *Id.* at 347.

that Congress had assigned FDA “difficult (and often competing) objectives.”¹⁰⁹ Moreover, the Court observed that FDA’s device regulations require the agency to “achieve a somewhat delicate balance of statutory objectives,” which could be “skewed” by allowing state tort claims.¹¹⁰ The prospect of state tort liability would “dramatically increase the burdens facing potential applicants,”¹¹¹ and it would provide “an incentive to submit a deluge of information that [FDA] neither wants nor needs, resulting in additional burdens on the FDA’s evaluation of an application.”¹¹²

In *Buckman*, the Supreme Court deemed one of FDA’s regulatory review processes—in fact, its device clearance process, the complexity of which pales in comparison to the agency’s review and approval of new drugs—to be sufficiently comprehensive and complex, and to require a “delicate” enough balancing of competing considerations, to warrant protection from interference from state tort requirements under the doctrine of obstacle preemption. How the same court came to the opposite conclusion about the agency’s drug labeling review is an intriguing question.

B. The Majority’s Reasoning

1. Congressional Intent

The *Levine* majority first rejected obstacle preemption because it found no evidence in the seventy-year history of the FDCA that Congress viewed state law suits as an obstacle to the objectives of the statute.¹¹³ Among other considerations, the majority observed that “despite its 1976 enactment of an express pre-emption provision for medical devices, Congress has not enacted such a provision for prescription drugs.”¹¹⁴ The majority took congressional “silence” on the issue to be “powerful evidence” that the legislature did not intend FDA labeling decisions to preempt state law.¹¹⁵ There are at least three problems with this argument.

First, the Court reads too much into the existence of an express preemption provision for medical devices. That provision must be understood within the larger history of medical device regulation, which contrasts in crucial respects with the history of new drug regulation. Unlike drugs, medical devices were largely

108. *Id.* at 348.

109. *Id.* at 349.

110. *Id.* at 348.

111. *Id.* at 350.

112. *Id.* at 351.

113. *Wyeth v. Levine*, 129 S. Ct. 1187, 1200 (2009).

114. *Id.* (citations omitted).

115. *Id.*

unregulated¹¹⁶ at the federal level before 1976, when injuries associated with the Dalkon Shield intrauterine contraceptive device provided the impetus for passage of the Medical Device Amendments (MDA).¹¹⁷ The MDA gave FDA the authority to require premarket approval of high-risk devices and enhanced enforcement authorities with respect to devices.¹¹⁸ Congress included an express preemption provision in the MDA specifically because—in the absence of any federal regulation of medical devices—states had already begun legislating in response to the Dalkon Shield crisis, resulting in thirteen separate device regulation statutes by 1976.¹¹⁹ The Supreme Court recognized this history in *Riegel v. Medtronic*,¹²⁰ when it concluded that the express preemption provision reaches state common law as well as state regulatory law.¹²¹ There was never a comparable moment in the history of state and federal new drug regulation. Although some states and local jurisdictions had enacted rudimentary food and drug laws before 1906,¹²² the Congress that enacted the FDCA in 1938 following the elixir sulfanilamide disaster did not have to contend with a patchwork of state laws comparable to the patchwork that concerned Congress in 1976. In light of this history, the majority's

116. Medical devices were subject to misbranding and adulteration proscriptions, but not premarket testing requirements, under the 1938 statute. Federal Food, Drug, and Cosmetic Act, Pub. L. No. 75-717, §§ 301(b), 501, 502, 52 Stat. 1040, 1042, 1049–51 (1938) (codified as amended at 21 U.S.C. §§ 331, 351, 352 (2006 & Supp. 2009)). On more than one occasion, the lack of a comprehensive scheme for oversight of devices led FDA to classify as a drug something that today would be considered a medical device. *See, e.g.*, *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 799 (1969) (finding it reasonable for the Secretary to deem an antibiotic sensitivity disc a “drug” thus subject to premarket clearance requirement).

117. Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 539; *see also* Robert S. Adler & Richard A. Mann, *Preemption and Medical Devices: The Courts Run Amok*, 59 MO. L. REV. 895, 912 n.84 (1994) (“The Dalkon Shield was cited numerous times during the debates on the MDA in both the House and Senate.”).

118. Medical Device Amendments of 1976, sec. 2, §§ 513–521, 90 Stat. at 540–74 (codified as amended at 21 U.S.C. §§ 360c–360k).

119. Robert B. Leflar & Robert S. Adler, *The Preemption Pentad: Federal Preemption of Products Liability Claims After Medtronic*, 64 TENN. L. REV. 691, 703 & n.66 (1997). The House Committee on Interstate and Foreign Commerce cited this patchwork of state regulation and concern about burdening interstate commerce as the reason for the express preemption provision. H.R. REP. NO. 94-853, at 45 (1976). Although the drafters of the report recognized that some state regulation would be a useful supplement to the federal program, they noted a desire to avoid overlapping and conflicting regulations that would burden the device industry unnecessarily. *Id.* at 45–46. Concern for small manufacturers in the medical device industry, in the face of conflicting state laws, may have been a complementary motivation for the express preemption provision. According to one study, small manufacturers (defined as those suppliers selling less than \$1 million worth of merchandise per year to hospitals) made up 91.5% of the market in the early 1970s. *Medical Device Amendments, 1973: Hearing on S. 2368, S. 1446, and S. 1337 Before the Subcomm. on Health of the S. Comm. on Labor and Public Welfare*, 93rd Cong. 472–73 (1973) (statement of the Health Industries Association).

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

121. *Id.* at 324–25.

122. *See generally* PETER BARTON HUTT ET AL., *FOOD AND DRUG LAW: CASES AND MATERIALS* 8 (3d ed. 2007) (noting establishment of city, county, and state boards of health prior to the 1938 statute, as well as District food and drug legislation from the 1880s).

emphasis on the existence of an express preemption for medical devices and Congress' failure to make the preemption provision more generally applicable is misplaced. Both facts can be explained without inferring anything about congressional intent with respect to the force of drug provisions enacted earlier.

Second, the Court's previous jurisprudence strongly disfavors drawing inferences about congressional intent from congressional silence.¹²³ It is especially peculiar to infer from the lack of an express preemption provision that there could be no conflict preemption. It is precisely under those circumstances—when there is no applicable express preemption provision—that the question of conflict preemption arises.¹²⁴ Moreover, the Court has made it clear that it is inappropriate to conclude from the presence of a limited express preemption provision—or a saving provision, for that matter—that Congress intended to disallow the operation of conflict preemption principles.¹²⁵ Without conflict preemption principles, “state law could impose legal duties that would conflict directly with federal regulatory mandates”¹²⁶ Such an interpretation of a federal statute would effectively

123. See *Wyeth v. Levine*, 129 S. Ct. 1187, 1216–17 (2009) (Thomas, J., concurring) (“The fact that the Court reaches the proper conclusion does not justify its speculation about the reasons for congressional inaction. In this case, the Court has relied on the perceived congressional policies underlying inaction to find that state law is not pre-empted. But once the Court shows a willingness to guess at the intent underlying congressional inaction, the Court could just as easily rely on its own perceptions regarding congressional inaction to give unduly broad pre-emptive effect to federal law.”); *Brown v. Gardner*, 513 U.S. 115, 121 (1994) (“[C]ongressional silence ‘lacks persuasive significance’” (quoting *Pension Benefit Guar. Corp. v. LTV Corp.*, 496 U.S. 633, 650 (1990))); *Cent. Bank of Denver v. First Interstate Bank of Denver*, 511 U.S. 164, 185 (1994) (“[I]t is not plausible to interpret the statutory silence as tantamount to . . . implicit congressional intent”); *Zuber v. Allen*, 396 U.S. 168, 185 (1969) (“Legislative silence is a poor beacon to follow in discerning the proper statutory route.”); *Castro v. Chi. Hous. Auth.*, 360 F.3d 721, 728–29 (7th Cir. 2004) (“[A]ll we can deem from congressional silence on the issue is just that—that Congress was silent on the issue. . . . [I]nferences from congressional silence are treacherous; oversights are common in the hurly-burly of congressional enactment; omissions are not enactments; and even deliberate omissions are often subject to alternative interpretations” (quoting *Alto Dairy v. Veneman*, 336 F.3d 560, 566 (7th Cir. 2003))); *Am. Online, Inc. v. United States*, 64 Fed. Cl. 571, 578 (2005) (“Silence in the legislative history about a particular provision ordinarily is not a good guide to statutory interpretation”).

124. See *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 387–88 (2000) (“A failure to provide for preemption expressly may reflect nothing more than the settled character of implied preemption doctrine that courts will dependably apply, and in any event, the existence of conflict cognizable under the Supremacy Clause does not depend on express congressional recognition that federal and state law may conflict.” (citing *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941))); *Geier v. Am. Honda Motor Co.*, 529 U.S. 861, 884–85 (2000) (“[C]onflict pre-emption is different [from express preemption] in that it turns on the identification of ‘actual conflict,’ and not on an express statement of pre-emptive intent. . . . Indeed, one can assume that Congress or an agency ordinarily would not intend to permit a significant conflict.”).

125. *Geier*, 529 U.S. at 870–71 (rejecting arguments that the presence of a limited express preemption provision and/or a saving provision affected the operation of “ordinary conflict pre-emption principles”); *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287–88 (1995) (repudiating the interpretation of a previous case to mean that “implied pre-emption cannot exist when Congress has chosen to include an express pre-emption clause in a statute”).

126. *Geier*, 529 U.S. at 871.

“permit[] that law to defeat its own objectives, or . . . to ‘destroy itself.’”¹²⁷ Thus, neither the absence of a preemption provision, nor even the presence of such a provision that does not happen to apply to the case at hand, grounds any conclusion about conflict preemption.

Third, it is not correct that Congress has been silent on the issue. This assertion ignores section 202 of the 1962 amendments to the FDCA.¹²⁸ Section 202 was a response to the Supreme Court’s field preemption decision six years earlier in *Pennsylvania v. Nelson*.¹²⁹ In *Nelson*, the Supreme Court held that, even where “Congress has not stated specifically whether a federal statute has occupied a field in which the States are otherwise free to legislate,” the federal statute can nonetheless preempt the entire field.¹³⁰ Members of Congress were concerned that there was no language in the bill that became the 1962 amendments that disavowed total field preemption.¹³¹ The member of Congress who introduced the language that would become section 202 explained that it solved the problem presented by *Nelson* because the amendment meant “that this Food and Drug Act shall not be construed as the intent of Congress to abolish all State laws on the same subject where they are not in conflict with the Federal law.”¹³² Section 202 therefore provides that nothing in the 1962 amendments should “be construed as invalidating any provision of State law [that] 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.”¹³³ By enacting section 202, Congress both disavowed field preemption and acknowledged the possibility of conflict preemption.¹³⁴

127. *Id.* at 872 (quoting *Am. Tel. & Tel. Co. v. Cent. Office Tel., Inc.*, 524 U.S. 214, 228 (1998) (Rehnquist, C.J., concurring)).

128. Drug Amendments of 1962, Pub. L. No. 87-781, § 202, 76 Stat. 780, 793.

129. 350 U.S. 497, 500–02 (1956).

130. *Id.* at 501–02.

131. 108 CONG. REC. 21,046 (1962) (statement of Rep. Smith of California).

132. *Id.* at 21,083 (statement of Rep. Smith of Virginia).

133. Drug Amendments of 1962 § 202 (emphasis added).

134. That Congress intended section 202 to endorse conflict preemption principles is confirmed by its use of the words “direct and positive” to describe the type of conflict required for preemption to occur. *Id.* The Supreme Court had used these same words to describe conflict preemption in *Kelly v. Washington*, 302 U.S. 1, 10 (1937), which was a leading preemption case when Congress enacted the 1962 legislation. *See, e.g.*, *Huron Portland Cement Co. v. City of Detroit*, 362 U.S. 440, 447 (1960) (discussing *Kelly* in preemption case); *id.* at 449 (Douglas, J., dissenting) (same). The *Kelly* Court held that Congress may preempt only those state laws that conflict with federal law because “[t]here is no constitutional rule [that] compels Congress to occupy the whole field.” *Kelly*, 302 U.S. at 10. In stating that conflict preemption occurs “only where the repugnance or conflict is so ‘direct and positive’ that the two acts cannot be reconciled or consistently stand together,” the Court used the phrase “direct and positive” to distinguish the more limited effects of conflict preemption from the sweeping effects of field preemption. *Id.* (internal quotations omitted). Section 202 embodied this same distinction.

2. *No Deference Due*

The majority also rejected obstacle preemption on the ground that no deference was due to FDA's conclusion—as expressed in the Federal Register preamble to new physician labeling regulations in 2006¹³⁵—that certain state law failure-to-warn claims threaten the agency's role as the federal agency responsible for evaluating and regulating drugs. The agency's view “does not merit deference,” the majority wrote, because (1) there was a “procedural failure” in the physician labeling rulemaking in that interested parties lacked an opportunity to comment on the issue; (2) it conflicted with congressional intent; and (3) it reversed the agency's longstanding contrary position.¹³⁶ As discussed in the prior section, the evidence on congressional intent is more supportive of obstacle preemption than the majority's opinion allows. The majority's treatment of FDA's view is also troubling.

The position taken by FDA in the preamble to its final 2006 professional labeling regulations was not unprecedented; it was in fact consistent with many of the agency's previous statements. The Department of Justice, on behalf of FDA, has repeatedly argued for obstacle preemption of specific state law requirements in cases before the federal courts.¹³⁷ The agency has also issued regulations

135. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3933–36 (Jan. 24, 2006).

136. *Wyeth v. Levine*, 129 S. Ct. 1187, 1201 (2009).

137. *See, e.g., Eli Lilly & Co. v. Marshall*, 850 S.W.2d. 155, 159 (Tex. 1993) (“Lilly and the FDA urge that just such a conflict is presented here: by compelling disclosure of what the regulations promise will remain confidential, the trial court's order stands as an obstacle to the effective operation of the FDA's reporting system, and they argue, will effectively destroy it.”); Amicus Brief Supporting Buckman Co., *supra* note 99, at 10 (arguing that state fraud-on-the-FDA claims “conflict with the important federal interest in permitting FDA to decide for itself whether it has been defrauded, and, if so, what sanction is appropriate” and the agency's “decision to grant market clearance” for the defendant's device); Brief for United States as Amicus Curiae, *Jones v. Rath Packing Co.*, *supra* note 23, at 9 (arguing that the California's flour labeling requirements stood as an obstacle to the accomplishment of federal statutory objectives); Amicus Brief for United States in Support of Defendant, *Motus v. Pfizer*, *supra* note 23, at 1–2 (arguing that failure-to-warn suit based on a proposed warning that FDA had considered and rejected would “undermine the agency's authority to protect the public health”); Brief of United States, *supra* note 100, at 5 (arguing that plaintiffs' request for an injunction “poses an obstacle to the full objectives of Congress by attempting to substitute [the] Court's judgment for FDA's scientific expertise”); Amicus Brief of United States in Support of SmithKline, *supra* note 23, at 22–23 (arguing that using the proposed warning “would conflict with federal law and pose an obstacle to accomplishing Congress's full purposes and objectives”); Responsive Memorandum of United States FDA and USDA, *supra* note 23, at 23 (arguing that New York's requirement that nutritious cheese alternatives bear the “imitation” label would “interfere with FDA's goal of encouraging the development of such products,” and thereby “stand[] as an obstacle to the accomplishment and execution of the full purposes and objectives . . . of FDA's regulations”) (internal quotations omitted); Statement of Interest of United States, *supra* note 99, at 7 (arguing that claims for injunctive relief in the form of labeling modifications would “frustrate the FDA's ability effectively to regulate prescription drugs by having the Court substitute its judgment for FDA's scientific expertise”).

preempting specific state law requirements on grounds of obstacle preemption.¹³⁸ Although amici have identified a few statements suggesting the contrary, many of these are compatible with the agency's position in 2006 when they are understood in context.¹³⁹ Others may, in fact, represent conflicting views from different periods

138. In 1977, FDA preempted state law labeling requirements for over-the-counter (OTC) drugs and other products in self-pressurized containers propelled by chlorofluorocarbons to promote its "interest in uniform labeling requirements . . ." Certain Fluorocarbon (Chlorofluorocarbon) Propellants in Self-Pressurized Containers, 42 Fed. Reg. 22,018, 22,026 (Apr. 29, 1977). In 1982, FDA found that state law labeling requirements for tamper-resistant packaging "would effectively negate" the uniform national standards that FDA had determined were necessary "throughout the country" to protect the public health. Tamper-Resistant Packaging Requirements for Certain Over-the-Counter Human Drug and Cosmetic Products, 47 Fed. Reg. 50,442, 50,448 (Nov. 5, 1982). Again in 1982, FDA determined that "a single national pregnancy-nursing warning with a specified text is necessary to ensure that OTC drugs are used safely and for their intended purposes." Pregnant or Nursing Women; Delegations of Authority and Organization; Amendment of Labeling Requirements for Over-the-Counter Human Drugs, 47 Fed. Reg. 54,750, 54,756 (Dec. 3, 1982) (citing Over-the-Counter Human Drugs Which Are Generally Recognized as Safe and Effective and Not Misbranded; Proposed Amendment of General Provisions, 47 Fed. Reg. 39,470, 39,471 (Sept. 7, 1982)). In 1985, FDA proposed a rule that preempted state law labeling requirements regarding the link between oral aspirin and Reye Syndrome after determining that a "multiplicity of warning statements" would risk "consumer confusion" and thus interfere with FDA's "well-established policy of promoting uniformity in the area of labeling." Proposed Labeling for Oral Aspirin-Containing Drug Products, 50 Fed. Reg. 51,400, 51,402-03 (Dec. 17, 1985); see also Labeling for Oral and Rectal Over-the-Counter Aspirin and Aspirin-Containing Drug Products, 51 Fed. Reg. 8180, 8180 (Mar. 7, 1986) (final rule). In 1994, FDA proposed a rule that preempted state law requirements for the disclosure of adverse event-related information treated as confidential under agency regulations in order to prevent "interfere[nce] with the agency's objective of ensuring the safety of human drugs, biologics, and devices." Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules, 59 Fed. Reg. 3944, 3944 (Jan. 27, 1994); see also Protecting the Identities of Reporters of Adverse Events and Patients; Preemption of Disclosure Rules, 60 Fed. Reg. 16,962, 16,962 (Apr. 3, 1995) (final rule). Finally, in 1997, FDA proposed to preempt state requirements for the format and content of OTC drug labeling based on concerns that they "would interfere" with the agency's objective of "uniformity." Over-the-Counter Human Drugs; Proposed Labeling Requirements, 62 Fed. Reg. 9024, 9040 (Feb. 27, 1997). The passage of a federal statute mandating uniform requirements for OTC drugs subsequent to the publication of this proposal "supersede[d] the agency's proposed regulation preempting State and local labeling requirements." Over-the-Counter Human Drugs; Labeling Requirements, 64 Fed. Reg. 13,254, 13,272 (Mar. 17, 1999) (final rule).

139. For example, former Commissioners Kennedy and Kessler summarize a 1979 preamble as stating that "FDA labeling decisions do not 'influence civil tort liability of the manufacturer . . .'" Brief of Amici Curiae Former FDA Commissioners Dr. Donald Kennedy and Dr. David A. Kessler in Support of Respondent at 10 n.4, *Wyeth v. Levine*, 129 S. Ct. 1187 (2009) (No. 06-1249) [hereinafter Brief of Amici Curiae Former FDA Commissioners] (quoting Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs, 44 Fed. Reg. 37,434, 37,447 (June 26, 1979)). But the Commissioners truncated the sentence, which actually states that "[i]t is not the intent of FDA to influence the civil tort liability of the manufacturer." Labeling and Prescription Drug Advertising, 44 Fed. Reg. at 37,437 (emphasis added). The context makes clear that the agency was assuring a physician commentator that its labeling review process was not designed to influence how liability would be allocated between doctors and drug companies in product liability or medical malpractice suits. See *id.* FDA's intent was simply "to ensure that a complete and accurate explanation of the drug is provided to the medical community." *Id.* This response has no implications for FDA's views on whether its regulations preempt conflicting state requirements. See *id.* (replying to comments about tort liability but not discussing preemption). To give another example, the same brief points to the

in the agency's history. But these statements do not establish a settled position, nevermind a "traditional" view,¹⁴⁰ especially in light of explicit evidence to the contrary. It is therefore a mistake to characterize the agency's statements in 2006 as a departure from its previous views.

The agency's comments in 2006 must be understood within the context in which they arose. The 2006 preamble was the culmination of a multi-year effort to modernize agency regulations governing the content and format of physician labeling,¹⁴¹ specifically to enhance the safe and effective use of prescription drugs by creating a package insert that "make[s] it easier for health care practitioners to access, read, and use information in prescription drug labeling."¹⁴² Among other things, this effort led to the creation of a new *Highlights* section for physician labeling, which includes important introductory information on no more than half a

preamble to a proposed rule from 1994 in which FDA made the general statement that FDA "recogniz[es] that 'product liability plays an important role in consumer protection . . .'" Brief of Amici Curiae Former FDA Commissioners, *supra*, at 10 n.4 (quoting Protecting the Identities of Reporters of Adverse Events and Patients, 59 Fed. Reg. at 3948). Though cited as contradictory, this excerpt is compatible with FDA's position in the 2006 preamble, which indicated that the agency's approval of prescription drug labeling should "preempt[] state law only to the extent required to preserve Federal interests," and that it seeks to limit preemption "to the 'minimum level necessary to achieve the objectives of the [FDCA] . . .'" Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3969 (quoting Exec. Order No. 13132, 64 Fed. Reg. 43,255, 43,257 (Aug. 10, 1999)).

140. See *Levine*, 129 S. Ct. at 1202 (claiming that "FDA traditionally regarded state law as a complementary form of drug regulation").

141. The agency issued a new content and format proposal in December 2000. Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics; Requirements for Prescription Drug Product Labels, 65 Fed. Reg. 81,082 (Dec. 22, 2000). Before issuing this new proposal, "the agency evaluated the usefulness of prescription drug labeling" under its existing regulations, using "focus groups, a national physician survey, a public meeting, and [a] written comment[]" process. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3922. The agency developed a prototype for new labeling, issued a proposal with that prototype for public comment, and then spent five years reviewing the comments and finalizing the new requirements. *Id.* This was part of "a broad effort to improve the communication to health care practitioners of information necessary for the safe and effective use of prescription drug[]" labeling. *Id.* at 3928; see also Jacobson & Feigl, *supra* note 60 (describing FDA's 2006 labeling revisions as the "culmination of over ten years of study").

142. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3922. Package inserts for new drugs had increased considerably in detail, complexity and length. See U.S. FOOD & DRUG ADMIN. & INST. FOR SAFE MEDICATION PRACTICES, AN INTRODUCTION TO THE IMPROVED FDA PRESCRIPTION DRUG LABELING 7 (2006), available at <http://www.ismp.org/fda/ImprovedFDAPrescriptionDrugLabeling.pdf> (noting that over time, drug labeling changed in length, detail, and complexity); Lars Noah, *Medicine's Epistemology: Mapping the Haphazard Diffusion of Knowledge in the Biomedical Community*, 44 ARIZ. L. REV. 373, 440 (2002) (discussing the increase in detail of package inserts, and noting that the intent of the FDA rulemaking was to make prescription drug labeling a better source of information for physicians); Raymond L. Woosley, *Drug Labeling Revisions—Guaranteed to Fail?*, 284 JAMA 3047, 3048 (2000) (noting that package inserts for new drugs "have increased in length more than [five]-fold" and that FDA has surveyed physicians about optimal labeling because of concerns about the effectiveness of the insert packaging).

page unless FDA grants a waiver.¹⁴³ The *Highlights* section is intended to be a brief summary of key safety and effectiveness information.¹⁴⁴ It draws attention to the information that health care practitioners most commonly reference and consider most important, and it guides them to related sections in the *Full Prescribing Information*.¹⁴⁵ FDA also reordered and reorganized the *Full Prescribing Information*, creating a hierarchical structure to give greater prominence to the most commonly referenced information and to minimize redundancy.¹⁴⁶

Given that FDA was engaged in rulemaking focused on enhancing the role and function of professional labeling, it seems unremarkable that the agency became more focused on obstacle preemption (i.e., on the possibility that state law requirements might frustrate the objectives of the federal labeling scheme). In fact, the agency received several comments expressing concern about the product liability implications of the new *Highlights* requirement; these comments compelled the agency to consider the issue.¹⁴⁷ Therefore, in the preamble to the

143. 21 C.F.R. § 201.57(a) (2009); see also Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3930 (noting FDA's proposal to require a *Highlights* section and comments received on that subject).

144. Specific rules govern the content and format of the *Highlights* section. 21 C.F.R. § 201.57(a). With respect to warnings and precautions, for example, it identifies only the most clinically significant risks and concisely summarizes the salient features of those risks. *Id.* § 201.57(a)(10); Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3939. The *Table of Contents* for the *Full Prescribing Information* serves as a navigational tool that references all sections and subsections in the *Full Prescribing Information*, some of which are not referenced in the *Highlights*. § 201.57(b); see also Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3941 (stating FDA's intent to require an *Index* and *Highlights* sections and the comments on this proposal).

145. CTRS. FOR DRUG EVALUATION & RESEARCH & BIOLOGICS EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: LABELING FOR HUMAN PRESCRIPTION DRUG AND BIOLOGICAL PRODUCTS—IMPLEMENTING THE NEW CONTENT AND FORMAT REQUIREMENTS 7 (2006) [hereinafter LABELING GUIDANCE], available at <http://www.fda.gov/ohrms/dockets/98fr/05d-0011-gdl0001.pdf>. The *Full Prescribing Information* is the most substantive portion of the package insert, containing all information FDA found necessary for the safe and effective use of the drug. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3927.

146. Press Release, U.S. Food & Drug Admin., FDA Announces New Prescription Drug Information Format to Improve Patient Safety (Jan. 18, 2006), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108579.htm>. For example, as a result of feedback from two national physician surveys, the *Indications and Usage* and the *Dosage and Administration* sections were moved to the beginning of the *Full Prescribing Information*, while *Warnings and Precautions* were consolidated into a single section, and *Drug Interactions* and *Use in Specific Populations* appear now as distinct sections. *Id.*; LABELING GUIDANCE, *supra* note 145, at 3–4. In addition, some formerly optional sections (such as *Clinical Studies*) are now required. LABELING GUIDANCE, *supra* note 145, at 3.

147. Several commenters inquired whether the *Highlights* requirement might make manufacturers more vulnerable to product liability claims for failure to warn because this section of the labeling includes only limited safety information. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3933. The agency also received comments that the new requirements might have product liability implications for drugs approved prior to June 30, 2001, because these drugs were not subject to the *Highlights* requirement. *Id.* A dramatic increase in

final rule, FDA restated and elaborated on its belief that certain state law claims alleging failure to provide adequate warning of a drug's risks are preempted by the provisions of the FDCA that authorize FDA to approve drug labeling.¹⁴⁸

Finally, the assertion of procedural deficiency seems a bit odd and unfair, considering that FDA's preamble was not meant to have the force of law. Preambles are advisory opinions.¹⁴⁹ Had the agency intended to publish a preemptive regulation with the force of law, it presumably would have done so.¹⁵⁰ The agency's statement of its beliefs about the relationship between its decisions and state law requirements could just as easily have been contained in a brief to the Court,¹⁵¹ a Federal Register notice, or another agency publication. There is no legal requirement, and no compelling policy reason, to subject statements of this sort to "notice and comment." As the majority itself noted, the weight to be given an agency's views on obstacle preemption depends on their "thoroughness, consistency, and persuasiveness,"¹⁵² not on whether stakeholders have participated in their development. Failure to engage in notice and comment should not render the agency's views "inherently suspect."¹⁵³

C. Policy Considerations

Near the conclusion of its opinion, the majority rehearsed a number of claims made by amici for the respondent, apparently in support of its conclusions that FDA has historically viewed state tort law as complementary rather than preempted and that FDA's stated views on obstacle preemption are not, in fact, its authentic views.¹⁵⁴ Specifically, the majority asserted that (1) FDA has limited resources to monitor the drugs on the market, (2) manufacturers have superior access to safety

product liability litigation in recent years may also explain the agency's decision to lay out its views more comprehensively than before. See generally Lisa Girion, *State Vioxx Trial Is Set as Drug Suits Boom*, L.A. TIMES, June 27, 2006, at C1 (discussing how trials about the drug Vioxx have made the pharmaceutical industry the nation's top target of product liability suits).

148. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3935–96.

149. *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 25 (D.D.C. 1997) ("[The] preamble . . . constitutes an advisory opinion binding on the agency unless repudiated by the agency . . ."); 21 C.F.R. § 10.85(d)(1) (defining an *advisory opinion* as "[a] statement of policy or interpretation made in . . . [a]ny portion of a Federal Register notice other than the text of a proposed or final regulation, e.g., . . . a preamble to a proposed or final regulation").

150. See *supra* note 138. The majority effectively concedes this point. *Wyeth v. Levine*, 129 S. Ct. 1187, 1203 (2009) ("[W]e have no occasion in this case to consider the pre-emptive effect of a specific agency regulation bearing the force of law.").

151. Indeed, they were also contained in the Solicitor General's brief to the Supreme Court in the *Levine* case. See Amicus Brief Supporting *Wyeth*, *supra* note 99, at 26–27 (describing the brief as an elaboration of FDA's views as expressed in the 2006 preamble).

152. *Levine*, 129 S. Ct. at 1201.

153. *Contra id.* (stating that FDA's views on state law are "inherently suspect" in light of FDA's failure to offer States or interested parties "notice or opportunity for comment").

154. *Id.* at 1202–03 & n.12.

information about marketed drugs, (3) state tort suits uncover unknown drug hazards, (4) state tort suits provide incentives for manufacturers to disclose safety risks promptly, and (5) state tort suits serve a distinct compensatory function that may motivate injured persons to come forward with information.¹⁵⁵

The majority's reliance on these assertions is troubling. As a preliminary matter, they appear to be immaterial to the question of what FDA believes about the preemptive effects of its labeling determinations. Beyond that, they are disputable claims for which little evidence was provided to the Court. We disagree, for example, that FDA has inadequate resources to monitor the drugs on the market. Although FDA's general funding level has not kept pace with its statutory mandate,¹⁵⁶ drug safety is the most generously funded agency function in the agency's annual government appropriation,¹⁵⁷ and it receives considerable supplemental funding from user fees paid by the regulated parties.¹⁵⁸ The agency's Center for Drug Evaluation and Research has almost 3,000 full-time equivalent employees, approximately one quarter of everyone employed by the agency.¹⁵⁹

The suggestion that state tort suits reveal safety risks known to the manufacturer but unknown to FDA is puzzling in light of the agency's comprehensive new drug application, safety update report, postmarket safety reporting, and annual report requirements.¹⁶⁰ The majority may be implying that state tort law is somehow necessary to induce non-compliant manufacturers to comply with FDA's requirements.¹⁶¹ But the reporting requirements are already backed by criminal and civil enforcement authority,¹⁶² and the agency itself can and

155. *Id.* at 1202. The majority concluded that "the FDA long maintained that state law offers an additional, and important, layer of consumer protection that complements FDA regulation." *Id.* at 1202–03.

156. See generally Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 ADMIN. L. REV. 431, 450–52 (2008) (describing the gap that exists between the funds FDA needs and the amount of funds actually appropriated).

157. See U.S. DEP'T OF HEALTH & HUMAN SERVS., FISCAL YEAR 2010: FOOD AND DRUG ADMINISTRATION JUSTIFICATION OF ESTIMATES FOR APPROPRIATIONS COMMITTEES 17 (2009), available at <http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/BudgetReports/ucm153374.htm> (noting that in FY 2010, FDA's human drugs program was slated to receive \$458 million from FDA's federal budget appropriation, as compared to \$206 million for the biologics program and \$315 million for devices and radiological health).

158. *Id.* at 86 (noting that in FY 2010, the human drugs program has been projected to receive an additional \$450 million in user's fees).

159. *Id.* at 265.

160. See 21 C.F.R. §§ 314.50, .80, .81 (2009) (describing the content and form of drug applications and the reporting requirements for drug applicants).

161. See Brief of Amici Curiae Former FDA Commissioners, *supra* note 139, at 11 n.5 ("Many of the recent failure-to-warn cases . . . allege that the drug's manufacturer withheld important safety data from FDA.").

162. 21 U.S.C. §§ 331, 333 (2006).

does police compliance.¹⁶³ At its core, the majority's argument seems to be that the federal scheme cannot accomplish its mission without the help of state tort law. It strikes us as strange not to allow the federal scheme to operate unhampered by conflicting state requirements before drawing this debatable conclusion.

D. The Future of Obstacle Preemption

The future for obstacle preemption in pharmaceutical litigation after *Levine* is cloudy. The majority gave no deference to FDA's view that its statutory objectives are frustrated by state tort suits that impose different labeling requirements than its own.¹⁶⁴ Instead, based on arguments put forward by amici, it posited that state tort litigation in fact complements the federal regulatory scheme.¹⁶⁵ The decision did leave open the possibility of an agency rulemaking with preemptive effect, and Justice Breyer noted this option in his concurrence.¹⁶⁶ Thus, one clear path forward would be rulemaking on the preemption question. Apart from this, it is unclear whether this Court, or a differently composed Court at a later time, could be persuaded to reconsider the weight due to FDA's views or the proper relationship between federal drug labeling requirements and state tort law.

The majority's unquestioning acceptance of the far-reaching assertions of amici for the respondent is very troubling. Not only does the majority's rejection of obstacle preemption on the basis of these assertions strike us as incorrect, but it also strikes us as profoundly bad public policy. FDA is an expert agency entrusted by Congress with a mandate that involves complex technical judgments and delicate balancing of the risks and benefits of drug products at a societal level. The agency's ability to make those determinations and strike those balances is, and will be, significantly compromised by private lawsuits that allow juries to introduce

163. See Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities; Final Policy, 56 Fed. Reg. 46,191, 46,192 (Sept. 10, 1991) ("The fraud policy . . . ensure[s] . . . that . . . decisions on pending applications are made based upon reliable data; . . . resources are not wasted[;] . . . applications containing fraudulent data are removed from the review process; . . . [a]pproval of applications containing fraudulent data is withdrawn; and . . . [m]arketed products that may be affected by wrongful acts do not pose a threat to the public health."); U.S. FOOD & DRUG ADMIN., APPLICATION INTEGRITY POLICY PROCEDURES 2 (1998), available at <http://www.fda.gov/downloads/ICECI/EnforcementActions/ApplicationIntegrityPolicy/UCM072631.pdf> (providing the specific procedures for the policy that "focuses on the integrity of data and information in applications submitted for [FDA] review and approval").

164. *Wyeth v. Levine*, 129 S. Ct. 1187, 1201 (2009).

165. *Id.* at 1202–03 & nn.12–13.

166. Justice Breyer wrote:

The FDA may seek to determine whether and when state tort law acts as a help or a hindrance to achieving the safe drug-related medical care that Congress sought. It may seek to embody those determinations in lawful specific regulations describing, for example, when labeling requirements serve as a ceiling as well as a floor. And it is possible that such determinations would have pre-emptive effect. I agree with the Court, however, that such a regulation is not at issue in this case.

Id. at 1204 (Breyer, J., concurring) (citations omitted).

considerations unrelated to science and the public health into labeling determinations.

CONCLUSION

There are compelling policy arguments in favor of a state tort scheme that is not preempted by federal law. Foremost among them is that individuals who have suffered injuries after taking drugs deemed safe and effective by FDA should receive compensation for those injuries. We recognize the appeal of this argument, and we do not challenge the instinct that gives rise to it. Nonetheless, we question the conclusion that tort suits against pharmaceutical companies are an effective way to compensate the injured. To the extent that state tort suits permit punitive damages, of course, they are not meant to serve a compensatory function; the purpose and appropriateness of punitive damages is a separate question. As a means of compensating people who have been injured, though, tort litigation has consistently proven to be expensive, inconsistent, and more rewarding for lawyers than for the injured.¹⁶⁷

Whether tort litigation is an appropriate mechanism for redressing injuries is a complex policy question that is well beyond the scope of this Article. Still, we cannot help but conclude that, if the goal is to compensate the injured, there are undoubtedly better ways—ways that do not impede the very system that we rely on to protect us from those injuries. Perhaps it is time for policy makers to consider alternative compensation systems for injuries arising out of the use of approved prescription drugs.¹⁶⁸

167. See Jason C. Miller, Note, *When and How to Defer to the FDA: Learning from Michigan's Regulatory Compliance Defense*, 15 MICH. TELECOMM. & TECH. L. REV. 565, 568–69 (2009) (noting that private litigation is an expensive, duplicative, and inefficient method of compensating victims and that it disproportionately rewards attorneys). Tort litigation has also been shown to inhibit drug development and drive some drugs off the market. See Louis Lasagna, *The Chilling Effect of Product Liability on New Drug Development*, in THE LIABILITY MAZE: THE IMPACT OF LIABILITY LAW ON SAFETY AND INNOVATION 334, 336 (Peter W. Huber & Robert E. Litan eds., 1991) (“[P]roduct liability issues prevent needed pharmaceutical research from being carried out and cause drugs with acknowledged utility to be eliminated from the marketplace.”). Furthermore, it provides a particular disincentive for the development of treatments for high-risk populations, such as pregnant women. See COMM. ON POPULATION, NAT’L RESEARCH COUNCIL & DIV. OF INT’L HEALTH, INST. OF MED., DEVELOPING NEW CONTRACEPTIVES: OBSTACLES AND OPPORTUNITIES 141 (Luigi Mastroianni, Jr. et al. eds., 1990) (“[P]roducts liability litigation and the impact of that litigation on the cost and availability of liability insurance have contributed significantly to the climate of disincentives for the development of contraceptive products.”); STEVEN GARBER, PRODUCT LIABILITY AND THE ECONOMICS OF PHARMACEUTICALS AND MEDICAL DEVICES 63 (1993) (“[P]roducts for patients with high rates of unexplained background injuries appear especially hazardous from a legal point of view—birth defects are the most prominent example.”).

168. There are models in states, at the federal level, and in other countries for consideration and possible adaptation. See, e.g., 30 U.S.C. §§ 901–962 (2006 & West Supp. 2009) (Black Lung Benefits Act); 42 U.S.C. §§ 247d to 247d-6e (authorizing the Secretary to make grants and conduct investigations into the cause, treatment, or prevention of a public health emergency); 42 U.S.C. §§ 300aa-1 to -34 (establishing the National Vaccine Injury Compensation Program (VIC Program) to provide

compensation for vaccine-related injury or death); 42 U.S.C. § 2210 (Price-Anderson Indemnity Amendments to the Atomic Energy Act of 1954); Air Transportation Safety and System Stabilization Act, Pub. L. No. 107-42, §§ 401–409, 115 Stat. 230, 237–41 (2001) (creating the September 11th Victim Compensation Fund); CAL. HEALTH & SAFETY CODE § 199.50 (AIDS Vaccine Victims Compensation Fund) (repealed 2010); Christopher Hodges, *Nordic Compensation Schemes for Drug Injuries*, 29 J. CONSUMER POL'Y 143, 143–47 (2006) (describing voluntary national compensation system for drug-related injuries that became effective in 1978, as well as similar schemes in Finland, Denmark, and Norway); Accident Comp. Corp., History of ACC in New Zealand, <http://www.acc.co.nz/about-acc/overview-of-acc/introduction-to-acc/ABA00004> (last visited May 31, 2010) (describing New Zealand's Injury Prevention Rehabilitation and Compensation Act 2001).