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Cover Page Footnote

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SACRIFICIAL LAMBS: COMPENSATING FIRST SUBSCRIBERS TO FDA-APPROVED MEDICATIONS FOR POSTMARKETING INJURIES RESULTING FROM UNLABELED ADVERSE EVENTS

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In recent years, the U.S. Food and Drug Administration (FDA) and the pharmaceutical industry have become easy targets for society's growing distrust of the federal government's ability to protect its citizens from serious health risks.[1] Whether because of reports of the FDA's repeated failures to identify serious adverse effects associated with prescription medications or because of stories of pharmaceutical manufacturers withholding safety data and falsifying trial results to gain marketing approval, the public's confidence in the industry and its regulators has dissipated.[2] Perhaps the public is correct.

The majority of Americans believe that an FDA approval equates to "the Good Housekeeping seal of approval."[3] In reality, however, at the time of approval and introduction into the open market, prescription medications carry significant, unknown health risks.[4] When these adverse effects are ultimately discovered, the results can be catastrophic.[5] For example, in 2007, eight years after receiving marketing approval from the FDA, the diabetes drug Avandia was found to increase the risk of heart attacks in patients taking the medication.[6] In 2006, thirteen years after FDA approval, the medication Trasylol—used to reduce bleeding during surgery—was found to increase the risks of kidney failure, heart attack, and stroke.[7] In 2004 and 2005, four and five years after their initial approvals, respectively, Cox-2 inhibitors[8] Bextra and Vioxx were withdrawn from the market after it was discovered that they

1. *See* Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419, 431 (2010) (citing a drop in the public's confidence in the FDA).

2. *See, e.g.*, *id.* at 428–31; Jeanne Lenzer, *Scandals Have Eroded US Public's Confidence in Drug Industry*, 329 BRIT. MED. J. 247, 247 (2004).

3. *Risk and Responsibility: The Roles of FDA and Pharmaceutical Companies in Ensuring the Safety of Approved Drugs, Like Vioxx: Hearing Before the H. Comm. on Gov't Reform*, 109th Cong. 2 (2005) [hereinafter *Risk and Responsibility Hearing*] (statement of Rep. Tom Davis, Chairman, H. Comm. on Gov't Reform). *But see* Evans, *supra* note 1, at 428 (arguing that many people overestimate the risk-benefit data available when a drug is approved by the FDA).

4. *See infra* notes 6–10 and accompanying text (providing examples of cases in which drugs with unknown side effects were approved).

5. *See* Evans, *supra* note 1, at 429–30 (explaining the negative consequences for patients taking drugs with unknown harmful effects).

6. Steven E. Nissen & Kathy Wolski, *Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes*, 356 NEW ENG. J. MED. 2457, 2458, 2467 (2007).

7. Dennis T. Mangano et al., *The Risk Associated with Aprotinin in Cardiac Surgery*, 354 NEW ENG. J. MED. 353, 361 (2006); Kris Hundley, *Researcher Beat Pfizer, Then Lost to It*, ST. PETERSBURG TIMES, Sept. 26, 2009, at 1A.

8. Cox-2 inhibitors are a type of non-steroidal anti-inflammatory drug (NSAID). *See, e.g.*, David J. Graham, *Cox-2 Inhibitors, Other NSAIDs, and Cardiovascular Risk: The Seduction of Common Sense*, 296 J. AM. MED. ASS'N 1653, 1653 (2006).

increased the risks of heart attack and stroke.[9] In total, millions of patients were potentially exposed to risks that they might otherwise have avoided if the serious side effects were discovered earlier.[10]

Unfortunately, these examples cannot be dismissed as isolated incidents.[11] Postmarketing discovery of adverse effects is common[12] and continues today.[13] Moreover, the significance of these later-discovered side effects might be marginalized were it not for the enormity of the patient population impacted.[14] In some cases, a single drug will have been prescribed to millions of patients for years before a serious, previously unknown adverse effect is discovered.[15] If one was able to pinpoint the cause of the FDA's inability to detect these health risks before approval, the problem of postmarketing discovery of adverse effects might be eliminated altogether.[16] Instead, to borrow from the medical lexicon, a constellation of factors ultimately contributes to the present reality that as many as half of all approved drugs have an unknown side effect when released.[17]

Critics have accused the FDA of an inability—be it through underfunding,[18] understaffing,[19] general incompetence,[20] or collusion with manufacturers[21]—to

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9. *Cox-2 Selective (Includes Bextra, Celebrex, and Vioxx) and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm103420.htm (last updated Nov. 27, 2012).

10. At the very least, the public should be made aware of the risks. *See, e.g.*, Steve Sternberg, *Diabetes Drug Called Heart Death Risk*, USA TODAY, May 22, 2007, at 1A (suggesting how the FDA and pharmaceutical companies failed to inform the public that a blockbuster drug increased the risk of heart disease by thirty percent); *see also* Evans, *supra* note 1, at 427 (noting that Americans spend $230 billion on prescription drugs annually).

11. *See infra* notes 12–13 and accompanying text.

12. *See, e.g.*, Alex Berenson, *In the Money, and in Court: Drug Industry Braces for New Suits over Even More of Its Products*, N.Y. TIMES, Apr. 22, 2006, at C1 (noting that, in the wake of the Vioxx litigation, plaintiffs' attorneys in products liability suits claimed that pharmaceutical companies marketed their drugs while hiding early indications of side effects).

13. *See, e.g.*, Duff Wilson, *F.D.A. Puts New Limits on Cholesterol Drug*, N.Y. TIMES, June 9, 2011, at B2 (noting that new safety restrictions were placed on cholesterol-lowering medications more than ten years after receiving marketing approval from the FDA).

14. *See, e.g.*, *The Adequacy of FDA to Assure the Safety of the Nation's Drug Supply: Hearings Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce*, 110th Cong. 59 (2007) [hereinafter *Adequacy of FDA Hearings*] (testimony of David J. Graham, Associate Director, Science and Medicine, FDA Office of Surveillance and Epidemiology) (asserting that Vioxx caused up to 140,000 heart attacks in Americans, of which 60,000 resulted in death).

15. *See, e.g.*, Berenson, *supra* note 12, at C1 (citing examples of drugs with unknown side effects being prescribed to a large pool of users).

16. *See* Evans, *supra* note 1, at 425–27.

17. *Id.* at 430 (quoting BENGT D. FURBERG & CURT D. FURBERG, EVALUATING CLINICAL RESEARCH 8 (2d ed. 2007)).

18. *See, e.g.*, *Risk and Responsibility Hearing*, *supra* note 3, at 43 (statement of Rep. Henry A. Waxman, Member, H. Comm. on Government Reform) (highlighting the FDA's acknowledgment that it lacks sufficient resources to inspect prescription drug promotional

require sufficient pre-approval clinical testing of medications to monitor sufficiently manufacturers' compliance with those tests or to monitor adequately the safety of approved medications once on the open market.[22] Given the FDA's conflicting mandate: "[to get] new[,] safe[,] and effective drugs to market quickly and efficiently," the drug approval process vis-à-vis safety assessment lends itself to second-guessing.[23] In light of the failures of adverse event detection, this mandate could suggest that the FDA has made a conscious decision to emphasize expediency at the expense of safety.[24] Like

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materials for information on accuracy, safety, and efficacy); 153 CONG. REC. 25,038 (2007) (statement of Sen. Edward Kennedy) (noting that the 2006 revenues for a single prescription drug were more than two hundred times the entire FDA budget dedicated to postmarketing surveillance for the same time period).

19. *Should FDA Drug and Medical Device Regulation Bar State Liability Claims?: Hearing Before the H. Comm. on Oversight & Gov't Reform*, 110th Cong. 7 (2008) (statement of Rep. Tom Davis, Member, H. Comm. on Oversight & Gov't Reform); *see also* Tom Costello, *100 Days Later, Nation Waits for FDA Overhaul*, NBCNEWS.COM (April 26, 2009, 12:33:50 AM), www.nbcnews.com/id/30388073/#.UTpDZfJBA78 (suggesting that the FDA can only inspect one percent of imported foods because of a lack of personnel).

20. *Adequacy of FDA Hearings*, *supra* note 14, at 60 (testimony of David J. Graham, Associate Director, Science and Medicine, FDA Office of Surveillance and Epidemiology) (claiming that the FDA's failure to protect the public health was rooted in its institutional decision-making process).

21. *Id.* (arguing that the FDA improperly regards the pharmaceutical industry as a client).

22. Efthimios Parasidis, *Patients over Politics: Addressing Legislative Failure in the Regulation of Medical Products*, 2011 WIS. L. REV. 929, 932 ("FDA epitomizes 'the hollow government syndrome—an agency with expanded responsibilities, stagnant resources, and the consequent inability to implement or enforce its statutory mandates.'" (quoting Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 ADMIN. L. REV. 431, 432 (2008))).

23. U.S. FOOD & DRUG ADMIN., PRESCRIPTION DRUG USER FEE ACT (PDUFA) IV: DRUG SAFETY FIVE-YEAR PLAN 2008-2012, at 2 (2008), *available at* http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM119244.pdf; *see also* Catherine T. Struve, *The FDA and the Tort System: Postmarketing Surveillance, Compensation, and the Role of Litigation*, 5 YALE J. HEALTH POL'Y L. & ETHICS, 587, 596–97 (2005) (finding the FDA's promotion of innovation, which lends itself to early drug release, counterintuitive to its mission of protecting consumers' safety).

24. As further proof of the FDA's commitment to expediency, Congress enacted the Food and Drug Administration Modernization Act (FDAMA) in 1997, which codified the FDA's longstanding practice of fast-tracking approval of a drug that has the potential to address unmet needs for a serious or life-threatening condition. Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, § 112, 111 Stat. 2996, 2309–10 (codified at 21 U.S.C. § 356 (2006)); *see also* Charles Steenburg, *The Food and Drug Administration's Use of Postmarketing (Phase IV) Study Requirements: Exception to the Rule?*, 61 FOOD & DRUG L.J. 295, 330 & n.360 (2006) (citing S. REP. NO. 105-43, at 43 (1997)). By definition, drugs approved on a fast-track basis have been proven neither safe nor effective, but rather are approved based on a "predict[ed] clinical benefit." 21 U.S.C. § 356(b)(1); *see also id.* § 356(b)(2) (authorizing the FDA to condition approval on postmarketing studies that confirm a clinical benefit); *id.* § 356(b)(3)(B)–(C) (authorizing the FDA to withdraw approval if postmarketing data shows no clinical benefit or finds the product unsafe or ineffective).

Those who would take issue with the expedited approval process must also note that the fast-track approval guidelines themselves were the direct result of criticism of Congress's

their counterpart in the drug approval process, manufacturers have done little to engender support from the public, routinely withholding safety data from the FDA.[25]

In the case of Avandia, both the FDA and GlaxoSmithKline (GSK), the drug's manufacturer, overlooked clinical trial data that supported a link between the medication and heart attacks, leaving a third party to discover the risk when it analyzed the publicly available data.[26] Evidence further suggested that GSK conducted an earlier safety study that identified the cardiac risks at issue, but suppressed the data and did not submit it to the FDA.[27] Similarly, Bayer, Trasylol's manufacturer, was found to have withheld information from the FDA study that suggested a link between its medication and the increased risks of heart attack and stroke.[28] Likewise, in the case of Cox-2 inhibitors, not only have critics suggested data withholding by the manufacturers,[29] but they have further alleged that the FDA was complicit in the data suppression, asserting that it was aware of the data's absence yet did nothing to expose publicly the drug's risks.[30]

The purpose of this Article is not to disparage the FDA or the pharmaceutical industry. Rhetoric and animus do not improve public health

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mid-twentieth century strengthening of FDA regulations to require "proof of safety and efficacy for all new drugs," which critics viewed as preventing patients suffering from life-threatening illnesses from timely receiving treatment. *See, e.g.*, Parasidis, *supra* note 22, at 942–44; Steenburg, *supra* note 24, at 319 ("In the case of HIV and cancer treatments that conceivably could extend the lives of patients without any other options, withholding approval potentially consigned patients to a premature grave. The corresponding risk of subjecting patients to the side effects of drugs that failed to live up to their original billing struck many people—particularly patients themselves—as comparatively trivial.").

25. *See* Gardiner Harris, *Drug Maker Hid Test Data, Files Indicate*, N.Y. TIMES, July 13, 2010, at A1.

26. *Id.* ("The heart risks from Avandia first became public in May 2007, with a study from a cardiologist at the Cleveland Clinic who used data the company was forced by a lawsuit to post on its own Web site.").

27. *Id.*

28. *Building a 21st Century FDA: Proposals to Improve Drug Safety and Innovation: Hearing Before the S. Comm. on Health, Educ., Labor, and Pensions*, 109th Cong. 41 (2006) (statement of Jim Guest, President and Chief Executive Officer, Consumers Union) (noting that Trasylol's manufacturer, Bayer, withheld from the FDA news of a study that showed an increased risk of "death, serious kidney damage, congestive heart failure and stroke").

29. *Paid to Prescribe? Exploring the Relationship Between Doctors and the Drug Industry: S. Hearing Before the Special Comm. on Aging*, 110th Cong. 50 (2007) [hereinafter *Paid to Prescribe Hearing*] (testimony of Peter Lurie, Deputy Director, Public Citizen's Health Research Group, Washington, D.C.) (noting Pfizer's publication of incomplete trial data on its drug, Celebrex, because Pfizer knew the full data set was not persuasive in demonstrating the drug's benefit).

30. *Id.*; *see also Adequacy of FDA Hearings*, *supra* note 14, at 75–76 (testimony of David J. Graham, Associate Director, Science and Medicine, FDA Office of Surveillance and Epidemiology) (discussing data suppression).

any more than they serve as a detterent to those who would undermine it.[31] Rather, to better serve the public welfare as it relates to FDA-approved medications, focus must be on rapid identification of all serious health risks associated with marketed pharmaceuticals, thereby reducing unexpected injuries and compensating those injured by the formerly unknown risks.[32] To this end, Congress and the FDA took a significant step forward in achieving rapid detection of unknown, serious health risks in marketed medications in 2007.[33] The Food and Drug Administration Amendments Act of 2007 (FDAAA)[34] marked a change in the agency's supervision of pharmaceutical manufacturers and, particularly, its regulation and enforcement of postmarketing surveillance of FDA-approved medications.[35]

Before 2007, the FDA was limited in its ability to monitor a medication's safety after granting marketing approval.[36] Although the FDA served as a repository for postmarketing adverse-event data reported by manufacturers, physicians, and patients through its Adverse Event Reporting System (AERS) database,[37] before 2007 the FDA did not routinely monitor the database for evidence of a drug's previously unknown side effects.[38] Further, the AERS database was limited in its information pool.[39] To make matters worse, when a possible unlabeled side effect was identified, the FDA lacked authority to require the manufacturer to conduct postmarketing trials to determine

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31. *Cf.* Robert H. Eckel & Ronald M. Krauss, *American Heart Association Call to Action: Obesity as a Major Risk Factor for Coronary Heart Disease*, 97 CIRCULATION 2099, 2099–100 (1998) (urging action on the part of healthcare providers, legislators, insurers, and the public so that effective treatments could be formed).

32. Robert G. Hauser, *Here We Go Again—Another Failure of Postmarketing Device Surveillance*, 366 NEW ENG. J. MED. 873, 874 (2012).

33. Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823 (codified in scattered sections of 21 U.S.C.).

34. *Id.*

35. *See id.* § 905, 121 Stat. at 944–45.

36. In actuality, postmarketing surveillance was entrusted almost exclusively to the manufacturers. *See, e.g.*, Laura B. Faden & Christopher-Paul Milne, *Pharmacovigilance Activities in the United States, European Union and Japan: Harmonic Convergence or Convergent Evolution?*, 63 FOOD & DRUG L.J. 683, 686 (2008) (stating that, under previous law, the industry was responsible for any surveillance activities).

37. *See, e.g.*, *Adverse Event Reporting System (FAERS) (Formerly AERS)*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm (last updated Sept. 10, 2012) [hereinafter *FDA Adverse Event Reporting System*] (providing frequently asked questions on FAERS).

38. *See, e.g.*, Struve, *supra* note 23, at 601 (citing a 2002 internal FDA survey, which found that respondents were not confident in the monitoring process once drugs were approved and that the FDA was incapable of monitoring or acting on gathered information).

39. *See* discussion *infra* Part I.A. Specifically, the database was not linked to other patient information sources (such as Medicare and insurance company databases) across which searches could identify entire patient populations that were prescribed a suspected drug. *See, e.g.*, 153 CONG. REC. 25,163 (2007) (statement of Sen. Judd Gregg).

causation.[40] The FDA also lacked the ability to require the manufacturer to change the drug's label to warn consumers of newly discovered risks.[41]

Through passage of the FDAAA, Congress required the FDA to "conduct regular, bi-weekly screening[s] of the [AERS] database, and post quarterly reports on the AERS website of any new safety information or potential signal of serious risk identified within the last quarter."[42] Congress ordered the FDA to develop and implement a single, comprehensive data network of patient healthcare information, including all serious adverse drug experiences,[43] which would become known as the Sentinel System and would contain at least 100 million patients' data by July 1, 2012.[44] Congress authorized the FDA to require that manufacturers conduct postmarketing clinical trials when a previously unknown safety risk is identified and to make the suspect drug's continued marketing contingent upon completion of the required analysis.[45] Further, Congress empowered the FDA to require drug manufacturers to change their labels.[46]

Despite the number and significance of the changes to the FDA's regulatory authority, the FDAAA forsakes or, at best, ignores those patients first exposed to FDA-approved medications—patients whose reactions to the medications make the FDAAA's amplified postmarketing surveillance system relevant and effective.[47] Even with the FDAAA's increased focus on postmarketing surveillance, the FDA will not be able to eliminate unknown adverse effects before a percentage of patients has experienced the side effects after the drug has been approved for marketing.[48] In fact, the Sentinel System is specifically designed to discover previously unknown adverse events *post*marketing.[49]

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40. *See* 153 CONG. REC. 25,162–63 (statement of Sen. Michael Enzi).

41. *See id.* at 25,163–64 (statement of Sen. Judd Gregg) (finding that the FDA now has express authority to accomplish this).

42. Faden & Milne, *supra* note 36, at 686; *see also* 21 U.S.C. § 355(k)(5)(A) (Supp. IV 2011).

43. A "serious adverse drug experience" is defined as any adverse event associated with a drug that results in death, immediate risk of death, hospitalization, incapacity, birth defect, etc. 21 U.S.C. § 355-1(b)(1), (4) (Supp. IV 2011).

44. *Id.* § 355(k)(3); *see also* Parasidis, *supra* note 22, at 951–52 (describing the FDAAA's requirement to track postmarket safety concerns). In response, the Sentinel Initiative was created, which "aims to create a nationwide electronic reporting system for monitoring medical product safety." *Id.*

45. 21 U.S.C. § 355(o) (Supp. IV 2011).

46. *Id.* § 355(o)(4)(E).

47. *See, e.g.*, 153 CONG. REC. 25,162–63 (2007) (statement of Sen. Michael Enzi) (giving several examples of how the bill expands the FDA's ability to handle safety problems occurring post-approval, including requiring label changes).

48. Hauser, *supra* note 32, at 874 (describing the current surveillance system as "passive").

49. *See id.* (characterizing the Sentinel Initiative as "active," and detailing the real-time network's intent to identify safety concerns in a timely manner).

Discovery of these effects will always lag behind the injuries that make their detection possible.[50] Thus, a drug's first subscribers unwittingly serve as participants in the drug's extended "clinical trial," but without the disclosures and protections normally afforded to such participants.[51] When new side effects are identified postmarketing, these first subscribers are left without recourse for their injuries.[52]

Rather than relying on the lengthy and fickle litigation process for compensation or further burdening an insurance network at its breaking point, an alternative compensation scheme must be implemented to compensate for injuries caused by a drug's unknown side effects.[53] Accordingly, this Article proposes the creation of an FDA-administered fund from which injury claims attributable to unlabeled adverse effects of FDA-medications would be paid. Not unlike state and federal workers' compensation plans, the fund would insure people who suffer injury from an unlabeled side effect after taking an FDA-approved medication.[54] This compensation system would be funded entirely by pharmaceutical manufacturers, with contribution to the fund a prerequisite of drug approval.[55]

This Article proceeds as follows. Part I of this Article details the FDA's postmarketing surveillance authority pre-FDAAA and the significant changes that the Act and its incorporated Sentinel System provided to the FDA's ability to monitor medications on the open market. Part II explains why the legal system fails to sufficiently compensate those injured by prescription medications, regardless of the manufacturer's level of fault. Part II further explores the stress placed on public and private insurance plans to budget for and compensate parties following injuries from unknown risks. Part III proposes the adoption of a no-fault compensation system that would replace

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50. 21 U.S.C. § 355(o)(3)(c).

51. *See infra* Part I.C.

52. *See infra* Part II (finding that neither tort nor insurance claims sufficiently protect first subscribers to newly approved medications).

53. This Article proposes that the alternative compensation scheme articulated herein should apply only to those expenses incurred by consumers in the open market following injury from an *unlabeled* adverse event occurring in the *postmarketing* period. When known side effects of a marketed drug are disclosed in a product's labeling, a physician can make an informed decision as to whether or not to prescribe the drug to a patient and warn the patient about the possible side effects; insurers can plan for labeled risks and fund accordingly. *See, e.g.*, Parasidis, *supra* note 22, at 932 ("If marketed products contain unreliable risk-benefit disclosures, providers are unable to evaluate treatment options accurately and the ability of patients to provide informed consent is compromised."). Conversely, clinical trial participants knowingly consent to experimental treatment on the understanding that their participation will help discover unknown health risks, which the FDA will use to warn physicians and patients following marketing approval. This Article addresses those patients who bridge the gap between these two groups—that is, those who do not consent to experimental therapy but are also without complete knowledge of all potential risks associated with a drug at the time of prescription.

54. *See infra* Part III.A.

55. *See infra* Part III.B.2.

litigation and insurance as the primary source of recompense for unlabeled drug-related injury and addresses several key considerations in implementing such a plan.

I. IDENTIFYING UNKNOWN ADVERSE DRUG REACTIONS IN THE POSTMARKETING PERIOD

"Despite [the FDA's] vigilant premarket review, . . . all possible side effects of a drug can't be anticipated based on preapproval studies involving only several hundred to several thousand patients . . . ."[56] Stated more bluntly, virtually every drug approved by the FDA for marketing in the United States contains undiscovered health risks that will only become known after the drug is exposed to a larger patient population.[57] For this reason, "[a] vital part of [the FDA's] mission is to monitor the safety and effectiveness of drugs that are currently available to the American people."[58] Until 2007, however, the FDA's ability to conduct postmarketing surveillance was hampered by a lack of complete access to healthcare data.[59] Contrary to its common meaning, the FDA's postmarketing surveillance was reactionary and dependent upon others to notify it of potential adverse health effects.[60] As a result, although the FDA could *monitor* the safety of approved drugs retroactively, it could not *protect* initial consumers of newly approved medications by detecting latent risks; it could only notify the public of newly discovered risks after unknown side effects were reported.[61]

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56. *Postmarketing Surveillance Programs*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/ucm090385.htm (last updated Aug. 19, 2009); *see also* Evans, *supra* note 1, at 456 (discussing the delicate ethical balance between the necessity of testing drugs before approval and the need to quickly introduce new drugs to the market).

57. Struve, *supra* note 23, at 598–99 (stating that premarket studies are not foolproof and inevitably miss a side effect or complication).

58. *Surveillance: Post Drug-Approval Activities*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/default.htm (last updated Nov. 10, 2010).

59. U.S. FOOD & DRUG ADMIN., THE SENTINEL INITIATIVE: ACCESS TO ELECTRONIC HEALTHCARE DATA FOR MORE THAN 25 MILLION LIVES 1–2, 4 (2010) [hereinafter SENTINEL 2010 REPORT], *available at* http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM233360.pdf.

60. "Surveillance" is defined as to "watch" or to "guard" against. OXFORD ENGLISH DICTIONARY 309 (2d ed. 1989). Before 2007, the FDA's postmarketing surveillance system was a wholly passive one. *See* SENTINEL 2010 REPORT, *supra* note 59, at 1–2, 4 (describing adverse-event surveillance systems as passive because, for the FDA to be aware of a drug's adverse effects, it relies on and require recognition and reports of safety concerns); *see also, e.g.*, Anna B. Laakmann, *Collapsing the Distinction Between Experimentation and Treatment in the Regulation of New Drugs*, 62 ALA. L. REV. 305, 337 (2011) (arguing that the FDA's surveillance program is reactive and lacks the FDA's "systematic rigor" characteristic of its approval process); Parasidis, *supra* note 22, at 950 (stating that the FDA has consistently relied on passive surveillance methods).

61. Parasidis, *supra* note 22, at 948 (outlining the enactment of the FDAAA).

A. The FDA's Pharmacovigilance Program Before 2007

Until 2007, the FDA's postmarketing surveillance of approved drugs consisted almost exclusively of its Adverse Event Reporting System (AERS).[62] The AERS database comprises information received both from manufacturers, who must report to the FDA, and from healthcare professionals, consumers, and patients that report information voluntarily.[63] Federal regulations require pharmaceutical manufacturers to report to the FDA all adverse experiences "associated with the use of a drug in humans."[64] Specifically, a manufacturer's postmarketing surveillance obligations include, but are not limited to:

- Prompt review of "all adverse drug experience information obtained or otherwise received by the [manufacturer] from any source . . . ."[65]
- Development of "written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to [the] FDA."[66]

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62. *See Prescription Drug User Fee Act (PDUFA): Adding Resources and Improving Performance in FDA Review of New Drug Applications*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119253.htm (last updated May 3, 2010) [hereinafter *PDUFA White Paper*] (stating that the AERS database provided the FDA with most of its postmarketing safety data before the FDAAA was passed); *see also* Parasidis, *supra* note 22, at 950 (characterizing the AERS database as the FDA's "primary source" for postmarketing safety data).

63. *FDA Adverse Event Reporting System*, *supra* note 37; *see also* Laakmann, *supra* note 60, at 337 ("FDA postmarketing monitoring involves a system of mandatory reporting of adverse drug reactions (ADRs) by manufacturers and voluntary ADR reporting by health professionals and patients."). However, no affirmative duty to search for adverse events exists. Parasidis, *supra* note 22, at 950; *see also* Laakmann, *supra* note 60, at 337 (stating that firms must only disclose those adverse effects reported by physicians and consumers). Consequently, some commentators criticize the FDA's postmarketing surveillance program as encouraging drug manufacturers to sit on their hands rather than actively pursue safety information on their products. *See, e.g.*, Struve, *supra* note 23, at 602 (declaring that drug manufacturers are disincentivized from identifying adverse drug effects because disclosing such information may harm the business).

64. 21 C.F.R. § 314.80(a), (c) (2012). Federal regulations require that manufacturers submit all adverse event reports to the FDA on Form FDA 3500A or a comparable form or electronic format. *Id.* § 314.80(f). This form requires manufacturers to report: (1) patient identifying information, including age, sex, and weight at the time of the event; (2) the adverse event experienced and subsequent outcome (e.g., death); (3) the date of the event; (4) a description of the event; (5) relevant patient laboratory data; (6) other relevant patient medical history; (7) the suspect drug, including dose, frequency of use, administration method, therapy dates, and reason(s) for use; and (8) whether the event ceased after discontinuation of the drug and/or reappeared after reintroduction of the drug. *See* U.S. FOOD & DRUG ADMIN., FORM FDA 3500A, at 1, http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/ucm082728.pdf [hereinafter FORM FDA 3500A]. Although adverse event reports submitted voluntarily are not governed by similar federal regulation, the FDA established the MedWatch program in 1993 that allows physicians to submit adverse drug events electronically. Laakmann, *supra* note 60, at 337.

65. 21 C.F.R. § 314.80(b).

- Disclosure of "each adverse drug experience that is both serious and unexpected" no later than fifteen days after receipt of the information.[67]
- Disclosure of all other adverse drug experiences (i.e., either not serious, or expected, or both) "at quarterly intervals, for [three] years from the date of approval of the application, and then at annual intervals."[68]

Although seemingly comprehensive in the data captured, solely relying on AERS as a postmarketing risk-detection tool proves the inability to detect unknown health risks, undermining the AERS database's effectiveness.[69]

Postmarketing surveillance exists to ensure that accurate and comprehensive warnings regarding a product's safety are disseminated upon the detection of a health risk.[70] As required by federal regulation, a drug's label must be updated to disclose clinically significant adverse reactions and other potential safety hazards when a causal connection has been established with the drug, though such causation does not have to be definitive.[71] Problematically, however, adverse event reports by themselves cannot be used to establish a causal link between the medication and injury.[72]

Before 2007, the FDA's pharmacovigilance program "principally involve[d] the identification and evaluation of safety signals," which are defined as "an excess of adverse events compared to what would be expected to be associated with a product's use."[73] A signal's identification is derived from analysis of

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66. *Id.*

67. *Id.* § 314.80(c)(1)(i). The regulations define "serious adverse drug experience" as one that results in death, life-threatening injury, inpatient hospitalization, disability, or birth defect. *Id.* § 314.80(a). An "unexpected" experience is one not already listed in the labeling for the medication. *Id.*

68. *Id.* § 314.80(b)–(c).

69. *See, e.g.*, Laakmann, *supra* note 60, at 338–39; Parasidis, *supra* note 22, at 951 (criticizing the FDA's current postmarketing framework); Struve, *supra* note 23, at 603–05.

70. *See Postmarketing Surveillance Programs*, *supra* note 56.

71. *See, e.g.*, 21 C.F.R. § 201.57(c)(6)(i) (2012). Some scholars suggest a "causal association" may be based on temporality between exposure to the drug and observed adverse effect, dose-response relationship, biological plausibility, and replication of the finding. Saad A.W. Shakir & Deborah Layton, *Causal Association in Pharmacovigilance and Pharmacoepidemiology: Thoughts on the Application of the Austin Bradford-Hill Criteria*, 25 DRUG SAFETY 467, 469–70 (2002).

72. *FDA Adverse Event Reporting System*, *supra* note 37 (describing the FAERS's shortcomings and reasons why it cannot be used in calculating the incidence of an adverse medical error in the U.S. population); *see also* Struve, *supra* note 23, at 604 (arguing that a substantial number of adverse event reports received may not involve a causal link between the drug and the injury). These flaws are significant because, without proof of a causal relationship, a manufacturer is not required to warn of a health risk identified postmarketing. 21 C.F.R. § 201.57(c)(6)(i).

73. U.S. FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: GOOD PHARMACOVIGILANCE PRACTICES AND PHARMACOEPIDEMIOLOGIC ASSESSMENT 4 (2005) [hereinafter GOOD

adverse events (or "case reports") submitted to the FDA by pharmaceutical manufacturers, healthcare professionals, or consumers and is stored in the FDA's AERS database.[74] Yet, as previously mentioned, federal regulations only mandate that manufacturers[75] report adverse events,[76] whereas healthcare providers and patients only report these events voluntarily.[77] Moreover, there is no control over duplication in AERS reporting.[78] As a result—and as the FDA readily admits—case reports are both under- and over-reported.[79] Because the total number of adverse events is unknown and the total number of prescriptions can only be estimated,[80] a true incidence rate cannot be determined.[81]

PHARMACOVIGILANCE PRACTICES], *available at* http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126834.pdf. The FDA defines pharmacovigilance "to mean all scientific and data gathering activities relating to the detection, assessment, and understanding of adverse events." *Id.*

74. *See FDA Adverse Event Reporting System*, *supra* note 37.

75. 21 C.F.R. § 314.80(c)(1)(iii) (2012) (mandating that the section applies to those in the chain of supply, such as packers and distributors).

76. *Id.* § 314.80(c); *see also FDA Adverse Event Reporting System*, *supra* note 37 ("Reporting of adverse events from the point of care is voluntary in the United States.").

77. *FDA Adverse Event Reporting System*, *supra* note 37. Because adverse event data reported from the point of care is voluntary, the data submitted to the FDA is woefully inadequate. *See, e.g.*, Laakmann, *supra* note 60, at 338 (noting that physicians under-report adverse events to the FDA's system and that such reports are only the "'proverbial tip of the iceberg of drug reactions and interactions'" (quoting Barbara A. Noah, *Adverse Drug Reactions: Harnessing Experiential Data to Promote Patient Welfare*, 49 CATH. U. L. REV. 449, 469 (2000))); Parasidis, *supra* note 22, at 950–51 (noting that adverse event data reported voluntarily "account[s] for less than five percent of all reported adverse events").

78. *See* Manfred Hauben et al., *'Extreme Duplication' in the US FDA Adverse Events Reporting System Database*, 30 DRUG SAFETY 551, 551–54 (2007) (describing how a scientific study found that the data in the FDA's AERS database is highly duplicated and identifying some explanations for such duplication).

79. *See* Lanh Green, Office of Surveillance and Epidemiology, Presentation to the 42nd Annual Meeting of the Drug Information Association: Postmarketing Pharmacovigilance Practice at FDA (June 21, 2006), *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ucm119101.pdf (citing both the failure to report adverse events and the duplication in reporting by multiple sources—e.g., manufacturers and healthcare professionals—as skewing the true number of adverse events associated with a medication).

80. *See, e.g.*, Parasidis, *supra* note 22, at 951 ("[F]rom an epidemiological standpoint, 'the FDA does not know how many people are using the drug' and does not have adequate information about those who are." (quoting David A. Kessler & David C. Vladeck, *A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims*, 96 GEO. L.J. 461, 490 (2008))).

81. *See Adequacy of FDA Hearings*, *supra* note 14, at 60 (statement of Steven E. Nissen, Chairman, Department of Cardiovascular Medicine, Cleveland Clinic Foundation) ("The post-marketing surveillance system for drugs and devices functions poorly. Adverse event reporting is voluntary and studies show that only 1 to 10 percent of serious adverse events are ever reported to the agency. Accordingly, the actual incidence of serious or life-threatening complications cannot be calculated accurately."); *see also FDA Adverse Event Reporting System*, *supra* note 37 ("[The] FDA does not receive reports for every adverse event or medical error that

Further complicating matters, adverse-event data does not account for confounding factors such as concomitant medications being taken by the patient and the attendant risks associated with those drugs.[82] Additionally, the data neither provides for the overall health profile of the patient[83] nor serves as proof that the patient actually suffered the reported injury.[84] Therefore,

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occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event . . . in the U.S. population."). Moreover, even when adverse events are timely reported to the FDA, additional problems with assessment of the data can arise because the FDA does not require electronic submission of adverse event reports. *See Adverse Events Reporting System (FAERS) Electronic Submissions*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm (last updated Sept. 10, 2012) (noting that electronic submissions of adverse effect reports are encouraged for their efficiency and cost-effectiveness). For those reports submitted on paper forms, data is manually coded into the AERS database, creating the potential for human error that an adverse event will be misclassified. *See* Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements, 74 Fed. Reg. 42,184, 42,188 (proposed Aug. 21, 2009) (finding that conversion of paper-submitted reports to an electronic form is time consuming, expensive, and open to error); *see also PDUFA White Paper*, *supra* note 62 (stating that over 100,000 manufacturers' reports must be converted to the FDA's electronic database).

"The FDA's inability to calculate 'the true frequency of adverse events in the population,' . . . 'makes it hard to establish the magnitude of a safety problem, and it makes comparisons of risks across similar drugs difficult.'" Laakmann, *supra* note 60, at 338 (quoting U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-06-402, DRUG SAFETY: IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESSES 24–25 (2006)). As the FDA itself stated in discussing the evaluation of safety signals: "Like the proverbial search for a needle in a haystack, the number and variety of reports, together with the number and variety of products and the lack of reliable usage information, make it difficult to distinguish variability and *noise* from a real concern." FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS., MANAGING THE RISK FROM MEDICAL PRODUCT USE: CREATING A RISK MANAGEMENT FRAMEWORK 67 (1999), *available at* http://www.fda.gov/downloads/safety/safetyofspecificproducts/ucm180520.pdf.

82. Although Form FDA 3500A asks the manufacturer to list all concomitant medications being used by the patient at the time of the adverse event, the report and the FDA analyst reviewing it are unable to distinguish which drug, if any, actually caused the event. FORM FDA 3500A, *supra* note 64, at 1, 9.

83. *See, e.g.*, CTR. FOR DRUG EVALUATION & RESEARCH (CDER), CTR. FOR BIOLOGICS EVALUATION & RESEARCH (CBER), FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS, GUIDANCE FOR INDUSTRY: POSTMARKETING SAFETY REPORTING FOR HUMAN DRUG AND BIOLOGICAL PRODUCTS INCLUDING VACCINES (DRAFT) 38–39 (2001) [hereinafter DRAFT POSTMARKETING SAFETY REPORTING], *available at* http://www.fda.gov/downloads/BiologicsBloodVaccines/Guidance-ComplianceRegulatoryInformation/Guidances/Vaccines/ucm092257.pdf (stating that medical records are not included with adverse event reports).

84. For example, unverified claims of adverse drug experiences on which a lawsuit against a prescription drug manufacturer is premised nonetheless create an obligation on the part of the manufacturer to report those claimed events to the FDA. *See* 21 C.F.R. § 314.80(b)–(c) (2012) (obligating manufacturers to review and report "all adverse drug experience information obtained or otherwise received by the applicant *from any source*, foreign or domestic" (emphasis added)); *see also, e.g.*, DRAFT POSTMARKETING SAFETY REPORTING, *supra* note 83, at 8 (requiring only

alternative causation theories cannot be dismissed.[85] Accordingly, case reports do not provide sufficient information to determine a causal association between medication and adverse event.[86]

Before 2007, the FDA's principal postmarketing surveillance method could not reasonably demonstrate that an identified risk in fact bore any association to the medication at issue.[87] Even when the FDA identified a potential health risk through the AERS database, it could not require or suggest a labeling change to the manufacturer on that basis alone.[88] Pursuant to agency guidance documents, the FDA could only ask manufacturers to "evaluate individual case reports for clinical content and completeness . . . [and] look for features that may suggest a causal relationship between the use of a product and the adverse

knowledge of an identifiable patient, reporter, suspect drug, and adverse outcome to trigger a reporting obligation on the part of the manufacturer).

85. Some critics of the FDA's adverse-event reporting system suggest that voluntary reports issued from the point of care will be written to shift blame from the provider to the manufacturer, which can result in an erroneous perception of an increased number of adverse events attributable to the product itself, rather than to user error. *See e.g.*, James T. O'Reilly, *Pin the Tail on the Other Donkey: Allocating and Avoiding Injury Losses After Drug or Device Approval*, 62 FOOD & DRUG L.J. 559, 562 (2007) ("The Medwatch form [3500A] sets the choice: 'Product Problem' or 'Product Use Error;' the device or drug's failed result in the clinical setting is more likely to be attributed by the hospital risk manager to a 'failed' product." (citation omitted)). But conversely, with consumers increasingly able to obtain prescription drugs over the Internet, the possibility that many adverse drug experiences will go unreported, due to the lack of physician involvement, increases exponentially. *See* Bryan A. Liang & Tim Mackey, *Searching for Safety: Addressing Search Engine, Website, and Provider Accountability for Illicit Online Drug Sales*, 35 AM. J.L. & MED. 125, 128–31 (2009).

86. *Compare* 21 C.F.R. § 314.80(a) (defining "adverse drug experience" as "[a]ny adverse event associated with the use of a drug in humans, *whether or not considered drug related*") (emphasis added), *with* GOOD PHARMACOVIGILANCE PRACTICES, *supra* note 73, at 4 (stating that the "actual risk to patients cannot be known from [adverse event] data because it is not possible to characterize all events definitively and because there is invariably under-reporting of some extent and incomplete information about duration of therapy, numbers treated, etc."). *See also* Rider v. Sandoz Pharm. Corp., 295 F.3d 1194, 1199 (11th Cir. 2002) (finding that case reports are only reported data and not based on any scientific methodology); Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1411 (D. Or. 1996) (stating that the lack of controls in case reports makes them unreliable as scientific means of establishing causation); Haggerty v. Upjohn Co., 950 F. Supp. 1160, 1165 (S.D. Fla. 1996) (noting that case reports cannot replace scientific studies); Casey v. Ohio Med. Prods., 877 F. Supp. 1380, 1385 (N.D. Cal. 1995) (finding that case reports do not provide reliable scientific evidence of causation).

87. *See* 153 CONG. REC. 25,162–63 (2007) (statement of Sen. Michael Enzi) (stating that the FDA has no active surveillance system in place to monitor adverse events and that its ability to monitor a drug is curbed after it has entered the market).

88. *See* 21 C.F.R. § 201.57(c)(6)(i) (2012) (requiring reasonable evidence of a causal association); *see also* GOOD PHARMACOVIGILANCE PRACTICES, *supra* note 73, at 8 ("Data mining is not a tool for establishing causal attributions between products and adverse events.").

event."[89] The guidance documents, however, did not create legal obligations and manufacturers were free to decline the FDA's suggestions.[90]

Although binding, federal regulations governing AERS proved similarly ill-equipped to direct an investigation into the reported event's cause.[91] Until 2007, federal regulations did not affirmatively empower the FDA to require manufacturers to conduct postmarketing clinical trials following identification of potential health risks from AERS data.[92] Although 21 C.F.R § 314.80 requires that manufacturers promptly investigate serious and unexpected adverse events,[93] it does not require a manufacturer to determine the event's causation.[94] Thus, as with FDA guidance documents, the FDA lacked the power to force manufacturers to discover the causal association in order to effect labeling changes.[95]

Moreover, depending on the adverse effect's severity and whether it was already listed on the product's label, a manufacturer may not report the event for months or years.[96] Consequently, the FDA could operate for a significant

89. GOOD PHARMACOVIGILANCE PRACTICES, *supra* note 73, at 6.

90. *Id.* at 1 (explicating that the guidance documents did not mandate any action and should be viewed as recommendations only).

91. *See The Public's Stake in Adverse Event Reporting*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm179586.htm (last updated Aug. 20, 2009) (finding that other causes, and not just a drug, may also lead to an adverse event).

92. *See* Evans, *supra* note 1, at 478–79 (detailing the FDAAA's expansion of the FDA's powers); *see also infra* notes 142–46 and accompanying text.

93. 21 C.F.R. § 314.80(c)(1)(i)–(ii) (2012) (requiring manufacturers to "promptly investigate all [serious and unexpected] adverse drug experiences" and "submit followup reports within 15 calendar days of receipt of new information or as requested by [the] FDA"); *see also id.* § 314.80(c)(2)(i) (describing reporting requirements for nonserious and expected adverse events).

94. *See id.* § 314.80(c)(1)(ii) (acknowledging that, "[i]f additional information is not obtainable, records should be maintained of the unsuccessful steps taken to seek additional information"); *see also* U.S. FOOD & DRUG ADMIN., COMPLIANCE PROGRAM GUIDANCE MANUAL ch. 53, pt. V, at 2 (2012), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/UCM332013.pdf (requiring manufacturers to follow up on unexpected and serious adverse events but declining to require ultimate proof of causation).

95. *See supra* note 40 and accompanying text (stating that, before 2007, the FDA could not require manufacturers to conduct follow-up trials during the postmarketing stage to determine whether a drug caused potential side effects that were previously unknown).

96. The Code of Federal Regulations defines a "serious adverse drug experience" as one that "results in" death or other life-threatening injury. 21 C.F.R. § 314.80(a) (2012). Because case reports do not demonstrate causation, whether the experience resulted in the injury may be open to debate. This could potentially cause a serious event to be misclassified and reported much later than what the regulations require for serious and unexpected events. *See, e.g.*, *id.* § 314.80(c)(2)(i) (permitting manufacturers to delay reporting of all nonserious or expected adverse events for as many as twelve months from receipt of information).

period of time under the assumption that a potential risk did not exist when, in fact, the drug manufacturer possessed contradictory data.[97]

Even if sufficient postmarketing data existed to prove a causal association between a drug and a side effect,[98] before 2007 the FDA lacked the power to force a labeling change.[99] Rather, the FDA could only suggest modifications, which typically resulted in protracted negotiations with the manufacturer,[100] which delayed, or even prevented, the dissemination of updated warnings to physicians and the public.[101] Although the FDA could withdraw a medication's marketing approval if the manufacturer refused labeling

97. *See, e.g.*, Letter from Pub. Health Serv., U.S. Food & Drug Admin., to Gregory Irace, President and Chief Exec. Officer, Sanofi-Aventis (Jan. 28, 2011), *available at* http://www.fda.gov/ICECI/ENforcementActions/WarningLetters/ucm243585.htm (issuing a warning letter to Sanofi-Aventis after discovering that the pharmaceutical company was potentially 896 days late in reporting a drug's adverse effects to the FDA). Reports of serious risks need not be reported to the FDA in the fifteen-day window if that risk is already reflected in the labeling. 21 C.F.R. § 314.80(c).

98. This information would have to come from sources other than AERS data, such as data from clinical trials.

99. In testimony before the House Committee on Government Reform, the acting director of the FDA's Center for Drug Evaluation and Research admitted the FDA's lack of authority to require Merck to modify its labeling for Vioxx:

> Mr. WAXMAN. I want to go back to that give and take of the FDA negotiating changes in the label with the company. It seems like you had what you thought ought to be disclosed and the company did not quite agree with it, and you are not in a position legally to order it, even though you thought the public and the doctors ought to have this, particularly the doctors ought to have this warning information in light of the new studies.
>
> Dr. GALSON. Right.

Risk and Responsibility Hearing, *supra* note 3, at 64 (exchange between Rep. Henry A. Waxman, Member, H. Comm. on Gov't Reform and Steven Galson, Acting Director, Center for Drug Evaluation & Research, U.S. Food & Drug Administration); *see also id*. at 40 (statement of Steven Galson, Acting Director, Center for Drug Evaluation & Research, U.S. Food & Drug Administration) (noting, in response to the question why the FDA could not dictate labeling changes to Merck for its medication Vioxx, that "[t]he label by law belongs to the product, which belongs to the company [and] we can work together with [the manufacturer and] . . . most of the time we are very, very successful in getting what we want").

100. CTR. FOR DRUG EVALUATION & RESEARCH (CDER), CTR. FOR BIOLOGICS EVALUATION & RESEARCH (CBER), FOOD & DRUG ADMIN., U.S. DEP'T OF HEALTH & HUMAN SERVS, GUIDANCE FOR INDUSTRY: SAFETY LABELING CHANGES—IMPLEMENTATION OF SECTION 505(O)(4) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT (DRAFT) 2 (2011) [hereinafter GUIDANCE FOR INDUSTRY: SAFETY LABELING CHANGES], *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM250783.pdf.

101. *See, e.g.*, Gardiner Harris, *F.D.A. Official Admits 'Lapses' on Vioxx*, N.Y. TIMES, Mar. 2, 2005, at A15 (citing the FDA's Deputy Director of the Office of New Drugs as stating that the FDA took too long to obtain information about health risks onto its Vioxx label and blaming the manufacturer for the delay).

recommendations, the agency admitted that it would rarely exercise such authority when there were patients benefitting from the drug.[102]

B. Improved Detection Through the FDAAA and Sentinel System

> The changes made in the drug safety components of [the FDAAA] are critical to restoring peace of mind to Americans who want to be assured that the drugs they take to treat illnesses and chronic medical conditions can be relied upon and trusted.
>
> —Sen. Michael Enzi, R-Wyo.[103]
>
> We cannot wait another month, another week—or even another day. We must take action here and take action now to send [the FDAAA] to the President.
>
> —Sen. Edward Kennedy, D-Mass.[104]

In 2007, Congress took action to rectify the shortcomings of the FDA's postmarketing surveillance of pharmaceutical products, overwhelmingly voting in favor of the Food and Drug Administration Amendments Act of 2007.[105] The FDAAA authorized the FDA to require drug manufacturers to conduct postmarketing clinical studies and trials to assess a medication's known and potential risks and identify additional, serious risks.[106] In direct response to the limitations of the AERS database, the FDAAA ordered the creation of a national healthcare data network—the Sentinel System—that was to comprise, by July 1, 2012, data from no less than 100 million patients.[107] Further, the FDAAA granted the FDA the authority to order labeling changes upon the discovery of "new safety information," and it created civil penalties for

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102. GUIDANCE FOR INDUSTRY: SAFETY LABELING CHANGES, *supra* note 100, at 2; *see also* Evans, *supra* note 1, at 504; Barbara J. Evans, *Congress' New Infrastructural Model of Medical Privacy*, 84 NOTRE DAME L. REV. 585, 632–33 (2009).

103. 153 CONG. REC. 25,162–63 (2007) (statement of Sen. Michael Enzi).

104. 153 CONG. REC. 25,037 (2007) (statement of Sen. Edward Kennedy).

105. The FDAAA passed through the House of Representatives by a vote of 405 to 7 and was approved unanimously in the Senate. *See* 153 CONG. REC. 24,773 (2007); *see also* 153 CONG. REC. 25,048 (2007). The bill was signed into law on September 27, 2007. Press Release, The White House Office of Commc'ns, President Bush Signs H.R. 2669 and H.R. 3580 into Law (Sept. 27, 2007).

106. 21 U.S.C. § 355(o)(3) (Supp. IV 2011). The FDAAA authorizes the FDA to require manufacturers to conduct postmarketing studies "[t]o assess a known serious risk related to the use of the drug involved"; "[t]o assess signals of serious risk related to the use of the drug"; and "[t]o identify an unexpected serious risk when available data indicates the potential for a serious risk." *Id.* § 355(o)(3)(B); *see also* Faden & Milne, *supra* note 36, at 688. Importantly, the FDAAA further empowers the FDA with authority to levy monetary sanctions against manufacturers that refuse to conduct such postmarketing studies and trials. 21 U.S.C. § 333(f)(4)(A) (Supp. IV 2011) (providing civil monetary penalties of up to $250,000 for single violations limited to $1 million per proceeding, with an increase of up to $10 million when the responsible party continues the violation after receiving notice from the Secretary).

107. 21 U.S.C. § 355(k)(3)(B)(ii)(II) (Supp. IV 2011).

violations of such orders.[108] The Act was the largest reform in half a century.[109]

The FDAAA rejects the concept that preclinical trials could identify all of a medication's potential side effects, thereby shifting the FDA's regulatory focus to identifying risks after marketing approval.[110] As noted by one scholar, the FDA's role as the market's gatekeeper acknowledges the reality that some products will enter the market with latent risks.[111] The FDAAA is relevant because it "adds [the] capability to detect and manage risks after products pass through the gate."[112]

Working in conjunction with the AERS database,[113] the Sentinel System allows the FDA to query patient healthcare data when a drug's safety is in question.[114] In order to rule out alternative causation theories, the FDA can now use the Sentinel System to pursue the question of causation by searching 100 million patients' healthcare data to determine a drug's users, the users' overall health profiles (including concomitant medications), and the side effects experienced.[115] The benefits of this system are exponential:

> With claims data for 100 million people, the [Vioxx] problem could have been spotted in fewer than 3 months. If [the] FDA had had the necessary data networks in place to do large-scale observational studies in 1999, *all of the people killed or injured by Cox-2 painkillers after August 1999 (i.e., three months after Vioxx went on sale) might have been spared*.[116]

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108. *Id.* § 355(o)(4)(E).

109. *See* Evans, *supra* note 1, at 422–23 (quoting Mark McClellan, *Drug Safety Reform at the FDA—Pendulum Swing or Systematic Improvement?*, 356 NEW ENG. J. MED. 1700, 1700 (2007)).

110. *See id.* at 457–58 (stating that the FDA's pre-1962 evidentiary paradigm, with its reliance on premarketing trials for determining adverse effects, was "beyond repair").

111. *Id.* at 477 (arguing that safety is not compromised by reacting to postmarketing reports).

112. *Id.* ("The gate is intrinsically porous, . . . key constituencies such as the medical profession and academics overestimated the power of premarket testing and consequently showed 'little, if any, leadership' in developing and using postmarket risk-benefit data. In [the] FDAAA, Congress has supplied the missing leadership." (quoting Kenneth L. Melmon, *Attitudinal Factors that Influence the Utilization of Modern Evaluative Methods*, *in* INST. OF MED., MODERN METHODS OF CLINICAL INVESTIGATION 135, 144 (Annetine C. Gelijns ed., 1990))).

113. SENTINEL 2010 REPORT, *supra* note 59, at 2 (asserting that the Sentinel System will augment the FDA's current postmarket surveillance systems).

114. *Id.* at 3 (calling this monitoring "active surveillance").

115. *See* Evans, *supra* note 102, at 588–89 (noting that the Sentinel System will provide the ability to examine a patient's entire medical record to conclusively determine whether a drug's ingestion caused an adverse effect). *But cf. supra* notes 73–86 and accompanying text (noting the FDA's inability to determine the true incidence rate of a newly identified side effect based solely on adverse event reports).

116. Evans, *supra* note 1, at 456 (emphasis added) (footnote omitted).

This statement assumes, however, that review of the Vioxx patients' claims data would have been focused on the adverse health effect at issue.[117] Ultimately, although the Sentinel System's use of active postmarketing surveillance will discover postmarketing health effects faster, the possibility of eliminating those effects entirely is not feasible.[118]

C. Cracks in the Façade: The FDAAA's 10,000-Patient Donut Hole

Despite the FDAAA's significant leap forward in postmarketing surveillance, the Sentinel System has value only if some percentage of patients experience a previously undetected adverse event during the postmarketing period.[119] Even post-FDAAA, some lag time between marketing and health risk detection will persist.[120] To Congress's credit, it did not shy away from these facts in drafting the Act; it embraced them.[121]

The FDAAA directs the FDA to conduct routine surveillance of newly approved drugs[122] and the AERS database,[123] and then report its findings to the public.[124] For all newly approved medications, the FDA must publicly report, "by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, . . . any new risks not previously identified,

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117. *Cf. id.* at 441 (noting that knowledge about what possible adverse effects might occur is necessary to assess safety data drawn from clinical trials).

118. SENTINEL 2010 REPORT, *supra* note 59, at 4.

119. *See* Evans, *supra* note 1, at 453 (arguing that a larger sample size provides more accurate data).

120. For the FDA's post hoc analysis of postmarketing surveillance data to have any effect, analysts must have predetermined criteria to which their review is targeted. *See, e.g.*, *id.* at 441. Until these targeted criteria are determined, preliminary reviews of Sentinel System data must first identify the potential unknown risks, with later analysis devoted to incidence rates and severity, creating an inherent delay in identifying, assessing, and warning of newly discovered risks. More generally, the FDA cannot simply release all adverse-event data immediately upon discovery. A due diligence period is required to substantiate the noted effect. *See, e.g.*, Kristen Rosati, *Using Electronic Health Information for Pharmacovigilance: The Promise and the Pitfalls*, 2 J. HEALTH & LIFE SCI. L. 171, 229–30 (2009) ("Drug safety 'signals' may be observed in an analysis, often requiring follow-up to obtain more information to confirm causation, such as comparing the findings across multiple information sources to confirm the validity of the conclusions. During the 'gray zone' that exists between the first drug safety signal and confirmation (or refutation) of the signal's validity, pharmacovigilance experts are wary about communicating their findings to others. False positives run the risk of alarming patients, potentially causing them to stop medication therapy that may have real benefit to them.").

121. 153 CONG. REC. S11,833 (daily ed. Sept. 20, 2007) (statement of Sen. Michael Enzi) (stating that the FDAAA strengthens the FDA's ability to address postmarketing drug safety).

122. *See, e.g.*, 21 U.S.C. § 355(k)(3)(E) (Supp. IV 2011).

123. *Id.* § 355(k)(5) (requiring the FDA to screen the AERS system bi-weekly and to post quarterly reports detailing any new safety information found within the previous quarter).

124. *See, e.g.*, *id.* § 355(r)(1) ("[The FDA] shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that . . . improves communication of drug safety information to patients and providers.").

potential new risks, or known risks reported in unusual number."[125] Implicit in these requirements, however, is that the new data comes at the expense of a drug's first subscribers who suffer the unknown adverse effects.[126]

Mandated surveillance and public disclosure of postmarketing safety data are critical to reassure the public about an approved drug's safety and to expedite updated warnings to both consumers and healthcare professionals.[127] Further, surveillance and disclosure complement the FDA's newly prescribed authority to require updated labeling of pharmaceutical products by creating a framework through which "new safety information"[128] will be promptly identified.[129] More subtly and controversially, however, the FDAAA provides a de facto post-approval clinical trial for all new drugs, involving no fewer than 10,000 participants and conducted during the first eighteen months after market approval.[130]

1. Protections Afforded Clinical Trial Participants

Clinical trials are an essential pillar of the drug approval process.[131] Before a new drug can be marketed in the United States, the FDA must first find that the drug is both safe and effective[132] and that its benefits outweigh its risks.[133] These criteria are proved through the mandatory human clinical trials that are typically conducted in three phrases.[134] Phase I trials assess side effects associated with the drug and how the drug is metabolized in the human body.[135] Less than 100 individuals participate in these trials.[136] Conversely,

125. *Id.* § 355(r)(2)(D).

126. *See supra* notes 5–10 and accompanying text.

127. *See* SENTINEL 2010 REPORT, *supra* note 59, at 2; *see also* Evans, *supra* note 102, at 590; Ralph F. Hall, *The Risk of Risk Reduction: Can Postmarket Surveillance Pose More Risk than Benefit?*, 62 FOOD & DRUG L.J. 473, 474 (2007); Lance L. Shea et al., *Cause and Effect? Assessing Postmarketing Safety Studies as Evidence of Causation in Products Liability Cases*, 62 FOOD & DRUG L.J. 445, 446 (2007).

128. 21 U.S.C. § 355(o)(4)(A) (Supp. IV 2011).

129. *Id.*

130. *Id.* § 355(r)(2)(D).

131. *See* Anna B. Laakmann, *Collapsing the Distinction Between Experimentation and Treatment in the Regulation of New Drugs*, 62 ALA. L. REV. 305, 315 (2011).

132. 21 C.F.R. § 314.2 (2012).

133. *Id.* §§ 314.2, 314.105, 314.125 (2012); *see also* Rebecca S. Yoshitani & Ellen S. Cooper, *Pharmaceutical Reformulation: The Growth of Life Cycle Management*, 7 HOUS. J. HEALTH L. & POL'Y 379, 382 (2007) (stating that, in order to receive FDA approval, clinical studies must prove a drug's safety and effectiveness and must show that the risks in its consumption are less than the benefits gained).

134. 21 C.F.R. § 312.21 (2011); *see also* W. Christopher Matton & F. Scott Thomas, *The Continuing Balance: Federal Regulation of Biotechnology*, 44 JURIMETRICS 283, 297–98 (2004) (concluding that each phase increases the number of participants and, therefore, the quality of data).

135. 21 C.F.R. § 312.21(a).

136. *Id.* (finding the number generally to be between twenty and eighty participants).

Phase II trials are concerned with the drug's effectiveness for its specified use.[137] Phase II trials are relatively small but larger than Phase I, involving less than 1,000 patients.[138] Phase III trials gather additional information on the drug's safety and effectiveness so that the drug's benefit/risk relationship can be assessed.[139] Phase III trials are the largest, comprising several hundred or several thousand participants.[140]

Since 1970, manufacturers have conducted postmarketing (Phase IV) clinical trials on FDA-approved medications.[141] Phase IV trials assess the drug's efficacy and safety over long-term administration and also examine the benefits of alternative dosages, including "use of the drug in other patient populations or other stages of the disease."[142] Although some suggest that the FDA ostensibly mandated early Phase IV trials as a condition of a drug's approval,[143] the authority to order such studies was premised on an unstable regulatory foundation until passage of the FDAAA[144] and was seldom invoked.[145] With the passage of the FDAAA, however, the FDA can now require a drug manufacturer to conduct postmarketing clinical trials upon identification of "new safety information" obtained in the post-approval period.[146]

All clinical research is governed by federal regulations,[147] which provide significant protections to clinical trial participants.[148] Pursuant to regulations

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137. *Id.* § 312.21(b).

138. *Id.* (finding the number to be no more than several hundred participants).

139. *Id.* § 312.21(c).

140. *Id.*

141. Steenburg, *supra* note 24, at 300.

142. *See, e.g.*, 21 C.F.R. § 312.85 (2011) (stating that it took seven years after passing the Kefauver-Harris Amendments for the FDA to require a Phase IV study).

143. Steenburg, *supra* note 24, at 300 (noting approval of Parkinson's drug Levodopa on the condition that certain long-term studies continue after approval).

144. *See id.* at 301 (noting that the FDA worked to codify Phase IV studies by promulgating a rule); *see also* Evans, *supra* note 1, at 477–79 (stating that the FDA claimed it had those extended powers before the FDAAA but had exercised them with caution because they were not expressly granted).

145. Evans, *supra* note 1, at 478. In 1992, the FDA formally adopted regulations empowering it to require postmarketing studies, albeit under specified and limited circumstances, for drugs addressing serious or life-threatening injury. 21 C.F.R. § 314.510 (2011). In 1997, Congress codified FDA regulations requiring postmarketing trials in this context. 21 U.S.C. § 356(a)(2)(a) (2006).

146. 21 U.S.C. § 355(o)(3)(C) (Supp. IV 2011). The FDAAA defines new safety information to include: "information derived from a clinical trial, an adverse event report, a postapproval study . . . ; data derived from the postmarket risk identification and analysis [Sentinel] system"; or "other scientific data deemed appropriate" by the FDA about a serious risk "that [FDA] has become aware of . . . since the drug was approved." 21 U.S.C. § 355-1(b)(3) (Supp. IV 2011).

147. 21 C.F.R. § 50.1 (2011); 45 C.F.R. §§ 46.101(a)(2), 46.102(e) (2011); Matton & Thomas, *supra* note 134, at 316 (concerning "protection of human subjects").

148. *See infra* notes 149–55 and accompanying text.

promulgated by the FDA[149] and the U.S. Department of Health and Human Services (HHS),[150] a new drug's clinical trial research conducted in support of market approval must minimize all potential risks "[b]y using procedures [that] . . . do not unnecessarily expose subjects to risk," and which "[r]isks . . . are reasonable in relation to anticipated benefits."[151] Moreover, trial sponsors must obtain participants' informed consent before conducting the trial.[152] This consent must include a statement to the participant that contains "[a] description of any reasonably foreseeable risks or discomforts to the subject"; "[a] disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject"; and, when appropriate, "[a] statement that the particular treatment or procedure may involve risks to the subject . . . *which are currently unforeseeable*."[153] If the trial involves more than minimal risk, the sponsor must disclose information regarding compensation and medical treatments that may be required should injury result.[154] Beyond regulatory protections, trial sponsors can also obtain insurance policies to compensate trial participants for injuries incurred during the trial.[155]

2. Protections Denied First Subscribers Post-FDAAA

As previously mentioned, one significant component of the FDAAA's new postmarketing surveillance regime is its requirement that the FDA publicly report an analysis of those reports identifying a new drug's adverse reactions received after the drug's marketing approval.[156] In compiling and assessing information for the new drug's initial summary analyses, the FDA will use both its old, passive AERS system and the new, active Sentinel System.[157] Moreover, the FDA intends to prioritize its active surveillance using data obtained through postmarketing surveillance sources such as adverse event

149. *See* 21 C.F.R. §§ 50.1(a), 56.101(a) (2011) (outlining the scope of protections afforded).

150. *See* 45 C.F.R. 46.101(a) (2011).

151. 21 C.F.R. § 56.111(a)(1)–(2) (2011); 45 C.F.R. § 46.111(a)(1)–(2) (2011).

152. 21 C.F.R. § 50.20 (2011); 45 C.F.R. § 46.116 (2011).

153. 45 C.F.R. § 46.116(a)(2), (4); § 46.116(b)(1) (emphasis added); *see also* 21 C.F.R. § 50.25(a)–(b) (2011).

154. 45 C.F.R. § 46.116(a)(6); 21 C.F.R. § 50.25(a)(6). As defined in the regulations, "*[m]inimal risk* means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." 21 C.F.R. § 56.102(i) (2011) (emphasis added); 45 C.F.R. § 46.102(i) (2011) (emphasis added).

155. *But see* William M. Sage, *Some Principles Require Principals: Why Banning "Conflicts of Interest" Won't Solve Incentive Problems in Biomedical Research*, 85 TEX. L. REV. 1413, 1453 (2007) (noting that, "unlike other countries, the United States does not require research institutions to have clinical trials insurance, and compensation policies for research injuries are erratic and incomplete").

156. 21 U.S.C. § 355(r)(2)(D) (Supp. IV 2011).

157. *See, e.g.*, *id.* § 355(r)(2)(C)–(D); SENTINEL 2010 REPORT, *supra* note 59, at 2 (stating that this creates a more comprehensive system).

reports[158] to identify previously unknown risks.[159] In outlining what would become the Sentinel System, the FDAAA required the FDA to establish procedures to identify and report trends in the data to the Secretary of HHS.[160]

Consequently, the FDA must conduct observational studies by querying the Sentinel System for adverse drug reaction reports on a drug's first subscribers.[161] Whether this activity rises to the level of a clinical trial is debatable,[162] but the distinction may be irrelevant.[163] There is no dispute that the FDA's conduct in querying the Sentinel System based on adverse reaction reports *observes* individuals taking a specified medication *and measures outcomes*.[164] Conversely, whether or not the FDA's data can be viewed as observational clinical trials, the queries are necessarily systematic investigations involving human subjects "designed to develop or contribute to generalizable knowledge" about a drug.[165]

Because the queries into the Sentinel System data contribute to the FDA's understanding of a drug's risks, the question remains whether these first subscribers should receive the same protections as those of postmarketing clinical trial participants.[166] Unlike trial participants, early subscribers to an FDA-approved drug are not required to receive information regarding

158. SENTINEL 2010 REPORT, *supra* note 59, at 3 ("[The] FDA will prioritize safety questions that have emerged from premarket or postmarket safety data sources (e.g., clinical trial data, spontaneous adverse event reports) and submit them to a Coordinating Center for evaluation by data partners that are part of Sentinel's 'distributed system.'").

159. 21 U.S.C. § 355(r)(2)(D).

160. *Id.* § 355 (k)(3)(C)(i)(IV)–(V). The procedures used would assure data dissemination in a timely manner, all while considering its comprehensiveness and standardization. *Id.* § 355(k)(3)(C)(ii).

161. *See* Evans, *supra* note 1, at 507; *see also Surveillance: Post Drug-Approval Activities*, *supra* note 58.

162. *Understanding Clinical Trials*, U.S. NAT'L INSTS. HEALTH, http://clinicaltrials.gov/ct2/info/understand#Q19 (last reviewed Aug. 2012).

163. *See supra* notes 147–48, 156 and accompanying text.

164. *See* SENTINEL 2010 REPORT, *supra* note 59, at 3 (discussing methods employed by the Sentinel System).

165. 45 C.F.R. § 46.102(d) (2011). Some may argue that the FDA's Sentinel System queries are exempt from HHS guidelines because they involve "the collection or study of existing data, documents, records," and, therefore, are exempt from HHS policies on the protection of human research subjects. 45 C.F.R. § 46.101(b)(4) (2011). Although the argument appears plausible, it misses the point. Without those early subscribers to the medication, whose injuries make the FDA's queries possible, the FDA would not have a basis to conduct the search. The information exists only because patients were allowed to take a newly approved medication without first receiving the protections afforded trial participants. *But see* Evans, *supra* note 102, at 626–27 (arguing that neither FDA nor HHS regulations apply to patient data "that are fully identified, identifiable by researchers, coded, or de-identified/anonymized").

166. Evans, *supra* note 1, at 456 (noting that relying on postmarket drug studies to detect risks poses ethical problems because the participants may become ill).

alternative treatments or disclosures of potentially unknown risks.[167] Likewise, because subscription to a newly approved medication can pose potentially significant risks, early subscribers would not receive the same compensation or medical treatment that clinical trial participants would receive should injury occur.[168]

The rationale behind the FDAAA's passage lies in the inevitability of postmarketing discovery of adverse health risks that could not have been identified during the pre-approval clinical trial phases.[169] As scholars and members of Congress have correctly noted, a compromise between expediency and safety must be reached in the drug approval process.[170] The FDAAA acknowledges that previously unknown side effects will be discovered postmarketing.[171] Therefore, the question arises as to how first subscribers injured during the postmarketing period should be compensated.[172]

II. AN ARGUMENT AGAINST EITHER TORT LITIGATION OR THE INSURANCE INDUSTRY PROVIDING RELIEF FOLLOWING UNLABELED POSTMARKETING INJURIES

By expanding the FDA's postmarketing surveillance authority, the FDAAA has created a void filled with unprotected patients.[173] First subscribers do not receive the disclosures, possible compensation, or healthcare provided to trial participants.[174] Nor do they benefit from long-term study of a drug that identifies the medication's health risks.[175] These first subscribers, constituting the first 10,000+ FDAAA-designated users, do not willingly agree to exploratory treatment.[176] Moreover, their physicians are not sufficiently informed of all the medication's risks because they are still being discovered at

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167. The warnings afforded participants in clinical trials pursuant to federal regulations do not apply to postmarket studies because the drug has already been approved. *See* 45 C.F.R § 45.116(a) (2011).

168. *See* INST. OF MED., ETHICAL AND SCIENTIFIC ISSUES IN STUDYING THE SAFETY OF APPROVED DRUGS 172 (2012) (discussing the ethical issues associated with postmarket drug studies because risks and benefits associated with taking certain FDA-approved drugs need not be weighed evenly).

169. Evans, *supra* note 1, at 425 (noting that the pretrial evidentiary data's weight is being reassessed).

170. *See, e.g.*, *id.* at 456 (asking whether it is ethical to expose patients to drugs for which some side effects may be unknown); *see also* 153 CONG. REC. 25,037 (2007) (statement of Sen. Edward Kennedy).

171. *See* Evans, *supra* note 1, at 443 (noting the inherent shortcomings of premarket drug clinical studies to detect all side effects).

172. *Cf. id.* at 456 (stating that reliance on postmarket drug studies to detect risks poses ethical problems).

173. *See supra* note 125 and accompanying text.

174. *See supra* note 167.

175. *See* Evans, *supra* note 1, at 477.

176. *See id.* at 456.

their patients' expense.[177] Thus, these first subscribers and their physicians cannot weigh the treatment's risks and benefits when some of those risks are unknown.[178] When injuries occur, first subscribers are left with two equally insufficient and unappealing options: tort litigation and health insurance claims.[179] For the following reasons, neither of these options is sufficient.[180]

A. The Inherent Inequality of Recovery from Litigation

Recovery under tort law requires the injured party to prove both causation and the manufacturer's liability for the injury.[181] Unfortunately, in the context of adverse health effects first discovered during the postmarketing period, finding proof of causation can be problematic and establishing liability exceedingly difficult.[182] As a result, using tort law remedies to provide relief from newly discovered adverse health effects is, at the individual level, limited at best.[183] Moreover, when this type of relief is expanded to society as a whole (e.g., in cases where similar adverse health effects are experienced by multiple users), additional concerns regarding unequal treatment of similarly situated parties arise, further diluting tort law's overall effectiveness at compensating injuries.[184]

Generally, under products liability laws, a business that sells or distributes a defective product is subject to liability for harm that the product causes.[185] Traditionally, the bases for a products liability cause of action include a claim that the product was defectively manufactured, defectively designed, or not accompanied by proper instructions and warnings.[186] In drug litigation,

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177. *See id.* at 477 (noting that the Sentinel System's efficacy is predicated on the discovery of unknown side effects during the postmarket study period).

178. *See id.*

179. *See* O'Reilly, *supra* note 85, at 567; *see also* RESTATEMENT (THIRD) OF TORTS: PRODUCT LIABILITY § 1 (1998) (noting the availability in tort to recover for defective products).

180. *See infra* Part II.A–B.

181. *See* RESTATEMENT (THIRD) OF TORTS: PRODUCT LIABILITY § 1 cmt. a; *see also In re* Hawaii Fed. Asbestos Cases, 699 F. Supp. 233, 236 (D. Haw. 1988) (stating that the plaintiff need only show that the product was defective and a proximate cause of the harm), *aff'd*, 960 F.2d 906 (9th Cir. 1992).

182. *See, e.g.*, Evans, *supra* note 1, at 457 (arguing that finding late-emerging risks is an unreasonable expectation, but the public believes that these should be discovered before a drug's approval).

183. David G. Owen, *Dangers in Prescription Drugs: Filling a Private Law Gap in the Healthcare Debate*, 42 CONN. L. REV. 733, 738 (2010) (noting that one area of unsettled law relating to prescription drugs is the extent of manufacturers' liability when unforeseeable dangers are present).

184. *See, e.g.*, O'Reilly, *supra* note 85, at 569 (arguing that even patients who take the allegedly defective drug must show that it was the drug that caused the injury and not something else).

185. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 1.

186. *See, e.g., id.* § 2.

failure-to-warn claims largely predominate.[187] Although an injured party may choose to pursue warning claims under strict liability, negligence, or breach of warranty theories of liability,[188] courts typically apply a negligence standard in assessing the warning's validity[189] by relying on the concept of foreseeability.[190] Foreseeability requires the plaintiff to prove that the manufacturer was aware, or should have been aware, of the risk of the injury sustained and failed to warn of it.[191]

Because an adverse health effect that is discovered after marketing approval is, by definition, previously unknown to the manufacturer,[192] the patient sustaining the injury almost certainly will be unable to recover under any applicable tort theory.[193] State products liability laws are virtually uniform in

187. *See* Owen, *supra* note 183, at 751 (detailing several warning issues that tend to arise in drug cases); *see also* Rosati, *supra* note 120, at 231 (characterizing improperly labeled drugs as "defective").

188. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 cmt. n; Owen, *supra* note 183, at 752.

189. Owen, *supra* note 183, at 752–53 & n.77 (citing cases in which courts have applied a negligence standard).

190. *See, e.g.*, RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 cmt. m(2) (1998) (stating that most jurisdictions find a duty to warn of risks where those risks were known or should have been known to a reasonable person).

191. *See, e.g.*, Opera v. Hyva, Inc., 450 N.Y.S.2d 615, 618 (N.Y. App. Div. 1982) ("Where the theory of liability is failure to warn or adequately instruct, negligence and strict products liability are equivalent causes of action."); RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 cmt. m(2) (proposing that there is little substantive difference between the terms "reasonableness" and negligence with respect to strict liability claims). Because failure to warn claims generally include some element of foreseeability, a breach of warranty theory is similar to its strict liability and negligence counterparts because all three require some type of actual or constructive knowledge of the risk imputed to the manufacturer. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 cmt. n. Moreover, those states that do not require proof of actual or constructive knowledge of the risk nevertheless require the plaintiff to prove that knowledge of the risk was known by or available to others. *See, e.g.*, Livingston v. Isuzu Motors, LTD., 910 F. Supp. 1473, 1497 (D. Mont. 1995).

192. Because this Article focuses on the FDA's improved efforts to detect previously unknown health risks during the postmarketing period, for purposes of this section, this Article assumes that the discovery during the postmarketing period of the adverse effect is legitimate and not the result of deliberate obfuscation by the manufacturer or lack of diligence in researching the risks of the product at issue. In such cases, an injured party would potentially be more likely to succeed in tort in obtaining relief from the manufacturer. *See, e.g.*, McNeil v. Wyeth, 462 F.3d 364, 369–70 (5th Cir. 2006) (finding that a genuine issue of material fact existed as to whether the manufacturer had sufficient evidence of a potential risk such that its failure to supplement the warnings for its drug misled physicians).

193. *See* LaMontagne v. E.I. Du Pont De Nemours & Co., 41 F.3d 846, 859 (2d Cir. 1994) (affirming a lower court's finding that the defendant was not required to warn of the risks associated with its product because the Connecticut products liability law for failure to warn is grounded in "the fundamental principle that a seller's duty to warn is premised on the existence of its knowledge or its reason to know of the hazards is evident"); *see also* Coburn v. Smithkline Beecham Corp., 174 F. Supp. 2d 1235, 1240–41 (D. Utah 2001) (noting that, because the duty to warn depends on the manufacturer's level of knowledge at the time of the drug's release,

their requirement that plaintiffs pursuing failure-to-warn claims prove that the manufacturer knew or should have known about the defect.[194] Even if a court were to find that the manufacturer knew of the relevant risk, the injured patient must still prove that the drug *caused* the injury.[195] As discussed previously, proof of causation on the basis of adverse reaction reports alone will not suffice.[196] Thus, although proof of causation is scientifically possible, the injured party will incur significant expense during litigation to prove that the drug caused the injury.[197] Consequently, the enormous costs of litigation diminish the amount of compensation received by the victim.[198] Further, relief ultimately comes after a significant delay from the time of injury[199] and, in cases where causation cannot be proven, recovery may be denied altogether.[200]

When extrapolated to the larger population of drug users, additional criticisms regarding the tort system's ability to effect prompt and equal relief become apparent.[201] As a preliminary matter, scholars agree that the tort

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knowledge attributable to the manufacturer can change in the case of a patient prescribed a medication at various points in time); John G. Fleming, *Drug Injury Compensation Plans*, 30 AM. J. COMP. L. 297, 308 (1982) ("[Negligence] does not cover 'development risks', i.e., risks which the manufacturer neither knew nor should have known at the time of marketing in the light of existing scientific knowledge."); Stephen Guest, *Compensation for Subjects of Medical Research: The Moral Rights of Patients and the Power of Research Ethics Committees*, 23 J. MED. ETHICS 181, 182 (1997) (noting, in the context of a clinical trial, that "an injured subject cannot easily claim that a risk was 'reasonably foreseeable in the ordinary course of events,' because the nature of experiment is such that a. unforeseeable events are to be expected and b. there is an inherent difficulty in establishing what the 'ordinary course of events' actually is").

194. *See, e.g.*, MISS. CODE ANN. § 11-1-63(c)(i) (Supp. 2011); *LaMontagne*, 41 F.3d at 859 (noting the applicability of a similar rule in Connecticut); Smith v. Eli Lilly & Co., 560 N.E.2d 324, 344 (Ill. 1990) (noting the applicability of similar rule in Illinois); Davis v. Wyeth Laboratories, Inc., 499 F.2d 121, 129 (9th Cir. 1968) (noting the applicability of a similar rule in Idaho). Moreover, even in states that define prescription drugs as "unreasonably dangerous" or "unavoidably unsafe" products—injuries from which would otherwise subject the drugs' manufacturers to strict liability—the manufacturer nonetheless is absolved from liability when the drug is accompanied by proper warnings. *See, e.g.*, Wagner v. Roche Labs., 671 N.E.2d 252, 256 (Ohio 1996); RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (1998).

195. *See* O'Reilly, *supra* note 85, at 560.

196. *See id.*

197. *Id.* (describing how a plaintiff must show, by a preponderance of the evidence, that a drug was the cause of harm, regardless of whether there are other plausible causes of the injury).

198. *See, e.g.*, Fleming, *supra* note 193, at 315 (suggesting that high litigation costs prevent plaintiffs from bringing claims).

199. *See* James P. George, *Access to Justice, Costs, and Legal Aid*, 54 AM. J. COMP. L. 293, 300 (2006) (describing delays in both state and federal civil litigation).

200. *See, e.g.*, Richardson v. Richardson-Merrell, Inc., 857 F.2d 823, 825 (D.C. Cir. 1988) (upholding the judgment notwithstanding the verdict in a drug manufacturing case in which the plaintiff was unable to establish causation).

201. *See* James R. Copland, *Administrative Compensation for Pharmaceutical- and Vaccine-Related Injuries*, 8 IND. HEALTH L. REV. 275, 282–84 (2011) (describing flaws in the tort system which compound as more litigants are involved).

system results in unequal treatment of similarly situated parties.[202] Two or more similarly situated plaintiffs litigating identical products liability suits against the same defendant, but in different jurisdictions, could have starkly different results.[203] One plaintiff may recover; the other may not. Alternatively, both may recover, but receive dramatically different compensation.[204]

Moreover, in pharmaceutical mass tort litigation, the ability to obtain uniformity in relief is further hamstrung by procedural rules and legal wrangling among the parties, precluding equality of treatment.[205] Because individual questions of causation and liability predominate in drug cases,

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202.

> Reformers are right to express serious concerns about horizontal inequity among both plaintiffs and defendants within the tort system. Plaintiffs with similar injuries are treated differently on the basis of both doctrinal and administrative considerations that are unrelated to the nature of their injuries. By the same token, defendants who commit similar wrongs are treated differently on the basis of considerations that are unrelated to the character and injurious tendency of their actions. Reformers are also accurate in noting the variability of outcomes due to differences in factors like the availability of evidence, financial differences, the quality of counsel, and jury composition.

Timothy D. Lytton et al., *Tort Litigation as a Lottery: A Misconceived Metaphor*, 52 B.C. L. REV. 267, 273 (2011) (footnotes omitted). *Cf.* Robert L. Rabin, *September 11 Through the Prism of Victim Compensation*, 106 COLUM. L. REV. 464, 472 n.35 (2005) (reviewing KENNETH R. FEINBERG, WHAT IS LIFE WORTH?: THE UNPRECEDENTED EFFORT TO COMPENSATE THE VICTIMS OF 9/11 (2005)) (noting, in the context of the September 11th Victim Compensation Fund of 2001, that "[i]n every case, across the entire spectrum of no-fault programs, from work-related to crime-related compensation and from injuries associated with military service to the unfortunate victims of vaccine-related mishaps, there is not a single program that grants recovery for wage loss reflecting the tort system's fundamental disregard for considerations of horizontal equity and need-based considerations"); *see also* Lytton et al., *supra*, at 273 (arguing that reformers are justified in their concerns over the horizontal inequity experienced among both plaintiffs and defendants).

203. *See* Alvin B. Rubin, *Mass Torts and Litigation Disasters*, 20 GA. L. REV. 429, 536–37 (1986) (highlighting the inequitable outcomes in mass torts litigation due to when and where both the injuries occur and the suits are filed).

204. *See, e.g.*, Joseph H. King, Jr., *Pain and Suffering, Noneconomic Damages, and the Goals of Tort Law*, 57 SMU L. REV. 163, 176 (2004) (noting the "wide disparity" in jury verdicts across jurisdictions caused by arbitrary concern with extraneous factors other than the actual injury); *see also* Fleming, *supra* note 193, at 316 (criticizing the tort system for "discriminat[ing] between different accident victims not according to their own deserts, but according to the culpability of the defendant"). The disparity in recovery from state to state further extends to punitive damages. *Compare* CAL. CIV. CODE § 3294(a) (West 1997) (allowing uncapped punitive damages in products liability cases), *with* VA. CODE ANN. § 8.01-38.1 (2007) (capping recovery of punitive damages at $350,000), *and* Miller v. Kingsley, 230 N.W.2d 472, 474 (Neb. 1975) (barring recovery of punitive damages).

205. *See* JoEllen Lind, *"Procedural Swift": Complex Litigation Reform, State Tort Law, and Democratic Values*, 37 AKRON L. REV. 717, 756–57 (2004) (noting difficulties faced by plaintiffs in mass tort litigation).

class-action-type relief is often unavailable.[206] In addition, because of pharmaceutical manufacturers' claims of the proprietary nature of internal documents, protective orders entered in individual actions prohibit or delay relevant information from becoming public, precluding those in other jurisdictions from obtaining and using that same material in their suits.[207]

Despite concerns over treatment inequalities, some commentators continue to support the tort system because it deters bad actors.[208] For the same reason, civil and criminal liability statutes are lauded as benefitting the marketplace by encouraging compliance with the FDA's manufacturing and marketing standards while simultaneously imposing significant financial penalties when manufacturers fail to comply.[209] In response, however, the pharmaceutical manufacturers' conduct over time has disproved the deterrent effect of litigation.[210] Additionally, despite the massive fines imposed on prescription drug manufacturers for federal law violations,[211] none of that money benefits

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206. *See, e.g.*, Zehel-Miller v. Astrazenaca Pharms., LP, 223 F.R.D. 659, 664 (M.D. Fla. 2004) (denying class certification in pharmaceutical products liability litigation because "individual questions concerning patient characteristics and medical history, physician involvement, dosage, causation and comparative or contributory negligence, eviscerate any notion that common issues predominate").

207. *Sunshine in Litigation Act of 2008: Hearing Before the Subcomm. on Commercial & Admin. Law of the H. Comm. on the Judiciary*, 110th Cong. 1 (2008) (statement of Rep. Linda T. Sánchez, Chairwoman, H. Subcomm. on Commercial & Admin. Law) (suggesting that confidentiality orders entered in products liability matters can have a deleterious effect on public health and safety because they prohibit dissemination of the information to the public).

208. Parasidis, *supra* note 22, at 991–92 (suggesting that state tort claims encourage companies to disclose information as quickly as it is available).

209. In recent years, the federal False Claims Act and Anti-Kickback Statute have been used to prosecute prescription drug manufacturers for false advertising and for providing remuneration to healthcare providers to encourage off-label prescription. 31 U.S.C. §§ 3729–3733 (2006 & Supp. IV 2011); 42 U.S.C. § 1320a-7b(b) (2006); *see also, e.g.*, Tim Mackey & Bryan A. Liang, *Off-Label Promotion Reform: A Legislative Proposal Addressing Vulnerable Patient Drug Access and Limiting Inappropriate Pharmaceutical Marketing*, 41 U. MICH. J.L. REFORM 1, 24–26 (2011). Additionally, intentional falsification and concealment of documents in response to an FDA request can result in criminal charges brought under the Sarbanes-Oxley Act of 2002. Pub. L. No. 107-204, 116 Stat. 745 (codified as amended in scattered sections of 11, 15, 18, 28, and 29 U.S.C.); *see also, e.g.*, United States v. Stevens, 771 F. Supp. 2d 556, 559–62 (D. Md. 2011) (citing 18 U.S.C. § 1519 (2006)).

210. *See supra* notes 12–13, 26–30 and accompanying text; *see also, e.g.*, Duff Wilson, *UCB Pays $34 Million and Pleads Guilty in Epilepsy Drug Fraud Case*, N.Y. TIMES PRESCRIPTIONS BLOG (June 9, 2011, 5:31 PM), http://prescriptions.blogs.nytimes.com/2011/06/09/ucb-pays-34-million-pleads-guilty-in-epilepsy-drug-fraud-case/ (stating that an epilepsy drug fraud case was one of many brought by the Justice Department for illegal marketing by a manufacturer).

211. *See, e.g.*, Press Release, U.S. Dep't of Justice, GlaxoSmithKline to Plead Guilty and Pay $3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data (July 2, 2012), http://www.justice.gov/opa/pr/2012/July/12-civ-842.html (noting GSK's agreement "to plead guilty and to pay $3 billion to resolve its criminal and civil liability arising from [its] unlawful promotion of certain prescription drugs, its failure to report certain safety data, and its civil liability for alleged false price reporting practices," making it "the largest health care fraud settlement in U.S. history and the largest payment ever by a drug company"); *see also* Press

those actually injured.[212] Thus, litigation has proven ineffective at providing comprehensive, equal relief to injured parties and is incapable of effecting improved conduct of manufacturers in the marketplace.[213]

B. The Undisclosed Burden on Public and Private Insurance—Shifting Costs to Responsible Parties

Absent a finding of fault on the pharmaceutical manufacturer, persons injured by a medication in the postmarketing period are forced to rely on insurance for relief.[214] Although the Patient Protection and Affordable Care Act (PPACA) significantly increased the availability of insurance coverage to the vast majority of Americans in 2010,[215] some of those increases will not occur for several years.[216] Moreover, the public and private costs to fund insurance programs are significant, particularly when the risks covered are unknown.[217] Using insurance to compensate postmarketing injury fails to

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Release, U.S. Dep't of Justice, Department of Justice Recovers $3 Billion in False Claims Cases in Fiscal Year 2010 (Nov. 22, 2010), http://www.justice.gov/opa/pr/2010/November/10-civ-1335.html [hereinafter 2010 DOJ Press Release] (highlighting a $2.3 billion settlement with Pfizer Inc., which included "$669 million recovered under the federal False Claims Act, $1.3 billion in criminal fines and forfeitures, and $331 million in recoveries for state Medicaid programs and the District of Columbia" and noting that "[t]he largest fiscal year 2010 False Claims Act recoveries came from the pharmaceutical and medical device industries, which accounted for $1.6 billion in settlements, including the $669 million from Pfizer Inc., $302 million from AstraZeneca, and $192.7 [million] from Novartis Pharmaceutical Corporation").

212. In fact, "'[q]ui tam' provisions under the False Claims Act allow private individuals acting as qui tam 'relators' [or whistleblowers] to bring a suit on the federal government's behalf involving past or present fraudulent acts." Mackey & Liang, *supra* note 209, at 24 n.115 (citing 31 U.S.C. § 3730(b) (2006)). Whistleblowers are entitled to beteween ten and fifteen percent of a suit's proceeds. 2010 DOJ Press Release, *supra* note 211. ("In fiscal year 2010, [whistleblowers] were awarded $385 million.").

213. *See supra* notes 210, 212 and accompanying text.

214. O'Reilly, *supra* note 85, at 567 (stating that private insurance may cover the injuries, but, for those who rely on government programs such as Medicare or Medicaid, the taxpayers are ultimately responsible for paying medical claims).

215. Patient Protection and Affordable Care Act (PPACA), Pub. L. No. 111-148, 124 Stat. 119 (2010) (codified as amended in scattered sections of 21, 25, 26, 29, and 42 U.S.C.), *amended by* Health Care and Education Reconciliation Act of 2010 (HCERA), Pub. L. No. 111-152, 124 Stat. 1029 (codified in scattered sections of 19, 20, 26, and 42 U.S.C.); *see also* Lawrence O. Gostin et al., *Restoring Health to Health Reform: Integrating Medicine and Public Health to Advance the Population's Well-Being*, 159 U. PA. L. REV. 1777, 1813 (2011) (discussing the PPACA and noting that the Act will expand public access to healthcare by expanding insurance coverage).

216. I.R.C. § 5000A(a), (d), (e) (Supp. IV 2011) (requiring every citizen to obtain healthcare coverage or pay a fine starting in 2014).

217. In fact, Congress appears determined to further reduce the availability of publicly funded healthcare options. *See, e.g.*, Jason Kane, *How Will Debt-Ceiling Deal Affect Medicare for Patients, Doctors?*, PBS NEWSHOUR: THE RUNDOWN BLOG (Aug. 4, 2011 12:16 PM EDT), *available at* http://www.pbs.org/newshour/rundown/2011/08/how-will-the-debt-deal-impact-medicare.html (noting, in the wake of the Fall 2011 federal debt-ceiling negotiations, the

provide complete relief because it accounts only for healthcare costs.[218] Insurance does not provide coverage for tangential losses such as lost wages or income.[219] Ultimately, reliance on insurance as a comprehensive means of providing economic relief following an adverse drug experience is misplaced.

Although estimates vary, various scholars suggest that the average cost to treat adverse drug experiences will soon eclipse $100 billion annually.[220] Moreover, because adverse drug experiences are routinely under-reported,[221] and because increased access to healthcare programs is forthcoming, these estimates are likely conservative.[222] Ultimately, the question becomes whether injuries from unlabeled adverse drug experiences sustained in the postmarketing period are even the type of injury that insurance, or even tort litigation, is intended to compensate.[223] To the contrary, because the pharmaceutical industry benefits from these injuries (allowing companies to improve their products' labeling, expand marketing, and avoid liability in the future), are the pharmaceutical manufacturers not the parties who should pay

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potential for cuts to Medicare and Medicaid as well as an increased eligibility age, co-pays, deductibles, and limitations on elderly supplemental insurance plans).

218. For example, although the PPACA outlawed high-deductible insurance plans, even under the new regime, certain deductibles persist. *See, e.g.*, Abigail R. Moncrieff, *The Freedom of Health*, 159 U. PA. L. REV. 2209, 2248 (2011). *But see* 42 U.S.C. § 18022(c)(2)(A) (Supp. IV 2011) (authorizing small group market plans to impose annual deductibles up to $2,000 for individual plans and $4,000 for all other plans).

219. *See* Amalea Smirniotopoulos, *Bad Medicine: Prescription Drugs, Preemption, and the Potential for a No-Fault Fix*, 35 N.Y.U. REV. L. & SOC. CHANGE 793, 852 (2011) (discussing the importance of wages as a remedy in mass tort litigation).

220. *See, e.g.*, Kristin C. Oberg, *Adverse Drug Reactions*, 63 AM. J. PHARM. EDUC. 199, 199 (1999) ("The national yearly cost of drug related morbidity and mortality was recently estimated at $76.6 billion. . . ."); T. Jeffrey White et al., *Counting the Costs of Drug-Related Adverse Events*, 15 PHARMACOECONOMICS 445, 450 (1999) (describing a study in which costs from adverse-drug reactions exceeded $130 billion nationally).

221. *See supra* note 77 and accompanying text.

222. *See* Nat'l Fed'n of Indep. Bus. v. Sebelius, 132 S. Ct. 2566, 2601 (2012) (finding that the PPACA requires expansion of Medicaid programs by 2014 to individuals under 65 who meet certain economic criteria). This expansion potentially would have extended Medicaid coverage to an additional 17 million individuals presently excluded from their state plans. *See, e.g.*, Abby Goodnough, *Lines Are Drawn over Opting out of Medicaid Plan*, N.Y. TIMES, July 13, 2012, at A1. It would also have provided those individuals with "access to the full apparatus of Medicaid-funded services for their primary conditions, while their providers [would have gained] access to more generous and secure funding," which would have given them "coverage to treat the physical and psychiatric co-morbidities that now often go unaddressed." Harold Pollack, *Health Reform and Public Health: Will Good Policies but Bad Politics Combine to Produce Bad Policy?*, 159 U. PA. L. REV. 2061, 2067 (2011). Nonetheless, following the Supreme Court's decision in *Sebelius*, a handful of state governors have suggested that, for budgetary reasons, they will consider opting out of the additional Medicaid coverage. *See Sebelius*, 132 S. Ct. at 2607–09 (holding that states are not required to expand Medicaid); *see also* Goodnough, *supra*, at A1.

223. Because these risks are unknown by definition, insurers are unable to properly estimate and apply them to insurance premiums. They are also not the type that make recovery under tort theories of law possible.

for that benefit by compensating the injured parties?[224] Although the PPACA currently requires pharmaceutical manufacturers to fund a portion of the new healthcare regime, that contribution does not cover the annual losses attributable to adverse drug experiences.[225] Further, the law does not require that the fees collected from the manufacturers go to the victims of drug injuries.[226]

Requiring the pharmaceutical industry to fully compensate those injured from unlabeled postmarketing adverse events will not cure any expected healthcare shortfall.[227] The fact remains, however, that neither the government nor the public should be responsible for compensating this group of individuals.[228] It is, instead, the group with the most vested interest in the issue, the pharmaceutical manufacturers, that should provide the just compensation to these injured parties.[229]

III. PROPOSING A NO-FAULT ALTERNATIVE

Neither the tort system nor the insurance system can fully and equally compensate early subscribers to prescription drugs who experience an unlabeled adverse event in the postmarketing period.[230] Relief in tort is often a quixotic pursuit, with very few able to prove liability for an injury,[231] and health insurance is expensive and often inadequate.[232] The 10,000-patient

224. David B. Resnik, *Compensation for Research-Related Injuries*, 27 J. LEGAL MED. 263, 266 (2006) ("The principle of justice requires the benefits and burdens of research be distributed fairly.").

225. The PPACA imposes an annual fee on prescription drug manufacturers that will collect a total of $28 billion between 2011 and 2019. *See* Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 9008(a)(1), (b), 124 Stat. 119, 862–63 (2010), *amended by* Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, § 1404(a)(1), (a)(2)(A), (a)(2)(B), 124 Stat. 1029, 1064 (codified as amended at I.R.C. § 4001 (Supp. IV 2011)). By contrast, extrapolating from existing data the estimated costs associated with adverse drug experiences over the same period could potentially exceed $1 trillion. *See supra* note 220 and accompanying text.

226. Pollack, *supra* note 222, at 2072 (finding a flaw in the ability of a congressional majority to cut or eliminate the appropriation on which the fund rests).

227. *See* Henry Huang & Farzad Soleimani, *What Happened to No-Fault? The Role of Error Reporting in Healthcare Reform*, 10 HOUS. J. HEALTH L. & POL'Y 1, 7 (2010) (noting that some critics of the no-fault compensation system worry that costs will drastically increase).

228. *See* Fleming, *supra* note 193, at 308 (suggesting that, because the victims of adverse events deserve compensation, they are essentially medical research volunteers); *see also infra* notes 301–03 and accompanying text.

229. *See* Resnik, *supra* note 224, at 266 (arguing that medication researchers are bound to minimize the harms that a participant receives).

230. *See* discussion *supra* Parts II.A–B.

231. *See supra* notes 192–93 and accompanying text.

232. *See supra* notes 214–18 and accompanying text.

donut hole created by the FDAAA requires more reliable protections for injuries sustained.[233]

Over the last century, numerous compensation schemes tailored to specific sources of harm have been imposed both legislatively and otherwise[234] to provide more efficient and uniform relief to injured parties.[235] In direct response to the tort system's vagaries, these plans attempt to rectify the perceived "lottery aspects" attributable to tort recovery while simultaneously reducing litigation costs.[236] Most significantly, for purposes of this Article, these alternative compensation schemes significantly relax the claimant's burden of proving causation and fault to qualify.[237]

Following in the footsteps of these existing plans, a similar compensation scheme should be adopted for patients exposed to a prescription drug in the drug's initial marketing months.[238] Although this Article does not advocate for

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233. *See supra* note 127 and accompanying text.

234. Workers' compensation plans are one of the earliest and most obvious examples of specialized compensation schemes, rising to prominence in the United States at the turn of the twentieth century. *See, e.g.*, Gregory P. Guyton, *A Brief History of Workers' Compensation*, 19 IOWA ORTHOPAEDIC J. 106, 107–08 (1999) (providing an overview of workers' compensation plans). Since the 1920s, the Warsaw and Montreal Conventions have governed personal injury and death claims arising from international air travel. *See* Convention for the Unification of Certain Rules Relating to International Transportation by Air, *opened for signature* Oct. 12, 1929, 49 Stat. 3000, 137 U.N.T.S. 11; *see also* Convention for the Unification of Certain Rules for International Carriage by Air, *opened for signature May 28, 1999*, S. Treaty Doc. No. 106-45 (entered into force Nov. 4, 2003). In the 1960s, Germany, Japan, and the United Kingdom established funds to compensate children born with birth defects caused by their mothers' ingestion of the drug thalidomide. Linda S. Mullenix, *Prometheus Unbound: The Gulf Coast Claims Facility as a Means for Resolving Mass Tort Claims—A Fund Too Far*, 71 LA. L. REV. 819, 908 (2011). In the U.S., alternative compensation structures have been created to address injuries sustained from sources as varied as vaccine exposure, black lung, and nuclear disaster. *See, e.g.*, 30 U.S.C. §§ 901–945 (2006) (black lung); 42 U.S.C. §§ 300aa-10 to -34 (2006) (vaccines); 42 U.S.C. § 2210 (2006) (nuclear disaster). More recently, plans have been developed to provide compensation to victims of the September 11, 2001 terrorist attacks and the 2010 Deepwater Horizon oil rig explosion and oil spill in the Gulf of Mexico. *See, e.g.*, Linda S. Mullenix & Kristen B. Stewart, *The September 11th Victim Compensation Fund: Fund Approaches to Resolving Mass Tort Litigation*, 9 CONN. INS. L.J. 121, 131–32 (2002); Alfred R. Light, *Designing the Gulf Coast Claims Facility in the Shadow of the Law: A Template from the Superfund § 301(E) Report*, 40 ENVTL. L. REP. NEWS & ANALYSIS 11121, 11121 (2010).

235. *See, e.g.*, Light, *supra* note 234, at 11,124, 11,127 (describing a study group's suggestions for remedying the compensation plans).

236. *See* Fleming, *supra* note 193, at 306; *see also* Peter H. Schuck, *Tort Reform, Kiwi-Style*, 27 YALE L. & POL'Y REV. 187, 188–89 (2008) (noting criticism of a fault-based tort system as evincing "false morality" and resulting in "unpredictable damage awards, and high transaction costs").

237. *See* Lawrence M. Solan & John M. Darley, *Causation, Contribution, and Legal Liability: An Empirical Study*, 64 LAW & CONTEMP. PROBS. 265, 269 (2001) (arguing that the standard of proof for plaintiffs in proving causation should be relaxed).

238. *See infra* Part III.A.

an across-the-board no-fault compensation scheme for drug-related injuries,[239] it does propose a specialized plan designed to address injuries caught in the gap between premarketing clinical study and widespread exposure following initial marketing.[240]

A. The Rationale for Adopting an Administrative Claims Fund

The FDAAA's regulation of postmarketing surveillance of prescription medications should be amended legislatively to include provisions that establish a no-fault compensation scheme to care for patients injured by an unlabeled adverse drug experience within the first eighteen months of marketing.[241] Pharmaceutical manufacturers would exclusively fund this compensation scheme, with contribution being a prerequisite to all new drug applications.[242] Moving away from tort liability in this context is warranted because a no-fault compensation system covering all injuries associated with unlabeled events will be more equitable.[243] Further, requiring contributions from the private industry will reduce the government's obligations and reduce the attendant tax liability imposed on the public to support the insurance system.[244] To maintain the role of litigation, however, the FDAAA's proposed amendments should include an opt-out provision that would allow individuals to exempt themselves from the compensation plan in order to pursue a tort claim.[245]

Modifying the FDAAA to guarantee relief to this discrete patient group is in line with the Act's policy goals.[246] Requiring pharmaceutical manufacturers to compensate early subscribers to a new medication serves as a logical trade-off to both Congress's and the industry's desires to expedite the approval of newly developed medications.[247] Early participants to a newly marketed drug provide

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239. *Cf.* Smirniotopoulos, *supra* note 219, at 834–35 (proposing a no-fault compensation scheme covering all drug and medical device injuries).

240. *See infra* Part III.A.

241. *See* 21 U.S.C. § 355(r)(2)(D) (Supp. IV. 2011); *see also supra* note 125.

242. *Cf.* Lytton et al., *supra* note 202, at 269 (explaining that no-fault accident compensation would be funded by direct payments into a fund financed by risk creators).

243. *See id.* at 279 (arguing that a no-fault compensation scheme would compensate more injured plaintiffs while also reducing administrative costs).

244. *See supra* note 217 and accompanying text (stating that Congress seems to want to reduce publicly funded healthcare options).

245. *See infra* Part III.B.3.

246. *See* 153 CONG. REC. 25,162–63 (2007) (statement of Sen. Michael Enzi) (describing a goal of offering a drug to the public while protecting those harmed by its adverse effects).

247. *See, e.g.*, *id.* at 25,037 (statement of Sen. Edward Kennedy) (noting that the FDAAA will provide "new research tools and better ways to evaluate the safety and effectiveness of drugs," while simultaneously expediting drug development and reducing development costs); *see also* Evans, *supra* note 1, at 444–50, 457–58 (noting that preapproval trials cannot eliminate the potential for risk in the postmarketing period).

value to the pharmaceutical industry by allowing expedited marketing approval, early signal detection, and expedited labeling changes.[248]

Pharmaceutical manufacturers receive significant financial benefits from a new drug's initial postmarketing evaluation.[249] From a financial transaction perspective, these "trial participants" should be compensated for the value added to a drug's worth as a result of the trial tests.[250] But, beyond compensation at the individual level, for Congress's policy initiatives to succeed and for the FDAAA to have value, society *needs* early subscribers to expedite detection of latent adverse effects.[251] Providing no-fault compensation to a newly approved medication's early subscribers will incentivize participation on the part of new patients and encourage physicians to prescribe new drugs.[252]

B. Considerations in Adopting a No-Fault System

Although a no-fault compensation system would improve horizontal equity in the type of relief provided to injured parties, it is not a cure-all.[253] Three principal and intertwined considerations must be addressed before adopting any no-fault plan: (1) eligibility; (2) administration and funding; and (3) limitations on recovery.[254]

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248. *Cf.* Light, *supra* note 234, at 11124 (relating, from the environmental context, supporters' arguments in favor of a compensation scheme alternative to tort litigation as "a useful method of cost allocation and sharing, and a socially responsible method of internalizing the emerging costs of industrial and technological development").

249.

> [In the FDAAA, Congress] gave [the FDA] a toolbox, a whole bunch of different things that they can now do so that drugs will be approved faster, *and then when that clinical trial that we call the whole population of the United States kicks in*, there is a mechanism for following all of those and finding small samples of problems, solutions to those small samples of problems, and the drug that is working for people across this Nation doesn't have to be pulled off the market. It can still work for the people who aren't affected by an adverse reaction. That is a major change we have been able to make.

153 CONG. REC. 25,162–63 (2007) (statement of Sen. Michael Enzi) (emphasis added).

250. *See* Resnik, *supra* note 224, at 266 (arguing that a subject is entitled to compensation or care for harms received during research).

251. Evans, *supra* note 1, at 455–56 (preferring postmarketing studies to premarketing observational clinical trials for purposes of identifying adverse effects).

252. *Cf.* Huang & Soleimani, *supra* note 227, at 30–31 (explaining that a no-fault compensation system provides incentives for doctors to report problems with drugs in the early stages).

253. *See supra* note 243 and accompanying text.

254. *See infra* Part III.B.1–3.

1. Eligibility

Every tort claim requires that the injured party prove that the defendant caused the injury.[255] This causation requirement takes on added significance in the prescription drug context.[256] Because prescription drug users are typically sick, often suffering from a myriad of physical maladies,[257] causation must be based on the outcome rather than the process.[258] Accordingly, even in a no-fault compensation system, the question of whether, and to what extent, causation can be proved must be answered to gain access to any relief.[259]

Specifically, because proof of causation places an onerous burden on injured parties,[260] no-fault compensation systems often invoke a relaxed standard of causation.[261] For example, under the National Vaccine Injury Compensation Program (NVICP),[262] which established a no-fault compensation fund to provide relief for harms resulting from vaccinations, so long as the sustained injury appears on the legislatively created Vaccine Injury Table, the injured party need only show that the vaccination was received and that the injury followed within the statutorily prescribed time period.[263] Moreover, although the NVICP requires proof of off-table claims by a preponderance of the evidence,[264] courts deciding the validity of off-table vaccine injury claims have

255. Solan & Darley, *supra* note 237, at 267 ("It is a legal maxim that people should be held liable for only harms that they have actually caused.").

256. *See infra* note 257 and accompanying text.

257. Robert L. Rabin, *Poking Holes in the Fabric of Tort: A Comment*, 56 DEPAUL L. REV. 293, 304 (2007); *see also* Donald G. Gifford, *The Peculiar Challenges Posed by Latent Diseases Resulting from Mass Products*, 64 MD. L. REV. 613, 695 (2005) (noting the inherent difficulties in establishing causation for latent diseases).

258. Schuck, *supra* note 236, at 199 (stating that causation is more often linked to pre-existing conditions, which the public does not desire to compensate for, rather than to the medication itself).

259. *See id.*

260. *See supra* notes 82–85, 197 and accompanying text (noting the potential for multiple co-factors contributing to adverse drug experiences, which poses a challenge for plaintiffs trying to prove actual causation).

261. *See* Janet Benshoof, *Protecting Consumers, Prodding Companies, and Preventing Conception: Toward a Model Act for NO Fault Liability for Contraceptives*, 23 N.Y.U. REV. L. & SOC. CHANGE 403, 424–25 (1997) (discussing how the Virginia Birth Injury Act and Longshore Act have relaxed the standard of causation required under their no-fault plans); *see also* Donald G. Gifford, *The Death of Causation: Mass Products Torts' Incomplete Incorporation of Social Welfare Principles*, 41 WAKE FOREST L. REV. 943, 971 (2006) (noting several no-fault compensation plans with relaxed causation requirements).

262. 42 U.S.C. §§ 300aa-10 to -34 (2006).

263. Derry Ridgway, *No-Fault Vaccine Insurance: Lessons from the National Vaccine Injury Compensation Programs*, 24 J. HEALTH POL. POL'Y & L. 59, 63 (1999); *see also* 42 U.S.C. § 300aa-14 (establishing time periods within which specified injuries must have occurred to merit a claim).

264. 42 U.S.C. § 300aa-13(a)(1)(A).

incorporated the relaxed standard of causation for table claims when deciding off-table claims as well.[265]

This emphasis on temporal proximity between exposure to the drug and injury as evidence of causation has been adopted by at least one foreign country in implementing its own no-fault drug-injury compensation scheme.[266] In 1978, Sweden adopted a national pharmaceutical insurance system to compensate drug-related injuries.[267] To establish a causal connection between drug and injury, the claimant only needs to "prove that there is a preponderate probability that the injury was caused by the drug," which can be demonstrated by showing "a chronological connection" between ingestion and harm.[268]

Outside of the drug context, analogous domestic and foreign administrative compensation schemes likewise relax causation requirements to expedite relief to injured parties.[269] For example, workers' compensation plans replace proof of actual causation with proof that the injury was sustained during employment.[270] In essence, workers' compensation plans substitute proof of causation with proof of temporality.[271] The rationale behind this construct of workers' compensation plans turns on the questions of probability and who was most likely responsible.[272] New Zealand famously abolished tort law

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265. Betsy J. Grey, *The Plague of Causation in the National Childhood Vaccine Injury Act*, 48 HARV. J. ON LEGIS. 343, 394 (2011) (arguing that the Federal Circuit requires a lower level of proof in vaccine cases to prove causation because the expert opinion of the physician and the patient's medical records can be sufficient).

266. *See infra* notes 267–68 and accompanying text.

267. Lotta Westerhäll, *Disbursement of Indemnity for Injuries Related to Reproductive Drugs and Devices: A Swedish Perspective*, 23 N.Y.U. REV. L. & SOC. CHANGE 443, 443 (1997) (characterizing the pre-1978 system as "weak"). Although tort remedies remain available to Swedish citizens for drug injuries, most injured plaintiffs seek recovery through the pharmaceutical insurance system. *Id.* at 445.

268. *Id.* at 448. (describing the pharmaceutical insurance system's unique rule for establishing causation).

269. *See, e.g.*, Gary T. Schwartz, *Auto No-Fault and First-Party Insurance: Advantages and Problems*, 73 S. CAL. L. REV. 611, 616–19 (2000) (describing state no-fault automobile insurance statutes that provide coverage for economic loss up to specified threshold levels without a showing of fault).

270. Schuck, *supra* note 236, at 199 (generalizing workers' compensation plans as requiring proof only that the injury occurred on the job).

271. *See* Gifford, *supra* note 261, at 965 (providing examples of workers' compensation liability coverage for injuries that occurred while performing job-related functions or that were caused by the employers' conduct).

272.

> The inquiry under the compensation statutes was . . . not who in any individual work-accident case had caused the injury in question, but rather who—employers or employees—was best described as responsible for the aggregate toll of casualties in a given industry. . . . Causation would, in a sense, be determined by legislative fiat for compensation cases as a whole on the theory that employers were best described as the cause of the injury in the majority of the cases; the individualized causation inquiry of tort law would be replaced by an inquiry into

remedies for all personal injury claims in favor of a no-fault compensation scheme in 1974[273] and exemplifies this rationale in its continued reliance on temporality and probability in assessing causation.[274]

More recent federal legislation and executive action in the United States perpetuate the themes of temporality and probability in providing no-fault compensation schemes for injuries sustained in specific contexts.[275] For example, following the 9/11 terrorist attacks, Congress enacted the September 11th Victim Compensation Fund of 2001, a no-fault compensation system covering all persons who were immediately affected by the attack and suffered physical harm.[276] Similarly, the Gulf Coast Claims Facility, the administrative fund developed to compensate injuries resulting from the 2010 Deepwater Horizon oil rig explosion, "presumes" compensability based on "proximity to the coast, or from direct dependence on natural resources such as beaches and fish."[277]

Despite a reduced burden of proof, to make a prima facie case under a no-fault compensation scheme, the claimant must also meet a threshold burden-of-production requirement to establish eligibility.[278] Taking elements from the various alternative compensation arrangements discussed above, a workable proposal for claims assessment can be outlined.[279]

Under the NVICP, for example, the claimant must produce an affidavit and supporting documentation demonstrating that he or she received the vaccination at issue, sustained an injury listed in the Vaccine Injury Table or other injury caused by the vaccine, that the injury was sustained in the relevant time period outlined in the Act, and that the claimant has not previously been compensated for his or her injuries.[280] Similarly, under both the September 11th Victim's Fund and the Gulf Coast Claims Facility, personal injury and

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> the status of the parties accompanied by an unrebuttable presumption of employer causation based on statistical tendencies.

JOHN FABIAN WITT, THE ACCIDENTAL REPUBLIC: CRIPPLED WORKINGMEN, DESTITUTE WIDOWS, AND THE REMAKING OF AMERICAN LAW 173 (2004).

273. *See* Schuck, *supra* note 236, at 188–89 (further explaining that this reform was not demanded by the public but was the result of a small dedicated group working with judges).

274. *See, e.g.*, Accident Compensation Act 2001, pt. 2, § 30(3)–(4), sched. 2 (N.Z.) [hereinafter New Zealand Accident Compensation Act], *available at* http://www.legislation.govt.nz/act/public/2001/0049/latest/DLM99494.html (providing that proof of causation is not required for specific injuries resulting from workplace exposures to specified "agents, dusts, compounds, [and] substances").

275. *See infra* notes 276–77 and accompanying text.

276. Pub. L. No. 107-42, § 405(c)(2)(A), 115 Stat. 230, 239 (2001), *amended by* Pub. L. No. 111-347, § 202(d)–(e), 124 Stat. 3623, 3662 (2011).

277. *See, e.g.*, Light, *supra* note 234, at 11126 (discussing the Gulf Coast Claims Facility and the facility administrator's thoughts on determining compensability for certain classes of individuals).

278. *See infra* notes 280–81 and accompanying text.

279. *See infra* notes 290–91 and accompanying text.

280. 42 U.S.C. § 300aa-11(c) (2006).

wrongful death claimants must produce, inter alia, medical records demonstrating the injury or death, medical records reflecting diagnosis by a physician, records showing expenditures for care, information showing location of injury, and information regarding other means of compensation available to the claimant.[281] Other administrative compensation programs largely follow suit, requiring proof of temporality or proximity, and at least some suggestion by a physician of a causal association.[282]

Once the burdens of production and proof are met, many alternative compensation schemes entitle the body administering the claims to challenge causation.[283] For example, the NVICP allows HHS to deny relief when alternative causation is found.[284] In such a case, however, the burden of proof shifts to the agency.[285] Moreover, evidence showing alternative causation does not overcome the legal presumption created by the Vaccine Injury Table.[286]

In the context of the FDAAA, requiring the injured party to prove actual causation unduly burdens the injured party and can preclude recovery.[287] Also, attempting to create a table of compensable injuries akin to the NVICP would prove unworkable because the injuries are unknown.[288] Instead, as workers' compensation schemes and recent federal legislation have demonstrated,

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281. *See* 28 C.F.R. § 104.21(b)(3) (2011) (providing criteria for submitting a claim under the September 11th Victim Compensation Fund); *see also* BDO CONSULTING, INDEPENDENT EVALUATION OF THE GULF COAST CLAIMS FACILITY REPORT OF FINDINGS AND EVALUATIONS, app. at Ex. Q (2012), *available at* http://www.justice.gov/iso/opa/resources/66520126611210351178.pdf.

282. *See, e.g.*, 20 C.F.R. §§ 718.101–.107 (2011) (requiring, for purposes of a claim under the federal Black Lung Program, proof of injury as demonstrated by medical evidence); U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-060-230, FEDERAL COMPENSATION PROGRAMS: PERSPECTIVE ON FOUR PROGRAMS 37 (2005) [hereinafter FEDERAL COMPENSATION PROGRAMS], *available at* http://www.gao.gov/assets/250/248586.pdf (noting the requirement under the Black Lung Program that proof of a claim must be supported by a statement from a pulmonary specialist); *see also* New Zealand Compensation Act, *supra* note 274, at pt. 3, § 55(1)(a) (requiring the claimant to supplement his or her claim with a "certificate by a registered health professional").

283. *See, e.g.*, Benshoof, *supra* note 261, at 424–25 (noting that, under the NCVIA, the Virginia Birth Injury Act, and the Longshore Act, once the claimant demonstrates an injury, the defendant can rebut it by showing a lack of causal connection); Ridgway, *supra* note 263, at 63 (noting that HHS may dispute causation for injuries on the Vaccine Table by showing an alternative cause).

284. 42 U.S.C. § 300aa-13(a)(1) (2006) (stating that compensation will not be granted if a preponderance of the evidence indicates that the vaccine did not cause the injury).

285. Ridgway, *supra* note 263, at 63 (indicating that HHS must prove alternative causation).

286. *Id.*

287. *See supra* notes 82–85, 197 and accompanying text.

288. *See supra* note 17 and accompanying text (noting the potential for unknown side effects with prescription drugs); *cf.* 42 U.S.C. § 300aa-14(a) (2006) (limiting the presumption of causation to a predefined list of injuries).

temporality is the touchstone of an effective no-fault compensation plan.[289] Accordingly, compensation under any proposed FDAAA modification must be based on the temporality between drug ingestion and the incidence of adverse symptoms.[290] Specifically, this Article proposes that proof of causation for postmarketing unlabeled events should be deemed satisfied by a showing that the patient ingested the medication and was injured thereafter.[291] In compensating injuries from unlabeled adverse events, the FDAAA should require claimants to submit documentation proving: (1) receipt of the drug; (2) diagnosis of injury; and (3) suggestion of causation by or association to ingestion of the medication.[292] As with the NVICP, the administrative board charged with adjudicating claims shall be allowed the opportunity to disprove causation, but must do so by showing an alternative cause.[293]

2. Administration and Funding

Because of the federal government's exclusive regulatory control over the pharmaceutical industry, and the aforementioned benefits provided to that industry by first subscribers to new drugs, this Article proposes that the no-fault compensation scheme for first subscribers be administered by a federal agency and funded entirely by the industry.[294] Although the proposal of a precise administrative structure for claims made by first subscribers to a newly approved drug is beyond the scope of this Article, because of the large patient population impacted by the no-fault compensation fund[295] and its geographic scope, the administration of the fund sensibly should reside within

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289. *See supra* notes 270–72, 275–77 and accompanying text (discussing the temporality standard applied in workers' compensation plans, the September 11th Victims Fund, and the Gulf Coast Claims Facility).

290. *See infra* note 291 and accompanying text. In fact, FDA regulations already provide a framework for labeling changes that rely on temporal proximity between ingestion and injury. *See, e.g.*, 21 C.F.R. § 201.57(c)(6) (2012) (stating that drug "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug"). Some scholars have suggested a temporal relationship between exposure to the drug and observed adverse effect may be the basis. *See supra* note 71 and accompanying text.

291. *Cf.* Ridgway, *supra* note 263, at 63 (noting, in the context of the NVICP, that "[i]f the *first manifestation* of a named injury occurs within the stated time period following vaccination (for example, the first seizure as a manifestation of a seizure disorder), the injury is presumed to have been caused by the vaccine" (emphasis added)).

292. *See supra* notes 280–82 and accompanying text (showing what the plaintiffs must produce in similar no-fault plans).

293. *See supra* notes 283–86 and accompanying text.

294. *See supra* Part III.A.

295. At minimum, that number is 10,000 patients per each prescription drug approved after creation of the fund. *See supra* note 125 and accompanying text. For perspective, in 2011 the FDA approved thirty-five new medicines. Press Release, U.S. Food & Drug Admin., FDA: 35 Innovative New Drugs Approved in Fiscal Year 2011 (Nov. 3, 2011), *available at* http://www.fda.gov/NewsEvents/%20Newsroom/PressAnnouncements/ucm278383.htm.

the federal government, whose institutional knowledge in administering similar funds would benefit those developing this new plan.[296] As other scholars have proposed, one logical place to situate the fund's management would be HHS, one division of which already administers the NVICP.[297] From an administrative standpoint, asking HHS to govern a fund that would bear many of the same characteristics as the NVICP is intuitive.[298] Moreover, as others have noted, separating fund administration from the FDA's governance over drug approval avoids the problem of agency capture.[299] Conversely, by keeping review within HHS, safety information could be disseminated to the FDA for its use in drug safety assessment.[300]

Similarly, asking members of the pharmaceutical industry to finance this proposed compensation structure offers the most logical option with respect to funding the plan.[301] For obvious reasons (i.e., because the manufacturers' products caused the injuries at issue), similar no-fault compensation programs are funded by industry,[302] including vaccine injury programs in Norway, Sweden, Taiwan, and the United States.[303] Further, the infrastructure designed to collect revenue is already in place and requires only an increase in the amounts to be collected to fund this new administrative fund.[304] Both the FDAAA and the PPACA impose annual fees on prescription drug manufacturers in order to fund, respectively, a rejuvenated FDA drug safety

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296. *See supra* notes 263–65 and accompanying text for a discussion of a similar federal fund.

297. *See, e.g.*, Smirniotopoulos, *supra* note 219, at 848–49.

298. Under the NVICP, following a claimant's application to HHS, special masters appointed by the U.S. Court of Federal Claims determine the claimant's eligibility. *See, e.g.*, Ridgway, *supra* note 263, at 63. These decisions are then subject to approval by the Court of Federal Claims and are appealable to the U.S. Court of Appeals for the Federal Circuit. *Id.* This same structure could be expanded and applied with only slight modification to handle claims made by the first 10,000 drug users to a newly marketed drug for unlabeled adverse effects.

299. *See, e.g.*, Smirniotopoulos, *supra* note 219, at 849 (arguing for separation of the drug compensation fund from the FDA so as to insulate it from undue influence, an issue experienced in the past); *cf.* Mullenix, *supra* note 234, at 823 (criticizing the administrator of the Gulf Coast Claims Facility as "a heroic 'special master' with limitless unreviewable discretion, who also is in the employ of the malefactor").

300. *See supra* Part I.B.

301. *See* Fleming, *supra* note 193, at 306 (articulating the common refrain in support of alternative compensation plans as providing for more efficient allocation of resources, which, in this case, would be to ask pharmaceutical manufacturers to fund a plan from which they would benefit); *see also supra* note 251 and accompanying text.

302. The Black Lung Program is funded by an excise tax on coal mined and sold in the United States. FEDERAL COMPENSATION PROGRAMS, *supra* note 282, at 15. The Price-Anderson Act, which was designed to compensate victims of nuclear accident, is funded by nuclear licensees. Mullenix & Stewart, *supra* note 234, at 138–40.

303. *See, e.g.*, Geoffrey Evans, *Vaccine Injury Compensation Programs Worldwide*, 17 VACCINE S25, S26 tbl.1 (1999) (discussing vaccine injury compensation programs worldwide).

304. *See infra* notes 305–07 and accompanying text.

regime and healthcare reform.[305] Imposing an additional fee on prescription drug makers, which could be incorporated into the FDAAA's existing fee structure, would establish private liability insurance for injuries sustained in the relevant period.[306] This insurance structure would be no different from those employed by other no-fault compensation schemes.[307]

3. Limitations on Recovery

In order to avoid an endless stream of claims directed to the fund for newly discovered adverse drug effects, limitations on recovery must be imposed.[308] This Article suggests the following restrictions on access to the fund: (1) time limitations for asserting claims; (2) limitations on specified damages amounts for all injuries and aggregate caps on recovery; and (3) availability of relief pursuant to tort causes of action only after the exhaustion of remedies under the administrative system.[309]

Imposing a time bar on access to the fund is no different from statutes of limitations barring state-law tort claims, and it parallels existing no-fault compensation funds.[310] As this Article has already proposed, claims to be covered by the fund would be limited to those *sustained* during the first eighteen months after marketing approval, parallel to the time period established by the FDAAA for initial review and assessment of newly approved drugs.[311] For purposes of *filing* a claim, this Article proposes extending the time to assert a claim to one year after the close of the FDA's initial eighteen-month review, equaling thirty months after receipt of FDA marketing approval.

This extension avoids fraud and allows for time to identify latent or unrecognized diseases or symptoms.[312] Further, this extension takes advantage of the FDA's existing obligation under the FDAAA to "prepar[e], by 18

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305. *See, e.g.*, Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, § 103(a)–(b), 121 Stat. 823, 826–28 (codified at 21 U.S.C. § 379h(a)(2)–(3), (b) (Supp. IV 2010)) (establishing a prescription drug user fee to be paid, in part, by prescription drug manufacturers); Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 9008(a)(1), (b), 124 Stat. 119, 859–60 (2010), *amended by* Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, § 1404(a)(1), (a)(2)(A), (a)(2)(B), 124 Stat. 1029, 1064 (codified as amended at I.R.C. § 4001 (Supp. IV 2011)) (establishing an annual fee on prescription drug manufacturers).

306. *See supra* Part III.A.

307. *See supra* notes 234–38 and accompanying text.

308. Similar no-fault compensation funds have also imposed certain limitations. For example, a fund established to compensate victims of 9/11 prevents claims from being filed more than two years after the fund's creation. Air Transportation Safety and System Stabilization Act, Pub. L. No. 107-42, § 405(a)(3), 115 Stat. 230, 238 (2001).

309. *See infra* notes 310–27 and accompanying text.

310. *See, e.g.*, Air Transportation Safety and Stabilization Act, § 405(a)(3) (barring claims filed more than two years after the fund's establishment).

311. *See supra* Part I.C.

312. *See, e.g.*, RESTATEMENT (SECOND) OF TORTS § 899 cmt. e (1979).

months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports received for the drug, including identification of any new risks not previously identified."[313] A filing extension beyond the eighteen-month assessment window provides early subscribers an opportunity to review the FDA's postmarketing report on a drug and determine whether symptoms observed or injuries sustained could potentially be attributable to the drug.[314] A one-year extension for filing claims will ensure that new subscribers are not unnecessarily barred from recovery for legitimate harms.[315]

Beyond time limitations on recovery, this Article further proposes the imposition of maximums on recovery by a patient and on the manufacturer's total monetary liability for any one drug.[316] Regarding individual recovery, patients' recovery must be limited to calculable, economic loss,[317] and then only to predetermined amounts as set by the fund's administrative review board.[318] For purposes of determining baseline claims amounts, fund administrators could rely on claims tables from workers' compensation statutes, analogous statutory funds like the NVICP,[319] and commonly used actuarial models.[320] In order to estimate fee amounts to be imposed on manufacturers to finance this fund, it is equally necessary to cap total liability per drug.[321] Once damages tables are developed for individual claims, the amount of liability for each drug is arguably finite. Those individual claims amounts can be used to determine the total potential monetary exposure

313. 21 U.S.C. § 355(r)(2)(D) (Supp. IV 2011).

314. *See infra* note 315 and accompanying text.

315. Conversely, the administrative review board could potentially use reliance on the FDA's eighteen-month new drug assessment to deny a claim that does not appear on the report. The board could argue that sufficient postmarketing testing has not revealed a link to the claimed injury.

316. In addition, this proposal would account for relief obtained through other means (e.g., life insurance) and use those amounts received to offset recovery under the plan. *See, e.g.*, Mullenix, *supra* note 234, at 859 (noting the use of the collateral source rule in administration of both the September 11th Victim Compensation Fund of 2001 and the Gulf Coast Claims Facility).

317. Damages for pain and suffering, and any other noneconomic losses, should not be covered under this program. *Cf. id.* at 854 (noting the exclusion of pain and suffering awards from claims submitted under the September 11th Victim Compensation Fund of 2001). In fact, the September 11th Victim Compensation Fund of 2001 provides a comprehensive definition of economic loss, which could be used as a model for any compensation structure adopted for the FDAAA. Air Transportation Safety and System Stabilization Act, Pub. L. No. 107-42 § 402(5), 115 Stat. 230, 237 (2001).

318. *See infra* notes 319–20 and accompanying text.

319. *See, e.g.*, 42 U.S.C. § 300aa-15 (2006).

320. Mullenix, *supra* note 234, at 854.

321. *See infra* note 322 and accompanying text.

attributable to each newly approved drug and establish a cap on the amounts recoverable for injuries claimed attributable to that medicine.[322]

Lastly, this Article proposes that any adopted plan provide an opt-out opportunity to claimants who wish to pursue relief through tort litigation.[323] Retaining the possibility of tort litigation incentivizes manufacturers to work to prevent harm through continued study and observation of their product in the postmarketing period.[324] Historically, no-fault plans that have not included an opt-out provision have been criticized as intending to serve only industry manufacturers.[325] Conversely, to discourage claimants from forgoing administrative relief in favor of litigation, the proposal would require that claimants first exhaust all available administrative relief before pursuing any possible legal claim.[326] Ultimately, to ensure finality to all claims administered pursuant to the fund, claimants to the fund would be required to waive all legal claims arising from the injuries sustained.[327]

IV. CONCLUSION

This Article has proposed amending the FDAAA to establish a no-fault compensation scheme designed to provide administrative relief to those injured by newly approved prescription drugs during the first eighteen months of the drug's marketing. The FDAAA, in its laudable efforts to improve postmarketing detection of adverse drug experiences attributable to newly approved drugs, has extended observational study of new medications to their first subscribers.

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322. At least one other no-fault compensation fund has instituted a similar cap on liability. *See, e.g.*, Mullenix & Stewart, *supra* note 234, at 140–41 & nn. 86 & 92 (noting the Price-Anderson Act's de facto cap on liability in light of its funding requirements, and the Supreme Court's upholding of the cap in the face of a challenge under the Due Process Clause). *But see id.* at 140 n.86 (noting criticism of the Price-Anderson Act "for setting a limit on liability, in light of the possibility that [funds collected from industry] may not be enough to compensate claimants adequately in the event of an extraordinary nuclear occurrence").

323. Opt-out provisions like the one proposed herein are commonplace in the context of no-fault compensation schemes. *See, e.g.*, 42 U.S.C. § 300aa-11(a)(2)(A) (2006) (providing opt-out criteria for NVICP).

324. *See* Benshoof, *supra* note 261, at 414 (1997). Examples of bad actors within the pharmaceutical industry persist. *See supra* notes 26–30 and accompanying text. However, a compensation plan should be able to separate those greedy and dishonest manufacturers from those acting in good faith. Benshoof, *supra* note 261, at 412.

325. Benshoof, *supra* note 261, at 416–17 (finding that such no-fault plans eliminated many economic safety incentives for manufacturers).

326. *Cf. id.* at 414 (noting a claimant's ability to waive a damages award under NVICP to pursue a civil claim against a manufacturer only after having "fully adjudicate[d] [his or her] claims through the compensation program" (citing 42 U.S.C. §§ 300aa-11(a)(2)(A), 21(a) (2006))).

327. *Cf.* Mullenix & Stewart, *supra* note 234, at 130 (noting that "[t]he centerpiece concept" of the September 11th Victim Compensation Fund of 2001 "is that claimants give up their rights and ability to resolve their claims through the tort litigation system").

An administrative fund serving this patient group is warranted here precisely because traditional tort remedies are practically unavailable to this patient population. Moreover, an administrative fund, financed by the pharmaceutical industry, is intuitive because the information gleaned from this type of postmarketing study inures to the benefit of the industry itself. The FDA's eighteen-month postmarketing surveillance improves manufacturers' abilities to provide comprehensive warnings associated with their products to the public, increasing their products' marketability, while simultaneously reducing manufacturers' exposure to tort claims for failure to identify and warn of these same risks. With the enactment of the FDAAA, the continued viability of newly approved prescription drugs rests on the backs of these first subscribers. This Article asks only that prescription drug manufacturers do the right thing by compensating those who make the continued marketing of their products possible.