

University of Michigan Journal of Law Reform

Volume 30
Issues 2&3

1997

Statutory Compliance and Tort Liability: Examining the Strongest Case

Michael D. Green
University of Iowa College of Law

Follow this and additional works at: <https://repository.law.umich.edu/mjlr>



Part of the [Administrative Law Commons](#), [Food and Drug Law Commons](#), and the [Torts Commons](#)

Recommended Citation

Michael D. Green, *Statutory Compliance and Tort Liability: Examining the Strongest Case*, 30 U. MICH. J. L. REFORM 461 (1997).

Available at: <https://repository.law.umich.edu/mjlr/vol30/iss2/12>

This Symposium Article is brought to you for free and open access by the University of Michigan Journal of Law Reform at University of Michigan Law School Scholarship Repository. It has been accepted for inclusion in University of Michigan Journal of Law Reform by an authorized editor of University of Michigan Law School Scholarship Repository. For more information, please contact mjlr.repository@umich.edu.

STATUTORY COMPLIANCE AND TORT LIABILITY: EXAMINING THE STRONGEST CASE[†]

Michael D. Green*

Professor Green addresses the matter of the proper balance between the tort system and regulation in the context of prescription drugs and the FDA's vigorous oversight of the industry. He articulates several reasons why a regulatory compliance defense, in which tort law would defer to FDA regulation, is quite attractive. Despite the superior expertise of the FDA in assessing the benefits and risks of a drug, a regulatory compliance defense is considerably more problematical than might appear at first glance. Ascertaining compliance with FDA requirements could be a lengthy and complicated inquiry that would either replace or supplement the issues that arise in current drug product liability litigation. Particularly in the period after a drug is approved and marketed, yet when additional risks emerge, a regulatory compliance defense might impede efforts to assure that current information is promptly disseminated to physicians who make prescribing decisions. Professor Green concludes by suggesting that a regulatory compliance defense may have an impact on the types of drug litigation that occur, but expresses doubt that drug litigation would disappear.

The broad issue the Symposium session on government compliance addresses is the overlap—perhaps conflict—between safety regulation and tort law. Both are concerned with the control of accidental risk and the attempt to find some reasonable balance between accidental harm and human activity.¹ Section 7(b) of the *Restatement (Third) of Torts: Products*

† © 1996 Michael D. Green, all rights reserved.

* Professor of Law, University of Iowa College of Law. B.S. 1972, Tufts University; J.D. 1975, University of Pennsylvania Law School. My thanks to Steven Garber and Lars Noah for their comments and suggestions about a draft of this Article, to Richard Merrill for sharing his thoughts with me about this subject, and to Sarah Livingston and Russ Markhovsky for their superb research assistance.

1. See Steven Shavell, *Liability for Harm Versus Regulation of Safety*, 13 J. LEGAL STUD. 357, 357 (1984) (discussing the behavioral incentives created by both tort liability and government regulation). Of course, the tort system also serves a compensatory function that regulation does not. A national health care system might take some of the wind out of the compensatory sails of the tort ship, especially in the context of pharmaceutical iatrogenic injury (accidental harm resulting from medical treatment). For a discussion of the advantages and disadvantages of tort and regulation in providing appropriate incentives for safety, see 2 AMERICAN LAW INST., REPORTERS' STUDY: ENTERPRISE RESPONSIBILITY FOR PERSONAL INJURY 85-89 (1991).

Liability reflects hornbook tort law: Compliance with a safety statute is relevant and admissible with regard to whether the defendant met the applicable tort standard of care, but not dispositive.² Asymmetrically, failure to comply with a safety standard is a per se violation of the standard of care imposed by tort law.³

The explanation for this contrasting treatment is that safety standards prescribe only minimum standards. Rather than defining the appropriate level of care, governmental standards merely provide a floor of safety below which no one subject to that standard should descend.⁴ If that characterization of safety statutes and regulation is correct, then the hornbook rule⁵ and the *Restatement (Third)* are on quite solid ground.⁶

This Article examines the strongest case for accepting regulatory standards as conclusive of liability for tort law purposes. The toughest challenge to section 7 and its provision that compliance with a safety statute is merely a matter for the finder of fact and is not legally dispositive is the pharmaceutical arena,⁷ which is regulated extensively by the U.S. Food and

2. Comment e to section 7 suggests that in some specific instances compliance with a governmental safety standard might be treated as legally conclusive in a tort action. See RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 7 cmt. e (Tentative Draft No. 2, 1995) [hereinafter Tentative Draft No. 2].

3. See *id.* § 7(a). This rule, however, is subject to the possibility of excuse or justification for the violation. See *Tedla v. Ellman*, 19 N.E.2d 987, 990-91 (N.Y. 1939) (holding that violation of a safety statute may be excused when circumstances are such that the safer course of action is to not comply with statutory requirement); RESTATEMENT (SECOND) OF TORTS §§ 288A, 288B (1965) (providing excuses for violation of a statute or regulation that, when present, prevent the violation from constituting negligence per se).

4. See Judith P. Swazey, *Prescription Drug Safety and Product Liability*, in THE LIABILITY MAZE 291, 306 (Peter W. Huber & Robert E. Litan eds., 1991).

5. See W. PAGE KEETON ET AL., PROSSER AND KEETON ON THE LAW OF TORTS § 36, at 233 (5th ed. 1984).

6. But see Lars Noah, *Reconceptualizing Federal Preemption of Tort Claims as the Government Standards Defense*, 37 WM. & MARY L. REV. 903, 964-67 (1996) (suggesting that the "floor but not ceiling" explanation is antiquated and does not reflect the vigor, comprehensiveness, and optimality of contemporary safety regulation).

7. I limit my consideration to prescription drugs and do not consider medical devices because courts have found tort liability of medical device manufacturers preempted by the federal regulatory scheme, although the Supreme Court's recent decision in *Medtronic, Inc. v. Lohr*, 116 S. Ct. 2240 (1996), has overturned those decisions preempting claims involving medical devices that have not undergone premarketing approval by the FDA. Federal preemption, as the *Restatement (Third)* explains, is not a matter of tort law, but rather derives from the Supremacy Clause of the U.S. Constitution, U.S. CONST. art. VI, § 1, cl. 1, in this case implemented by Congress' decision to make its legislative pronouncements the sole legal authority applicable to a given regulatory situation. See Tentative Draft No. 2, *supra* note 2,

Drug Administration (the FDA).⁸

There are several reasons for scrutinizing prescription drugs and the FDA. First, the prescription drug industry is the most heavily regulated industry (for safety purposes) in this country today.⁹ The United States leads other Western countries in its vigilance in protecting its citizenry from the risks of prescription drugs;¹⁰ indeed, the FDA has been criticized severely for its overprotectiveness of the populace.¹¹ Unlike many other

§ 7 cmt. e (discussing differences between state and federal preemption). For discussions of federal preemption in the area of FDA-regulated medical devices, see Brian J. Donato & Mary Beth Neraas, *Federal Preemption of Product Liability Claims Involving Drugs and Medical Devices Regulated Under the Federal Food, Drug, and Cosmetic Act*, 48 FOOD & DRUG L.J. 305 (1993); Lars Noah, *Amplification of Federal Preemption in Medical Device Cases*, 49 FOOD & DRUG L.J. 183 (1994).

The considerations relevant to preemption as compared to those relevant to a statutory compliance defense are quite different, as the medical device preemption cases illustrate. Prior to *Lohr*, some courts held that medical devices approved by the FDA, but without any premarketing FDA review, were protected from state tort liability by preemption. See cases cited *infra* note 112. These medical devices were exempt from premarketing review pursuant to section 510(k) because they were "substantially equivalent" to medical devices on the market before the FDA was authorized to regulate medical devices in 1976. Although as a matter of preemption law that may or may not have been a correct interpretation of Congress' intent, it surely would be poor tort law to provide a statutory compliance defense for a product that effectively has undergone no regulatory review for safety. For an explanation of how preemption of state tort claims might be understood as a federal common law rule providing a defense for compliance with governmental safety standards, see Noah, *supra* note 6, at 971-78.

8. See, e.g., STEVEN GARBER, *PRODUCT LIABILITY AND THE ECONOMICS OF PHARMACEUTICALS AND MEDICAL DEVICES* 27-33 (1993) (describing the extent of FDA regulation of pharmaceuticals).

9. The former director of the FDA's Bureau of Drugs observed, "Drugs and medical devices are today the most heavily regulated consumer product in our society." J. Richard Crout, *The Drug Regulatory System: Reflections and Predictions*, 36 FOOD DRUG COSM. L.J. 106, 113 (1981).

10. One measure of commitment to safety is investigative thoroughness as measured by length of time spent; the FDA's vigilance by this measure is well documented. See, e.g., COMPTROLLER GEN., *REPORT TO THE SUBCOMMITTEE ON SCIENCE, RESEARCH, AND TECHNOLOGY, THE FOOD AND DRUG ADMINISTRATION'S PROCESS FOR APPROVING NEW DRUGS* 25-30 (1980) (describing delays in the approval of new drugs in the United States compared to other countries); WILLIAM M. WARDELL & LOUIS LASAGNA, *REGULATION AND DRUG DEVELOPMENT* 55-78 (1975) (finding that new drugs were approved more quickly in Great Britain); William M. Wardell, *Introduction of New Therapeutic Drugs in the United States and Great Britain: An International Comparison*, 14 CLINICAL PHARMACOLOGY & THERAPEUTICS 773 (1973) (finding that, in general, new drugs were approved more rapidly by drug regulators in Great Britain than in the United States).

11. The criticism began in the early 1970s when Sam Peltzman published his pioneering work that identified the "drug lag"—delay in the approval of pharmaceuticals by the FDA compared to other Western countries and the consequent cost to U.S. patients because of the delayed availability of new drugs. See Sam Peltzman, *An Evaluation of Consumer Protection Legislation: The 1962 Drug*

regulatory contexts, the FDA extensively regulates drugs from cradle to grave, and it is difficult to identify areas of potential risk reduction that the FDA does not address in its regulations.¹² Indeed, as explained below, the vast majority of products liability litigation concerns the provision of warnings and information about safe use of drugs, a major area of FDA regulation. In short, pharmaceuticals present the toughest challenge to the black letter provision of section 7 of the *Restatement (Third)*, and they are the strongest case for accepting governmental safety standards as conclusive when an injured plaintiff sues a pharmaceutical manufacturer for iatrogenic injuries allegedly caused by a pharmaceutical.

Second, the matter of a statutory compliance defense for the pharmaceutical industry comprises quite a prominent aspect of contemporary tort reform legislation. Partially as a consequence of the vigor of FDA regulation and partially as a consequence of the perceived socially detrimental effects of the present system of products liability law and its application to prescription drugs, there has been a great deal of contemporary activity and interest in changing the effect of FDA approval or compliance in products liability litigation. Several states have enacted statutes providing,¹³ a number of commentators have

Amendments, 81 J. POL. ECON. 1049 (1973). Throughout the remainder of the 1970s, the drug lag was the subject of extensive commentary and criticism. See BARUCH A. BRODY, *ETHICAL ISSUES IN DRUG TESTING, APPROVAL, AND PRICING: THE CLOT-DISSOLVING DRUGS* 164-65 (1995) (generally describing two critiques of the FDA: one by Peltzman, who analyzed the economic effects of the 1962 FDA legislation and another by William Wardell, who analyzed the clinical costs and benefits of the drug lag in the United States).

12. See Beth E. Myers, *The Food and Drug Administration's Experimental Drug Approval System: Is It Good for Your Health?*, 28 HOUS. L. REV. 309, 310-25 (1991) (describing in detail the FDA's approval process and the breadth of the FDA's regulatory scope).

13. See, e.g., MICH. COMP. LAWS ANN. § 600.2946(5) (West Supp. 1995) (providing that a pharmaceutical manufacturer is not liable for a drug approved by FDA, subject to exceptions for fraud on or bribery of FDA); N.J. STAT. ANN. § 2A:58C-4 (West 1987) (creating a rebuttable presumption that a warning approved by the FDA is adequate); OHIO REV. CODE ANN. § 2307.80(C) (Anderson 1995) (barring punitive damages against manufacturer of drug manufactured and labeled in compliance with FDA requirements); OR. REV. STAT. § 30.927 (1995) (barring punitive damages in a pharmaceutical case in which drug and labeling was approved by FDA, provided material information was not withheld or misrepresented); UTAH CODE ANN. § 78-18-2 (1992) (prohibiting the award of punitive damages if the drug causing the claimant's harm received premarketing approval or licensure by the FDA, unless it is shown by clear and convincing evidence that the drug manufacturer knowingly withheld or misrepresented material and relevant information); see also Teresa Moran Schwartz, *Punitive Damages and Regulated Products*, 42 AM. U. L. REV. 1335, 1341 n.37 (1993) (citing statutes that create a presumption of non-liability when statutory compliance

advocated,¹⁴ and Congress has considered seriously¹⁵ special treatment of pharmaceuticals and other products regulated by the FDA. The basic thrust of this legislative reform would be to insulate manufacturers of pharmaceuticals approved by the FDA or manufacturers who comply with applicable FDA regulations from tort liability, or, alternatively, from liability for punitive damages.

Third, the *Restatement (Third)* itself leaves open a small window for a stronger role for compliance with governmental safety regulation. Comment e to section 7 suggests that common law courts might decide that a safety statute or regulation is sufficiently current, protective, salient, and the product of untainted regulatory expertise to treat the safety standard as

existed); Paul Dueffert, Note, *The Role of Regulatory Compliance in Tort Actions*, 26 HARV. J. ON LEGIS. 175, 178 (1989) (detailing state statutes that provide a rebuttable presumption that a product is not defective if in compliance with relevant safety standards).

14. See GARBER, *supra* note 8, at 192-93; AMERICAN LAW INST., *supra* note 1, at 83-110; Richard M. Cooper, *Drug Labeling and Products Liability: The Role of the Food and Drug Administration*, 41 FOOD DRUG COSM. L.J. 233, 233-34 (1986); Charles J. Walsh & Marc S. Klein, *The Conflicting Objectives of Federal and State Tort Law Drug Regulation*, 41 FOOD DRUG COSM. L.J. 171, 183-84 & nn.59-60 (1986); Note, *A Question of Competence: The Judicial Role in the Regulation of Pharmaceuticals*, 103 HARV. L. REV. 773 *passim* (1990); see also Robert F. Service, *Panel Wants to Break R&D Barrier*, 272 SCI. 1258, 1258 (1996) (reporting on Institute of Medicine recommendation that companies who obtain FDA approval for a new contraceptive be insulated from product liability); Gregory C. Jackson, Comment, *Pharmaceutical Product Liability May Be Hazardous to Your Health: A No-Fault Alternative to Concurrent Regulation*, 42 AM. U. L. REV. 199, 235-36 (1992) (recommending replacement of tort law for pharmaceutical injuries with a no-fault compensation scheme).

The pharmaceutical industry itself, as one might expect, has been quite active in lobbying on a variety of fronts for greater deference by the tort system to FDA regulatory determinations. See, e.g., Comments of Eli Lilly and Company on the *Restatement (Third) of the Law of Torts: Products Liability*, Preliminary Draft No. 1, at 12 (Aug. 9, 1993) (on file with the *University of Michigan Journal of Law Reform*) ("A jury should not be allowed to remake the FDA's decision.").

15. Several versions of the Common Sense Products Liability and Legal Reform Bill of 1995 contained a provision that would have precluded the awarding of punitive damages against a manufacturer or product seller of a drug that was subject to premarket approval by the FDA with respect to the safety of the formulation or performance aspect of the drug and was approved by the FDA. See H.R. 956, 104th Cong. § 201(F)(1)(A) (1995) (Versions 4, 5, 6, and 7). If the manufacturer or product seller of a drug intentionally withheld from or misrepresented to the FDA information that is material and relevant to the claimant, the provision precluding punitive damages would not apply. *Id.* § 201(F)(1)(B). This provision was removed from the succeeding versions of the bill. See H.R. 956, 104th Cong. (1995) (Versions 8, 9, and 10). The most recent appearance of this provision was in H.R. 2425, 104th Cong. § 15312(e)(a)(A)-(B) (1995).

conclusive in a products liability suit.¹⁶ Thus, the *Restatement (Third)* recognizes both that all safety statutes and regulations are not alike and that some are more deserving of respect in tort suits than others, thereby suggesting that common law courts consider adopting a more powerful role for those safety standards that are sufficiently rigorous.

The recognition that adopting a statutory compliance defense requires consideration of the specific standard or regulatory scheme is quite sound. The variety of industries and risks that are regulated, the variety of means employed to regulate risks, the strengths and weaknesses of those different regulatory schemes, the seriousness and intrusiveness of the regulatory scheme, and the resources available to the regulatory agency have important implications in considering the proper role for other regulatory rules in tort suits.¹⁷ Thus, this Article opts to address a single regulatory scheme, albeit the one for which the strongest case might be made for a compliance defense.

Finally, by addressing the most pervasive regulatory situation, we should be able to learn much about whether and when the tort system should defer to a greater extent to regulation. To the extent that a governmental compliance defense is problematic even in the strongest case—as this Article argues—then, a fortiori, the case for a broader umbrella for a government standards defense is weaker.

Let us begin by considering what can be said in favor of adopting a regulatory compliance defense for products liability claims that arise from prescription drugs. The predominant argument is that the overlap of regulation and tort law results

16. See Tentative Draft No. 2, *supra* note 2, § 7 cmt. e. The taint concern is that an industry may “capture” the regulatory agency, which then acts to benefit the industry, rather than consumers or overall social welfare. For one of the early accounts of the life cycle of an agency progressing to the stage of industry capture, see MARVER H. BERNSTEIN, *REGULATING BUSINESS BY INDEPENDENT COMMISSION* 74–95 (1955). The regulatory-capture theory of agency action has been quite popular since the 1970s. See George J. Stigler, *The Theory of Economic Regulation*, 2 *BELL J. ECON. & MGMT. SCI.* 3 (1971) (arguing that regulations are initiated, constructed, and implemented for the benefit of the regulated industry).

17. See generally CARL F. CRANOR, *REGULATING TOXIC SUBSTANCES: A PHILOSOPHY OF SCIENCE AND THE LAW* 104–08 (1993) (discussing the large number of regulatory statutes and agencies concerned with carcinogenic agents); Noah, *supra* note 6, at 977 n.285 (citing support for the proposition that products regulated by the FDA most deserve the protections of a government standards defense); W. Kip Viscusi et al., *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, 24 *SETON HALL L. REV.* 1437, 1475–79 (1994) (arguing for national standards in pharmaceutical litigation because of the distinct issues peculiar to the industry).

in overdeterrence, which in the drug context has several undesirable aspects:

(1) Manufacturers are deterred from research and development of new and effective drugs, the benefits of which are lost to society;¹⁸

(2) Manufacturers who do develop new drugs will test them longer and more carefully, thereby delaying the availability of the drug and its therapeutic advantages to society;¹⁹

(3) Beneficial drugs are withdrawn from the market;²⁰

(4) Shortages in supplies and suppliers of pharmaceuticals will occur, as has been most notable in the vaccine area;²¹

(5) Dual systems overlap, which results in duplicated administrative costs; unnecessary administrative costs are a concern especially in light of the substantial administrative costs of the tort system.²²

The premises for the overdeterrence argument are that (1) the FDA provides optimal levels of safety precautions, rather than a floor or minimum standard; (2) the FDA is more accurate than a court or jury at identifying the appropriate level of safety precaution;²³ and (3) where activities are subject to regulation, retention of tort liability systematically will impose

18. See, e.g., *Punitive Damages: Tort Reform and FDA Defenses: Hearings on S. 671 and S. 672 Before the Senate Comm. on the Judiciary*, 104th Cong. 141-42 (1995) (statement of Sen. Nancy Landon Kassebaum).

19. See Walsh & Klein, *supra* note 14, at 194.

20. See S. REP. NO. 102-215, at 38 (1991); GARBER, *supra* note 8, at 82-86; WALTER OLSON, *THE LITIGATION EXPLOSION* 164 (1991); C.I. Barash & Louis Lasagna, *The Bendectin Saga: "Voluntary" Discontinuation*, 1 J. CLINICAL RES. & DRUG DEV. 277, 289 (1987); Howard A. Denmark, *Improving Litigation Against Drug Manufacturers for Failure to Warn Against Possible Side Effects: Keeping Dubious Lawsuits from Driving Good Drugs Off the Market*, 40 CASE W. RES. L. REV. 413, 415 (1989-90); Bruce N. Kuhlik & Richard F. Kingham, *The Adverse Effects of Standardless Punitive Damage Awards on Pharmaceutical Development and Availability*, 45 FOOD DRUG COSM. L.J. 693, 700-01 (1990).

21. See INSTITUTE OF MED., *VACCINE SUPPLY AND INNOVATION* 27-44 (1985); Teresa Moran Schwartz, *Prescription Products and the Proposed Restatement* (Third), 61 TENN. L. REV. 1357, 1401-02 (1994).

22. See AMERICAN LAW INST., *supra* note 1, at 89.

23. See Peter Huber, *Safety and the Second Best: The Hazards of Public Risk Management in the Courts*, 85 COLUM. L. REV. 277, 329-35 (1985); W. Kip Viscusi & Michael J. Moore, *Rationalizing the Relationship between Product Liability and Innovation*, in *TORT LAW AND THE PUBLIC INTEREST* 125 (Peter H. Schuck ed., 1991); Walsh & Klein, *supra* note 14, at 193. Complementing this argument is that, if anything, the FDA is overly conservative about approving new drugs. Thus, FDA regulation alone is biased and results in excessive caution at the cost of greater therapeutic benefits. See, e.g., Henry Grabowski, *Product Liability in Pharmaceuticals: Comments on Chapters Eight and Nine*, in *THE LIABILITY MAZE* 360, 364 (Peter W. Huber & Robert E. Litan eds., 1991).

excessive liability and litigation costs on the regulated industry.²⁴ Often the excess cost problem is not the result of adverse judgments, but a result of litigation costs.²⁵ In the Bendectin litigation, for example, Marion Merrell Dow, the manufacturer, has not yet suffered an adverse final judgment, yet it has incurred an estimated \$100 million bill in defending itself in the litigation.²⁶

This Article proceeds first by providing background with a summary of the provisions of the *Restatement (Third)* relating to pharmaceutical products liability cases and identifying the significant substantive issues likely to arise in conventional pharmaceutical products cases. The Article next examines the case for a government standards defense.

The Article agrees with the proponents of an FDA approval defense that the FDA provides optimal standards for pharmaceutical approval and that FDA expertise should receive deference. FDA approval of a new pharmaceutical is based on a determination that the social benefits of the drug outweigh

24. See AMERICAN LAW INST., *supra* note 1, at 87; Cooper, *supra* note 14, at 237.

In addition to these aspects of overdeterrence, the argument is sometimes made that permitting a jury to find inadequate a drug warning that the FDA has approved and mandated is unfair to the manufacturer. See *Hurley v. Lederle Lab.*, 863 F.2d 1173, 1179-80 (5th Cir. 1988) (making this argument especially in light of FDA restrictions on manufacturers' ability to add additional warnings); Margaret Gilhooly, *Innovative Drugs, Products Liability, Regulatory Compliance, and Patient Choice*, 24 SETON HALL L. REV. 1481, 1485 (1994).

Conversely, the relatively low level of tort claims against the pharmaceutical industry, when set against a backdrop of more than 2.2 billion prescriptions, 60,000 reported adverse drug reactions, and substantial number of deaths may be worthy of note. See Swazey, *supra* note 4, at 326; see also Samuel Shapiro et al., *Fatal Drug Reactions Among Medical Inpatients*, 216 JAMA 467 (1971) (finding that pharmaceuticals administered to hospital patients were responsible for deaths of .44% of patients). The Rand Institute has found that between 1974 and 1986, there were, on average, fewer than 200 pharmaceutical lawsuits filed per year in the federal courts, exclusive of Bendectin and Dalkon Shield suits. See TERENCE DUNGWORTH, PRODUCTS LIABILITY AND THE BUSINESS SECTOR: LITIGATION TRENDS IN FEDERAL COURT 40 (1988). Another study found a similar incidence of pharmaceutical lawsuits in federal courts. See W. Kip Viscusi et al., *A Statistical Profile of Pharmaceutical Industry Liability, 1976-1989*, 24 SETON HALL L. REV. 1418, 1420-22 (1994). A General Accounting Office study of verdicts in products liability cases in five states found that approximately 50% were litigated in state court and 50% in federal court, which would suggest that the total number of pharmaceutical products cases is 400 per year, exclusive of mass litigations. See U.S. GEN. ACCOUNTING OFFICE, GAO/HRD-89-99, PRODUCT LIABILITY: VERDICTS AND CASE RESOLUTION IN FIVE STATES 20-21 (1989).

25. See GARBER, *supra* note 8, at 93.

26. See *Punitive Damages: Tort Reform and FDA Defenses: Hearings on S. 671 and S. 672 Before the Senate Comm. on the Judiciary*, 104th Cong. 141-42 (1995) (statement of Sen. Nancy Landon Kassebaum); MICHAEL D. GREEN, BENEDECTIN AND BIRTH DEFECTS: THE CHALLENGES OF MASS TOXIC SUBSTANCES LITIGATION 335 (1996).

its risks.²⁷ Thus, FDA review of drugs cannot be characterized as setting a minimum, as opposed to an optimal standard. Second, the FDA's judgments on New Drug Applications (NDAs) are about as good as any human system can produce in terms of assessing risks and comparing them with therapeutic benefits—certainly better than the common law courts can provide, at least to the extent accuracy is the goal.²⁸

Notwithstanding the superior expertise and optimal standards (at least with regard to safety concerns)²⁹ of the FDA, a government compliance defense is far more problematic than most of the contemporary proponents of such a reform have recognized. The third Part of this Article explains that any such defense would have to be limited to those instances in which the manufacturer complied with all relevant statutory and regulatory requirements both pre-approval and post-approval. Once statutory and regulatory compliance become the standard for a defense, the difficulties of such a defense begin to emerge.

Part Four explains why any compliance defense would be likely to shift the focus of pharmaceutical tort litigation rather than to prevent it. Indeed, the inquiry into compliance issues may be no more appropriate for common law courts than the issues confronting the courts in contemporary pharmaceutical litigation. In short, a compliance defense does not hold much promise for reducing transaction costs; instead, it may exacerbate them by adding an additional layer of litigation filled with peripheral issues for meritorious cases.

The final section of the Article expresses concern about the adequacy of FDA resources to oversee the industry in the post-approval period when additional risks are identified. Removing the incentives provided by the tort system for prompt warnings of newly emergent risks and limitations on efficacy may have an unfortunate impact on prompt dissemination of this infor-

27. See Richard A. Merrill, *Compensation for Prescription Drug Injuries*, 59 VA. L. REV. 1, 9–10 (1973).

28. Some argue that accuracy should not be exalted as the single or primary goal of adjudicatory processes. Thus, for one who believes grass roots democratic participation is central to the adjudicatory process, jury determinations in the litigation context are preferable to the FDA, despite the latter's expertise and more accurate decisionmaking. Cf. Charles Nesson, *The Evidence or the Event? On Judicial Proof and the Acceptability of Verdicts*, 98 HARV. L. REV. 1357, 1377–92 (1985) (arguing that public acceptance and the projection of public norms is as important a goal for an adjudicative system as accuracy).

29. See *infra* notes 52–61 and accompanying text.

mation. Finally, attempting to compromise (or create a more focused reform) by making the defense only applicable to punitive damages (as a number of state statutes have done) may, perversely, exacerbate the problems of employing a government standards defense.

I. PHARMACEUTICAL PRODUCTS LIABILITY LITIGATION

Before proceeding to consider how a government compliance defense would operate, we should recognize the special character of pharmaceutical products liability litigation. With the advent of the *Restatement (Third)*, we can skip past the confusion engendered by section 402A comment k of the *Restatement (Second) of Torts*,³⁰ and consider the application of the functional approach to drug litigation wisely adopted by the Reporters and the special design standards for pharmaceutical litigation.

In the mix of pharmaceutical products liability litigation, manufacturing defects are infrequent³¹ and quite uncontroversial.³² The FDA prescribes good manufacturing practices that, along with technological capabilities of the industry, result in the sale of very few dangerously adulterated drugs. The *Restatement (Third)* imposes strict liability for manufacturing defects, and comment a to section 7 explains why compliance with safety standards regarding the manufacturing process should not insulate the manufacturer from strict

30. The core difficulty is that comment k provides more limited liability standards for manufacturers of "unavoidably unsafe" products, and the courts have struggled with which products this encompasses. See Richard C. Ausness, *Unavoidably Unsafe Products and Strict Products Liability: What Liability Rule Should be Applied to Sellers of Pharmaceutical Products?*, 78 KY. L.J. 705, 712-19 (1989-90) (claiming that the "unavoidably unsafe" designation generally has been limited to "chemical drugs, antibiotics, vaccines, blood or medical devices," but that courts have disagreed over which products within these categories should be so designated); Joseph A. Page, *Generic Product Risks: The Case Against Comment k and for Strict Tort Liability*, 58 N.Y.U. L. REV. 853 (1983) (discussing the problems in interpreting comment k). Compare *Feldman v. Lederle Lab.*, 479 A.2d 374, 380 (N.J. 1984) (drugs are generally subject to strict products liability; some drugs, determined on a case-by-case basis, may be afforded comment k protection), with *Brown v. Superior Ct.*, 751 P.2d 470, 481-82 (Cal. 1988) (no strict products liability available for design defect claims involving pharmaceuticals).

31. See Swazey, *supra* note 4, at 305.

32. See Schwartz, *supra* note 21, at 1369.

liability for manufacturing defects.³³ Section 8(b)(1) of the *Restatement (Third)* extends strict liability for manufacturing defects to pharmaceuticals.³⁴

The analysis for design defects in drugs is quite different and driven by the unique character of most drugs. Unlike durable goods, drugs cannot be designed in an alternative fashion, at least not in light of current technological capabilities.³⁵ With the *Restatement (Third)*'s adoption of a risk-benefit test for design defects and its insistence on proof of an alternative design, one might think that there would therefore be no place for a design defect theory involving pharmaceuticals.³⁶

But the *Restatement (Third)* does have a very limited provision for a design defect claim in the case of pharmaceuticals:

A prescription drug or medical device is not reasonably safe due to defective design when the foreseeable risks of harm posed by the drug or medical device are sufficiently great in relation to its foreseeable therapeutic benefits so that no reasonable health care provider, knowing of such foreseeable risks and therapeutic benefits, would prescribe the drug or medical device for any class of patients.³⁷

In failing to demand proof of a reasonable alternative design as is mandated for other product design claims,³⁸ the *Restatement (Third)* might be understood to recognize the way in which drugs (and other chemicals) differ from durable goods

33. See Tentative Draft No. 2, *supra* note 2, § 7 cmt. a (stating that statutes or regulations relating to manufacturing defects usually address quality control levels, and quality control levels are irrelevant because liability for manufacturing defects is liability without fault).

34. See *id.* § 8(b)(1) (incorporating the general standards for liability for a manufacturing defect contained in section 2(a)). Thus, if a drug is contaminated, adulterated, or otherwise not in conformity with the drug's specifications, the manufacturer will be strictly liable for any harm caused by the flaw. See *id.*

35. But see *infra* note 53.

36. This observation is inapplicable to medical devices. Pharmaceuticals differ from most products because it is difficult to change the design of a given drug; medical devices, such as the Dalkon Shield with a multifilament tailstring, although subject to FDA regulation, do not share that characteristic with drugs.

37. Tentative Draft No. 2, *supra* note 2, § 8(c).

38. See *id.* § 2(b). A narrow exception disregards the requirement of a reasonable alternative design when the "extremely high degree of danger posed by [the product's] use or consumption so substantially outweighs its negligible utility that no rational adult, fully aware of the relevant facts would choose to use or consume the product." *Id.* § 2(b) cmt. d; see also *id.* § 2(b) cmt. d, illus. 5 (describing an exploding cigar as an example of such a product).

in their amenability to design change. The inclusion of medical devices in section 8(c) contradicts this explanation for the different treatment of pharmaceuticals, however, as most medical devices are more like durable goods than drugs in their amenability to design modification. Rather, the limited design claim provided in section 8(c) reveals two principles that are in tension.

First, design defect claims are permitted without proof of an alternative design, thereby permitting courts and juries to do for pharmaceuticals what the *Restatement (Third)* does not permit for durable goods—to make an overall risk-benefit judgment for the drug or medical device, and, if the risks inherent in the pharmaceutical outweigh its benefits to patients, to declare the pharmaceutical defective. This expansion of design defect liability for pharmaceuticals as compared to durable goods reflects a number of courts that have permitted, in limited fashion, a design defect claim to be made for prescription drugs.³⁹ At the same time, the expansion is quite limited, permitting a finding of defect only in a limited range of circumstances.⁴⁰ Comment f reveals that the goal of the *Restatement (Third)* is to maximize the availability of pharmaceuticals and medical devices, provided that adequate warnings accompany them.⁴¹ Unstated but nevertheless prominent in the close confinement of the design claim is reliance on the FDA and its screening of new drugs and medical devices to ensure that their benefits outweigh the risks.⁴² Thus, we see that the efficacy of FDA regulation affects the substantive standards for drug liability as well as the question of a regulatory defense.

Nevertheless, we should expect that design claims in pharmaceutical litigation will be relatively rare.⁴³ The vast bulk of pharmaceutical litigation is in the warnings area and that will

39. See *id.* § 8 reporters' note cmt. f (stating that the recent trend has been toward greater judicial review in this area).

40. See *id.* § 8.

41. See *id.* § 8 cmt. f (stating that "as long as a given drug provides or device provides net benefits for some category of patients, it should be available to that group, albeit with appropriate warnings and instructions").

42. See James A. Henderson, Jr., *Prescription Drug Design Liability Under the Proposed Restatement (Third) of Torts: A Reporter's Perspective*, 48 RUTGERS L. REV. 471, 473-74 (1996).

43. See GARBBER, *supra* note 8, at 39-40 (noting that it "seems rare for design defects to be found"); Henderson, *supra* note 42, at 492 (positing that the *Restatement (Third)* "reflects the view that courts are institutionally unequipped to substitute their approval of a proposed new drug, on a case-by-case basis, for that of the FDA").

continue for the foreseeable future.⁴⁴ The predominant claim in most warnings cases concerns risks that emerged after the drugs were approved by the FDA and made available to the public.⁴⁵ In the warnings litigation arena, the major issues that arise include: (1) whether the drug causes an adverse reaction or disease from which the plaintiff suffers;⁴⁶ (2) where adverse reactions or diseases are shown to exist, whether the manufacturer had adequate knowledge of the dangers to have a duty to warn;⁴⁷ and (3) the adequacy of any provided warnings.⁴⁸ The primary liability issues that might be affected by a government standards defense would be causation, and the adequacy, accuracy, and timeliness of drug labeling providing information about the risks entailed in use of a pharmaceutical.

II. THE CASE FOR AN FDA APPROVAL DEFENSE

There are three frequently raised objections to a government standards defense: (1) governmental regulation is designed to provide a minimum, rather than an optimal, level of safety; (2) regulatory capture;⁴⁹ and (3) government standards are often outdated⁵⁰ or do not exist for the specific risk of which the plaintiff complains.⁵¹ In those situations the common law system is better situated to decide whether the manufacturer

44. See GEORGE EADS & PETER REUTER, *DESIGNING SAFER PRODUCTS: CORPORATE RESPONSES TO PRODUCT LIABILITY LAW AND REGULATION* 38 (1983) ("In the case of pharmaceuticals, most suits involve warning labels.")

45. See Jeffrey N. Gibbs & Bruce F. Mackler, *Food and Drug Administration Regulation and Products Liability: Strong Sword, Weak Shield*, 22 *TORT & INS. L.J.* 194, 228 (1987) ("A review of . . . cases shows that the great majority of suits are predicated on actions or omissions that took place *after* the drug or device entered the market."). For an explanation of why post-marketing risks and warnings play such a prominent role in pharmaceutical products liability litigation, see *infra* text accompanying notes 124-33 and accompanying text.

46. See, e.g., *DeLuca v. Merrell Dow Pharm., Inc.*, 911 F.2d 941, 943 (3d Cir. 1990).

47. See, e.g., *Feldman v. Lederle Lab.*, 479 A.2d 374, 388-89 (N.J. 1984); *McEwen v. Ortho Pharm. Corp.*, 528 P.2d 522, 528 (Or. 1974).

48. See, e.g., *McEwen*, 528 P.2d at 536; *Grundberg v. Upjohn Co.*, 813 P.2d 89, 92 (Utah 1991).

49. See sources cited *supra* note 16.

50. See, e.g., Teresa Moran Schwartz, *The Role of Federal Safety Regulations in Products Liability Actions*, 41 *VAND. L. REV.* 1121, 1151-52 (1988) (explaining that obsolescence can occur through changes in technology, inadequate resources of the regulating agency, and the general slowness of regulatory bodies).

51. See, e.g., *id.* at 1143.

has met appropriate standards with regard to safety. At least with regard to the FDA's decision to approve a new pharmaceutical, I do not believe that any of these objections to a regulatory compliance defense have much force.

When the FDA approves a new drug, it is not providing safety minima. What the FDA does when it approves a drug is determine that because the drug's efficacy sufficiently outweighs its risks of adverse reactions, it should be available for patients, albeit with appropriate warnings of those adverse reactions.⁵² Because the unique constitution of drugs does not allow the possibility of building in marginal additional safety through design changes, all we can ask in terms of safety is that the benefit/risk relationship is positive, that adequate testing is conducted to identify risks, and that available information about known risks is provided. Unlike durable goods, pharmaceuticals cannot be designed differently, in the sense of modifying (or adding to) the product so as to build in more safety.⁵³ We simply do not know how to rearrange the electrons or move the relative position of, say, the carbon and hydrogen molecules so as to squeeze out the drug's tendency

52. See Merrill, *supra* note 27, at 9-10; see also Grundberg, 813 P.2d at 97 (finding the FDA's "extensive regulatory scheme capable of and appropriate for making the preliminary determination regarding whether a prescription drug's benefits outweigh its risks").

53. A couple of exceptions exist. Combination drugs contain multiple active ingredients and can be designed differently by removing or adding active ingredients. For example, Fiorinal, a prescription drug for headaches, originally contained a barbiturate, aspirin, caffeine, and phenacetin (an analgesic). In 1981, phenacetin was removed from the market because of safety concerns, and Fiorinal was redesigned without the phenacetin component. See *Aspirin / Acetaminophen Combination Poses Safety Question at FDA*, FOOD & DRUG LETTER (Washington Bus. Info., Inc.), May 22, 1981, at 3 (reporting that phenacetin was about to be banned from marketed drugs); see also *Combinational Chemistry Hits the Drug Market*, 272 SCI. 1266 (1996) (describing recent scientific developments that permit the manipulation of organic molecules to create many chemically similar substances that can be tested for potential in treating diseases). The second exception concerns the recommended dosage; experience with a drug may reveal that the same therapeutic benefits can be obtained with a lower dose, and decreasing the dose reduces the risk of adverse side effects. See, e.g., *Brochu v. Ortho Pharm. Corp.*, 642 F.2d 652, 658-59 (1st Cir. 1981) (upholding a jury finding that warnings were inadequate because they did not mention a correlation between dosage level and risk of adverse reaction); U.S. FOOD AND DRUG ADMIN., REPORT OF THE HALCION TASK FORCE 14 (1996) [hereinafter HALCION TASK FORCE REPORT] (noting that the recommended dosage for Halcion was reduced in response to adverse reactions); GARBER, *supra* note 8, at 24-25 (describing the process of redesigning drugs with more chemical particularity to minimize side effects); *Improved Safety with Low-Estrogen Oral Contraceptives*, FDA MED. BULL., May 1994, at 3-4 (finding that low-dose oral contraceptive users had a lower risk of thromboembolism than higher-dose oral contraceptive users).

to cause nausea or cell mutation, while retaining its beneficial physiological effects. Thus, the regulatory overseer cannot, as with an automobile or industrial machine, specify certain minimum standards for safety design (e.g., driver-side airbag; point-of-operation guards) that might be characterized as a safety floor. Rather, with nonmodifiable drugs, the FDA must decide whether the therapeutic benefits of a new pharmaceutical outweigh the risks it poses through adverse side effects. In these cases, a regulatory approval defense is most attractive: the FDA has made a risk-benefit analysis of the drug, which is precisely the issue that will arise in a products liability design defect claim. If one accepts the proposition that the FDA is more accurate than courts in making such determinations, as argued below,⁵⁴ a regulatory compliance defense for design defect claims for drugs approved by the FDA appears justified.

Consistent with the above, one might think that the FDA should not approve a new drug whose efficacy-safety balance is less favorable than another drug available to treat the same condition.⁵⁵ Efficacy-safety ratios, however, emerge from clinical (epidemiological) studies that examine the benefits and adverse reactions among *groups* of patients. But there is much variability among individuals, and a drug that better treats one individual may not work similarly for another. Thus, even drugs that emerge in epidemiological studies as less beneficial than their competitors for the *group* studied may be more beneficial for some *individual* patients. Physicians, exercising good prescribing practices, will try initially the most beneficial drug. If it is not effective or if the patient cannot tolerate its side effects, then the physician will prescribe an alternative drug that may not have fared as well overall in epidemiological studies, but which may turn out to be better for that specific patient. At bottom, the issue is the provision of adequate information to physicians making the prescription decision—revealing the overall efficacy-safety balance of a drug and identifying any known individual factors that make a drug

54. See *infra* notes 62–72 and accompanying text.

55. The pharmaceutical industry managed to block inclusion of inter-drug efficacy comparisons in the 1962 amendments to the Food, Drug, and Cosmetic Act. The FDA, however, has asserted the right to disapprove an NDA based on comparative safety. See, e.g., John C. Ballin, *Who Makes the Therapeutic Decisions?*, 242 JAMA 2875, 2875 (1979) (criticizing the FDA for attempting to limit the availability of drugs to those that are safest).

more or less efficacious or safe for certain patients. The FDA has the authority to require a drug's label to provide this information.⁵⁶

If a new drug passes the risk-benefit screening test, the drug labeling then seeks to minimize potential adverse effects through explanations of contraindications and precautions for those taking the drug. Individual autonomy is fostered by warning of the side effects that cannot be avoided or minimized. Because information about both the benefits and risks of pharmaceuticals is so costly to obtain, pharmaceuticals have been regulated since 1906 and today are extensively regulated not only for information-enhancing purposes (ensuring that a drug's labeling is accurate and complete) but also for pure consumer protection (keeping unsafe drugs off the market).⁵⁷

Pharmaceutical regulation entails premarketing approval; before a prescription drug may be marketed, regulatory approval is required. This means that we have, *ex ante*, the regulatory agency's assessment and approval of the drug, the IND testing, and the labeling provided with the drug. Post-marketing regulation, in which compliance is not determined unless and until someone raises the issue of noncompliance, is a much more uncertain environment for use of a government compliance defense.

Premarketing approval also provides the FDA with a strategy for dealing with the perennial problem of inadequate regulatory resources for enforcement. The FDA is woefully underfunded for its mandate, which includes regulatory oversight of products that account for more than twenty-five percent of all American consumer purchases.⁵⁸ A 1991 study of the FDA reported, "It is glaringly apparent that the FDA cannot now execute all of its statutory responsibilities within the limitations of existing resources, a conclusion that is repeated throughout this report."⁵⁹ The budget for the entire

56. 21 C.F.R. §§ 201.56–201.57, 201.100 (1996).

57. See Peter Temin, *The Origin of Compulsory Drug Prescriptions*, 22 J.L. & ECON. 91, 103–04 (1979).

58. See John K. Iglehart, *The Food and Drug Administration and Its Problems*, 325 NEW ENG. J. MED. 217, 217 (1991).

59. ADVISORY COMM. ON FOOD & DRUG ADMIN., FINAL REPORT 11 (1991) [hereinafter ADVISORY COMMITTEE REPORT]; cf. *Medtronic, Inc. v. Lohr*, 116 S. Ct. 2240, 2246–48 (1996) (stating that inadequate resources of the FDA to review applications for approval of new medical devices has resulted in many medical devices being submitted to FDA under a premarketing notification provision for devices "substantially equivalent" to those marketed before the Medical Devices Amendments of 1976).

human drug division of the FDA totalled a mere \$272 million in 1996.⁶⁰ Premarketing approval means that the effects of inadequate regulatory resources can be managed without compromising safety concerns—consideration of an application for approval of a new drug can be deferred and approval delayed. This strategy may have adverse consequences for those patients for whom the drug will be therapeutically beneficial,⁶¹ but the trade-off is to protect against adverse drug effects.

Finally, it seems plain that the FDA, with its expertise, can reach more accurate decisions than can a common law jury. Even the most vociferous critics of a regulatory compliance defense do not argue otherwise.⁶² The experience with the Bendectin litigation—in which plaintiffs, over a fifteen-year period, obtained favorable jury verdicts in about forty percent of cases tried before juries despite a strong consensus in the medical, scientific, and FDA communities that Bendectin is not a teratogen—is one striking and popular bit of evidence supporting this proposition.⁶³

Thus, if we could freeze time at the point of FDA approval of a new drug, a regulatory compliance defense might be reasonable. I am inclined to think that the FDA's initial approval of a drug and labeling requirements for that drug is about as good as we can do. That is not to suggest that the

60. See *FDA Talk Paper No. T96-17: 1997 Budget Proposed for FDA*, Mar. 19, 1996, at 3, available in WL, Diogenes Database. The 1994 and 1995 budgets for the human drug division were estimated at \$242 million and \$254 million, respectively. See *Hearings on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations for 1995 Before the Subcomm. on Agric., Rural Dev., Food and Drug Admin., and Related Agencies of the House Comm. on Appropriations*, 103d Cong. 217 (1994).

61. See *supra* note 11 and accompanying text.

62. For example, one set of critics argues against a government compliance defense because of concerns about the FDA's resources and ability to oversee the IND testing process. See Thomas Koenig & Michael Rustad, *His and Her Tort Reform: Gender Injustice in Disguise*, 70 WASH. L. REV. 1, 48 (1995). So long as any defense requires compliance with FDA standards, however, any manufacturer who failed to comply with IND requirements would not have the benefit of the defense. See Schwartz, *supra* note 50, at 1127-35.

63. See Joseph Sanders, *From Science to Evidence: The Testimony on Causation in the Bendectin Cases*, 46 STAN. L. REV. 1, 5-8 (1993). If Bendectin is a teratogen, it is such a weak one that despite extensive scientific study, existing scientific methods are unable to detect it. With such a weak teratogen, no Bendectin plaintiff should be able to succeed in proving that her birth defect was more likely than not caused by Bendectin. See GREEN, *supra* note 26, at 328-29.

FDA is perfect—surely it is not.⁶⁴ Decisionmaking with imperfect information in a scientifically complex arena that requires balancing health benefits with the adverse effects that are inevitable with physiologically active agents is not easy and will result, with some frequency, in incorrect or dubious outcomes.⁶⁵ The question, however, is not perfection but the best alternative. And in that respect, the FDA beats anything else available.⁶⁶

Most importantly, strong influences drive the FDA toward being more cautious with regard to approval of new drugs. Before the drug-lag criticism that began in the mid-1970s,⁶⁷ the FDA was subject to the harsh glare of public criticism when it approved a drug that subsequently was revealed to have serious hazards.⁶⁸ The media and Congress regularly denounced the

64. See Paul J. Quirk, *Food and Drug Administration*, in *THE POLITICS OF REGULATION* 191, 203–07 (James Q. Wilson ed., 1980). Quirk asserts that FDA decisionmaking is problematic for several reasons. The FDA must rely on manufacturer-sponsored studies and is inclined to approve drugs despite marginal deficiencies in testing methods. The FDA's effectiveness in evaluating manufacturer's drug studies is limited by its inability to attract high-caliber scientists and its poor management. Animal testing and limited human testing may not identify the hazards of a new drug. Further, after the FDA approves a drug, it lacks authority to continue monitoring the drug. The FDA cannot monitor the way in which doctors prescribe the drug or whether they misuse it. *See id.*

There is no shortage of critics who allege shortcomings in the FDA's regulatory activities, ranging from a failure to take a leadership role in examining high drug prices to the generic drug scandals of the 1980s. The vast majority of this criticism of the FDA is unrelated to its role in assessing the safety of new drugs (at least when it has full information). This criticism is often related to the lack of resources available to the Agency in enforcing its mandate. *See generally* HERBERT BURKHOLZ, *THE FDA FOLLIES* 4 & n.1 (1994) (identifying the FDA's ineffective assessment of new drugs as only one of several criticisms of the FDA; other criticisms are budget-based, including a threadbare budget, an inability to accommodate an expanding AIDS drug market, and improper or infrequent inspection of food and drug factories).

65. *See* Quirk, *supra* note 64, at 206 (explaining that the FDA's evaluation of relative risks and benefits of a drug under consideration for approval is complicated by the fact that "these benefits and risks are often subject to extreme uncertainty"). Of course, hindsight will show some decisions to have been unwise. By "incorrect" or "dubious," I mean as judged according to the information (or absence of information) available at the time of the FDA's decision.

66. *See id.* at 220–21 (discussing a study in which a consumer-oriented panel studied FDA new drug approvals and, although reviewers disagreed with some FDA judgments, disagreements revealed no bias on the FDA's part to prefer erroneously approving NDAs (citing REVIEW PANEL ON NEW DRUG REGULATIONS, INTERIM REPORT: FDA'S REVIEW OF INITIAL IND SUBMISSIONS: A STUDY OF THE PROCESS FOR RESOLVING INTERNAL DIFFERENCES AND AN EVALUATION OF SCIENTIFIC JUDGMENTS (1977))).

67. *See* Crout, *supra* note 9, at 114.

68. *See* STEPHEN BREYER, *REGULATION AND ITS REFORM* 132 (1982) (describing economic and political pressures faced by FDA officials that cause them to overemphasize safety regulation); Quirk, *supra* note 64, at 217–18 (describing the external

FDA for errors of commission. By contrast, the failure to approve (or delay in approving) a beneficial drug was not the subject of public or congressional concern. Former FDA Commissioner Alexander Schmidt addressed the FDA's false negative bias:

For example, in all of FDA's history, I am unable to find a single instance where a Congressional committee investigated the failure of the FDA to approve a new drug. But, the times when hearings have been held to criticize our approval of new drugs have been so frequent that we aren't able to count them. . . . The message to FDA staff could not be clearer. Whenever a controversy over a new drug is resolved by its approval, the Agency and the individuals involved likely will be investigated. Whenever such a drug is disapproved, no inquiry will be made. The Congressional pressure for our negative action on new drug applications is, therefore, intense. And it seems to be increasing as everyone is becoming a self-acclaimed expert on carcinogens and drug testing.⁶⁹

I do not want to be understood as claiming that the pharmaceutical industry and its interests play no role in influencing FDA decisionmaking. The industry is plainly better organized, has more extensive contact with, and is far more able to affect FDA decisionmaking than the handful of consumer protection organizations, such as Public Citizen, that are involved in drug

pressures placed on the FDA in the approval of new drugs; cf. GARBER, *supra* note 8, at 32 (arguing that economic incentives cause the FDA to be overcautious when approving new drugs).

69. Alexander Schmidt, *The FDA Today: Critics, Congress, and Consumerism*, Address Before the National Press Club (Oct. 29, 1974), *quoted in* HENRY G. GRABOWSKI & JOHN M. VERNON, *THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS* 5 (1983). Grabowski and Vernon observe:

In point of fact, the institutional incentives confronting FDA officials strongly reinforce the tendency to avoid type 2 errors [approving dangerous drugs] at the expense of type 1 errors [failing to approve efficacious drugs]. An FDA official who approves a drug subsequently shown to be not safe or effective stands to bear heavy personal costs. . . . The costs of rejecting a good drug are borne by outside parties (drug manufacturers and sick patients who might benefit from it).

GRABOWSKI & VERNON, *supra*, at 10.

regulation.⁷⁰ The FDA is made up of a large number of individuals and some, no doubt, will have sympathies and interests that align with industry interests. The political winds often shift, depending on the current Administration, and those winds often play a role in the regulatory teeth of federal agencies.⁷¹ Rather, the claim is that any pro-industry bias or influence that may exist with regard to the new drug approval process in the FDA has been outweighed by countervailing risk aversion born of concern about public and congressional calumny in the event of the approval of a new drug that turns out to be a successor to thalidomide. Frances Kelsey, the FDA official who refused to approve thalidomide for sale in the United States, was accorded hero status for her role in protecting Americans from the horrific effects of that drug.⁷²

In short, given the expertise of the FDA and the political incentives that operate on it, a regulatory compliance defense for drugs approved by the FDA appears promising. It would lead to greater accuracy in the adjudication of tort cases and might provide a measure of confidence to pharmaceutical manufacturers that would generate a modestly more robust new drug development process. But before we enact legislation embodying such a reform, an important qualification and an

70. See JOHN ABRAHAM, *SCIENCE, POLITICS AND THE PHARMACEUTICAL INDUSTRY: CONTROVERSY AND BIAS IN DRUG REGULATION* 22–25 (1995) (distinguishing regulatory capture from differing ability of various interest groups to organize and thereby influence regulation); EADS & REUTER, *supra* note 44, at 37 (describing interactions between regulators and officials of companies in the regulated industry that, while short of regulatory capture, affect the regulatory process); JAMES Q. WILSON, *BUREAUCRACY: WHAT GOVERNMENT AGENCIES DO AND WHY THEY DO IT* 80–85 (1989) (describing how different political contexts influence agency decisionmaking); Paul Sabatier, *Social Movements and Regulatory Agencies: Toward a More Adequate—and Less Pessimistic—Theory of Clientele Capture*, 6 POLY SCI. 301, 325–27 (1975) (arguing that regulatory capture is not inevitable).

71. See SUSAN J. TOLCHIN & MARTIN TOLCHIN, *DISMANTLING AMERICA: THE RUSH TO DEREGULATE* 39–43 (1983) (noting how the Reagan administration sought deregulation immediately after the inauguration); Quirk, *supra* note 64, at 218 (stating that “the FDA’s political environment allows for—and indeed probably causes—noticeable fluctuation in the orientation of the agency over time”); ABRAHAM, *supra* note 70, at 80.

72. See BURKHOLZ, *supra* note 64, at 109–10. After reviewing more than 100 congressional investigations of the FDA, the former chief counsel for the FDA wrote: “No FDA official has ever been publicly criticized for *refusing to allow* the marketing of a drug. Many, however, have paid the price of public criticism, sometimes accompanied by an innuendo of corruptibility, for approving a product that could cause harm.” Richard A. Merrill, *Can the FDA Do Anything Right?*, VA. L. SCH. REP., Summer 1978, at 19, 22, quoted in Sidney A. Shapiro, *Limiting Physician Freedom to Prescribe a Drug for any Purpose: The Need for FDA Regulation* 73 NW. U. L. REV. 801, 813 n.86 (1978).

explanation of why the reform may provide less than initially meets the eye is necessary. The next section provides the qualification; the remainder of this Article addresses the explanation.

III. AN IMPORTANT (AND A CONTINGENT) QUALIFICATION ON ANY FDA COMPLIANCE DEFENSE

Preliminarily, and I believe uncontroversially, we should recognize that any defense based on FDA regulation would have to be structured as a compliance with FDA regulatory standards rather than as a defense based on FDA approval of the drug in question. The reason is quite simple but based on a fact that is not well known: the FDA's approval of a drug, which includes a determination of the appropriate labeling (i.e., warnings) is wholly dependent on testing performed and reported by the sponsoring manufacturer.⁷³ The FDA conducts none of the testing to demonstrate that a proposed new drug is safe and effective required by the 1962 Kefauver-Harris Amendments to the Food, Drug, and Cosmetic Act⁷⁴ for approval of new drugs by the FDA. The FDA does review the results of the tests performed by the manufacturer and submitted as part of its NDA; sometimes the FDA will request additional information or tests.⁷⁵ In the end, it is the FDA that makes the judgment whether a drug is safe and efficacious. Any conclusion that the FDA's approval represents a considered assessment that an approved drug's therapeutic benefits outweigh its risks, however, is unwarranted without manufacturer investigation that complies with FDA requirements for adequate and well-controlled studies of the new drug, accurate reporting of the results of those tests, and truthful responses to inquiries by the FDA.⁷⁶

73. See 21 U.S.C. § 355(b)(1) (1994); see also Merrill, *supra* note 27, at 17 n.59. For one commentator unaware of this fact, see Dueffert, *supra* note 13, at 206 (asserting that "a drug . . . must undergo extensive testing by the Food and Drug Administration").

74. 21 U.S.C. § 355(b)(1)(A)(1994); see also David A. Kessler, *The Regulation of Investigational Drugs*, 320 NEW ENG. J. MED. 281, 281 (1989) ("[T]he FDA itself does not investigate new drugs or conduct clinical trials.").

75. See Merrill, *supra* note 27, at 17 n.59.

76. A regulatory compliance defense, as opposed to an FDA approval defense, thus responds to the critics of any defense based upon governmental regulation who argue

Once again, we must recognize the reality of regulatory resource constraints: The FDA does not have the resources to monitor and ensure universal compliance of a large, technologically complex, and informationally massive industry.⁷⁷ Sometimes it is the tort system that uncovers instances of noncompliance with FDA regulatory standards, rather than the FDA itself.⁷⁸ Nor can the FDA bring suit for every violation of which it may become aware. Often informal negotiations between the FDA and pharmaceutical companies take place, especially when the situation falls in a regulatory gray area.⁷⁹ Given the non-specific phrasing of many regulatory requirements (such as "efficacy" and "safety") and the vagaries of cost-benefit analyses, those instances are not uncommon. Here, the tort system operates to provide a stick (though its size is often quite varied depending on the personal injury implications of any violation) that supplements FDA enforcement: violations of FDA safety regulations that are the legal cause of patient injuries result in negligence per se.⁸⁰ There is good reason to

that the FDA is dependent on data from the industry it is supposed to regulate. See John G. Culhane, *The Limits of Product Liability Reform Within a Consumer Expectation Model: A Comparison of Approaches Taken by the United States and the European Union*, 19 HASTINGS INT'L & COMP. L. REV. 1, 75 n.303 (1995) (listing authors who have criticized the FDA for inadequately protecting the public); Schwartz, *supra* note 21, at 1387 (arguing that because the FDA has failed to require strict compliance with its stringent safety standards, unsafe medical devices and prescription drugs have reached the market); see also GARBER, *supra* note 8, at 127-28 (noting that serious safety shortfalls that become known are more often the result of lack of compliance with FDA standards than inadequate FDA standards).

77. See ADVISORY COMMITTEE REPORT, *supra* note 59, at 25 ("Unfortunately, recent events have raised doubts about the FDA's current capacity to conduct effective law enforcement. The generic drug scandal exposed the Agency's vulnerability to shoddy, and sometimes fraudulent, data submitted in support of new product approvals."); see also Cooper, *supra* note 14, at 240; Schwartz, *supra* note 21, at 1387-89 (attributing the FDA's regulatory failures to both decreased resources and increased responsibilities).

78. See, e.g., HALCION TASK FORCE REPORT, *supra* note 53, at v, 18 (noting that a tort suit first uncovered evidence of errors in IND studies for Halcion that were due to poor oversight by manufacturer and may have been intentional). See generally Carl T. Bogus, *War on the Common Law: The Struggle at the Center of Products Liability*, 60 MO. L. REV. 1, 85 (1995) ("The common law provides a mechanism for developing information—sometimes by prying it from the manufacturer's hands . . .").

79. See GREEN, *supra* note 26, at 49, 183 (detailing how informal pressure by the FDA resulted in Richardson-Merrell ceasing its promotional efforts for Bendectin).

80. The stick is variable because, as with violations of other federal regulations, many FDA violations may only be tangentially implicated in adverse drug effects, and so the violation would not be a cause in fact or proximate cause of damages. See *Sheridan v. United States*, 969 F.2d 72, 75 (4th Cir. 1992) (finding that violation of a federal regulation did not necessarily establish proximate cause); *Stanton v. Astra Pharm. Prods., Inc.*, 718 F.2d 553, 565 (3d Cir. 1983) (finding that violation of a

believe that the threat of tort liability assists considerably in effective enforcement of the nation's drug laws by the FDA, both by encouraging voluntary compliance and by providing leverage for the FDA in informal negotiations.⁸¹

Thus, the qualification reveals a silver lining: in addition to the stick of negligence per se, a regulatory compliance defense would add the carrot of a defense to a tort suit for complying with FDA regulatory requirements in the IND process. This incentive should influence manufacturers' compliance. Of course, the incentive is prospective only: we can affect only behavior in the future; testing of drugs that has already occurred at the time of adoption of any defense would be unaffected. The carrot should also provide the FDA greater leverage in its negotiations with drug manufacturers with regard to an NDA.

Another qualification and concern deserves mention. Both the drug-lag scholarship and, even more significantly, the emergence of the AIDS scourge have had an enormous impact on the FDA in its review and approval of new drugs. In recent years, the FDA has been criticized publicly for delays in approval of new drugs, as exemplified in a harsh editorial in the *Wall Street Journal* concerning the FDA's delay in approving a drug (t-PA) designed to prevent clotting in heart attack victims:

regulation was not enough to establish cause in fact, although the court uses "proximate cause" language). Not every jurisdiction subscribes to the legal proposition that violation of a regulatory safety provision is negligence per se. *See, e.g., Sheridan*, 969 F.2d at 75 (applying Maryland law); *Eimers v. Honda Motor Co.*, 785 F. Supp. 1204, 1208-09 (W.D. Pa. 1992) (applying New York law).

81. Penalties imposed on manufacturers for violating the Food, Drug, and Cosmetic Act or FDA regulations are considerably more meager than the damages that might be imposed on a manufacturer, as a result of tort actions. *See Viscusi et al., supra* note 17, at 1455 n.66. A variety of criminal statutes may be applicable in the event of willful misconduct by a manufacturer, and penalties imposed pursuant to such statutes can be more substantial than the civil penalties. *See, e.g., Talbott v. C.R. Bard, Inc.*, 865 F. Supp. 37, 41-42 (D. Mass. 1994) (involving a heart catheter manufacturer's executives who pleaded guilty to a variety of criminal charges resulting in criminal and civil penalties exceeding \$61 million), *aff'd*, 63 F.3d 25 (1st Cir. 1995), *cert. dismissed*, 116 S. Ct. 1892 (1996); *see also* GREEN, *supra* note 26, at 86 (noting the criminal penalties imposed on Richardson-Merrell for false reporting of studies in connection with MER/29). Of course, criminal charges are rarely filed against manufacturers who violate FDA regulations.

Thus because of the potential amount of damage awards the tort system plays an important role in making FDA regulations more effective. *See, e.g., GARBBER, supra* note 8, at 125 (stating that potential liability costs create an incentive for regulatory compliance). A regulatory compliance defense would not seem, on the surface, to affect this role, but we should be wary of the law of unintended consequences.

Patients will die who would otherwise live longer. Medical research has allowed statistics to become the supreme judge of its inventions. The FDA, in particular its bureau of drugs under Robert Temple, has driven that system to its absurd extreme. . . . The advisory panel's suggestion that TPA's [sic] sponsor conduct further mortality studies poses grave ethical questions. . . . We'll put it bluntly: Are American doctors going to let people die to satisfy the bureau of drugs' chi-square studies?⁸²

By the mid-1980s the FDA began responding to this criticism and had modified its practices to speed the approval of especially valuable drugs. The issue of delay in approving drugs and in making them available, especially to terminally ill patients, has taken on increasing significance in the quest to find drugs to ameliorate, cure, or prevent AIDS. As a result, the FDA has adopted provisions to permit desperately ill patients to obtain drugs before preapproval testing is complete and to speed the approval of new drugs with the promise of providing significant therapeutic advantages for those with conditions that are life-threatening or risk irreversible serious health consequences.⁸³

Although a recent General Accounting Office study found that the FDA has reduced the delay in approving new drugs significantly,⁸⁴ political pressure continues to mount for further

82. *Human Sacrifices*, WALL ST. J., June 2, 1987, at 30. Subsequent research found that t-PA reduced mortality in heart attack victims from an average of 7.3% with alternative treatments to 6.3% percent with t-PA. See The GUSTO Investigators, *An International Randomized Trial Comparing Four Thrombolytic Strategies for Acute Myocardial Infarction*, 329 NEW ENG. J. MED. 673, 677 (1993).

The FDA has, over the past 15 years, become more responsive to the drug-lag criticism. See BRODY, *supra* note 11, at 52. The deregulation fervor that marked the Reagan administration no doubt contributed to the sensitivity and responsiveness of the FDA. See generally TOLCHIN & TOLCHIN, *supra* note 71, at 94 (noting the dramatic increase in drug approvals in 1981).

83. See BRODY, *supra* note 11, at 169-81 (describing three programs that responded to the need for quicker access to AIDS treatments).

84. See U.S. GEN. ACCOUNTING OFFICE, GAO/T-PEMD-96-9: FDA REVIEW TIMES: TESTIMONY BEFORE THE SUBCOMMITTEE ON HEALTH AND ENVIRONMENT OF THE HOUSE COMMITTEE ON COMMERCE 8-9 (1996) (noting that during the six-year period of 1987-1992, time for FDA approval dropped from 33 months to 19 months; approval times for drugs that are new molecular entities is tending toward two years in all Western countries); see also David A. Kessler et al., *Approval of New Drugs in the United States: Comparison with the United Kingdom, Germany, and Japan*, 276 JAMA 1826 (1996) (reporting that U.S. drug approvals are comparable with Great Britain and ahead of Germany and Japan).

reform in the new drug approval process.⁸⁵ Although the reforms to date appear quite modest and generally beneficial, continued pressure to accelerate, streamline, outsource, or compromise the approval process may affect the arguments above about the optimality of FDA decisions about NDAs. As David Kessler, then-Commissioner of the FDA, has observed:

On analysis, it is important to recognize that the FDA could easily accelerate the availability of new drugs. Likewise, it could provide greater assurances that drugs reaching the market are safe and effective. Neither goal alone is sufficient, however. The agency's job is to balance the need to make drugs available quickly with the need to ensure that patients do not receive unsafe or ineffective products. Since it cannot pursue any single objective, criticism can always be leveled against the FDA from either direction.⁸⁶

IV. THE TRANSACTION COSTS OF A COMPLIANCE DEFENSE

A. Preapproval Regulation

To appreciate what will be required if a compliance-with-FDA-standards defense is adopted, we should briefly consider the new drug testing process.⁸⁷ As the following discussion will reveal, the process of testing a new drug is lengthy,

85. See *Revitalizing New Product Development From Clinical Trials Through FDA Development: Hearing on S.1477 Before the Senate Comm. on Labor and Human Resources*, 104th Cong. 1 (1996) (opening statement of Sen. Kassebaum on reform of FDA approval on drugs and devices); Jocelyn Kaiser, *FDA Reform Starts Down the Track*, 271 SCI. 1228, 1228 (1996) (discussing a proposed bill that would force the FDA to speed up its review process or contract out new drug applications for faster processing).

86. Kessler, *supra* note 74, at 286.

87. The condensed and stylized account of new drug testing set forth below is drawn from GREEN, *supra* note 26, at 50-51. For more detailed explanations of the NDA testing process, see Kessler, *supra* note 74, at 281-85. See also JERRY T. GIBSON, *MEDICATION, LAW AND BEHAVIOR* 123-45 (1976) (detailing the three-phase procedure of the Investigational New Drug Application and the subsequent NDA required by the FDA); WARDELL & LASAGNA, *supra* note 10, at 19-25 (describing post-1962 developments in the new drug approval process).

complicated, and heavily regulated by the FDA.⁸⁸ The process is also one that evolves in response to advancements in the sciences employed. A study that might meet the FDA standard for an adequate and well-controlled study in 1962 might not meet the same standard if performed today.⁸⁹ Ascertaining compliance by the pharmaceutical manufacturer and, if non-compliance occurred in some respect, its implications in a hypothetical causal chain that led to the plaintiff's injury is likely to entail substantial, perhaps enormous, transaction costs.⁹⁰

Animal studies are required before an IND, which is required as a condition for shipping unapproved drugs in interstate commerce, is filed with the FDA. These studies are conducted in the laboratory on animals or through in vitro (test tube) testing of animal or human tissue. Dozens, hundreds, or even thousands of biologically active agents may be tested in this initial stage of drug development for every drug that receives final approval. The winnowing of potential new drugs during the IND process is in significant part responsible for the fact that it takes, on average, twelve years and costs more than \$200 million to develop and obtain approval for a new drug.⁹¹ If the initial phase of testing by the manufacturer (or a private laboratory hired by the manufacturer) is successful, an IND is filed with the FDA. The FDA must decide whether, based on the results of the laboratory testing, human clinical testing should be permitted. The IND submission does not require positive approval by the FDA—it becomes effective unless the FDA objects within thirty days of submission.⁹²

Human subject testing entails three phases.⁹³ In the initial phase, the drug is tested on a limited group of humans to understand absorption, elimination, metabolism, and toleration by a relatively small group (usually less than a

88. Some of the FDA's regulation of the IND process is motivated by concern for the safety of the subjects involved in the IND testing process. That aspect of the FDA's regulations need not concern us, as they would not bear on post-marketing risks for patients injured by a pharmaceutical.

89. See Kessler, *supra* note 74, at 286.

90. See Schwartz, *supra* note 50, at 1130–31 (noting that regulatory agencies may not have considered the precise issue before a court, weakening the justification for courts' reliance on agency standards).

91. See Joseph A. Di Masi et al., *Cost of Innovation in the Pharmaceutical Industry*, 10 J. HEALTH ECON. 107, 125 (1991).

92. See 21 C.F.R. § 312.40(b)(1) (1996).

93. See *id.* § 312.21.

hundred) of healthy human subjects. Toxicity is also examined, but the initial phase ordinarily does not attempt to assess the efficacy of the drug. If the first phase is completed successfully, the next stage is to study patients who have the disease or condition that the investigational drug is designed to treat. This initial efficacy examination (safety is also assessed) is conducted as a controlled study on a smaller cohort of patients (several hundred) than the third phase, which entails expanded clinical testing of the drug. The third phase typically involves several thousand patients to provide improved ability to detect infrequent effects that the drug may have on patients who take it. Most often the human subject testing is conducted by medical center researchers who are hired by the sponsoring manufacturer. The third phase is often conducted by multiple private physicians who are supervised by and report to the manufacturer to obtain access to the number of patients required for the third phase. In all cases, however, clinical investigators report to the manufacturer, not to the FDA.⁹⁴ By statute, the studies conducted must be "adequate and well-controlled."⁹⁵ Because the perfect clinical study has yet to be performed, this general standard gives the FDA considerable discretion to require the sponsoring manufacturer to conduct additional studies (in what might be termed a fourth phase).

If the IND testing proves successful, the manufacturer submits an NDA to the FDA, which must approve the NDA before the manufacturer may market the drug. NDAs must contain the results of all animal and human testing, proposed usage of the drug, and the proposed labeling (including warnings) that will accompany the drug. An NDA typically consists of a hundred thousand pages or more—the NDA for Prozac consisted of a million pages that included reports on twenty-five premarketing studies of the drug.⁹⁶ FDA review of an NDA

94. See 21 U.S.C. § 355(i) (1994).

95. *Id.* § 355(d).

96. See Materials submitted by James T. Burns, Eli Lilly & Co., for the Colloquy on Products Liability: Comprehensive Discussions on the *Restatement (Third) of Torts: Products Liability* 12 (Mar. 22–23, 1996) (on file with the *University of Michigan Journal of Law Reform*); see also *Revitalizing New Product Development from Clinical Trials Through FDA Review: Hearing of the Senate Comm. on Labor and Human Resources*, 104th Cong. 5 (1996) (statement of Sen. Nancy Landon Kassebaum) (referring to a recent NDA that contained 200,000 pages). See generally John A. Norris, *Fulfilling FDA's Vision of Faster Drug Review*, in *FOOD AND DRUG ADMIN., FDA CONSUMER SPECIAL REPORT, FROM TEST TUBE TO PATIENT: NEW DRUG DEVELOPMENT IN THE UNITED STATES* (1988), reprinted in *BIOTECHNOLOGY: NEW*

often entails negotiation between the sponsor and the agency about the adequacy of the clinical data generated by the NDA studies and the contents of the drug's labeling. The latter addresses the conditions for which the drug is approved, a great deal of information about how the drug should be used, and safety related information that includes contraindications, known adverse effects, and precautions in usage to avoid identified risks.⁹⁷ Because drugs cannot be modified to reduce risk, full information about the inherent and avoidable risks posed by the drug are essential aspects of the drug's safety. We should understand that the drug's labeling is an essential element of an NDA approval by the FDA.

The IND process has three important consequences for a government compliance defense. First, as previously mentioned, because all information relevant to the regulatory decision is developed by the sponsor (or its agents), the defense must be available only if the sponsor complied with all regulatory requirements. The mere fact of government approval of the product should not provide adequate grounds for the defense.⁹⁸ Despite the theoretical existence of FDA enforcement of its IND and NDA regulations and the tort stick of negligence per se for violation of government safety standards, the pharmaceutical industry's history is littered with instances of deliberate or negligent withholding of information from the FDA in the new drug approval process.⁹⁹ If a government standards

DEVELOPMENTS IN FEDERAL POLICIES AND REGULATIONS 130 (Practising Law Institute ed., 1988) (describing NDA's generally, including their length).

97. See Quirk, *supra* note 64, at 202.

98. See 21 U.S.C. § 355(b)(1)(A) (1994) (requiring that an NDA contain "full reports of investigations" conducted on the drug for which the sponsor seeks approval).

99. See *Benedi v. McNeil—P.P.C., Inc.*, 66 F.3d 1378, 1389 (4th Cir. 1995) (involving a manufacturer failing to provide drug experience reports on a timely basis); *Hearings on Preclinical and Clinical Testing by the Pharmaceutical Industry Before the Subcomm. on Health of the Senate Comm. on Labor and Pub. Welfare and the Subcomm. on Admin. Practice and Procedure of the Senate Comm. on the Judiciary*, 94th Cong. 725 (1975) (statement of a former FDA Commissioner characterizing the problem of false and misleading reporting to the FDA as "serious and grave"); ABRAHAM, *supra* note 70, at 92–96 (summarizing the inaccurate and incomplete data submitted to the FDA in support of the NDA for Naproxen); GARBER, *supra* note 8, at 188 (noting that "there is substantial evidence of incomplete compliance with FDA regulations"); GREEN, *supra* note 26, at 83–86, 128–29 (describing the events surrounding the cover-up of Bendectin's adverse effects); Merrill, *supra* note 27, at 5–6 (1973) (recounting McNeil Laboratories' concealment of the adverse effects of Flexin); Schwartz, *supra* note 13, at 1348–52 (describing several instances in which drug manufacturers concealed the adverse effects of new drugs from the FDA); *Excerpts from Dr. Goddard's Address*, N.Y. TIMES, Apr. 7, 1966, at 24 (expressing dismay on the part of the then FDA Commissioner, Dr. Goddard, at poor quality and dishonesty in the submission of investigational drug studies).

defense is to serve the public interest instead of serving as a shield for industry misfeasance, the defense must be structured as a compliance, rather than an approval, defense.¹⁰⁰ Initially, I assume that the defense would still be available despite a failure to comply with regulations if the failure would not have made any difference in the FDA's consideration of the NDA or in the proposed labeling. Thus, unless it were shown that the FDA would have refused to approve the drug or insisted on additional information in the labeling that would have affected the plaintiff's use of the drug, a plaintiff still could not prevail. This treatment is not the only possibility, and later this Article considers alternatives.

Second, once we recognize that the defense is based on compliance,¹⁰¹ the advantage of *ex ante* approval is lost: once

Of course, all of these instances of withholding (or mischaracterization) of information from the FDA represent a partial numerator without a denominator—that is they reveal nothing about the rate at which such episodes occur. My intuition is that today they represent a reasonably small percentage of NDAs, but, of course, others might have different intuitions. Nevertheless, given the small number of drug products liability cases currently brought, *see supra* note 24, another important question about which I have no evidence is the percentage of lawsuits in which the manufacturer has failed to provide complete information to the FDA.

100. The Michigan statute, which provides that a drug is not defective if approved by the FDA, is the most problematic of the existing state reform provisions. *See* MICH. COMP. LAWS ANN. § 600.2946(5) (West Supp. 1995). The statute has an exception for fraud on the FDA that, had the fraud not existed, would have resulted in a denial of approval. The Michigan statute, however, immunizes the drug manufacturer who knowingly submits false data minimizing a side effect from which a plaintiff subsequently suffers, if submission of accurate information would have resulted not in denial of the NDA, but in a requirement for warnings in the drug labeling or limitations on prescribing the drug. Consider Accutane: the drug causes birth defects but is nevertheless available on the market with extensive precautions required before prescribing to women of child-bearing age. *See* PHYSICIANS' DESK REFERENCE 2076–79 (1996); *Birth Defects Caused by Isotretinoin—New Jersey*, 124 ARCHIVES OF DERMATOLOGY 838, 838 (1988). Under the Michigan statute, a manufacturer could not be held liable even if it intentionally had failed to reveal to the FDA any evidence of the drug's teratogenicity during preapproval testing. To take another egregious example, Michigan's statute would have immunized the manufacturer of thalidomide and its U.S. licensee from any products liability claim that it negligently conducted preapproval testing of the drug. The drug was never approved in the United States by the FDA because it had been developed, tested, and marketed in Europe, and its teratogenicity was discovered before the FDA completed its review of the NDA. Several thalidomide children were born in the United States during the course of a shamelessly excessive preapproval clinical testing that was designed to promote the drug. *See* GREEN, *supra* note 26, at 64–78 (describing thalidomide's journey from development and marketing in Europe to lawsuits in the United States).

101. Some state statutes that provide a defense based on FDA approval have exceptions for the situation in which a manufacturer engages in fraudulent misrepresentation or withholds information required to be submitted to the FDA. *See* sources cited *supra* note 13. However, if the justification for an FDA regulatory oversight

suit is brought, courts will have to examine compliance *ex post*. The tort system, not the FDA, will be required to make a determination of the manufacturer's compliance with requirements governing the testing of new drugs and accurate reporting of the outcome of the testing. This leads ineluctably to the third concern: the enormously complicated—both factually and legally—inquiry that will be required to determine compliance. When we recall the extensive testing required and examine the complexity of that testing and the reporting of the results to the FDA, we should become quite leery of the inquiry that a government compliance defense will impose on courts, juries, and pharmaceutical products liability litigants.

A recent report by an FDA task force investigating allegations of misconduct in connection with the prescription drug Halcion nicely captures the difficulties that can arise:

The review has required the Task Force to address events and processes retrospectively, going back more than two decades, and to evaluate those events, keeping in mind how regulatory and scientific approaches have changed over time. Actions or choices that may seem clear today may have been less obvious to the decision makers involved in the issues at the time decisions were being made. In addition, the Task Force observes that the debate over Halcion's safety and efficacy and the actions of Upjohn and the FDA involve complex scientific and regulatory issues about which reasonable people may differ.¹⁰²

The extensiveness of pre-approval testing and the written record documenting it (the NDA on file with the FDA) may, with some frequency, contain a variety of mistakes, deceptions, or other culpable conduct ("errors"), ranging from the minor to

defense is the FDA's superior information and technical expertise, then it should not matter why the FDA does not have relevant information. If the FDA does not have the information for any reason, the basis for displacing tort law is missing, provided, of course, that the missing information would have had an impact on the FDA's decisionmaking. *Cf. Stanton v. Astra Pharm. Prods., Inc.*, 718 F.2d 553, 580–81 (3d Cir. 1983) (finding manufacturer negligent in part because it failed to provide adverse drug reaction reports required by FDA regulations).

102. HALCION TASK FORCE REPORT, *supra* note 53, at i. The Task Force concluded that the Department of Justice would have to determine whether there was a violation of criminal laws that prohibit fraud on a federal agency. *See id.* at ii–iii, 29.

the egregious.¹⁰³ If, after extensive discovery,¹⁰⁴ errors are uncovered, two and possibly three further inquiries would be required: (1) does the error raise a legitimate issue about whether the manufacturer met existing FDA requirements for the IND process; (2) if yes, would the drug and its existing labeling nevertheless have been approved by the FDA despite the error; and (3) and if the labeling would have been different, would any modification have affected the adverse reaction suffered by the plaintiff?

The courts will have to conduct this inquiry for the most part without the benefit of a prior FDA judgment on the first two matters. In those instances in which the errors discovered were previously unknown to the FDA, the court must determine whether the errors compromised the FDA's conclusion that "adequate and well-controlled studies" were conducted. This sort of general, imprecise, contextual, and normative inquiry, often handled within the FDA by informal negotiation with a manufacturer whose NDA raises questions rather than through formal determinations of compliance, is not the sort of inquiry that falls squarely within the institutional competence of common law courts. The question of compliance may also require interpretation and application of specific and quite complicated FDA regulatory standards.¹⁰⁵

Assessing the significance of noncompliance will be difficult as well. The inquiry will be the hypothetical question of what would have happened within the FDA if the error had not

103. See *supra* note 99 and accompanying text.

104. Discovery might extend as far as deposing individual physicians, their nurses, and office staff who participated in multi-center clinical testing and obtaining patient records, in situations in which carelessness or worse is suspected in the phase three NDA testing. See GREEN, *supra* note 26, at 176.

105. For example, FDA regulations for the content of an NDA, which comprise 10 pages in the Code of Federal Regulations, require that the manufacturer provide the following:

A description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from clinical investigations, including controlled and uncontrolled studies of uses of the drug other than those proposed in the application, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers.

21 C.F.R. § 314.50(d)(5)(iv) (1996); *cf. Stanton*, 718 F.2d at 558-63 (holding that a manufacturer who negligently failed to comply with adverse drug reporting requirements was negligent per se).

occurred. Because the FDA limits the circumstances under which its employees are allowed to testify in court,¹⁰⁶ the courts will be left to answer that question without the most salient evidence available. Or, we may be confronted with the spectacle of one former FDA official testifying about what action she would have taken, while another retired FDA official explains that he would have done something quite different.¹⁰⁷ These counterfactual inquiries are not the stuff from which confidently accurate outcomes are reached in litigation.

Of course, we could fashion a compliance defense that would not require this inquiry—once noncompliance was determined the defense would be unavailable—but only at the cost of driving a quite substantial—perhaps fatal—wedge into the protection afforded by the defense.¹⁰⁸ If the compliance defense is lost any time there is some default by the manufacturer in meeting FDA requirements, the protection afforded by the defense would begin to resemble Swiss cheese.¹⁰⁹

Concerns similar to these have led a number of courts to decline to adopt a noncompliance exception for federal preemption of tort claims involving medical devices. Thus, in *Kemp v. Pfizer, Inc.*,¹¹⁰ the court refused to permit the plaintiff to prove her allegations that defendants had committed fraud by deceiving the FDA about the safety of the Shiley heart valve

106. See 21 C.F.R. § 20.1 (1995) (prohibiting an FDA employee from testifying in court about “any information acquired in the discharge of his official duties” unless previously authorized by the FDA Commissioner).

107. Such an episode occurred in the Bendectin litigation, when a former FDA pharmacologist testified that had she seen the original of a study that was sanitized by the manufacturer before its submission to the FDA, she would have recommended that the drug’s approval be withdrawn or, at least, that a birth defect warning be provided. See GREEN, *supra* note 26, at 140. The manufacturer then had the FDA Commissioner at the time testify that he would have overridden any such recommendation. Trial Transcript at 8116, *Mekdeci v. Merrell Nat’l Lab.*, No. 7-255-Orl-Civ (M.D. Fla. Mar. 14, 1980).

108. Other options include employing an objective “materiality” standard, see *infra* text following note 119, and shifting the burden of proof on causation to the defendant. See Frank M. McClellan et al., *Strict Liability for Prescription Drug Injuries: The Improper Marketing Theory*, 26 ST. LOUIS U. L.J. 1, 34–35 (1981).

109. Although such a rule would gut the defense, there is some justification for it. The defense is provided because of the superior expertise of the FDA in making judgments about drug safety and appropriate labeling. If a manufacturer’s nontrivial error deprives the FDA of relevant information in making that determination, asking the courts to determine what the FDA would have done is at least modestly inconsistent with the justification behind the defense. Of course, there may be cases in which the FDA has already responded to the newly emergent information that was not made available at the time of NDA approval.

110. 835 F. Supp. 1015 (E.D. Mich. 1993).

because of concern that permitting such an exception to preemption would create such an enormous hole in the defense as to render it futile in protecting manufacturers from tort suits.¹¹¹ The court also expressed its doubt about the ability of judges and juries to “untangl[e] the bramble of procedures and regulations governing pre-market approval and later reporting requirements.”¹¹² In several similar contexts, courts have foregone resolving questions about regulatory standards and compliance without prior administrative agency consideration, recognizing the expertise and discretion reposed in the administrative agency responsible for oversight.¹¹³

Another significant matter is the extent to which a compliance defense will obviate the need for courts and juries to resolve the difficult causal questions that arise in drug cases: whether the drug is capable of causing disease, and if so, whether it caused the individual plaintiff's disease or injury.¹¹⁴

111. See *id.* at 1021.

112. *Id.* at 1022. See also *Michael v. Shiley*, 46 F.3d 1316, 1329 (3d Cir.) (“In sum this claim requires a court, applying state law, to perform the same functions initially entrusted to the FDA.”), *cert. denied*, 116 S. Ct. 67 (1995); *Reeves v. Acromed Corp.*, 44 F.3d 300, 307 (5th Cir. 1995) (“Given the FDA's central role in reviewing and approving devices under the MDAs [Medical Device Amendments], the FDA is in the best position to decide whether [the device manufacturer] withheld material information from the agency and, if so, the appropriate sanction.”), *cert. denied*, 115 S. Ct. 2251 (1995). *But cf. Medtronic, Inc. v. Lohr*, 116 S. Ct. 2240, 2256 (1996) (holding that plaintiff's state law claim that defendant's violations of FDA regulations were negligent or resulted in a defective product was not preempted by Medical Device Amendments).

The First Circuit extended this position to its extreme in *Talbot v. C.R. Bard, Inc.*, 63 F.3d 25 (1st Cir. 1995), in which the court held the plaintiff's state law claim was preempted by the Medical Device Amendments to the Food, Drug, and Cosmetic Act, 21 U.S.C. § 360k(a) (1988), despite the fact that the manufacturer pled guilty to defrauding the FDA in its applications for premarketing approval of the heart catheter that failed during surgery and killed the plaintiff's decedent. The court expressed the concern that the FDA was the entity with the expertise to determine compliance and that leaving such a determination to state courts in products liability actions might result in “numerous inconsistent interpretations and applications” of the Medical Device Amendments. *Id.* at 29–30.

113. See *Lowe v. Sporicidin Int'l*, 47 F.3d 124, 130 (4th Cir. 1995) (concluding that comparing advertisements with approved labeling of a pesticide “does not clearly establish—one way or the other—whether the advertisement claims ‘substantially differ’ from the labeling claims,” which agency regulations prohibit); *Sandoz Pharm. Corp. v. Richardson-Vicks, Inc.*, 902 F.2d 222, 230–31 (3d Cir. 1990) (declining to decide whether an ingredient in cough medicine was properly labeled “active” or “inactive,” pursuant to regulations of the FDA where the FDA had not yet addressed the question).

114. Because of the nature of scientific evidence, which is almost always developed in studies involving groups, both inquiries are logically necessary. See generally *Linda Bailey et al., Reference Guide on Epidemiology*, in REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 121, 167 (Federal Judicial Center 1994) (discussing the role of science in proving general causation and the legal treatment of specific causation).

Assessing causation has been one of the most controversial aspects of modern pharmaceutical litigation¹¹⁵ and eliminating the need for juries to delve into the complex and difficult scientific issues required for this inquiry might be a significant advantage.

To the extent that a regulatory compliance defense prevents suits from being filed, all issues are eliminated from jury consideration. In those cases litigated by a plaintiff claiming a failure to comply with FDA regulations, however, I am not sure that the causal issues could be avoided, at least not in all cases. Even if the fact finder were persuaded that the manufacturer violated FDA requirements and that the FDA would not have permitted the pharmaceutical on the market, the manufacturer should still not be held liable if the drug does not cause the type of injury suffered by the plaintiff or did not cause the particular plaintiff's injury. Thus, manufacturers should be free, as they are without a regulatory compliance defense, to show that plaintiff's injury is the result of some cause other than the manufacturer's drug or that the drug does not cause the injury from which the plaintiff suffers. Otherwise, the defendant's actions simply have not caused the plaintiff's harm. Of course, there may be cases in which causation is not contested, as in a case in which the issue is the adequacy of a warning of an admitted side effect. However, even without a regulatory compliance defense, the jury would not be required to address these causal issues.

Another quite different concern is the subtle and subconscious biases that affect investigators conducting the studies required for approval of a new drug. The concern is not with outright deceptions, but with the effect of the financial consequences of the test's outcome either on the manufacturer conducting them or even on independent investigators hired by the manufacturer to conduct the tests. Both personal relationships with the sponsor and the prospect of future grant support may play an influential role. One empirical study of independent researchers found that the source of funding was associated with the outcome of the study.¹¹⁶

115. See MARCIA ANGELL, *SCIENCE ON TRIAL: THE CLASH OF MEDICAL EVIDENCE AND THE LAW IN THE BREAST IMPLANT CASE* (1996); PETER W. HUBER, *GALILEO'S REVENGE: JUNK SCIENCE IN THE COURTROOM* 215-16 (1991).

116. See Richard A. Davidson, *Source of Funding and Outcome of Clinical Trials*, 1 J. GEN. INTERNAL MED. 155, 155 (1986). The results of this study may have been affected by confounding factors or by non-random selection bias—pharmaceutical

Studies funded by sources other than the sponsor favored the new therapy sixty-one percent of the time.¹¹⁷ By contrast, studies that were funded by the sponsor found the new therapy preferable eighty-nine percent of the time.¹¹⁸ This bias affects the accuracy of the testing conducted, thereby compromising regulatory decisionmaking. But this problem is not a new one nor one of which the FDA is unaware¹¹⁹ and therefore may be neutralized in the NDA review by FDA staff. At a minimum, it complicates and extends the FDA's review process; at worst, it may contribute to the post-approval risk problem, a matter discussed in the next section.

In the end, the concerns raised above, while serious, may not be fatal to a compliance defense. Trivial or modest errors that are immaterial are unlikely ever to be uncovered because of search costs. Errors that at least are related to serious adverse reaction risks will likely be uncovered, either by the FDA or by plaintiff's lawyers. The question of tying the error to the approval or labeling decision might be avoided by an objective materiality standard for errors, although that will require the courts to do that for which the FDA is far better suited. Although there are substantial investigative costs imposed by a compliance defense, at least there is reason to believe that the approval determination made by the FDA is a reasonably optimal one, one that is probably better than any alternative determination.

Thus, if we could freeze time (and our knowledge of risk) at the point of FDA approval of an NDA, we might be inclined to opt for an FDA compliance defense. But we cannot freeze time; it marches on and with it our storehouse of information changes, often radically. And it is the post-approval period that raises the most serious questions about the viability of a regulatory compliance defense because additional significant information is uncovered, manufacturers undertake marketing activity that affects the benefit-risk ratio of the drugs that are promoted, and the FDA has inadequate resources to enforce

companies are more likely to sponsor studies that show their drugs to be efficacious. *See id.* at 157; *see also* ABRAHAM, *supra* note 70, at 242-46 (explaining that inconsistencies in testing that support the commercial interests of the testers may result from shared "commercial perspectives" among industrial scientists and company managers); BRODY, *supra* note 11, at 145-50.

117. *See* Davidson, *supra* note 116, at 157.

118. *See id.*

119. *See* Quirk, *supra* note 64, at 205.

regulatory compliance. Most importantly, accommodation of these post-approval concerns in any regulatory compliance defense could make the defense largely chimerical. We simply may not be able to channel the expertise of the FDA in the pharmaceutical approval process into streamlining the tort system.

B. Post-Approval Risk Identification, Regulation, and Enforcement

The post-approval story begins with the recognition that after a drug's approval by the FDA and general distribution to the public much critical information emerges and activity occurs that exposes and affects a drug's risks and safety. We should also recall that these risks play a central role in most of the pharmaceutical litigation that takes place.¹²⁰ The three phases of the IND human testing process¹²¹ are inadequate to identify all of the significant adverse effects that a drug may cause. Identifying those previously undiscovered risks, taking appropriate precautionary actions, and taming the manufacturer's incentives to advertise and promote its drugs in a manner that encourages overuse (and thereby excess risk) or dangerous "off-label" uses¹²² are the post-approval areas of concern for a regulatory compliance defense.

A number of reasons explain the inability of the IND testing process to identify all of the risks associated with use of a drug. First, it is often difficult both to anticipate all of the adverse effects that a drug may cause and to build into the clinical investigations a mechanism to detect those side effects.¹²³

120. See Gibbs & Mackler, *supra* note 45, at 228.

121. See *supra* text accompanying notes 93-94.

122. Drugs are approved by the FDA to treat conditions for which the manufacturer has shown the drug to be safe and efficacious. Once the FDA approves a drug, physicians are free to prescribe it for other medical purposes. The FDA's authority with regard to off-label prescribing is limited to its control over manufacturers' advertising and promotion. Off-label prescribing of a drug may account for 25% or more of all prescriptions. See Milt Freudenheim, *FDA Gets Tough on Drugs Offered for Unapproved Uses*, N.Y. TIMES, June 29, 1991, at 1; see generally Lars Noah, *Constraints on the Off-Label Uses of Prescription Drug Products*, 16 J. PROD. & TOXICS LIAB. 139 (1994); Kaspar J. Stoffelmayr, Comment, *Products Liability and "Off-Label" Uses of Prescription Drugs*, 63 U. CHI. L. REV. 275 (1996).

123. See Gerald A Faich, *Adverse Drug Experience Reporting and Product Liability*, 41 FOOD DRUG COSM. L.J. 444, 444 (1986).

Second, because even the final and largest testing phase of the pre-marketing approval process is conducted on a limited number of human subjects,¹²⁴ if a given side effect is rare enough it may not emerge in the clinical testing phase.¹²⁵ Third, often the subjects involved in the clinical trial will be more homogenous than the population that will ultimately use the drug. Thus, inevitably, additional hazards of new drugs emerge as they are put into widespread use in a heterogeneous population.¹²⁶ Oral contraceptives had been marketed and used by thousands of women for three years before their tendency to cause blood clots in a small number of users was discovered.¹²⁷ Until recently, drugs were not tested on pregnant women during the IND process. For example, Bendectin, a drug for morning sickness, was never subjected to reproductive toxicity testing before its approval by the FDA.¹²⁸ Fourth, the widespread use of a newly approved drug may also provide new information that has implications for expanding or narrowing indications for use and about the efficacy of the drug; a drug may be used differently or for a longer period by the general population than those involved in clinical trials.¹²⁹ That information, which would affect prescribing practices, is also important information for proper use of the drug that should be included in the drug's labeling. Fifth, the IND testing process is unlikely to reveal interactions with other drugs.¹³⁰ Finally, the hazards of drugs causing diseases only after lengthy latency periods remain unknown until well into the post-approval period, as was the case with, for example, DES.¹³¹

124. See *supra* text accompanying notes 93-94.

125. See H.R. REP. No. 91-931, at 11-12 (1970).

126. See, e.g., GENERAL ACCOUNTING OFFICE, CHOLESTEROL TREATMENT: A REVIEW OF THE CLINICAL TRIALS EVIDENCE 3 (1996) (noting that clinical trials of the efficacy of drugs in reducing cholesterol levels ignored women, elderly, and minorities).

127. See HARRY F. DOWLING, MEDICINES FOR MAN: THE DEVELOPMENT, REGULATION, AND USE OF PRESCRIPTION DRUGS 59-60 (1970).

128. See GREEN, *supra* note 26, at 329-30.

129. See, e.g., HALCION TASK FORCE REPORT, *supra* note 53, at 14 (noting that the recommended dose for Halcion was reduced in response to adverse drug reports).

130. See David A. Kessler, *Introducing MEDWatch: A New Approach to Reporting Medication and Device Adverse Effects and Product Problems*, 269 JAMA 2765, 2765 (1993).

131. See ROBERTA J. APFEL & SUSAN M. FISHER, TO DO NO HARM: DES AND THE DILEMMAS OF MODERN MEDICINE 19-25 (1984); A.L. Herbst et al., *Adenocarcinoma of the Vagina: Association of Maternal Stilbestrol Therapy with Tumor Appearance in Young Women*, 284 NEW ENG. J. MED. 878, 880 (1971).

These impediments to complete identification of a drug's risks create a significant pocket of unknown hazards that exist despite FDA approval and even manufacturer compliance with FDA requirements for IND testing. The General Accounting Office (the GAO) recently studied the incidence of hazards that do not emerge until the post-approval period, their magnitude, and the impact on the drug's benefit-risk balance and the adequacy of the drug's labeling.¹³² The GAO reviewed all prescription drugs approved by the FDA from 1976 through 1985. By reviewing drugs removed from the market or drugs that had undergone a revision in their labeling indicating additional adverse effects, the GAO found that slightly more than half of 198 prescription drugs approved by the FDA had serious post-approval risks that went undetected in the IND phase.¹³³ Thus, it is sometimes said that the post-approval process constitutes "phase IV" of new drug testing.

The mechanism for tracking a drug's safety in the post-marketing period is the Adverse Reaction Report (ARR)¹³⁴ or its predecessor, the Drug Experience Report (DER). The ARR is a report of an adverse event after the use of a pharmaceutical by a physician or consumer to the manufacturer. Periodic reports are made to the manufacturer; by law manufacturers must report to the FDA "any adverse event associated with the use of a drug in humans, whether or not considered drug related."¹³⁵ Prompt reporting of serious and unexpected adverse drug experiences is required, as is any increase in frequency of a particular adverse event.¹³⁶ In theory at least, the FDA monitors adverse drug reactions (ADRs), looking for

132. See GENERAL ACCOUNTING OFFICE, *FDA DRUG REVIEW: POSTAPPROVAL RISKS 1976-85* (1990).

133. See *id.* at 3. The GAO defined serious risks as ones requiring withdrawal of the drug, changes in labeling that reflected a serious medical problem, or identification of a serious risk in the FDA Drug Bulletin. See *id.* at 3-4; see also GOODMAN AND GILMAN'S *THE PHARMACOLOGICAL BASIS OF THERAPEUTICS* 64 (Alfred G. Gilman et al. eds., 8th ed. 1990) (noting that 50% of adverse reactions are identified in the post-marketing period).

134. See 21 C.F.R. § 314.80 (1996); see also 50 Fed. Reg. 7471 (1985) (explaining that "the primary objective of the adverse drug experience reporting system is to signal potential serious safety problems with marketed drugs").

135. 21 C.F.R. § 314.80(a). The manufacturer also must submit reports periodically that describe its actions in response to the adverse drug experience information it has received, any post-approval studies that have been performed on the drug, published reports or studies of the drug, and any foreign experience with the drug. See *id.* § 314.80(b)-(d).

136. See *id.* § 314.80(c)(1).

trends that suggest the need for further investigation.¹³⁷ There are a number of forces at work that make (and have made) the ADR notification process less than entirely effective in identifying adverse side effects.¹³⁸ But the key concerns for purposes of a regulatory compliance defense are the significant role of the post-approval period in identifying new risks related to drugs, the incorporation of that information and its implications for prescribing practices into the drug's labeling, and the FDA's ability to monitor both manufacturer compliance and the information produced by the ADR process.

Reporting by manufacturers to the FDA, despite the legal requirement, has been less than perfect. Some notable examples of flagrant manufacturer disregard for this requirement have been documented, sometimes as the result of a tort suit.¹³⁹ More subtle defalcations are harder, if not impossible, to detect, yet no doubt exist.¹⁴⁰ The marketing and profit incentives for a pharmaceutical manufacturer are contrary to thorough and accurate gathering and reporting of ADRs.

If the FDA had adequate resources to monitor manufacturer post-approval reporting behavior, detect violations, impose adequate sanctions, and thereby provide an appropriate deterrent, we could be more sanguine about the efficacy of the ARR process.¹⁴¹ But, once again, there is the problem of inadequate regulatory resources.

137. See Thomas P. Gross, *The Analysis of Postmarketing Drug Surveillance Data at the U.S. Food and Drug Administration*, in *DRUG EPIDEMIOLOGY AND POST-MARKETING SURVEILLANCE 1* (Brian L. Strom & Giampaolo Velo eds., 1992).

138. The primary problem is the identification and reporting of adverse effects by patients and physicians. One study concludes that "less than one percent of serious ADRs are reported directly to the FDA." H. Denman Scott et al., *Rhode Island Physicians' Recognition and Reporting of Adverse Drug Reactions*, 70 R.I. MED. J. 311, 313 (1987). Recently the FDA announced a new program designed to increase reporting of adverse events by physicians. See Kessler, *supra* note 130, at 2767.

139. See, e.g., *Benedi v. McNeil-P.P.C., Inc.*, 66 F.3d 1378, 1379 (4th Cir. 1995) (finding that the defendant's withholding of ADR's from 1980 to 1988 from the FDA justified award of punitive damages); FDA, *NEW DRUG DEVELOPMENT IN THE UNITED STATES 50* (1990) (explaining criminal conviction of pharmaceutical employees who suppressed ADRs for the blood pressure medication Selacryn in the early 1980s); Merrill, *supra* note 27, at 5-6 (noting McNeil Laboratories' delay in notifying FDA of cases of liver damage of patients using its drug until three to five years after McNeil received information from physicians).

140. See GREEN, *supra* note 26, at 129 (describing how a drug manufacturer persuaded doctors who called to report birth defects associated with maternal use of a drug to characterize their calls as "inquiries" rather than reports so as to avoid having to report calls to the FDA as an ARR).

141. The enforcement provisions of the Federal Food, Drug, and Cosmetic Act are contained in 21 U.S.C. §§ 332-335 (1994).

Thus, any regulatory compliance defense should include compliance with post-approval FDA regulations regarding the adverse drug reporting program. This requirement then leads to the same problem identified with regard to preapproval regulatory compliance: The courts will have to confront and resolve the question of manufacturer compliance with adverse drug reporting regulations. This task will require factual, legal, and evaluative determinations as difficult as those required in determining the manufacturer's compliance with pre-approval testing and reporting requirements.¹⁴²

The silver lining in this ADR-regulation compliance requirement is that, like IND compliance, the carrot of a defense to tort liability is provided to manufacturers who do comply with the ADR regulations. How much incentive that carrot might provide depends on a number of other factors, including how competitive the market is for the drug in question, how significant the post-approval risks are in their impact on the market for the drug, and the significance of the drug in contributing to the manufacturer's overall profits. But the point is that we should expect some marginal effect on compliance with ADR reporting requirements.

The ADR process is not, however, an end in itself. It serves the instrumental functions of assuring that all identified risks are communicated to physicians who make the consumption decision and weeding out those drugs whose additional risks overtake the therapeutic benefits of the drug. At the same time, overwarning has its costs,¹⁴³ and the FDA frequently resists labeling changes that manufacturers propose.¹⁴⁴ Labeling changes for existing drugs require

142. See *Stanton v. Astra Pharm. Prods., Inc.*, 718 F.2d 553, 563 (3d Cir. 1983).

143. See Richard A. Epstein, *Legal Liability for Medical Innovation*, 81 CARDOZO L. REV. 1139, 1150 (1987) ("Warnings that are too severe are as bad as those that are too soft. Both tend to distort . . . the relevant patient or consumer choices. The full costs of overwarning would only be known if legal actions were available to people deterred from taking needed therapy by excessive warnings."); Margaret Gilhooley, *Innovative Drugs, Products Liability, Regulatory Compliance, and Patient Choice*, 24 SETON HALL L. REV. 1481, 1501 (1994) (expressing concern about information overload); Lars Noah, *The Imperative to Warn: Disentangling the "Right to Know" from the "Need to Know" about Consumer Product Hazards*, 11 YALE J. ON REG. 293, 381-91 (1994) (explaining two consequences of overwarning: overreaction and dilution in effectiveness); Viscusi et al., *supra* note 17, at 1468 (arguing that overwarning hinders the ability of doctors to distinguish the relative risks of certain drugs).

144. See Gilhooley, *supra* note 143, at 1485 & n.8 (listing cases that reflect FDA efforts to discourage warnings).

submission of a supplemental NDA,¹⁴⁵ as the labeling of a drug is integral to its receiving FDA approval. An exception permits a drug manufacturer to change its labeling and then to seek approval after the change,¹⁴⁶ but that exception is somewhat narrower than is evident. Manufacturers are reluctant to change their labeling without at least tacit informal approval by FDA staff in the reviewing division of the FDA's Center for Drug Evaluation and Research. Informal consultations are the norm, and unless the manufacturer can persuade FDA staff that a labeling change is desirable, subsequent disapproval along with the deterioration in good will with the FDA deters many manufacturers from making unapproved changes to labeling.¹⁴⁷

Thus, tort law currently provides significant incentives for pharmaceutical manufacturers to provide additional warnings in the labeling of drugs. Recall that inadequate warnings are the primary basis for pharmaceutical products liability claims.¹⁴⁸ The best prophylactic available to a drug manufacturer with liability concerns is to include information about all risks that emerge as promptly as possible. Thus, frequently the manufacturer is the aggressor seeking labeling changes with the FDA resisting such changes.¹⁴⁹ That is not to suggest that tort incentives are always the predominant incentive. Marketing concerns and competitive circumstances provide countervailing incentives that in some contexts will be more powerful.¹⁵⁰

145. See 21 C.F.R. § 314.70(b)(3) (1996).

146. See Gibbs & Mackler, *supra* note 45, at 233-34 (explaining the exception that allows manufacturers to strengthen warning labels, modify dosage, and delete unsupported effectiveness claims without FDA approval); Sheila R. Shulman & Marianne E. Ulcickas, *Update on ADR Reporting Regulations: Products Liability Implications*, 3 J. CLINICAL RES. & DRUG DEV. 91, 97 (1989) (noting that manufacturers' failure to share new information, even before receiving FDA approval of the labeling change, could result in the drug being misbranded).

147. See Cooper, *supra* note 14, at 236 (noting that manufacturers are reluctant to make labeling changes without FDA approval); Viscusi et al., *supra* note 17, at 1441 n.8 (describing informal negotiations over drug labeling between FDA and manufacturer).

148. See *supra* notes 44-48 and accompanying text.

149. See Viscusi et al., *supra* note 17, at 1468.

150. Again, the Bendectin experience is illuminating. The manufacturer negotiated with the FDA over labeling changes that would identify an association found between pyloric stenosis (a birth defect involving a blockage in the stomach) and maternal use of the drug. The manufacturer's concern was to minimize the risks that would be conveyed in the new labeling. This occurred against a background of severely declining sales of the drug. See GREEN, *supra* note 26, at 183-84.

What impact might an FDA compliance defense have on manufacturer incentives to communicate risks discovered post-marketing? This question becomes critical, and the answer reveals a dramatic shifting of roles. With a regulatory compliance defense available, manufacturers would no longer have an incentive to seek labeling changes that would disclose additional risks discovered in the post-marketing period. The impetus for such changes would be left to the FDA. Here, the compliance defense wipes out existing tort incentives, and we would be wholly reliant on the FDA and its enforcement of post-approval risk reporting regulation.¹⁵¹ The specter of inadequate resources available to the FDA makes this role reversal of significant concern. As one student of the FDA has explained, "FDA action to change drug labeling and advertising in response to new adverse information tends to be painfully slow. Sometimes this is due to litigation. . . . Other delays have been caused by organizational inefficiency and resources shortages."¹⁵² Moreover, unlike with the pre-approval situation in which inaction by the FDA prevents a drug and its risks from being available, there is no safety-enhancing temporizing strategy available in the post-approval period.

Yet the apparent shield of a regulatory-compliance defense in this post-approval period may be virtually illusory. The FDA has regulations that require that drug labels be modified to reflect newly emergent information relevant to use of the drug.¹⁵³ If a compliance defense included compliance with those regulations, the defense afforded a manufacturer by its pre-approval regulatory compliance would be quite compromised with respect to any post-approval information that identified greater risks or less efficacy than was the case at the time of FDA approval of the NDA. And, of course, once the compliance defense shield is breached—here, by the inquiry about whether the drug's labeling was modified in compliance with FDA regulations regarding post-approval data—our ability to contain the significant transaction costs imposed by the tort system is imperiled.

151. See Gilhooley, *supra* note 143, at 1490 (arguing that drug companies will be less likely to include warnings with reduced liability, leaving the FDA to warn consumers).

152. Quirk, *supra* note 64, at 224.

153. The FDA requires that the labeling of a drug be modified "as soon as there is reasonable evidence of an association of a serious hazard with a drug; a causal relationship need not have been proved." 21 C.F.R. § 201.57(e) (1996). In addition to serious hazards, less significant adverse effects must be disclosed in the package labeling. *See id.*

The final aspect to consider is pharmaceutical marketing—media advertising and promotional calls on individual physicians. One of the central tenets of the *Restatement (Third)*'s treatment of pharmaceuticals is the essential role played by physicians in making a considered assessment of the risks and benefits of employing pharmaceuticals in the treatment of a patient.¹⁵⁴ If physicians are to fulfill this role, at a minimum they will have to have accurate and thorough information about those risks and benefits.¹⁵⁵ The primary source of that information, as discussed above, is the drug's labeling. Pharmaceutical marketing is often another important source of information for physicians,¹⁵⁶ however, and there is good reason to believe that much pharmaceutical marketing is detrimental to that goal.¹⁵⁷ Furthermore, the pharmaceutical industry devotes considerable resources to marketing its products: in written advertisements in medical journals, in direct mail to physicians, in sponsoring educational and scientific programs, increasingly in direct-to-consumer advertising, and through sales calls by company representatives on physicians and others in the health care system who decide on drug purchases.¹⁵⁸ Here, again, the FDA's limited ability to enforce its own regulations that govern the post-approval marketing process raises serious concerns about any compliance defense, unless it were to include compliance with post-approval regulatory requirements as well.¹⁵⁹

154. See Tentative Draft No. 2, *supra* note 2, § 8 cmt. b (arguing that health care professionals are uniquely able to advise ill patients); see also Henderson, *supra* note 42, at 481 & n.54 (concluding that the knowledge of the physician combined with full manufacturer warnings and lack of third party effects warrants a denial of judicial review on drug design).

155. This is a very questionable proposition in any case. See Quirk, *supra* note 64 *passim*.

156. See *Drug Industry Antitrust Act: Hearing on S. 1552 Before the Subcomm. on Antitrust and Monopoly of the Senate Comm. on the Judiciary*, 87th Cong. 181–84, 319 (1961) (discussing the impact of direct mail advertisements on a physician's choice of which drug to prescribe).

157. See, e.g., Michael S. Wilkes et al., *Pharmaceutical Advertisements in Leading Medical Journals: Experts' Assessments*, 116 ANNALS INTERNAL MED. 912, 912 (1992).

158. Current estimates on marketing expenditures by the pharmaceutical industry are in the range of \$5 billion per year. See Charles J. Walsh & Alissa Pyrich, *FDA Efforts to Control the Flow of Information at Pharmaceutical Industry-Sponsored Medical Education Programs: A Regulatory Overdose*, 24 SETON HALL L. REV. 1325, 1326 n.1 (1994).

159. For a discussion of drug products liability cases in which plaintiffs asserted claims are based on the manufacturer's promotional efforts, see Janet Fairchild, Annotation, *Promotional Efforts Directed Toward Prescribing Physician as Affecting Prescription Drug Manufacturer's Liability for Product-Caused Injury*, 94 A.L.R. 3d 1080 (1979).

In theory, the FDA regulates all written marketing and advertising efforts by pharmaceutical manufacturers. The 1962 amendments to the Food, Drug, and Cosmetic Act transferred jurisdiction over prescription drug advertising to the FDA.¹⁶⁰ Advertising that is "false and misleading" is proscribed.¹⁶¹ Although the Act contains no definition of advertising, the FDA "has defined its authority in this area [labeling and advertising] to cover virtually any material issued by or sponsored by a drug manufacturer."¹⁶² Labeling includes material that accompanies the drug, while advertising includes any other efforts by the manufacturer to promote the drug.

The FDA has detailed regulations covering advertising and defining "false and misleading" advertising, but the essential concern is that any advertising should contain a "fair balance" of information that would be relevant to a decision by a physician to prescribe.¹⁶³ But there is no mandatory pre-advertising review,¹⁶⁴ and the FDA's most common response to advertising that it believes violates its advertising regulations is to send a letter to the manufacturer. This letter begins a negotiation process between the FDA and the manufacturer.

In the FDA's oversight of advertising, again limited regulatory resources and the consequent need to order priorities take their toll. There is good reason to believe that a substan-

160. See Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (codified in scattered sections of 21 U.S.C.). For a history of legal and congressional authority for the regulation of pharmaceuticals, see Walsh & Pyrich, *supra* note 158, at 1334-43.

161. See 21 U.S.C. § 352(a) (1994).

162. David A. Kessler & Wayne L. Pines, *The Federal Regulation of Prescription Drug Advertising and Promotion*, 264 JAMA 2409, 2409 (1990).

163. See *id.* at 2410. According to Kessler and Pines:

The agency's regulations list 33 ways an advertisement may be false or misleading. Most commonly, advertisements are judged false or misleading if they selectively or inaccurately represent or report data, or make claims of superiority, based on less than adequate and well-controlled scientific studies; if they use in vitro or animal data to suggest clinical significance when such significance has not been demonstrated; or if they represent that the drug's indications are broader than those approved by the FDA. In general, only information consistent with the approved labeling can be used in advertising.

Id.

164. Recently, the FDA has requested voluntary advance review of promotional copy. Some manufacturers have acceded and some have not. See *id.* No information is currently available about how many of the advertisements submitted are reviewed, the rigor of any reviews that are conducted, or whether this program has had an impact on the accuracy of pharmaceutical advertising.

tial amount of overclaiming and misleading information is peddled in drug advertising. A 1992 study assessed the accuracy of advertisements contained in medical journals.¹⁶⁵ It employed panels of three physicians who were expert in the field in which the drug was approved for use. The panels found that at least twenty percent of the advertisements they reviewed were misleading about the drug's efficacy, encouraged inappropriate use of the drug, or relied on inadequate studies to justify use of the drug.¹⁶⁶ Thirty percent were found to contain inappropriate claims that the drug being promoted was the drug of choice.¹⁶⁷ Forty percent lacked a balance between information on efficacy and safety,¹⁶⁸ and fifty-seven percent were determined to have failed to communicate adequately adverse effects and contraindications.¹⁶⁹ For virtually every one of the twenty-one categories, based on FDA regulations, that the authors used to determine if advertising was false and misleading, a substantial minority of advertisements failed.¹⁷⁰ Ninety-two percent of advertisements were not in compliance with at least one of the FDA's criteria.¹⁷¹ Perhaps most significantly, only forty-four percent of the reviewers felt that the advertisement would lead to proper prescribing if the doctor relied solely on the advertisement to make her prescribing decision.¹⁷²

165. See Wilkes et al., *supra* note 157, at 916-17. The authors had hoped to assemble panels of doctors who were independent of the industry by excluding all who had received more than \$300 in consulting, research, or honoraria from a pharmaceutical company in the past two years. The authors report that "[c]areful screening revealed an insufficient number of physicians who met this criterion." *Id.* at 914. For a critique of the methodology of this study, see Jacob Jacoby, *Misleading Research on the Subject of Misleading Advertising: The Wilkes et al. Investigation of Pharmaceutical Advertising in Leading Medical Journals*, 49 FOOD & DRUG L.J. 21 (1994), and Paul H. Rubin, *Are Pharmaceutical Ads Deceptive?*, 49 FOOD & DRUG L.J. 7 (1994).

166. See Wilkes et al., *supra* note 157, at 916.

167. See *id.*

168. See *id.*

169. See *id.*

170. See *id.* at 915.

171. See *id.* at 916.

172. See *id.* at 917. It appears that the same problems identified in advertising to physicians is occurring in the emerging direct-to-consumer advertising by the pharmaceutical industry. See *Drug Advertising: Is this Good Medicine?*, CONSUMER REP., June 1996, at 62 (noting that only 40% of advertisements evaluated contained accurate information about the drug's efficacy and fairly explained the risks involved).

The authors of the study concluded:

The finding of problems in a large proportion of pharmaceutical advertisements is troublesome, given research suggesting that drug advertising serves as a major source of information for practicing physicians. In an era where several similar drugs are often available for a given condition many of which serve the same function, it is more important than ever that physicians be provided with accurate, truthful information.

....

Standards for honesty, accuracy, and balance in pharmaceutical advertising currently exist in the form of FDA regulations, but these regulations appear to go unheeded.¹⁷³

Once again, the choice is between removing the apparently inadequate incentives provided by the tort system to keep advertising truthful or to create yet another hole in a regulatory compliance defense that would require assessments of whether drug advertising met the FDA's "false and misleading" standards,¹⁷⁴ and, if not, whether the violation of the FDA's advertising regulations can be linked causally to the plaintiff's injury. That inquiry will require assessing what the prescribing physician would have done had accurate information been provided in the manufacturer's advertising and might entail far longer causal chains, such as the reason why a group practice or other physician community preferred one drug therapy over other available treatments.¹⁷⁵

Another important marketing activity is the promotional process that goes on between pharmaceutical companies' agents, known as detailers, and physicians.¹⁷⁶ The FDA's legal

173. Wilkes et al., *supra* note 157, at 918.

174. 21 C.F.R. § 202.1(a)(5)-(7) (1996) (setting forth the FDA's detailed standards for advertisements that are "false, lacking in fair balance, or otherwise misleading").

175. See *supra* notes 106-05 and accompanying text.

176. See Lars Noah, *Death of a Salesman: To What Extent Can the FDA Regulate the Promotional Statements of Pharmaceutical Sales Representatives?*, 47 *FOOD & DRUG L.J.* 309, 310-12 (1992) (explaining detailer's function and importance in the drug industry); *Twilight of U.S. Detail Forces?*, *SCRIP*, Dec. 13, 1991, at 16 (estimating that as many as 50,000 detailers are employed by the pharmaceutical industry). For an explanation by a former detailer of the conflicting roles of marketing the employer's products and providing accurate information to physicians, see Comment, *The*

authority to regulate these oral communications is quite controversial.¹⁷⁷ Equally importantly, the FDA's practical ability to monitor these activities is virtually nil.¹⁷⁸ If there is industry exaggeration and hyping in media advertising, one suspects that it is far greater in the personal interactions between marketing agent and physician that are standard practice in the pharmaceutical field.¹⁷⁹ Overpromotion (including promoting off-label uses) claims based on marketing efforts by pharmaceutical representatives might furnish an attractive alternative theory for plaintiffs to pursue if a compliance defense removes other avenues.¹⁸⁰ Such claims might not be encompassed within a regulatory compliance defense, if, as many industry advocates claim,¹⁸¹ the FDA is without authority to regulate oral communications by salespeople, a matter that, presumably, would have to be decided in an overpromotion case. If the FDA does have regulatory authority and if its advertising regulations are applicable to oral marketing efforts, the questions about compliance with FDA standards discussed above for written advertising would necessarily arise.¹⁸²

CONCLUSION

I draw several conclusions from this analysis of a regulatory standards defense, especially in the context of prescription drugs. First, and most evidently, an FDA regulatory compliance defense is not nearly as neat nor as clean a reform

Ubiquitous Detailman: An Inquiry Into His Functions and Activities and the Law Relating to Them; 1 HOFSTRA L. REV. 183, 185-92 (1973).

177. See Noah, *supra* note 176, at 315-16; Walsh & Pyrich, *supra* note 158, at 1344-45.

178. See Noah, *supra* note 176, at 310 & n.6.

179. See, e.g., *Benedi v. McNeil-P.P.C., Inc.*, 66 F.3d 1378 (4th Cir. 1995); see also ANGELL, *supra* note 115, at 59 (quoting "obviously duplicitous" memorandum to detail persons explaining how to conceal from physicians tendency of new implants to leak fluid); Noah, *supra* note 176 *passim* (examining the unique difficulties of regulating oral promotion).

180. See, e.g., *Benedi*, 66 F.3d at 1389 (describing how a manufacturer instructed detail persons not to discuss with physicians a study identifying the risk of adverse reactions when their drug was combined with alcohol drinking).

181. See Kessler & Pines, *supra* note 162, at 2411.

182. See Kessler & Pines, *supra* note 162, at 2411 ("Until further judicial decisions or congressional action clarifies the FDA's specific authority in the area of promotion, the FDA will continue to assert broad jurisdiction.").

as many supporters may have envisioned. Although it might be reasonable to attempt some greater protection for prescription drugs based on regulatory compliance—for those risks for which post-approval information has not revealed different risks from those known at the time of FDA approval, or perhaps for punitive damages—complete immunity from suit based on FDA approval or even compliance with FDA regulations seems ill-advised.

Even a limited FDA regulatory compliance defense is not unproblematic. In the case of severe drug-related injuries, rather than avoiding litigation, such a defense is likely to shift the area of inquiry in current pharmaceutical litigation to other questions. These will include compliance by the manufacturer with FDA requirements during the IND process, the existence of newly emerged information that the FDA did not consider when approving the labeling and marketing and promotional efforts by the manufacturer that may be in violation of FDA requirements. The extensiveness of FDA regulations and the complexity of the pre-marketing testing process could transform that inquiry into a Serbian bog that would consume substantial resources.

At the same time, increasing the barriers to suit should deter some cases from being brought. Yet the cases that are likely to be squeezed out of the tort system may very well be meritorious,¹⁸³ albeit ones involving minor or modest injuries that do not affect a large number of individuals.¹⁸⁴ Increasing the threshold (and thereby the resources) required to bring a suit will enhance the trend toward high stakes, high damages, multiple claimant drug litigation, the only type in which the recoverable damages will be sufficient to support the costs of investigation and discovery regarding the question of regulatory compliance. The advantages of aggregation in pooling resources and information or even more informal information exchanges among plaintiffs' attorneys are simply not available for the relatively infrequent adverse effect.¹⁸⁵

183. By "meritorious" I mean cases that under the prevailing legal standard with a regulatory compliance defense should nevertheless result in a judgment for plaintiff.

184. The availability of punitive damages in the event of manufacturer noncompliance would modify this effect.

185. The claims I have made about the impact of a regulatory approval defense should be recognized as nothing more than armchair hypotheses. The proof is in the testing, and there are a number of states that have now adopted some form of a regulatory compliance defense. Those states provide an opportunity for empirical research of the effect of a compliance defense on pharmaceutical litigation. The

Compromising on a regulatory compliance defense by limiting it to punitive damages has much appeal. There is great consternation about punitive damages in the pharmaceutical industry. Plaintiffs still could recover compensatory damages without proof of regulatory noncompliance, but might be deterred from pursuing punitive damages by the large investigation costs. And if a defendant does comply with FDA regulations, why should it be subject to punitive damages? This compromise, however, has a serious disadvantage. Without providing any screening of a case, courts and juries will have to make assessments of causation and the adequacy of warnings in the traditional manner. Yet the substantial administrative costs entailed in determining regulatory compliance also will be incurred in those cases in which plaintiffs do decide to pursue claims for punitive damages. Despite the superficial appeal, this compromise adopts undesirable aspects of two different worlds. Given that punitive damages are awarded infrequently in products liability cases,¹⁸⁶ providing a regulatory compliance defense for punitive damages may entail employing a mountain to root out a molehill. There is also good reason to believe that much of the extreme fear of punitive damages is no more than that—exaggerated fear among manufacturers about the possibility of being tagged with a large punitive damage award—rather than based on

statutes are relatively recent, and given the low incidence of pharmaceutical products cases, it may be difficult to find an adequate sample. Moreover, while measuring the effect of a compliance defense on litigation may be realistic, I am dubious about the possibility of assessing the impact of any defense, even one on a federal level, on the pharmaceutical industry. That, after all, is the point of adopting such a reform.

186. Study after study reaches the conclusion that punitive damages are rare in personal injury and products liability litigation. See WILLIAM M. LANDES and RICHARD A. POSNER, *THE ECONOMIC STRUCTURE OF TORT LAW* 302-07 (1987); MARK PETERSON ET AL., *PUNITIVE DAMAGES: EMPIRICAL FINDINGS* (1987); MICHAEL RUSTAD, *DEMISTIFYING PUNITIVE DAMAGES IN PRODUCTS LIABILITY CASES: A SURVEY OF A QUARTER CENTURY OF TRIAL VERDICTS* 26 & 48-49 nn.3-5 (1991); U.S. DEPT' OF JUSTICE, OFFICE OF JUSTICE PROGRAMS, *CIVIL JUSTICE STUDY OF STATE COURTS, 1992: CIVIL JURY CASES AND VERDICTS IN LARGE COUNTIES* 6-9 (1995); Stephen Daniels & Joanne Martin, *Myth and Reality in Punitive Damages*, 75 MINN. L. REV. 1, 28-43 (1990); Edward Felsenthal, *Punitive-Damage Awards Found to be Generally Modest and Rare*, WALL ST. J., June 17, 1996, at B4; Michael J. Saks, *Do We Really Know Anything About the Behavior of the Tort Litigation System—And Why Not?*, 140 U. PA. L. REV. 1147, 1254-62 (1992); cf. GARBER, *supra* note 8, at 48 n.60 (citing an amicus brief filed in the U.S. Supreme Court by the Pharmaceutical Manufacturers Association and the American Medical Association that found an increase in trial awards of punitive damages from six awards from 1970 to 1979, to 17 from 1980 to 1984, to 35 from 1985 to 1988).

objective data or experience.¹⁸⁷ Enacting reform statutes that reflect those distorted perceptions may provide additional succor for them.

Of course, the question of the impact of a regulatory compliance defense on the pharmaceutical industry in terms of enhancing innovation and facilitating the introduction of new drugs is one that remains to be explored. That is a far more difficult endeavor, and I leave the task to others, recognizing, however, that the answer is an important variable in balancing the concerns expressed in this Article about the adverse impact of a compliance defense.

Perhaps even the initial premise of this Article is incorrect. Given the difficulties identified in implementing a regulatory compliance defense for pharmaceutical drugs, it may be that this is not the strongest arena for a compliance defense. It may be that a very clear and specific regulatory standard, developed in an open rulemaking process, would provide a more attractive candidate for such a defense.¹⁸⁸ I leave that question to others, because, as I hope this excursion through the FDA and its regulation of pharmaceuticals will persuade the reader, any effort to make changes to section 7 of the *Restatement (Third)* requires consideration of the specific regulatory scheme and the industry involved.¹⁸⁹ The devil is truly in the details, which must be examined carefully if reform of the current balance between tort and regulation is to be attempted.

187. See GARBBER, *supra* note 8, at 184–85, 196; Schwartz, *supra* note 13, at 1360; Viscusi et al., *supra* note 17, at 1476–77 & n.141.

188. I am grateful to Professor Lars Noah for this suggestion.

189. Cf. GARBBER, *supra* note 8, at 171–72 (“The policy implications here cannot be presumed to apply to other industries: Our conclusions stem from aspects of the market, technological, regulatory, and legal environments of the pharmaceutical and medical device industries that do not characterize U.S. industry at large.”).