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Medical Product Information Incentives and the Transparency Paradox

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Medical Product Information Incentives and the Transparency Paradox[†]

DANIEL R. CAHOY^{*}

[We] are faced with what may be the single greatest drug safety catastrophe in the history of this country or the history of the world. We are talking about a catastrophe that . . . should have been largely or completely avoided.

—Dr. David J. Graham of the FDA¹

Recent allegations that essential safety and efficacy information is often suppressed by medical product manufacturers or poorly evaluated by regulators have led to calls for greater information transparency. The public is justifiably concerned that its ability to conduct an informed risk-benefit assessment of drugs and medical devices is compromised. Several changes have already been made to federal regulatory law and medical research policy to mandate greater disclosure and more changes are being considered. However, it is possible that these measures may backfire by enhancing significant tort-based economic disincentives for generating new information. In other words, greater disclosure requirements could, paradoxically, lead to less information production. The resulting shortfall could be extremely dangerous and have a detrimental effect on health care for years to come. This Article addresses the crisis on the horizon and proposes a unique solution that connects tort law disincentives to information production incentives. It explains why an economically rational company would be expected to respond to transparency with less information and proposes a tort liability limitation as a solution that will encourage a cost-internalizing company to increase information production. This Article also considers the impact of the FDA's recent position on preemption along with other regulatory enhancements and concludes that these are effective, but second-best solutions.

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1. *FDA, Merck, and Vioxx: Putting Patient Safety First?: Hearing Before the S. Comm. on Finance*, 108th Cong. 125 (2004) (statement of Dr. David J. Graham, M.D., MPH, Associate Director for Science, Office of Drug Safety, Center for Drug Evaluation and Research, U.S. Dep't of Health and Human Servs., Fed. & Drug Admin.).

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INTRODUCTION

When results from clinical studies came to light in 2004 demonstrating that a popular and widely prescribed class of pain-relieving drugs could pose significant cardiac risks,² the ensuing controversy grabbed the nation's attention.³ It served as the tipping point for a wave of discontent that had been building for some time.⁴ Most importantly, the discussion exacerbated fears that government regulatory agencies, like the United States Food and Drug Administration (FDA), are not nearly potent enough to effectively investigate, assess, and resolve the risk-benefit equation for various products.⁵ Adding fuel to the fire was the concern that the regulated companies themselves may be negligently or intentionally concealing the true dangers of these and similar goods essential for basic health and quality of life.⁶ Since that time, it has

2. See Barbara Martinez, *Vioxx Lawsuits May Focus on FDA Warning in 2001*, WALL ST. J., Oct. 5, 2004, at B1 (detailing Merck's abrupt decision to pull its pain reliever, Vioxx, from the market after a placebo-controlled clinical trial affirmed information from earlier studies indicating a higher risk of cardiac arrest).

3. Cf. Gardiner Harris, *Drug Safety System is Broken, A Top F.D.A. Official Says*, N.Y. TIMES, June 9, 2005, at A24 ("This system has obviously broken down to some extent, as far as the fully informed provider and the fully informed patient." (quoting Dr. Janet Woodcock, FDA Deputy Commissioner of Operations)).

4. See, e.g., Allison Frankel, *Still Ticking*, AM. LAW., Mar. 2005, at 92 (providing a detailed description of the trials and tribulations faced by Wyeth in attending to litigation stemming from the 1997 discovery that its widely prescribed diet drug combination, fen-phen, caused heart valve damage); Barry Meier, *New Report Of Problems At Guidant*, N.Y. TIMES, July 30, 2005, at C1 (reporting on both the intense scrutiny surrounding medical device manufacturer, Guidant, related to the finding that one of its pacemakers has a tendency to short-circuit and the likelihood that the manufacturer was aware of the danger at least three years before the product was recalled).

5. The concern regarding the FDA's abilities continues, as noted in a recent Wall Street Journal editorial:

The notion that the FDA should "err on the side of safety" sounds like a tautology but is an affront to patients with incurable or poorly treatable diseases . . . we only damage them further with paternalistic public policy that prevents individuals from exercising their own judgment about risks and benefits.

Henry I. Miller, *Paternalism Costs Lives*, WALL ST. J., Mar. 2, 2006, at A14.

6. See Alex Berenson, *Despite Vow, Drug Makers Still Withhold Data*, N.Y. TIMES, May 31, 2005, at A1 (describing the criticism that Merck and Pfizer have faced for failing to disclose

become even more evident that the risk-benefit analysis for medical products is tremendously complex and may vary significantly depending on the individual.⁷ The result has been an unprecedented demand for change in the regulatory, corporate, and scientific environment surrounding the development and marketing of medical products. There is a common theme in this movement: public information disclosure.

The modern health care system depends on providers and consumers having sufficient information about safety and efficacy to make rational choices about available treatments. Manufacturers play an essential role in generating and collecting the information, which is then evaluated and disseminated through the regulatory process. Problems occur when that process breaks down and essential information is either not produced or effectively disclosed—creating information asymmetry.⁸ In the context of recent events, a consensus has emerged that too much information of the type most directly relevant to products already on the market—clinical studies (or trials) of the drug or device—is locked away from the public.⁹ Despite the established forces pushing disclosure, manufacturers may have too much flexibility to keep damaging information secret. Thus, the move toward greater disclosure in the conduct of industry-sponsored clinical trials is *de rigueur*, and initiatives exist that would operate on many levels to achieve this. If secrecy is the ill, transparency is the cure, so the argument goes.

Unfortunately, it is possible that these well-intentioned efforts toward greater disclosure may end up causing more harm than good. The one-sided nature of the discussion ignores the significant impact of post-marketing information-*creation* disincentives. In particular, the fact that the prospect of crippling tort liability hangs precipitously over every piece of negative information brought to light related to the safety or efficacy of a drug or medical device imposes an *ex post* transfer of costs on manufacturers. Because greater transparency generally means greater tort exposure, companies may make the logical choice to simply diminish the source of liability. In other words, companies may reduce the amount of information they create (e.g., by

clinical trial results indicating the dangers of COX-2 painkillers, as well as a lack of consensus in the industry on the appropriate amount of disclosure). As of this writing, Merck has successfully defended nine lawsuits related to its handling of Vioxx information disclosure, and lost five. See Heather Won Tesoriero, *Jury Awards \$47.5 Million to Man in Vioxx Retrial*, WALL ST. J., Mar. 13, 2007, at A3.

7. See, e.g., Miller, *supra* note 5, at A14. In one of the most striking representations of the individual nature of medical products, an FDA advisory panel voted to permit Vioxx back on the market due to its benefits for certain patients. See FDA, Summary Minutes, *Joint Meeting with the Arthritis Drug Advisory Committee* (Feb. 18, 2005), http://www.fda.gov/ohrms/dockets/ac/05/minutes/2005-4090M1_Final.htm. However, the FDA declined to follow that recommendation. See FDA, Public Health Advisory, *FDA Announces Important Changes and Additional Warnings for COX-2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)* (Apr. 7, 2005), <http://www.fda.gov/cder/drug/advisory/COX2.htm>.

8. A severe information asymmetry that results in one party's inability to rationally evaluate a transaction is considered a market failure. ROBERT COOTER & THOMAS ULEN, *LAW & ECONOMICS* 47 (4th ed. 2004) (“[S]evere asymmetries can disrupt markets so much that a social optimum cannot be achieved by voluntary exchange.”) Markets operate most efficiently when critical information is fully available to all parties. See, e.g., *id.*

9. See, e.g., Kay Dickersin & Drummond Rennie, *Registering Clinical Trials*, 290 JAMA 516, 516–17 (2003) (discussing the harm that results from clinical study information remaining confidential).

conducting fewer voluntary clinical trials). Measures meant to increase information may actually result in less. This transparency paradox could produce a more dangerous health care environment and eventually erode public confidence in the system.

Is there a way to resolve the transparency paradox by better balancing tort and regulatory incentives? A large body of literature has considered the proper role of regulation and tort law in medical product innovation or safety,¹⁰ but the issue of private firm information incentives has not been prominently addressed. Recent attempts by the FDA to attenuate tort liability through preemption address this problem to some degree,¹¹ but the impact may be less than could be achieved through a measure more specifically directed to information production. This Article presents a unique perspective on the problem and proposes that the key to resolving the crisis lies in addressing both creation disincentives as well as disclosure incentives. By applying a narrow variant of the familiar tort law limitation on evidence of subsequent remedial measures, this Article suggests that incentives for information creation will be greatly increased.

The Article begins in Part I by considering how private firms are encouraged to produce information in the first place. It describes the ex ante and ex post economic incentives that comprise the so-called dual-track system for generating information on medical products. In Part II, the Article explains how modern “practice-based” tort

10. See, e.g., STEVEN GARBER, *PRODUCT LIABILITY AND THE ECONOMICS OF PHARMACEUTICALS AND MEDICAL DEVICES* (1993); Richard A. Epstein, *Regulatory Paternalism in the Market for Drugs: Lessons from Vioxx and Celebrex*, 5 *YALE J. HEALTH POL'Y L. & ETHICS* 741 (2005); Marc T. Law, *How do Regulators Regulate? Enforcement of the Pure Food and Drugs Act, 1907–38*, 22 *J.L. ECON. & ORG.* 459 (2006); Richard L. Manning, *Products Liability and Prescription Drug Prices in Canada and the United States*, 40 *J.L. & ECON.* 203 (1997); 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 (2005). A major subset of Garber's work relates to the specific question of federal regulatory preemption of state tort law. See, e.g., Robert R. Gasaway, *The Problem of Federal Preemption: Reformulating the Black Letter Rules*, 33 *PEPP. L. REV.* 25 (2005); Michael D. Green, *Statutory Compliance and Tort Liability: Examining the Strongest Case*, 30 *U. MICH. J.L. REFORM* 461 (1996); James T. O'Reilly, *A State of Extinction: Does Food and Drug Administration Approval of a Prescription Drug Label Extinguish State Claims for Inadequate Warning?*, 58 *FOOD & DRUG L.J.* 287 (2003); David G. Owen, *Federal Preemption of Products Liability Claims*, 55 *S.C. L. REV.* 411 (2003); Sasha B. Rieders, *State Law Tort Claims and the FDA: Proposing a Consumer-Oriented Prescription in Medical Device Cases*, 25 *CARDOZO L. REV.* 1159 (2004); Teresa Moran Schwartz, *Regulatory Standards and Products Liability: Striking the Right Balance Between the Two*, *U. MICH. J.L. REFORM* 431 (1997). An entire symposium was held at Georgetown University on the regulatory compliance defense, producing several excellent articles on this topic. See, e.g., Michael D. Green & William B. Schultz, *Tort Law Deference to FDA Regulation of Medical Devices*, 88 *GEO. L.J.* 2119 (2000); Lars Noah, *Rewarding Regulatory Compliance: The Pursuit of Symmetry in Products Liability*, 88 *GEO. L.J.* 2147 (2000); Robert L. Rabin, *Keynote Paper: Reassessing Regulatory Compliance*, 88 *GEO. L.J.* 2049 (2000); Richard B. Stewart, *Regulatory Compliance Preclusion of Tort Liability: Limiting the Dual-Track System*, 88 *GEO. L.J.* 2167 (2000); see also W. Kip Viscusi, Steven R. Rowland, Howard L. Dorfman & Charles J. Walsh, *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, 24 *SETON HALL L. REV.* 1437 (1994).

11. See *infra* Part III.B.1.

disincentives arising from information disclosure can cause companies to produce less than the optimal amount of information. It demonstrates how recent enhancements to information disclosure incentives move the landscape closer to total transparency while the corresponding increases in creation disincentives remain unaddressed, setting the stage for a transparency paradox. The forgoing analysis leads to a proposal in Part III to resolve the paradox by creating a market-based information production incentive through limited tort reform. The second-best nature of an FDA preemption regime or enhanced regulatory authority is also discussed. In view of the enormous social benefits to increased information, the paper concludes that the production incentives outlined herein must be considered if the public is to have the ability to conduct anything approximating a rational evaluation of medical products.

I. INFORMATION INCENTIVES IN THE DUAL-TRACK MEDICAL PRODUCT INFORMATION CREATION AND DISCLOSURE FRAMEWORK

The decision to use or prescribe a drug or medical device is (or should be) a complex assessment of risk and benefit. An individual's decision regarding the safety profile of a particular product can be manipulated, though, by controlling the information the individual receives. No drug or device is completely "safe." Even regulatory agencies that approve the marketing of medical products plainly acknowledge the existence of risk.¹² But a patient or provider may determine that significant benefits outweigh the potential for harm and nevertheless choose to use a particular treatment.¹³ Thus, a rational risk-benefit analysis is an important part of

12. *E.g.*, FDA, MANAGING THE RISKS FROM MEDICAL PRODUCT USE: CREATING A MANAGEMENT FRAMEWORK, REPORT TO THE FDA COMMISSIONER FROM THE TASK FORCE ON RISK MANAGEMENT 21 (1999) [hereinafter FDA RISK MANAGEMENT REPT.] ("Although medical products are required to be safe, safety does not mean zero risk, since all medical products are associated with risks."). *See also* Miller, *supra* note 5 (noting, as a former FDA official, that all drugs have risks and there are dangers in reducing access to potentially harmful drugs if patients that would obtain significant benefits cannot obtain them).

13. If the absence of risk was the sole criteria for permitting medical products to enter the stream of commerce, almost nothing could be sold. Efficacy is really just a question of whether a medical treatment will have the effect it is represented to have under specified conditions. *See* 21 U.S.C. § 355(d)(5) (2000 & Supp. IV 2004) (an application must demonstrate that a new drug is backed by "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof"). Determining efficacy can be considerably more complex than safety, as there are many degrees, and the impact may vary by patient type or specific disease characteristics. *See* HENRY G. GRABOWSKI & JOHN M. VERNON, THE REGULATION OF PHARMACEUTICALS: BALANCING THE BENEFITS AND RISKS 3 (1983) (discussing the efficacy determination). Not surprisingly, the FDA has struggled to determine what evidence is appropriate to demonstrate efficacy adequate to permit approval. *See* Steven R. Salbu, *The FDA and Public Access to New Drugs: Appropriate Levels of Scrutiny in the Wake of HIV, AIDS, and the Diet Drug Debacle*, 79 B.U. L. REV. 93, 97-102 (1999) (discussing the difficulty in finding the perfect balance and noting the historical risks of under-inclusion and over-inclusion); Jeffrey E. Shuren, *The Modern Regulatory Administrative State: A Response to Changing Circumstances*, 38 HARV. J. ON LEGIS. 291, 308-13 (2001) (reviewing the gradual development of the FDA's assessment of efficacy in response to changing circumstances, including the AIDS public health crisis).

prescribing and using medical products, and it is utterly dependant on access to clear, current, and relatively complete safety and efficacy information.

Although a number of entities generate information about medical products, the company that manufactures or markets a product produces the lion's share.¹⁴ Most importantly, private companies carry out the essential clinical trials that directly address the effect of a medical product in a live patient population.¹⁵ For this reason, the current system absolutely depends on the existence of incentives that will compel companies to allocate their own resources to undertake medical product testing and analysis. Functionally speaking, there must be incentives to induce information creation as well as information disclosure. Both must be maximized to provide information sufficient for rational end-user analysis.

How do we craft information incentives for private firms? As a general matter, government and private sector creation and disclosure incentives are derived from two separate legal policy tracks. One depends on creating prospective—or ex ante— incentives to encourage the discovery of safety and efficacy issues before harm occurs. Included in this track are regulatory rules as well as market-based forces. A second, independent track creates retrospective—or ex post— incentives that punish companies

14. See Joe Collier & Ike Iheanacho, *The Pharmaceutical Industry as an Informant*, 360 LANCET 1405 (2002) (“Although the primary function of drug companies is to develop and market drugs, these companies spend more time and resources generating, gathering, and disseminating information.”); Jennifer Couzin, *Gaps in the Safety Net*, SCIENCE, Jan. 14, 2005, at 198, 196 (“FDA generally relies on companies to run postmarketing trials, called phase IV studies, often requesting them as a condition for a drug’s approval.”).

15. No study is considered as critical or useful in realistically gauging performance as one using human participants, also known as a clinical trial. See LAWRENCE M. FRIEDMAN, CURT D. FURBERG & DAVID L. DEMETS, *FUNDAMENTALS OF CLINICAL TRIALS* 1 (3d ed. 1998) (“It is only in the past few decades that the clinical trial has emerged as the preferred method in the evaluation of medical interventions.”). More specifically, the variant known as the randomized clinical trial (also referred to as a randomized controlled trial (RCT)) is considered the “gold standard” of medical research. See ROBERT J. LEVINE, *ETHICS AND REGULATION OF CLINICAL RESEARCH* 211 (2d ed. 1986) (“[T]he RCT is the *gold standard* for evaluating therapeutic efficacy.”) (emphasis in original); Dickensin & Rennie, *supra* note 9, at 516; Steven M. Teutsch, Marc L. Berger & Milton C. Weinstein, *Comparative Effectiveness: Asking the Right Questions, Choosing the Right Method*, 24 HEALTH AFF. 128, 129 (2005) (“When assessing efficacy, RCTs are considered to be the gold standard.”). In the modern world of medical product review, any conclusion regarding a medical product’s safety or efficacy ultimately depends on what is found in these small, controlled trials on humans. Of course, a number of pieces of information are relevant to the risk-benefit analysis. For example, an elucidation of the chemical structure, studies on stability, and descriptions of the physiochemical characteristics can tell a trained eye much about how a drug will be likely to act in a human physiological setting. See, e.g., FDA, *GUIDANCE FOR INDUSTRY: S7A SAFETY PHARMACOLOGY STUDIES FOR HUMAN PHARMACEUTICALS* 2–3 (2001) (explaining the rationale for the non-clinical pharmacology studies in drug approval applications). Similarly, the testing of certain medical devices in animals can be an accurate predictor of the toxicity and absorption profile in human patients. FDA, *FROM TEST TUBE TO PATIENT: IMPROVING HEALTH THROUGH HUMAN DRUGS* 16 (1999) [hereinafter TEST TUBE] (“[I]n animal testing, scientists measure how much of a drug is absorbed into the blood, how it is broken down chemically in the body, the toxicity of its breakdown products (metabolites), and how quickly the drug and its metabolites are excreted from the body.”).

for the harm resulting from the failure to discover or disseminate information. Such incentives include tort-based product liability and consumer protection litigation.

Ideally, the two tracks are complementary. For example, an *ex post* litigation incentive may fill in an *ex ante* regulatory gap to inspire a company to create or release information that would otherwise be withheld from the public. However, there is also a great potential for conflict. The independent nature of the incentive systems may result in the formation of unintended information disincentives. This occurs most prominently when the broad and uncontrolled nature of certain *ex post* liability resulting from *disclosure* abuts the limited power of *creation*-inducing *ex ante* incentives. In many cases, it is likely that the disincentives will be strong enough to reduce the production of important medical product information. For efficient flow, the impact of the two tracks on firm behavior must be assessed and balanced, particularly in crafting new measures that may disturb the status quo.

A. The Limited Nature of Ex Ante Incentives

From a societal perspective, the need to uncover medical product safety and efficacy information before harm results is obvious. It follows that there is an inclination to transfer the societal desire for loss avoidance to firms in the form of *ex ante* information production requirements. One is not at all surprised to find that a manufacturer encounters the strongest *ex ante* information disclosure and creation incentives through regulatory requirements for the sale of medical products. Powerful incentives derived from the need for marketplace success additionally exist to solicit voluntary information production. Together, these forces encourage the production of a great deal of important information.

But the *ex ante* system is far from complete. There are limitations in these incentives that necessarily leave significant information gaps. Thus, in view of their bounded nature, one must consider *ex ante* incentives with an eye toward how additional mechanisms can add to the risk-benefit picture.

1. Circumscribed Information Generation and Disclosure Through the Regulatory Process

The FDA—the U.S. federal agency that has the power to control the interstate marketing of medical products¹⁶—induces a substantial amount of information production, and its approval procedures are representative of the regulatory review process at its most sophisticated level.¹⁷ The *ex ante* information incentive structure in

16. In the United States, the FDA possesses the authority to regulate, *inter alia*, the marketing of drugs, § 355(a) (“No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.”), biologics, 42 U.S.C. § 262 (2000 & Supp. IV 2004) (“No person shall introduce or deliver for introduction into interstate commerce any biological product unless . . . a biologics license is in effect for the biological product . . .”), and medical devices, 21 U.S.C. §§ 360, 360e (2000 & Supp. IV 2004) (requiring approval for various classes of medical devices), including the decision whether to allow a sale at all.

17. Regulatory agencies in many other countries also play an important role in information production, and some—such as the European Union’s European Medicines Agency (EMA)

place here is extraordinarily straightforward. Firms must produce sufficient information to convince the FDA to approve the drug, biologic, or medical device as safe and effective for marketing.¹⁸ If an applicant cannot convince the FDA that the data is sufficient, the sunk research and development costs will never be recouped.¹⁹ Moreover, expected future revenue streams for the marketing of the drug will not be realized. Thus, it is to an applicant's advantage to make significant investments in information production.

The agency's role begins when an applicant files an application to use the drug or device in preliminary studies on humans.²⁰ This initial requirement is the jumping off point for the essential clinical trials that will form the basis for assessing safety and efficacy.²¹ Following the completion of clinical trials sufficient to satisfy the FDA's approval standards, a company may choose to submit a formal application for approval to market.²² In reviewing the application, the FDA may base its analysis on the

and Japan's Ministry of Health, Labor, and Welfare (MHLW)—possess a level of sophistication that comports with the FDA's. See EMEA, EUROPEAN MEDICINES AGENCY (June 2006), http://www.emea.eu.int/pdfs/general/direct/organigramme/EN_Organigramme.pdf; Thomas M. Moore & Siobhan A. Cullen, *Impact of Global Pharmaceutical Regulations on U.S. Products Liability Exposure*, 66 DEF. COUNS. J. 101, 105 (1999). All contribute to the information profile of a product with an international market. Although distinct information may be collected, information that is significant in understanding a product's safety-efficacy profile is even more likely to be shared between primary international regulatory agencies. See, e.g., FDA, CONFIDENTIALITY ARRANGEMENTS CONCLUDED BETWEEN THE EU (EC AND EMEA) AND THE U.S. FDA/DHHS IMPLEMENTATION PLAN FOR MEDICINAL PRODUCTS FOR HUMAN USE, <http://www.fda.gov/oia/arrangements0904.html>. Since, on balance, the incentives provided by the most prominent regulatory agencies are similar, a description of the FDA's basic system is representative.

18. See approval requirements under the Food, Drug, and Cosmetic Act (FDCA), covering drugs, § 355(d)(5), the Public Health Services Act (PHSA), covering most biologics not covered under the FDCA, 21 C.F.R. § 601.2 (2006), and the Medical Devices Act, 21 U.S.C. § 360(b) (2000 & Supp. IV 2004). The FDA's approach is holistic, weighing the strength of a patient's response to the treatment versus the risks. See Margaret Gilhooley, *When Drugs are Safe for Some but Not Others: The FDA Experience and Alternatives for Product Liability*, 36 HOUS. L. REV. 927, 938–40 (1999) (explaining that some uses pose significantly more risks than others and this must be taken into account in the review process). A very strong response may outweigh minor safety risks, and vice versa.

19. See GARBNER, *supra* note 10, at 41 (noting that the FDA affects economic outcomes primarily through its authority to restrict marketing of products).

20. Cf. Sharona Hoffman, *The Use of Placebos in Clinical Trials: Responsible Research or Unethical Practice?*, 33 CONN. L. REV. 449, 466–67 (2001) (describing the use of investigational new drugs in clinical trials).

21. The application for approval to test a new drug or biologic compound is known as an investigational new drug (IND) application. See § 355(i) (outlining the investigational drug exception). INDs mark the start of a long research process. See Richard J. Findlay, *Originator Drug Development*, 54 FOOD & DRUG L.J. 227, 228 fig.1 (1999) (figure showing timeline of drug development). Medical device premarketing studies require the filing of an investigational device exemption (IDE) and follow a similar, if less rigidly defined, investigation scheme. See 21 C.F.R. § 812.1 (2006).

22. Manufacturers submit a new drug application (NDA) in the case of a drug or a biologic license application (BLA) in the case of treatments with biotechnology origins like vaccines. See § 355(a); 21 C.F.R. § 314.2 (2006) (purpose of drug application process); 42 U.S.C. § 262 (2000 & Supp. IV 2004); 21 C.F.R. § 601.2 (2006) (applications for biologics and procedures

submitted information or request additional evidence such as new clinical trials to confirm the safety and efficacy profile of the treatment.²³

Strict regulatory standards ensure that a wealth of information results from the pre-approval process, and this stage in product development stands as the key *ex ante* information generation point. However, information disclosure is at a minimum. This is so because, to a great extent, the process surrounding regulatory applications and approvals is confidential and the information disclosure requirements are limited. Applicants do not have to publicly disclose that a preliminary study application has been filed, nor must they disclose to anyone but the FDA (and local institutional review boards) that one has been withdrawn.²⁴ Although applicants have the obligation to file periodic reports containing summary information on premarketing studies with the FDA,²⁵ the final details of the studies may be completely protected from disclosure under certain conditions such as application withdrawal.²⁶ Additionally, the submission of the approval application is itself confidential, as is the detailed review by the FDA.²⁷ Such restrictions provide a company with a great deal of control over information related to a new product, at least until marketing approval.

Perhaps more surprising, details of the studies and other data underlying an application may not be available even *after* it is approved. Although the approval package is nominally public—the FDA is authorized to release the submitted

for filing). In the context of medical devices, applicants submit either a premarket approval application (PMA) for particularly risky products, *see* 21 U.S.C. § 360e (2000 & Supp. IV 2004) (outlining premarket approval requirements); 21 C.F.R. § 814.1 (2006) (outlining requirement of having an approved premarket approval application)), or a premarket notification, *see* § 360(k); 21 C.F.R. § 807.81 (2006).

23. *See, e.g.*, TEST TUBE, *supra* note 15, at 34 (“If CDER’s [Center for Drug Evaluation and Research] evaluation of studies reveals major deficiencies, substantially more work by the sponsor may be needed, ranging from further analyses to the conduct of new studies . . .”).

24. *See* 21 C.F.R. § 312.130 (2006) (“The existence of an investigational new drug application will not be disclosed by FDA unless it has previously been publicly disclosed or acknowledged.”); 21 C.F.R. § 812.38 (2006) (“FDA will not disclose the existence of an IDE unless its existence has previously been publicly disclosed or acknowledged . . .”).

25. 21 C.F.R. § 312.33 (2006) (requiring IND annual reports); 21 C.F.R. § 812.150 (2006) (requiring IDE reports).

26. However, if an IND is withdrawn for safety reasons, the FDA and other parties associated with the clinical trials (e.g., investigators and institutional review boards) must be informed with the reason for withdrawal. 21 C.F.R. § 312.38 (2006). Additionally, IND sponsors must report adverse events within fifteen days after learning of them during a series of IND clinical trials. 21 C.F.R. § 312.32 (2006). Studies that relate to indications other than those sought in an NDA may be deemphasized if they are primarily related to efficacy as opposed to safety, and such studies must be reported, 21 C.F.R. § 314.50 (d)(5) (2006). However, the FDA states that they are primarily used to assess safety and suggests that they may be separated from the primary safety and efficacy studies in the application documentation. *See* FDA, GUIDELINE FOR THE FORMAT AND CONTENT OF THE CLINICAL AND STATISTICAL SECTIONS OF NEW DRUG APPLICATIONS 25–26 (1988) (CDER guidance on NDA formats).

27. 21 C.F.R. § 314.430(b) (2006) (“FDA will not publicly disclose the existence of an application or abbreviated application before an approvable letter is sent to the applicant . . .”); 21 C.F.R. § 601.51(b) (2006) (“The existence of a biological product file will not be disclosed by the Food and Drug Administration before a biologics license application has been approved . . .”); 21 C.F.R. § 814.9 (2006) (“Confidentiality of data and information in a premarket approval application (PMA) file.”).

information via a Freedom of Information Act (FOIA) request²⁸ absent “extraordinary circumstances”—FDA regulations make establishing extraordinary circumstances quite easy, and even routine.²⁹ An applicant may claim a number of reasons for requesting secrecy, including that many documents contain trade secrets or even that the data could be used by a competitor to seek approval marketing overseas.³⁰ Without an affirmative act on the applicant’s part, this information may not be released into the public domain.

The shroud of secrecy surrounding preliminary drug studies exists ostensibly to protect trade secret and other proprietary business strategy information.³¹ It is also probably recognition of the fact that information resulting from the studies can be quite preliminary and lead to misleading conclusions regarding treatment.³² In practice, the secrecy gives applicants an initial opportunity to conduct substantial testing outside of the public eye.

In view of the disclosure limitations, it is clear that the FDA’s preapproval rules are imperfect as an information production mechanism, but they are even more lacking in the postmarketing phase where the approval incentive is eliminated.³³ This is a critical information production point, because many of the most important safety and efficacy problems only become clear after a drug has entered the patient population.³⁴ Clinical

28. See Freedom of Information Act, 5 U.S.C. § 552(b) (2000 & Supp. IV 2004); 21 U.S.C. § 355(l) (2000 & Supp. IV 2004) (public disclosure of safety and effectiveness data); Pub. Citizen Health Research Group v. FDA., 185 F.3d 898, 901 (D.C. Cir. 1999) (affirming the FDA’s power to withhold IND studies based on Exemption 4 of FOIA). The FDA’s official policy is to make the “fullest possible disclosure of records to the public” consistent with its other goals and obligations. 21 C.F.R. § 20.20 (2006).

29. See DONALD O. BEERS, *GENERIC AND INNOVATOR DRUGS: A GUIDE TO FDA APPROVAL REQUIREMENTS* § 5.01 (1999) (“In fact, for almost every application, FDA has been willing to find ‘extraordinary circumstances’ for refusal to release such data . . .”).

30. *Id.*

31. 21 C.F.R. §§ 20.61, 314.430, 601.51 (2006). In fact, forced disclosure of trade secret information in order to obtain agency approval could be considered a taking. See *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1002–04 (1984) (disclosure of trade secrets submitted in compliance with Environmental Protection Agency regulations could constitute a taking).

32. Analogously, the FDA places some restraints on the ability of the manufacturers to advertise and otherwise disclose information during the approval process. See George W. Evans & Arnold I. Friede, *The Food and Drug Administration’s Regulation of Prescription Drug Manufacturer Speech: A First Amendment Analysis*, 58 *FOOD & DRUG L.J.* 365, 401–03 (2003).

33. See, e.g., 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, 343–61 (2006) (providing a very detailed review of the FDA’s authority to require or request postapproval studies and concluding that it must be based on strained statutory interpretation that is ultimately “dubious”); Struve, *supra* note 10, at 600–01 (stating that there are reasons to question the agency’s effectiveness in monitoring postmarketing safety and describing internal FDA survey results that reflect this sentiment).

34. Steenburg, *supra* note 33, at 375 (“Vioxx also highlights the reality that FDA is in a weaker position to press for Phase IV studies once a drug is on the market—a time when the need for such investigations can come into sharper focus.”). A survey of the origins of 206 “black box” warnings, the FDA’s most extreme caution, found that only twenty-nine percent were the result of premarketing clinical trials. See, e.g., Judith E. Beach, Gerald A. Faich, F. Gail Bormel & Frank J. Sasinowski, *Black Box Warnings in Prescription Drug Labeling:*

studies that occur after FDA approval are known as phase IV, or postmarketing studies.³⁵ Such studies are generally not required for most drugs and devices.³⁶ If an issue arises that is deemed too minor to preclude approval, the FDA will often seek agreement with an applicant to conduct postmarketing studies.³⁷ An applicant need not agree, but there may be a risk to objecting when approval has not been granted.³⁸ Even so, the FDA has very little authority to enforce the agreement.³⁹

Results of a Survey of 206 Drugs, 53 FOOD & DRUG L.J. 403, 408 (1998).

35. See LEVINE, *supra* note 15, at 6–7; Richard J. Findlay, *Originator Drug Development*, 54 FOOD & DRUG L.J. 227, 227 (1999) (“After FDA approval, postmarketing testing continues in Phase IV for, *inter alia*, side effects, clinical education, and possible new indications.”).

36. *But see* 21 U.S.C. § 356 (2000); 21 C.F.R. §§ 314.510, 601.41 (2004) (postmarketing studies may be required for fast-track approval applications); 21 C.F.R. §§ 314.55, 601.27 (2004) (postmarketing studies may be required for deferred pediatric approval).

37. See FDA, GUIDANCE FOR INDUSTRY, REPORTS ON THE STATUS OF POSTMARKETING STUDIES—IMPLEMENTATION OF SECTION 130 OF THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT OF 1997 4 (2006) [hereinafter FDAMA 130 GUIDANCE] (“A postmarketing study might be conducted because you and FDA *agree*, in writing, that one or more such study should be conducted.”) (emphasis in original). Annual reports of these, as well as required studies, must be submitted to the FDA. 21 U.S.C. § 356b (2000 & Supp. IV 2004); 21 C.F.R. § 314.81(b)(2)(vii) (2004).

38. Applicants are generally willing to make such concessions to ensure favorable treatment in the approval process. Steenburg, *supra* note 33, at 334–37 (“[C]ompanies may ‘agree’ to postmarketing commitments as a means to push drugs through the pipeline . . .”). In fact, a recent report estimated that seventy-three percent of new molecular entity drug approvals from 1998–2003 issue with postmarketing study commitments. Tufts Center for the Study of Drug Development, *FDA Requested Postmarketing Studies in 73% of Recent New Drug Approvals*, IMPACT REP., July–Aug. 2004, at 2.

39. The applicable statutes do not provide the FDA with the explicit power to enforce voluntary agreements to conduct studies. Theoretically, the FDA could determine that such a study was a record or report “necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for [revoking an approval under] subsection (e) of this section.” 21 U.S.C. § 355(k) (2000 & Supp. IV 2004); *see* Steenburg, *supra* note 33, at 343 (noting that the FDA relies on this interpretation for authority). In that case, a failure to conduct the study could be grounds for the FDA to begin revocation proceedings (which are by no means instantaneous). *See* § 355(e). The FDA has claimed such power in a 2002 report to Congress. *See* FDA, REPORT TO CONGRESS, REPORTS ON POSTMARKETING STUDIES [hereinafter FDAMA 130] (2002), *available at* <http://www.fda.gov/cber/fdama/pstmrktfdama130.pdf> (stating that in addition to authority to mandate deferred pediatric studies and accelerated approval studies, “FDA has authority to order an applicant to conduct a study if the information is necessary in order to facilitate a determination whether grounds exist for revocation of approval (21 U.S.C. § 355(k))”). It is also reflected in the relevant sections of the *Code of Federal Regulations*. *See* 21 C.F.R. §§ 314.530, 601.43 (2004). However, this appears to be a rather strained reading of the statute, as it actually refers to the reporting of studies conducted, not the failure to conduct a study. § 355(k). Rather, the FDA’s primary power seems to be a statutory right to publicly embarrass a company that does not comply:

If a sponsor fails to complete an agreed upon study required by this section by its original or otherwise negotiated deadline, the Secretary shall publish a statement on the Internet site of the Food and Drug Administration stating that the study was not completed and, if the reasons for such failure to complete the study were not

The FDA's ability to continue its evaluation after a product is on the market is significantly restrained by the content of the approval negotiation. The agency cannot require drug companies to conduct new trials once a drug is on the market.⁴⁰ Other information is gathered, but it may not be as useful in making medical treatment decisions.⁴¹ Information gaps must be filled, if at all, through the voluntary actions of private companies.⁴² Additional incentives must exist to induce such behavior.⁴³

satisfactory to the Secretary, a statement that such reasons were not satisfactory to the Secretary.

21 U.S.C. § 356b(d) (2000).

40. *FDA Calls for Warning Label Authority, Others Seek More Trials, National Registry*, 33 *Prod. Safety & Liab. Rep. (BNA) No. 11*, at 278 (Mar. 14, 2005) (citing the FDA's Deputy Director of the Office of New Drugs, Sandra Kweder) ("The FDA also does not have the authority to require drug companies to conduct new clinical trials after a drug is on the market."). There is, arguably, some ambiguity on this point. *See* Steenburg, *supra* note 33, at 345–47 (recounting several conflicting statements from government officials and legislators regarding the FDA's postmarketing authority); INSTITUTE OF MEDICINE OF THE NATIONAL ACADEMIES, *THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC* 155–56 (2007) [hereinafter IOM REPORT] ("FDA's statutory authority to require postmarketing studies has been a subject of debate for decades.").

41. For example, there are adverse event reports that describe a single patient's medical problem encountered while using the drug. *See* § 355(k); 21 C.F.R. §§ 310.305, 314.80 (2004) (drugs and biologics); *see also* 21 U.S.C. § 360l (2000) & 21 C.F.R. § 814.82 (2004) (medical devices). The FDA uses the reports to spot potential problems, and may even issue alerts to the public based on the information. Additionally, a manufacturer may make emergency changes to a label prior to FDA review in response to adverse incidents. 21 C.F.R. § 314.70(c)(2)(i) (2005). The reports themselves are fully available to the public, and easily viewed at the FDA's MedWatch website (which also provides the portal for reporting incidents). *See* MedWatch: The FDA Safety Information and Adverse Event Reporting Program, <http://www.fda.gov/medwatch/index.html> (last visited Apr. 2, 2007). As accessible as these data are, they often provide a significantly more ambiguous overview of safety than a large clinical trial. Given the uncontrolled nature of adverse incident reports, it can be difficult to make a causal link to the treatment or device in question. Moreover, reporting adverse incidents is mandatory only for manufacturers (over whom the FDA has regulatory authority). 21 C.F.R. §§ 314.80, 600.80, 803.50 (2004). Participation by physicians and patients, the parties who surely have the most information on adverse consequences, is entirely voluntary. FDA, *MedWatch—How to Report Serious Adverse Events*, <http://www.fda.gov/medwatch/how.htm> (last visited Apr. 12, 2007) (categorizing physician and consumer reporting as voluntary, but manufacturer, distributor, packer, and medical device user facility reporting as mandatory). Therefore, the picture provided by MedWatch is incomplete as well as imprecise.

42. A firm is permitted to conduct postmarketing studies by its own volition. The results of these phase IV studies must also be reported to the FDA in the case of drugs, but *not* in the case of biologics and medical devices. *See* 21 C.F.R. § 314.81(b)(2)(viii) (2004) (requiring that an annual report for approved application include the status of postmarketing studies other than required and agreed upon); FDAMA 130 GUIDANCE, *supra* note 37, at 6 ("Under existing rules, you, as an applicant for a biological product marketed under a biologics license application (BLA) . . . are not generally required to submit annual reports on the status of postmarketing studies."). The FDA apparently does not require medical device reports and records other than those pertaining to postmarketing surveillance. *See* 21 C.F.R. § 822.38 (2004).

43. There are, of course, practical limits to regulatory information creation. A medical product could undergo an infinite number of test and clinical studies, and risks would still remain. *See* Mary K. Olson, *Pharmaceutical Policy Change and the Safety of New Drugs*, 45

2. Market Incentives Encourage Information Production and Disclosure to Increase Sales and Firm Profile

The power of the marketplace can provide a serious counterweight to the disclosure limitations of regulatory incentives. Although the drug and medical device industry may be permitted to keep information secret in a number of cases, the economic benefits of early, limited disclosure can often outweigh the harm from a partial loss of confidentiality. For example, large pharmaceutical companies in particular are consumed by the need to demonstrate a future pipeline of new drugs as a measure of overall corporate health.⁴⁴ Smaller biotech or medical device companies may also feel pressure to establish that products in development are still moving through the FDA approval process.⁴⁵ One of the best ways of establishing the viability of promising new research is to disclose the existence of current preapproval studies.⁴⁶ Postmarketing studies may also be disclosed to create interest in new indications for an existing product.⁴⁷ And there may be considerable value in using clinical study information as a signal to other companies of a desire to move into a particular treatment area.

Companies may disclose clinical information directly through a variety of means including: websites, annual reports, or letters to physicians. Several independent news organizations also collect this information and make it available to the public.⁴⁸ Of

J.L. & ECON. 615, 618 (2002) (“Even though firms spend many years and invest millions of dollars to gather this evidence, it is impossible to resolve all uncertainty about drug safety (or effectiveness) at the time of FDA approval.”). Additionally, even if one could spend years conducting every form of clinical trial imaginable, many problems would not appear until the treatment reached a larger patient population. John P.A. Ioannidis, *Contradicted and Initially Stronger Effects in Highly Cited Clinical Research*, 294 JAMA 218, 220 (2005) (finding that, of forty-five highly cited clinical trials that showed a benefit for clinical intervention, fourteen (thirty-two percent) were either contradicted by, or found to show stronger effects than, subsequent studies).

44. See, e.g., Jesse Eisinger, *Long & Short: What Ails the Drug Industry? Go Ask Wall Street and Its Short-Term Vision*, WALL ST. J., Oct. 13, 2004, at C1 (considering the future pipelines of several pharmaceutical companies and the impropriety of focusing on short-term financial goals); John Simons, *Lilly Goes off Prozac*, FORTUNE, June 28, 2004, at 179 (“Lilly is a bright spot in Big Pharma, widely acknowledged to have the industry’s most bountiful pipeline of new products.”).

45. See Donna Marie DeCarolis & David L. Deeds, *The Impact of Stocks and Flows of Organizational Knowledge on Firm Performance: An Empirical Investigation of the Biotechnology Industry*, 20 STRATEGIC MGMT. J. 953, 964–65 (1999) (analyzing information that indicates the success of a biotechnology company, and concluding that reports of product pipelines are positively correlated).

46. In general, late-stage “phase III studies” are used because a company can be more confident that the treatment at issue will actually make it to market. On the other hand, the Imclone debacle certainly highlights the risks of over-confidence. See David Denby, *The Life of the Party*, FORTUNE, Jan. 26, 2004, at 99 (detailing the downfall of former Imclone CEO, Sam Waksal, for insider trading related to the cancer drug, Erbitux, which was thought to be days away from FDA approval in 2003).

47. See Howard L. Dorfman & Linda Pissott Reig, *Avoiding Legal and Ethical Pitfalls of Industry-Sponsored Research: The Co-Existence of Research, Scholarship, and Marketing in the Pharmaceutical Industry*, 59 FOOD & DRUG L.J. 595, 602, 612–13 (2004).

48. For example, the *Wall Street Journal* has an online column titled “Checkup” that breaks

course, the extent to which this may result in the selective disclosure of favorable information is an issue of concern for both the regulatory⁴⁹ and financial⁵⁰ communities. Further, the results of voluntarily disclosed studies are usually briefly summarized at best and one cannot realistically conduct an independent evaluation of the information.

Additionally, approval by the private scientific community can induce the voluntary disclosure of information that could otherwise be held in confidence under FDA regulations. In order to support a claim of efficacy, particularly in comparison to other available treatments, great weight is placed on the conclusions of the private sector (generally academic) medical establishment.⁵¹ The endorsement of researchers in the field can create a very strong economic incentive by dramatically increasing a product's sales and use. The most prominent journals have a tremendous impact and may individually build or destroy a product's market.⁵² Companies may even seek to engage in research beyond the requirements of FDA approval if it may lead to such broad acceptance. At the very least, there may be an incentive to disclose studies conducted as part of the application process. This marketplace disclosure outlet is certainly far from perfect,⁵³ but the increase in overall information production is likely significant.

down new drugs by condition and describes the clinical testing phase. See <http://online.wsj.com/article/0,,checkup,00.html> (subscription required for access).

49. See Dorfman & Reig, *supra* note 47, at 612–14.

50. The Securities and Exchange Commission (SEC), in particular, is concerned with companies misleading investors by manipulating studies related to FDA approval proceedings. The SEC has taken action against companies that present an incomplete picture of the available data. See *British Biotech PLC*, Admin. Proc. No. 3-9915, (Jun. 10, 1999), available at <http://www.sec.gov/litigation/admin/34-41505.htm> (instituting a 21C cease-and-desist proceeding against a biotechnology company that suggested favorable clinical trial results based on a measure disputed by the FDA).

51. Richard A. Rettig, *The Industrialization of Clinical Research*, 19 HEALTH AFF. 129, 141 (2000) (describing the dominance of academic health centers (AHC), but stating that they may be in decline). According to former *New England Journal of Medicine* editor, Marcia Angell, the percentage of studies conducted in academia may have already fallen below sixty percent. See MARCIA ANGELL, *THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT* 101 (2004).

52. See Collier & Iheanacho, *supra* note 14, at 1405 (“Drug companies recognise the enormous value of publishing clinical trial reports about their products in medical journals, especially when the journal is prestigious.”).

53. Critics have noted that published medical research can suffer from several institutional biases. For example, a detailed literature review conducted by the American Medical Association (AMA) found support for the notion that “[s]tudies with positive findings are more likely to be published than studies with negative or null results” See AMA, *CSA REPORT, INFLUENCE OF FUNDING SOURCE ON OUTCOME, VALIDITY AND RELIABILITY OF PHARMACEUTICAL RESEARCH* (June 2004), available at <http://www.ama-assn.org/ama/pub/category/14314.html>. Additionally, reviewers may be at least subconsciously biased against studies that contradict their own work, leading to a kind of inertia in clinical study publication. See Tom Reynolds, *Researchers Push for Publication, Registration of All Clinical Trials*, 95 J. NAT’L CANCER INST. 772 (2003) (studies indicate that many negative studies are never reported or even submitted for publication).

B. Ex Post Liability Creates Supplemental Incentives

Legal liability for wrongful behavior is one of the most important incentives for the creation and disclosure of information. While violating regulatory rules and industry norms can have economic consequences, it pales in comparison to the potential losses that may result from a single tort case involving punitive damages.⁵⁴ In addition, the courts provide a means for redressing a broader set of harms than encompassed by the mission of government regulatory agencies.⁵⁵ In the context of medical products companies, it is the desire to internalize the costs of future legal liability that promotes information creation and disclosure.

1. Tort Law as a Powerful Pro-Disclosure Incentive

To the extent that information disclosure impacts the safe use of a product, tort law acts as a supplemental means of punishing those whose secrecy creates unreasonable risks. Unlike regulation-based incentives, which encourage prophylactic behavior to identify and address safety and efficacy issues before injury, tort law is an ex post hammer that falls if the detrimental effects of undesirable behavior occur. From an economic perspective, it is expected that an appreciation of potential liability will create incentives to engage in early loss-avoidance behavior to internalize the costs of future harm.⁵⁶ This is the key to the second part of the “dual track” system of safety incentives.⁵⁷

54. Perhaps one of the most dramatic examples is a one-billion dollar verdict against American Home Products (now Wyeth) in a case involving the diet drug, fen-phen. Eric Seggebruch, *United States—Strategies and Tactics: Electronic Data in Litigation*, (July 30, 2004), http://194.88.95.39/i_article.asp?articleid=27545 (registration required for access). The size of the verdict may have been related to the discovery of an unusually damaging e-mail message by administrator Kay Anderson which was culled from Wyeth’s computer back-up tapes: “Do I have to look forward to spending my waning years writing checks to fat people worried about a silly lung problem . . . ?” *Id.* The one-billion dollar verdict was later reduced. Note that the costs of liability could to some degree be passed on to consumers, resulting in higher overall prices. This may partially explain differences between U.S. drug prices and those of similarly situated countries like Canada. See Manning, *supra* note 10, at 233–34.

55. See Rabin, *supra* note 10, at 2071–73 (referring to the compensation gap that would exist if tort law were to be completely supplanted by regulatory agency review). *But see* Stewart, *supra* note 10, at 2181–85 (arguing that compensation shortfalls only arise in the rare, strict-liability treatment of complex products liability, and the current system ends up perpetuating inequities based on disparate jurisdictional treatments).

56. See, e.g., COOTER & ULEN, *supra* note 8, at 309–10 (“The economic essence of tort law is its use of liability to internalize externalities created by high transactions costs.”); RICHARD POSNER, *ECONOMIC ANALYSIS OF LAW* 197–98 (5th ed. 1998).

57. See, e.g., 2 AM. LAW INST., REPORTERS’ STUDY ON ENTERPRISE RESPONSIBILITY FOR PERSONAL INJURY 87–89 (1991) [hereinafter, ALI REPORTERS’ STUDY] (describing tort law and regulation as a dual system of remedies); Stewart, *supra* note 10, at 2169–70 (essay by former Chief Reporter on the American Law Institute (ALI) study describing the impact of the dual-track system, which can be positive or negative depending on the circumstances of the regulatory environment). Some refer to it as “regulation through litigation.” See, e.g., Victor E. Swartz & Leah Lorber, *State Farm v. Avery: State Court Regulation Through Litigation Has Gone Too Far*, 33 CONN. L. REV. 1215, 1237 (2001).

In a highly regulated state prior to the marketing of a product, as in the preapproval stage of a drug or medical device, tort incentives may add little over regulatory and market incentives.⁵⁸ However, as detailed above, following the approval of a product, the incentives for mandatory information production dwindle.⁵⁹ At this point, a firm must see economic benefits to voluntarily producing information or such investments may not be made. When a company, through whatever means, discovers negative information, tort law can provide a powerful incentive to the extent the law places liability on a company that does not responsibly disclose the information to the appropriate regulators and in some instances the public.⁶⁰ Additionally, costs are reduced when such information is discovered early, before a greater number of people can be affected or the individual harm increases.⁶¹ A rational firm would be expected to invest in uncovering and releasing potentially damaging information in order to minimize these costs.

Ultimately, the strength of the tort incentive is linked to the acts for which a company may find itself liable. In the context of most high-risk products, the most concerning act is usually the marketing of a defectively designed product.⁶² Although drugs, biologics, and medical devices present the type of significant safety issues that would seem appropriate for design-defect cases, the viability of this cause of action has been significantly curtailed in most states. The rationale is overriding public policy: Most courts and commentators acknowledge the fact that it is extremely difficult—if not impossible—to produce a medical product that does not pose some risk of injury for at least part of the population, and valuable treatments might disappear if liability were automatic.⁶³ This notion has become famously enshrined in the widely adopted comment k to section 402A of the *Restatement (Second) of Torts*, which precludes

58. This is due to the comprehensive nature of mandatory information creation and disclosure as well as to the negligible tort liability that exists when most people are not at risk because a product is not on the market.

59. See *supra* notes 35–42 and accompanying text.

60. See Rabin, *supra* note 10, at 2068–69.

61. Medical products often require several years beyond approval to achieve peak sales. See Henry Grabowski, John Vernon & Joseph A. DiMasi, *Returns on Research and Development for 1990s New Drug Introductions*, PHARMACOECONOMICS, Supplement 3, 2002, at 11. Therefore, early investigations have a real chance of averting widespread harm. In many respects, the notion of early attention is the theory behind “medical monitoring” liability, which seeks to impose on a manufacturer the costs of monitoring persons who might fall ill due to their use of that manufacturer’s product. See Thomas C. Galligan, Jr., *The Risks of and Reactions to Underdeterrence in Torts*, 70 MO. L. REV. 691, 719–20 (2005).

62. Design-defect liability seeks to hold manufacturers responsible for the marketing of unreasonably dangerous products, regardless of fault. RESTATEMENT (SECOND) OF TORTS § 402A(2)(a) (1963) (“The rule . . . applies although . . . the seller has exercised all possible care in the preparation and sale of his product . . .”). The most common test asks whether a safer design was a reasonable alternative, considering the state of the art and market conditions, among other things. W. PAGE KEETON, PROSSER AND KEETON ON THE LAW OF TORTS 698–700 (5th ed. 1984).

63. See PRODUCTS LIABILITY: PHARMACEUTICAL DRUG CASES §4.02 (Donald E. Vinson & Alexander H. Slaughter eds., 1988) [hereinafter PRODUCTS LIABILITY]; see also M. Stuart Madden, *The Enduring Paradox of Products Liability Law Relating to Prescription Pharmaceuticals*, 21 PACE L. REV. 313, 321 (2001); Richard McCormick, *Pharmaceutical Manufacturer’s Duty to Warn of Adverse Drug Reactions*, 66 DEF. COUNS. J. 59, 61–62 (1999).

strict liability for “unavoidably unsafe” products, so long as adequate warnings are provided.⁶⁴

One recurrent theme in the unavoidably unsafe doctrine regarding drug and device strict product liability is the requirement for accurate information concerning safety and efficacy. Whether one considers a drug company’s determination of safer alternatives or a physician’s decision to prescribe to certain patients, a complete knowledge is presumed and the discovery of concealed information can defeat the standard defenses.⁶⁵ This necessarily directs the design defect inquiry to information disclosure, which is generally the scope of a failure-to-warn cause of action.⁶⁶ For that reason, it makes sense that failure-to-warn cases make up the bulk of medical products liability litigation.⁶⁷

Liability issues in failure-to-warn cases arise in the context of consumer injuries that could have been avoided if the proper information regarding the risks of use was disclosed.⁶⁸ The failure to warn could theoretically fall within any one of three possible tort causes of action: (1) a warning defect, implicating strict liability;⁶⁹ (2) a negligent act on the part of the manufacturer;⁷⁰ or (3) an intentional act.⁷¹ Because an intentional

64. RESTATEMENT (SECOND) OF TORTS § 402A cmt. k (1963). Comment k must be read in conjunction with comment j to understand the association between unavoidably unsafe products and warnings. *Id.* at cmt. k, j. This presumption of drug and device safety is taken even one step further by the most recent ALI articulation of the law, section 6 of the *Restatement (Third) of Torts*, which insulates a manufacturer from liability if a “reasonable healthcare provider” would prescribe the treatment or device for *any* class of patients. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 6(c) (1997). Section 6 was specifically drafted to address medical products and to bring uniformity to the somewhat disparate treatment of comment k. *See, e.g.*, Michael J. Wagner & Laura L. Peterson, *The New Restatement (Third) of Torts—Shelter from the Product Liability Storm for Pharmaceutical Companies and Medical Device Manufacturers?*, 53 FOOD & DRUG L.J. 225, 228 (1998) (“The *Restatement (Third)* was drafted with the hope of finally defining the law and setting forth specific rules addressing the unique characteristics of prescription drugs and medical devices.”); George W. Conk, *Is There a Design Defect in the Restatement (Third) of Torts: Products Liability?*, 109 YALE L.J. 1087, 1105–07 (2000) (criticizing the ALI for essentially adopting a super-negligence standard). This is generally perceived to be a strong move to restrict liability for design defects in most cases. *But see* William A. Dreier, *Manufacturers’ Liability for Drugs and Medical Devices Under the Restatement (Third) of Torts: Products Liability*, 30 SETON HALL L. REV. 258, 259–260 (1999) (arguing that a consideration of the entirety of section 6 suggests that manufacturers have not, in fact, been given such broad license to ignore product liability when producing products).

65. *See* Dreier, *supra* note 64, at 264.

66. Arguably, this is as it should be, a notion supported in the *Restatement (Third) of Torts. Id.* (“In a highly regulated industry in which the FDA acts as gatekeeper, the section breaks with the traditional tests for liability to focus on the real issues raised by most cases: adequate warnings.”).

67. *See* James A. Henderson, Jr. & Aaron D. Twerski, *A Proposed Revision of Section 402A of the Restatement (Second) of Torts*, 77 CORNELL L. REV. 1512, 1542 (1992) (“It is not at all difficult to summarize the standards courts have used in deciding prescription drug cases. The overwhelming majority of drug cases have been based on failure to warn.”).

68. *See* PRODUCTS LIABILITY, *supra* note 63, at § 4.23 (noting that some courts refuse to find liability if the failure to warn was not the cause in fact of the plaintiff’s injury).

69. *See id.* at § 4.09; McCormick, *supra* note 63, at 61–62.

70. *See* PRODUCTS LIABILITY, *supra* note 63, at § 4.08; McCormick, *supra* note 63, at 61–62.

failure to warn requires proof akin to common law fraud or false advertising,⁷² it may be more difficult to prevail under this theory.⁷³ However, negligent and strict liability failure-to-warn cases are common when a manufacturer is found to possess undisclosed information impacting the safety or efficacy profile of a medical product.⁷⁴ To prove a strict liability failure, a plaintiff must show that a manufacturer was, or should have been, aware of a product's dangerous propensities and that an insufficient disclosure was made.⁷⁵ A negligence case of this type is very similar. Many courts draw no distinction between strict liability and negligence in design defect cases.⁷⁶

Significantly, tort incentives that arise from failure to warn cases generally compel information disclosure but not creation. As a general matter, tort law places a requirement on manufacturers to disclose pertinent information that they already possess.⁷⁷ It may also mandate the creation of new information if done as part of routine product research and development or in response to a clear indication of a problem.⁷⁸ Expensive and speculative information creation efforts, such as the

71. JAMES M. BECK & ANTHONY VALE, *DRUG AND MEDICAL DEVICE PRODUCT LIABILITY DESKBOOK* § 2.13 (2d release 2005). However, it has been noted that intentional failures are frequently pled when it is clear that a manufacturer has engaged in a risk-benefit analysis in marketing a product. See Malcolm E. Wheeler, *A Proposal for Further Common Law Development of the Use of Punitive Damages in Modern Product Liability Litigation*, 40 ALA. L. REV. 919, 922–24 (1989) (“Modern substantive tort law principles tend to make punitive damages arguments of that nature available in every design-defect and inadequate-warning case.”).

72. See *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 528–30 (1992) (commenting on the alleged conspiracy by cigarette manufacturers to conceal the dangers of smoking).

73. BECK & VALE, *supra* note 71, at § 2.13 (“While fraud/intentional misrepresentation claims against manufacturers of prescription medical products are allowed if properly pleaded, claims of this nature have by and large met with only limited success.”).

74. See *infra* notes 101–102 and accompanying text.

75. See Bernard J. Garbutt III & Melinda E. Hofmann, *Recent Developments in Pharmaceutical Products Liability Law: Failure to Warn, the Learned Intermediary Defense, and Other Issues in the New Millennium*, 58 FOOD & DRUG L.J. 269, 269–72 (2003) (restating the general elements of a pharmaceutical failure-to-warn case).

76. See PRODUCTS LIABILITY, *supra* note 63, at § 4.12 (“[T]he distinction between these two theories is more semantic than real in a drug products liability case.”); Henderson & Twerski, *supra* note 67, at 1530–32 (arguing that since the risk-benefit test and foreseeability issues are generally applied to strict product liability for failure to warn, there is little reason to distinguish the two); McCormick, *supra* note 63, at 63 (citing cases holding that negligence and strict liability failure to warn are indistinguishable). One difference may be a slightly higher standard for assessing what knowledge a reasonably prudent manufacturer possesses and the acts it would take to fulfill one's duties in a negligence case, but it depends on the court. See *id.* at 63–65 (detailing cases wherein courts have attempted to determine how standards for negligent and strict liability failure to warn differ, particularly in the case of pharmaceuticals).

77. See BECK & VALE, *supra* note 71, at § 2.04[1] (citing cases and concluding that courts generally require a manufacturer to warn about risks of which it has actual or constructive knowledge).

78. See *id.* at § 3.07. For example, courts have found manufacturers liable under a tort theory based on the failure to adequately test the product. See, e.g., *Tinnerholm v. Parke, Davis & Co.*, 285 F. Supp. 432, 451 (S.D.N.Y. 1968) (manufacturer failed to discover dangers associated with the drug and warn physicians), *modified*, 411 F.2d 48 (2d Cir. 1969). But the duty to test is that which arises from the normal course of pharmaceutical research and development. Therefore, a products liability case premised on a failure to test can be viewed as a

postapproval initiation of large-scale clinical trials, simply to identify unknown safety issues, should not generally be considered to fall within one's loss-avoidance duties.⁷⁹ In other words, companies will usually not face liability for choosing not to conduct clinical studies merely for the purpose of confirming the safety and efficacy profile of an approved medical product.⁸⁰ In and of itself, this is not unreasonable because the mandated expense of forever trying to prove the absence of harm in approved products could have a negative impact on innovation. Conversely, when harm is found, courts rarely engage in hindsight analysis to imagine what studies might have uncovered defects that were not reasonably foreseeable at the time.⁸¹

Taken together, the various elements of tort liability create a very strong incentive for rapid and complete disclosure of safety and efficacy information. The economic risk in attempting to market while concealing the dangers generally outweighs the benefits, even for blockbuster drugs.⁸² However, the products liability regime is not the exclusive source of ex post incentive forces operating upon industry; one must also factor in the impact of state government intervention.

2. Pro-Disclosure Consumer Protection and Fair Competition Law Incentives Fill in Tort Law Gaps

In the same way that an individual may allege an intentional failure to warn that takes the form of common law fraud or false advertising, a similar action may be available through consumer protection and unfair competition statutes.⁸³ The incentive structure is for all intents and purposes equivalent: economic losses may result from a failure to disclose information that could have averted harm. Having the government as an actor may change one's assessment of probability or impact, however.

species of the standard failure-to-warn case, wherein a manufacturer allegedly breaches a duty to warn about dangers known or reasonably knowable. See PRODUCTS LIABILITY, *supra* note 63, at § 4.06.

79. See BECK & VALE, *supra* note 71, at § 2.04 [1].

80. See *id.* at § 3.07. California courts have recently addressed this issue. In *Valentine v. Baxter Healthcare Corp.*, 81 Cal. Rptr. 2d 252, 265 (Cal. Ct. App. 1999), the court determined that no independent duty to test exists. The court declared that the "imposition of liability for breach of an independent duty to conduct long-term testing, where the causal link to the known harm to plaintiff is the unknown outcome of testing that was not done, would be beyond the pale of any California tort doctrine." *Id.* (emphasis omitted).

81. Arguably, there is disagreement among jurisdictions on this point, but it appears that more recent cases tend to refrain from imposing a retrospective requirement to test. See BECK & VALE, *supra* note 71, at § 3.07 (citing one 1973 case essentially imposing a duty to test, but several more recent cases in accord with the proposition that no such requirement exists).

82. In many ways, blockbuster drugs may pose even greater liability issues because they provide so much of a company's profits that their loss can be devastating. For example, Merck's recently withdrawn Vioxx was responsible for approximately \$2.5 billion in yearly sales. See Aaron Smith, *Merck's Vioxx Bill Could Hit \$50 Billion*, CNN MONEY.COM, Aug. 22, 2005, <http://money.cnn.com/2005/08/22/news/fortune500/merck>. The withdrawal was partially responsible for Merck's fifty-nine percent plunge in earnings in the following year. Associated Press, *Merck Q2 Earnings Plunge on Charge*, CBS NEWS.COM, July 21, 2005, <http://www.cbsnews.com/stories/2005/07/21/ap/business/mainD8BFP8O80.shtml>.

83. See Garbutt & Hofmann, *supra* note 75, at 282–83 (describing private actions under consumer fraud and unfair competition statutes).

Laws that specifically address deceptive marketing (or more generally, unfair competition) are enforced by the state⁸⁴ and most include a private right of action.⁸⁵ If the government is involved, it may be able to benefit from certain advantages not available to private, common-law plaintiffs. Obvious examples include greater financial power to manage litigations, to utilize the experience of multiple cases, and potentially to extract greater remedies—even criminal penalties in some cases.⁸⁶ Additionally, since state statutes may prohibit false or misleading statements, per se, it may be possible to avoid important common-law tort defenses like the learned intermediary doctrine.⁸⁷ Arguably, a company has a stronger incentive to consent to a broad prospective resolution to the action, as the potential for future litigation is more onerous than in a common law tort case to address an individual harm or a class's common set of facts.

The use of consumer-protection and fair-competition laws to pursue product liability issues is by no means a new idea. Some refer to this as simply another form of regulation through litigation,⁸⁸ and it has figured prominently in cases related to such products as lead paint and tobacco.⁸⁹ The nature of the tobacco company litigation, in particular, is a model for the typical assertions and issues in a medical products case. In the context of a regulated product, containing mandated warnings and known dangers,

84. *See id.*

85. *See, e.g.*, ALA. CODE § 8-19-10 (LexisNexis 2002); CAL. BUS. & PROF. CODE §§ 17204, 17535 (West 1997 & Supp. 2006); CONN. GEN. STAT. ANN. § 42-110g(a) (West Supp. 2006); FLA. STAT. ANN. § 501.211(1) (West 2006); GA. CODE ANN. § 10-1-373 (2000); HAW. REV. STAT. § 480-13 (Supp. 2005); 815 ILL. COMP. STAT. ANN. 505/10a (West Supp. 2006); IND. CODE ANN. § 24-5-0.5-4 (West Supp. 2006); LA. REV. STAT. ANN. § 51:1409(A) (2003); ME. REV. STAT. ANN. tit. 5, § 213(1) (2002); MD. CODE ANN., COM. LAW § 13-408 (LexisNexis Supp. 2003); MASS. ANN. LAWS ch. 93A § 9 (LexisNexis 2005); MINN. STAT. ANN. § 8.31 (West 2005); N.J. STAT. ANN. §§ 56:8-18 to -19 (West 2001); N.Y. GEN. BUS. LAW § 349(h) (McKinney 2004); N.C. GEN. STAT. ANN. § 75-16 (West 2000); OHIO REV. CODE ANN. § 1345.09(B) (LexisNexis 1954, 1962, 1979, 1993, 2002); TENN. CODE ANN. § 47-18-109(a)(1) (2001); TEX. BUS. & COM. CODE ANN. § 17.50(b) (Vernon Supp. 2006); VT. STAT. ANN. tit. 9, § 2461(b) (1993); WASH. REV. CODE ANN. § 19.86.090 (West 1999); *see also* BECK & VALE, *supra* note 71, at § 3.08[1] (noting that private actions under consumer protection statutes are not always successful due to the perception that such statutes are misused as a basis for products liability claims); Trevor W. Morrison, *Private Attorneys General and the First Amendment*, 103 MICH. L. REV. 589, 605–06 (2005) (describing the general nature of such statutes).

86. Under consumer protection statutes, the criminal consequences are often classified as a misdemeanor. CAL. BUS. & PROF. CODE § 17500 (West 1997); N.Y. PENAL LAW § 190.20 (McKinney 1999); TEX. BUS. & COM. CODE ANN. § 17.12(d) (Vernon 2002).

87. *See* Garbutt & Hofmann, *supra* note 75, at 272–73, 282–83 (explaining the basic assumptions of the doctrine and noting that “[p]laintiffs increasingly have tried to avoid the effects of the learned intermediary doctrine by asserting state consumer fraud claims,” but the results have been “mixed”).

88. *See, e.g.*, W. Kip Viscusi, *Overview, in* REGULATION THROUGH LITIGATION 1, 7 (W. Kip Viscusi ed., 2002); Andrew P. Morriss, Bruce Yandle & Andrew Dorchak, 29 HARV. ENVTL. L. REV. 179, 203–04 (2005) (describing government regulation through litigation wherein new enforcement powers—beyond those typically applied to a regulated entity—are exercised).

89. *See* Edward T. Schroeder, Note, *A Tort by Any Other Name? In Search of the Distinction Between Regulation Through Litigation and Conventional Tort Law*, 83 TEX. L. REV. 897, 900–04 (2005).

consumers, and states on their behalf, were able to sue for harm caused by the alleged systematic fraudulent misrepresentation of the ill effects of using the product.⁹⁰ Of course, the outcome has been quite favorable to plaintiffs, as states have been extremely successful in extracting huge settlements, and a great deal of important information on the addictive properties of smoking has come to light.⁹¹ The same legal theories should apply in the context of a pharmaceutical company that covers up a safety issue to achieve a better marketing position. And similar to tort liability, consumer protection claims generally impact only information that companies have generated or plan to generate.⁹²

Taken together, consumer protection liability and medical products liability are presumed to act positively to increase the amount of information available while equitably allocating the risks of product defects between manufacturers and the public. Importantly, the ability of a strong ex post incentive track to induce information production is predicated on the notion that liability can be fully avoided through a company's good faith efforts. Unfortunately, the realities of litigation practice in the United States impose a retrospective marginal cost transfer that can significantly detract from the incentives.

II. THE TRANSPARENCY PARADOX: WHY MORE INFORMATION MEANS LESS

Since a rational assessment of medical product risks and benefits is so dependent on accurate information, it seems logical that any effort to increase its availability would have a positive effect. A general effort to force companies to disclose more information should provide for greater safety and smarter choices. However, this presumption is based on an incomplete picture. Specifically, it fails to take into account the fact that the above information incentive forces can be countered by the significant tort disincentives that accompany disclosure. Because greater disclosure enhances the disincentive effect, it is actually possible for an increase in information disclosure to result in less information creation such that production is reduced overall. This is the information paradox, and it confounds efforts to enhance the public's ability to exercise its judgment regarding the use of medical products.

90. See Wendy E. Wagner, *Rough Justice and the Attorney General Litigation*, 33 GA. L. REV. 935, 957–61 (1999) (detailing the organization of the collaborative attorneys general lawsuits against tobacco companies and why such action was necessary as a cure to the failure of private litigation); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 528–530 (1992) (holding that common law failure-to-warn actions are not precluded by federal labeling statutes).

91. See Wagner, *supra* note 90, at 966 (drawing conclusions as to the ultimate success of the attorneys general lawsuits).

92. This is because the cause of action is generally based on fraud, including “‘deception, misrepresentation, concealment [or] suppression’ of a material fact”—in other words, misrepresenting existing clinical data—rather than a failure to investigate potential safety problems. See Complaint at 17, *New York v. GlaxoSmithKline, PLC*, No. 04401707 (N.Y. Sup. Ct. N.Y. County June 2, 2004) [hereinafter *Glaxo Complaint*], available at http://www.oag.state.ny.us/press/2004/jun/jun2b_04_attach1.pdf (quoting N.Y. EXEC. L. § 63(12) (alteration in original)).

A. The Perverse Disincentives Created by Modern Tort Practice

The modern practice of mass tort litigation has evolved to create significant pressures on businesses that extend beyond traditional loss-avoidance incentives. These litigation pressures could be referred to as “practice-based” since they emanate from the methods and procedures employed by attorneys. Unlike conventional tort incentives, practice-based forces operate not to induce loss-avoidance, specifically, but rather to compel litigation-avoidance strategies. They derive from information distortions caused by the reactive, experimental nature of tort litigations, wherein liability may be sought without regard to clear evidence of negligent behavior.⁹³ The impact of practice-based forces is even greater when a large plaintiff pool exists.⁹⁴ In view of the limitations on *ex ante* and *ex post* incentives, practice-based pressures may lead companies to make an obvious but unfortunate strategic choice to avoid the litigation morass: create less information.

The net disincentive effect of practice-based incentives arises from the combination of the fact that tort and consumer protection incentives do not compel information creation⁹⁵ with the axiomatic imposition of tort costs following a negative disclosure.⁹⁶ In part, this is a consequence of the fact that newly discovered safety or efficacy problems can shift the risk-benefit balance.⁹⁷ A manufacturer-sponsored study to investigate new patient populations or uncover long-term effects may backfire by revealing previously unknown problems.⁹⁸ Such information may even remove the deference to a regulatory review that occurred without the benefit of the study,

93. This can be characterized as inefficiency based on incomplete information. *See* CONG. BUDGET OFFICE, *THE ECONOMICS OF U.S. TORT LIABILITY: A PRIMER* 14–16 (2003) [hereinafter CBO REPORT]. It can outweigh the benefits of the deterrent function of tort law, if sufficiently large. *See id.*; GARBER, *supra* note 10, at 180–83 (discussing the incentives produced by actual litigation and how they are significantly less efficient than the ideal of the tort system due to information distortions such as the uncertainty of liability).

94. For example, given the tens of millions of patients that take a drug like Vioxx, “[e]ven a fraction of a percent excess in the rate of serious [illness] would translate into thousands of affected people.” Eric J. Topol, *Failing the Public Health—Rofecoxib, Merck, and the FDA*, 351 *NEW ENG. J. MED.* 1707, 1708 (2004).

95. *See supra* notes 77–81 and accompanying text.

96. *See* Andrew E. Flasetti, *Fluoxetine-Induced Suicidal Ideation: An Examination of the Medical Literature, Case Law, and the Legal Liability of Drug Manufacturers*, 57 *FOOD & DRUG L.J.* 273, 290–92 (2002) (describing Eli Lilly’s experience with selective serotonin reuptake inhibitors (SSRI) pharmaceutical litigations at the turn of the twenty-first century, and arguing “while Lilly has yet to know defeat, the real loser likely will be the patient suffering from depression, as the pharmaceutical industry may limit or halt the production of products as a result of manufacturers repeatedly being found liable for purported effects of their products that have no rational basis of support in the scientific literature”). In some jurisdictions, the failure to warn is judged as a strict liability tort, meaning the reasonableness of a manufacturer’s actions is irrelevant. *See* BECK & VALE, *supra* note 71, at § 2.04[1].

97. *See* BECK & VALE, *supra* note 71, at § 3.02[5] (“If new information later tips the balance toward the risk of a product, or if new developments make possible a safer design, at that point further distributions of the product are not protected by comment k.” (quoting *Toner v. Lederle Labs.*, 732 P.2d 297, 307 (Idaho 1987))); *supra* notes 65–66 and accompanying text.

98. *See* Struve, *supra* note 10, at 602 (describing the countervailing forces in disclosing negative information in terms of liability and business losses).

depending on the jurisdiction.⁹⁹ The liability costs of such a study are therefore added on to a firm's marginal costs retrospectively.¹⁰⁰

Presenting an even greater liability issue is the fact that frequently a study with negative outcomes may confirm a problem that, in retrospect, was suggested by earlier evidence.¹⁰¹ Invariably, this opens up the possibility for a failure-to-warn action based on a lack of response to the known issues. As one plaintiff's attorney put it in comments on the attractiveness of Viagra lawsuits, "[a]nytime you get news of a post-market adverse event that is as serious as blindness, heart attack, stroke, the first thing you expect is that the company already knew about the problem."¹⁰² In view of this extreme liability, a manufacturer may reasonably conclude that the risks of generating potentially harmful information outweigh the benefits.¹⁰³

99. Professor Rabin cites this use of tort law as a means of bridging the gap in regulatory review and as an important function of private litigation. See Rabin, *supra* note 10, at 2077.

100. A case in point is pharmaceutical company Wyeth's recent experience with its hormone replacement therapy (HRT), Prempro. Evidence available at the time Prempro was released suggested that such estrogen-progestin combination products could have a prophylactic effect on heart disease; thus, many women were prescribed the drug for this off-label indication. See Writing Group for the Women's Health Initiative, *Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women*, 288 JAMA 321, 321-22 (2002). To further investigate the benefits of HRT, a long-term, randomized clinical trial was designed by the Women's Health Initiative, sponsored by the federal government, and aided by Wyeth's contribution of all medications used. See *id.* at 332. Stunningly, the trial contradicted previous findings and determined that the use of HRT actually increased the risk of heart attack. *Id.* at 330-31 ("At the end of the trial, the global index indicated that there were more harmful than beneficial outcomes in the estrogen plus progestin group vs [sic] the placebo group."). Not surprisingly, Wyeth faced the prospect of massive individual and class action litigation for alleged Prempro harm, primarily for the potential future impacts. See, e.g., Melissa Nann Burke, *Judge Rejects Class Action for Monitoring of Prempro Users*, LEGAL INTELLIGENCER, May 4, 2005, available at <http://www.law.com/jsp/article.jsp?id=111511119293> (certification of a class of over 700,000 women attempted but ultimately denied). Although the first of the "bellwether" cases ended favorably for Wyeth, *Today in Business*, N.Y. TIMES, Sep. 16, 2006, at C2, the company has lost others and still faces approximately 5000 lawsuits. *Wyeth to Pay \$3 Million in Cancer Suit*, N.Y. TIMES, Feb. 21, 2007, at C4. The class action filings are particularly interesting for their employment of the relatively novel request for "medical monitoring" of currently healthy patients due to the increased risk of heart attack. *Id.* If successful, it is possible that this new form of liability could become a significant burden for pharmaceutical and biotechnology companies. See David M. Studdert, Michelle M. Mello & Troyen A. Brennan, *Medical Monitoring for Pharmaceutical Injuries*, 289 JAMA 889, 893 (2003).

101. The Vioxx study is, of course, the most prominent example. See Anna Wilde Mathews & Barbara Martinez, *E-Mails Suggest Merck Knew Vioxx's Dangers at Early Stage*, WALL ST. J., Nov. 1, 2004, at A1; Barry Meier, *Merck Canceled an Early Study of Vioxx*, N.Y. TIMES, Feb. 8, 2005, at C1.

102. See Justin Scheck, *Attorneys Soft on Viagra Suits*, RECORDER, June 15, 2005, available at <http://www.law.com/jsp/article.jsp?id=1118739911459>; see also Justin Scheck, *Product Defect May Set Lawyer's Hearts Racing*, RECORDER, June 24, 2005, available at <http://www.law.com/jsp/article.jsp?id=1119517513020> ("There's nothing like a short-circuit inside thousands of people's chest cavities to jump-start plaintiff lawyers and shock the heart of a corporate defendant.").

103. Note that the clinical trials themselves are not without liability risk. Recently, pharmaceutical companies have come under fire on a number of claims related to clinical

The liability that follows disclosure is daunting enough, but practice-based tort forces further exacerbate the problem. In particular, information-creation disincentives are compounded by the increasing sophistication¹⁰⁴ of plaintiffs' attorneys in initiating lawsuits based on the early indications of a problem with an FDA-approved medical product.¹⁰⁵ For example, one of the largest and best-known lobbying groups for trial attorneys, the Association of Trial Lawyers of America (ATLA),¹⁰⁶ provides "litigation packets" containing specific advice, strategies, and even sample pleadings for lawyers interested in taking on clients harmed by drugs with as yet unclear risk-benefit profiles like Vioxx.¹⁰⁷ The production of such information is rapid, and manufacturers could reasonably be concerned that safety issues may be litigated before conclusive evidence is available. According to some observers, the goal of much early-stage litigation is a fast settlement.¹⁰⁸ Within a year of the disclosure of cardiac safety concerns with Vioxx, over four thousand cases were filed against manufacturer Merck & Co.,¹⁰⁹ and the number has grown to over twenty-eight thousand.¹¹⁰ However, after winning nine out of fourteen trials as of the beginning of 2007,¹¹¹ it is not at all clear that Merck acted wrongfully in all—or even many—of those lawsuits.¹¹² There are indications that

research, including wrongful death and the right to continue receiving drugs after the trial has ended. See Tresa Baldas, *Drug Trials on Trial*, NAT'L L.J., July 18, 2005, at 1.

104. Television and Internet advertising are now common ways for plaintiffs' attorneys to generate clients with injuries possibly related to specific drugs under public scrutiny. See Andrew Harris, *Law Firm's Vioxx Campaign Draws Audience—and Raises Questions*, N.Y.L.J., Mar. 18, 2005, available at <http://www.law.com/jsp/article.jsp?id=1110881109096> (describing an attorney's advertising campaign that includes advertising as well as a series of free dinner seminars); Leigh Jones, *Class Action Web Sites Untested*, NAT'L L.J., July 8, 2005 (discussing the issues in the use of websites to solicit clients related to products like Paxil).

105. See *Five Plaintiffs File Worldwide Class Action Saying Drug Caused Heart Attacks, Embolism*, 33 Prod. Safety & Liab. Rep. (BNA) No. 16, at 399 (Apr. 18, 2005); *Wave of Class Action Litigation Follows Merck's Withdrawal of Arthritis Drug VIOXX*, 32 Prod. Safety & Liab. Rep. (BNA), No. 43, at 996 (Nov. 1, 2004).

106. ATLA recently voted to change its name to the American Association for Justice. See Editorial, *Trial Lawyers for Justice*, L.A. TIMES, Aug. 11, 2006, at B12.

107. See Am. Trial Lawyers Ass'n, *Exchange Litigation Packet*, http://www.atla.org/LegalResearchServices/Tier3/Lit%20Packet%20Flyer_Current.pdf (last visited Oct. 22, 2006) ("Begin your search with ATLA Exchange Litigation Packets, and you'll gain practical, valuable case materials such as deposition transcripts and summaries, pleadings, trial transcripts, company manuals, and bibliographies of relevant reference materials.").

108. See, e.g., Michelle M. Bufano, *Keep from Drowning in a Sea of Mass Torts!*, PHARM. & MED. DEVICE L. BULL., Jan. 22, 2004, at 1 ("Keeping in mind that the goal of mass tort litigations is early settlement, a defendant's most important goal is to expose frivolous claims early.").

109. Alex Berenson, *First Vioxx Suit: Entryway into Legal Labyrinth?*, N.Y. TIMES, July 11, 2005, at C1.

110. Tesoriero, *supra* note 6. See also Barnaby J. Feder, *Lawyers Set to Bring More Suits*, N.Y. TIMES, Apr. 8, 2005, at C5 (stating that the FDA's decision to ban Bextra and add warnings to Celebrex "galvanized the informal network of lawyers pursuing death and injury suits aimed at the two drugs").

111. Tesoriero, *supra* note 6.

112. In fact, a recent investigation conducted by former U.S. District Judge John S. Martin concluded that the company did not act inappropriately or mislead the public with respect to Vioxx. REPORT OF THE HONORABLE JOHN S. MARTIN, JR. TO THE SPECIAL COMMITTEE OF THE BOARD OF DIRECTORS OF MERCK & CO, INC. CONCERNING THE CONDUCT OF SENIOR

the number of early stage, reactive lawsuits is increasing across the medical product industry,¹¹³ even as other mass torts may be waning.¹¹⁴

Even if a firm has acted responsibly and could prove it in court, it is not always clear that the tort system will yield reliable results. This is due in large part to problems the civil jury—the trier of fact in most products liability cases—will likely experience in making the necessary risk-benefit assessments.¹¹⁵ Evidence from litigation concerning drugs like Bendectin, medical devices like breast implants, and vaccines suggests that juries are not always good at assessing whether the harm in a particular case is outweighed by societal benefits.¹¹⁶ The uncertainty of jury verdicts can, completely aside from the merits of the case, dissuade corporate defendants from undertaking the risk of litigation.¹¹⁷ Additionally, cases involving large numbers of plaintiffs are ripe for fraud, which can dramatically drive up the costs. In a recent, dramatic example, a Duke University professor's audit of claims approved in the massive class action settlement concerning Wyeth's fen-phen drug found that seventy percent were manipulated and should have been denied.¹¹⁸

As a result of these transferred costs, manufacturers will likely be driven to undertake a course of reduced information production.¹¹⁹ From an economic

MANAGEMENT IN THE DEVELOPMENT AND MARKETING OF VIOXX 176–79 (Sept. 5, 2006), available at <http://161.58.184.45/martinreport/>. The objectivity of the report has been questioned, as it was prepared at the request of Merck's board of directors. John Carreyrou & Heather Won Tesoriero, *Merck Vioxx Probe Clears Officials*, WALL ST. J., Sept. 7, 2006, at D3 (“Plaintiffs’ attorneys dismissed the investigation as a whitewashing exercise.”).

113. See, e.g., Alex Berenson, *Trial Lawyers Are Now Focusing on Lawsuits Against Drug Makers*, N.Y. TIMES, May 18, 2003, at A1 (describing a new wave of products liability litigation in the pharmaceutical industry and noting that “the new lawsuits are much larger, covering more drugs and many more plaintiffs”).

114. A recent article in the *Wall Street Journal* states that companies facing some of the largest and most controversial litigations, involving products such as asbestos and silica, are seeing a significant decline. Paul Davies, *Plaintiffs’ Lawsuits Against Companies Sharply Decline*, WALL ST. J., Aug. 26, 2006, at A1. However, it is not clear that this drop has much connection to the pharmaceutical mass torts described above. See *id.* (“Despite the tougher landscape, plaintiffs’ lawyers are pushing ahead with a number of large-scale new actions [against Wyeth and Merck].”).

115. See Stewart, *supra* note 10, at 2171–73 (“[T]he tort litigation system generates seriously erroneous and inconsistent liability decisions, and results in over-deterrence with respect to regulated products that present complex scientific and technical questions regarding risk, benefit, and causation.”).

116. See *id.* (reviewing specific cases wherein jury verdicts appear to be at odds with reliable evidence and reasonable assessments).

117. See Daniel R. Cahoy & Min Ding, *Using Experimental Economics to Peek into the “Black Box” of Jury Behavior: A Proposal for Jury Research Reform*, 14 S. CAL. INTERDISC. L.J. 31, 40–44 (2004).

118. See Frankel, *supra* note 4 (describing the use of attorney “echo mills”—mass plaintiff processing sites screening for heart problems—and citing a study conducted by Dr. Joseph Kisslo of 926 claims that have passed through the settlement trust auditing system).

119. At the very least, the transferred costs may result in the termination of current studies that could produce dangerous outcomes. See, e.g., Benjamin Falit, *The Path to Cheaper and Safer Drugs: Revamping the Pharmaceutical Industry in Light of GlaxoSmithKine’s Settlement*, 33 J.L. MED. & ETHICS 174, 176 (2005) (“Aware that summaries of all *completed* trials will inevitably be released to the public, pharmaceutical companies will rationally choose to

perspective, it is the most rational course of action. If one presumes that manufacturers engage in voluntary information creation and disclosure to the extent that the marginal benefits of the studies (e.g., generating evidence of market advantages, discovering latent defects early to permit loss avoidance, and disclosing revised efficacy profiles to reduce patient risk) are equal to the marginal costs of the studies and future liability based on the information produced, a certain amount of information will be available to the public (see figure 1).¹²⁰

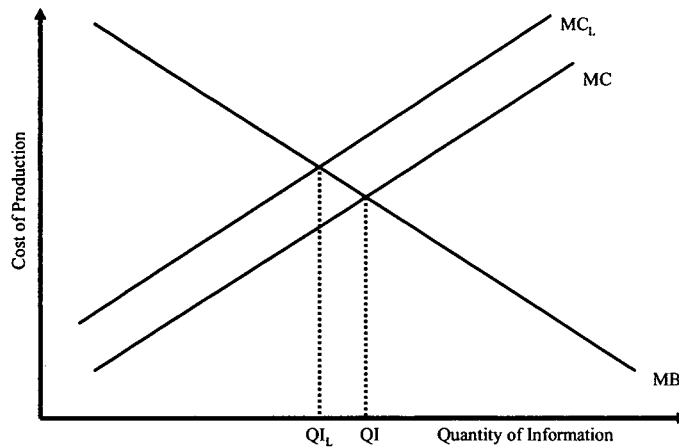


Figure 1. Ex Post Liability Impact on Voluntary Information Production. The marginal cost curve reflects the increased costs to the firm of producing additional information following approval. The marginal benefits curve reflects the benefits of producing information in terms of a firm's ability to internalize future harm from discovered defects. At the equilibrium point, the quantity of information "QI" will be produced. The legal system's ex post transfer of the costs of past harm revealed by additional information is represented by curve MC_L . Thus, liability resulting from new information can be expected to reduce the quantity of information to QI_L .

However, when liability is applied to the disclosure of information, regardless of one's negligence or otherwise bad acts, the marginal costs of information production increase retrospectively (see curve MC_L). That should move the equilibrium point of information costs and benefits back and thus suggests that a company will view less information as optimally efficient (see point QI_L). Significantly, this information-production disincentive could blunt both ex ante and ex post incentives to the extent they are voluntary.

Even if in some cases the economic consequences of practice-based liability are not so severe as to warrant a change in information production, it is quite possible that a company may employ a loss-avoidance heuristic that compels the same result. Heuristics are simple rules that reflect a decision maker's perception of his or her environment.¹²¹ They are not always accurate and may be skewed by anecdotal

prematurely terminate projects that are likely to produce negative results.") (emphasis in original).

120. Note that information produced to the public, QI, is a function of both information creation and disclosure.

121. See GARBER, *supra* note 10, at 69–71; Amos Tversky & Daniel Kahneman, *Judgment Under Uncertainty: Heuristics and Biases*, 185 SCIENCE 1124, 1124–25 (1974) [hereinafter

evidence of the bad outcomes of others.¹²² For example, a company may choose to avoid a course of action with substantial risks if that company or an industry cohort has faced extreme losses in the past for similar actions.¹²³ As a general matter, companies perceive litigation risks as greater than their actual economic impact.¹²⁴ Therefore, a heuristic for information production is likely to err on the side of less exposure.¹²⁵

Possible liability-avoidance measures a company might employ in response to either real or perceived liability risks include: (1) limiting the range of clinical studies that must be generated for approval by seeking a narrow indication;¹²⁶ (2) declining to engage in an independent evaluation of adverse incident reports; and, most importantly, (3) never initiating a postmarketing (phase IV) study unless absolutely necessary. As a result of ex post disincentives, opportunities to uncover serious safety and efficacy issues could be lost, and the health care environment could become significantly riskier.¹²⁷

Tversky & Kahneman, *Heuristics and Biases*]. Another way to look at the phenomenon is the “prospect theory” of decision making. This involves narrow outcome “framing” based on norms, habits, and expectancies of the decision maker and the weighting of those outcomes based on properties such as whether the decision maker places great value on loss aversion. Amos Tversky & Daniel Kahneman, *Rational Choice and the Framing of Decisions*, 59 J. BUS. S251, S257–60 (1986). Both concepts have been quite influential in management theory and political science. See Jack S. Levy, *Daniel Kahneman: Judgment, Decision, and Rationality*, 35 POL. SCI. & POL. 271, 271 (2002).

122. See Steven Garber, *Product Liability, Punitive Damages, Business Decisions and Economic Outcomes*, 1998 WIS. L. REV. 237, 249–251 (1998) (describing the misperceptions corporate decisionmakers are likely to incorporate into a tort liability assessment heuristic); Tversky & Kahneman, *Heuristics and Biases*, *supra* note 121, at 1124.

123. See Daniel S. Bailis & Robert J. MacCoun, *Estimating Liability Risks with the Media as Your Guide: A Content Analysis of Media Coverage of Tort Litigation*, 20 L. & HUM. BEHAV. 419, 420 (1996).

124. See GARBER, *supra* note 10, at 73 (noting that potential liability costs are often perceived as being much more substantial than they actually are).

125. See Cass Sunstein, Daniel Kahneman & David Schkade, *Assessing Punitive Damages (with Notes on Cognition and Valuation in Law)*, 107 YALE L.J. 2071, 2077 (1998) (“[A]s a practical matter, a risk of extremely high awards is likely to produce excessive caution in risk-averse managers and companies.”) (citing KENNETH R. MACCRIMMON & DONALD A. WEHRUNG, *TAKING RISKS: THE MANAGEMENT OF UNCERTAINTY* (1986)).

126. Because uses outside of the approved indications are available through off-label use, manufacturers may be allowed to retain these profits without the use risk. However, if there is insufficient support for off-label use, there is a risk in any related promotion manufacturers undertake. See Steven R. Salbu, *Off-Label Use, Prescription, and Marketing of FDA-Approved Drugs: An Assessment of Legislative and Regulatory Policy*, 51 FLA. L. REV. 181, 205–06 n.152 (1999) (describing arguments against permitting off-label use and explaining why they may be overstated).

127. Although reform of the tort system is a hot political topic, see, e.g., Mark Silva, *Bush’s Tort Reform Efforts to Start at “Judicial Hellhole,”* CHI. TRIB., Jan. 3, 2005, at 9 (detailing tort reform points pushed by the Bush administration and reflected in the President’s visit to Madison County, Illinois, notorious for its mass tort filings), it is not entirely clear that this issue would normally be included in the push. For example, plaintiffs’ attorneys would likely be reluctant to accept that there could be negative safety implications to tort litigation, and manufacturers would also seem less than inclined to admit that any safety study was foregone due to purely economic reasons.

B. Complete Information Disclosure Ratchets Up Production Disincentives

Most of the practice-based issues described above arise only when the information becomes public. As noted previously, there are many instances where manufacturers can generate information outside of the public eye¹²⁸ and in some cases, beyond the scrutiny of regulators.¹²⁹ There is, as a result, still somewhat of a de facto safe harbor for detailed clinical investigations that can provide information about medical products. It may permit additional information creation while providing a great incentive for secrecy when a problem is discovered, an arguably less than ideal result.

But change is afoot. Recently, the push for greater transparency in the medical product development process has led to a marked increase in disclosure incentives for several sources. More and more, companies are being called upon to immediately release information that is potentially relevant to the safety-efficacy equation.¹³⁰ This trend is likely to only increase. However, the continued pressure to quickly disclose information that can lead to legal liability may create ever-greater incentives for companies to refrain from creating the information in the first place. Thus, paradoxically, efforts to increase the flow of information may end up playing a role in reducing a large portion of it.

1. Increased Use of Government Online Clinical Study Databases

Before one can assess the information in a clinical trial, one must obviously know of its existence. This is actually a significant obstacle in the case of preapproval studies due to regulatory confidentiality protections. In a rather dramatic change in the information environment, the existence and details of such clinical trials are now being widely disseminated on Internet-based registries.¹³¹ One registry, known as "ClinicalTrials.gov,"¹³² is particularly significant in this regard because it is a government initiative and participation is mandatory for certain types of trials—it effectively trumps standard confidentiality.¹³³ Any study that concerns the effectiveness of a drug for the treatment of a "serious or life-threatening disease or condition" must be registered on the database.¹³⁴ Members of the general public can find information

128. In particular, one should note the significant amount of information submitted to the FDA during the approval process that may be held in confidence. *See supra* notes 24–30 and accompanying text.

129. While it is difficult to imagine much information related to drugs that could be withheld from the FDA, biologics and medical devices have an opening for voluntary postmarketing studies. *See supra* note 42 and accompanying text.

130. *See, e.g.,* Dickersin & Rennie, *supra* note 9, at 517–18.

131. The concept of mandatory clinical trial registries is actually not new; there have been limited registries since the 1960s. *See id.* at 518 (describing the early existence of clinical trial registries and noting that some were even searchable by computer). However, the accessibility provided by the Internet has breathed new life into such proposals.

132. The name of the database, maintained by the National Institutes of Health and developed by the National Library of Medicine, intuitively discloses its Web address: <http://www.clinicaltrials.gov/> (last visited Mar. 9, 2006).

133. *See supra* notes 24–30 and accompanying text.

134. 42 U.S.C.A. § 282(j)(3)(A) (2006). *See also* CENTER FOR DRUG EVALUATION AND RESEARCH & CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FDA., GUIDANCE FOR

about what drugs are being tested, where the trials are taking place, and who is sponsoring them, among other significant facts.¹³⁵ In truth, the database is somewhat limited as a safety or efficacy disclosure device because it does not always present the results of the trials.¹³⁶ However, the registry can be a starting point for locating information on safety or efficacy issues related to an approved drug. Once the existence of a study is disclosed, simply concealing the results may be an ineffective way of preventing negative information from escaping. The mere discrepancy between available drug study results and any additional trials listed on a website like ClinicalTrials.gov may be enough to provide a roadmap for compelling production during litigation discovery. At the least, it may create a strong presumption that the findings of the undisclosed study were unfavorable.¹³⁷

Unlike preapproval clinical studies, the existence of all postapproval clinical studies concerning drugs or biologics that were either required by the FDA or agreed upon by the applicant are considered public information.¹³⁸ This is a relatively recent change that resulted from the Food and Drug Administration Modernization Act of 1997.¹³⁹ Significantly, postapproval studies undertaken on an applicant's own initiative are not subject to the public disclosure provisions.¹⁴⁰ What has changed since 1997 is that the

INDUSTRY: INFORMATION PROGRAM ON CLINICAL TRIALS FOR SERIOUS OR LIFE-THREATENING DISEASES AND CONDITIONS 2 (2002), available at www.fda.gov/cber/gdlns/clintrial031802.pdf [hereinafter CLINICAL TRIALS GUIDANCE] (stating that § 282(j)(3)(A) requires the submission of information regarding clinical trials to test effectiveness). Non-effectiveness trials or trials concerning conditions not serious or life-threatening may also be submitted to the database. *Id.* The database is the result of the amendments made by the Food & Drug Administration Modernization Act. See Pub. L. No. 105-115, 111 Stat. 2296 (1997) (codified in scattered sections of 21 U.S.C.). See also Charles Marwick, *Implementing the FDA Modernization Act*, 279 JAMA 815, 815 (1998).

135. See CLINICAL TRIALS GUIDANCE, *supra* note 134, at 3 (listing the information to be disclosed to the clinical trial registry).

136. See *id.* at 7–8 (describing other information that can be voluntarily linked to a database entry). This is likely due to the fact that ClinicalTrials.gov was created at the behest of patient advocacy groups (particularly those concerned with less treatable conditions like AIDS and cancer) as a trial-locating device rather than a tool for evaluating safety data. See Alexa T. McCray, *Better Access to Information about Clinical Trials*, 133 ANNALS OF INTERNAL MED. 609, 610 (2000) (describing, in the words of ClinicalTrials.gov's creator, the origin and intent of the database).

137. Although it is not axiomatic that an unpublished study—one that essentially disappears from the public eye because it is abandoned or never submitted to a journal—has uncovered a problem, evidence exists that such studies tend to be more unfavorable than those that are published. See Dickersin & Rennie, *supra* note 9, at 517.

138. 21 U.S.C. § 356b(b) (2000).

139. Pub. L. No. 105-115, § 130, 111 Stat. 2296, 2331 (1997) (codified at 21 U.S.C. § 356b (2000)). Interestingly, the FDA's authority to require medical device manufacturers to undertake postmarketing surveillance was actually *weakened* in 1998 as a result of FDAMA. See CENTER FOR DEVICES AND RADIOLOGICAL HEALTH, FDA, GUIDANCE FOR INDUSTRY AND FDA STAFF: SMDA TO FDAMA: GUIDANCE ON FDA'S TRANSITION PLAN FOR EXISTING POSTMARKET SURVEILLANCE PROTOCOLS 1 (Nov. 2, 1998), available at <http://www.fda.gov/ohrms/dockets/98fr/980108gd.pdf> (stating that the former automatic requirement to conduct postmarketing surveillance has been limited to situations in which the failure of the device would have serious health consequences, is life-sustaining, or will be used in the body for more than one year).

140. See FDAMA 130 GUIDANCE, *supra* note 37, at 4 ("Voluntary studies are not subject to

FDA also lists basic information about each such trial in a searchable database available on its website.¹⁴¹ The results of the trials, however, are subject to the same confidentiality protections as preapproval studies.¹⁴² Moreover, they are not provided in redacted form alongside the preapproval studies on the Web.¹⁴³ However, compared to the availability of any of the above information only a few years ago, the content available on FDA websites is substantial, creating a serious litigation risk.

2. Medical Journals and Early Clinical Trial Citation

Concerned by the role that medical journals play in disseminating misleading information, editors of prominent publications have long sought to find a way to reduce the likelihood of study-selection bias.¹⁴⁴ In 2004, the International Committee of Medical Journal Editors (ICMJE), a group that includes members from such prestigious journals as the *Journal of the American Medical Association*, the *New England Journal of Medicine*, and the British journal *Lancet*, met to revise its Uniform Requirements for Manuscripts Submitted to Biomedical Journals (“Requirements”).¹⁴⁵ The Requirements reflect a voluntary agreement of basic standards for the review and publication of medical and scientific information. To effectuate change, the members included a relatively minor requirement for disclosure prior to publication, but in doing so, this *minor* requirement set in motion a potentially important limitation on secrecy.

The change adopted in the Requirements creates a new obligation on authors to register clinical trials as a precondition to consideration for publication.¹⁴⁶ To satisfy the ICMJE, the trial registry must be public and accessible without charge.¹⁴⁷ Moreover, it must be open to all submitters and electronically searchable, and it must include a mechanism to ensure the validity of the registration data.¹⁴⁸ It appears that the only registry that would qualify would be either a federal government-maintained website like ClinicalTrials.gov or a neutral, third-party website like Thomson’s CenterWatch or the Pharmaceutical Research and Manufacturers of America’s (PhRMA) ClinicalStudyResults.org.¹⁴⁹ Private company databases would presumably

506B’s reporting requirements . . .”).

141. See Postmarketing Study Commitments, <http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm> (last visited Nov. 20, 2006).

142. See FDAMA 130 GUIDANCE, *supra* note 37, at 15 (“[The] FDA will not make public any trade secrets, or any information that, if disclosed, might cause an unwarranted invasion of personal privacy.”) (internal citations omitted).

143. While preapproval studies are available on the FDA website, they are located in a separate database from postmarketing reports. See Drugs@FDA, <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/> (last visited Nov. 5, 2006).

144. See AMA, *supra* note 53 (describing several forms of medical research bias).

145. See Benjamin Falit, *Pharma’s Commitment to Maintaining a Clinical Trial Register: Increased Transparency or Contrived Public Appeasement*, 33 J.L. MED. & ETHICS 391, 392 (2005).

146. ICMJE, UNIFORM REQUIREMENTS FOR MANUSCRIPTS SUBMITTED TO BIOMEDICAL JOURNALS: WRITING AND EDITING FOR BIOMEDICAL PUBLICATION 21 (2006), <http://www.icmje.org/icmje.pdf> (“The ICMJE member journals will require, as a condition of consideration for publication in their journals, registration in a public trial registry.”).

147. *Id.* at 22.

148. *Id.*

149. The ICMJE issued a joint statement in 2004 in which it declared that the only registry

be too likely to vary in the quantity and quality of information and could perhaps incorporate bias.

As a result of the Requirements, a company must decide to make certain disclosures about a trial *before* the results are known if there is ever to be a chance of publishing in a prominent journal. If a medical product is to reach blockbuster status, this may be an incentive too great to ignore. There is evidence that the publication requirement is already having an effect¹⁵⁰ by increasing the number of disclosures to ClinicalTrials.gov and thereby reducing the tendency toward nondisclosure of trial information.

3. Legislative Proposals to Foreclose Opportunities to Retain Information in Confidence

To further reduce information asymmetry, some advocates urge the adoption of new federal legislation. Two recent efforts in Congress utilizing different approaches typify the call for reform: one seeks to increase the amount of information subject to mandatory disclosure via government information portals, while the other would have increased the penalties for failing to disclose important information.

The Fair Access to Clinical Trials Act ("FACT Act") of 2007 provides for a greatly expanded government clinical-studies database that would include a registry of new trials and, significantly, a results database.¹⁵¹ Participation in the FACT Act database would be mandatory for both publicly and privately funded trials from the phase II stage forward.¹⁵² In essence, the bill takes the ClinicalTrials.gov database and removes its "serious or life-threatening diseases and conditions" limitation.¹⁵³ Additionally, the FACT Act attempts to rein in the information disclosure restrictions on parties to contract research by prohibiting limits or unreasonable delay in discussing or publishing the results of clinical trials.¹⁵⁴ To ensure manufacturers do not take their research overseas to retain confidentiality, the bill also contains a section that would, under certain circumstances, include foreign clinical trials within the disclosure rules.¹⁵⁵ The other congressional reform effort, the Pharmaceutical Research and Manufacturers Accountability Act of 2005 ("PhRMA Act"), was introduced in the 109th Congress but did not become law.¹⁵⁶ It was directed to drugs only and would have increased the penalties for violations of existing FDA rules relating to adverse

known to meet all its criteria is ClinicalTrials.gov. Catherine D. DeAngelis et al., *Clinical Trial Registration: A Statement From the International Committee of Medical Journal Editors*, 292 JAMA, 1363, 1364 (2004). But it left open the possibility that other registries could satisfy the ICMJE's requirements. *Id.*

150. See Deborah A. Zarin, Tony Tse & Nicholas Ide, *Trial Registration at ClinicalTrials.gov Between May and October 2005*, 353 NEW ENG. J. MED. 2779, 2784 (2005) (finding a seventy-three percent increase in trial registrations on the government website, ClinicalTrials.gov, following the adoption of the Requirements).

151. S. 467, 110th Cong. at § 3(a)(3) (2007). Another bill, the Enhancing Drug Safety and Innovation Act of 2007, combines the expanded database provisions of the FACT Act with new requirements for FDA risk evaluation and mitigation strategies. See S. 484, 110th Cong. (2007).

152. See S. 467 § 3(a)(3).

153. See 42 U.S.C.A § 282(j)(3)(A) (2006).

154. S.467 § 5.

155. *Id.* § 3(n).

156. H.R. 870, 109th Cong. (2005).

incidents.¹⁵⁷ Specifically, the PhRMA Act raised the penalties for knowingly concealing information related to a “serious adverse drug experience”—a new subcategory of the general failure to adhere to the FDA’s reporting requirements described in the current statute—from one year and one thousand dollars to twenty years and two million dollars.¹⁵⁸ Most interesting is that this new liability was to be placed exclusively on either the CEO of the manufacturing company or on a member of the senior executive management group.¹⁵⁹ Additionally, the bill contained an attestation of compliance provision directed to the company CEO that smacks of Sarbanes-Oxley-style accountability.¹⁶⁰ The clear message is that the rules are adequate, but better enforcement is needed. Given reports of noncompliance with current regulations in key areas,¹⁶¹ that sentiment may be accurate as far as it goes and the bill could see reintroduction in the 110th Congress.

Because provisions like those in the PhRMA Act and the FACT Act can work side-by-side without conflict, it is possible that both could eventually become law. Indeed, they would also seem to complement other existing information-disclosure incentives without creating a preemption issue. Although the bills are somewhat duplicative of the disclosure incentives provided by either publication standards or state tort liability, there is arguably some additional force and consistency to enacting the rules into federal law.

4. More Aggressive Consumer Protection Litigation

Because consumer protection litigation is a field often directed by elected officials, it may be largely fueled by public outrage over industry behavior. If medical product companies believed that public policy or some other consideration insulated them from landing in that position, all doubt was eliminated in the summer of 2004. In the wake of the alleged suppression of important clinical trials related to the use of antidepressants, the New York State Attorney General’s Office pursued a campaign against several drug manufacturers over their efforts to selectively keep studies confidential.¹⁶² New York first filed suit against GlaxoSmithKline (GSK) for fraud in concealing studies regarding the effectiveness of SSRI inhibitors—specifically, the antidepressant medication paroxetine—in treating children with Major Depressive Disorder (MDD).¹⁶³ The complaint included several factual allegations suggesting that GSK

157. *Id.* § 2(a).

158. *Id.*

159. *Id.*

160. See Sarbanes-Oxley Act of 2002, Pub. L. No. 107-204, §§ 302(a), 906(a), 116 Stat. 745, 777, 806 (2002) (codified as amended at 15 U.S.C. § 7201 (Supp IV 2004)); H.R. 870 at § 2(b).

161. See *infra* notes 233–35 and accompanying text.

162. See Gardiner Harris, *Glaxo Agrees to Post Results of Drug Trials on Web Site*, N.Y. TIMES, Aug. 27, 2004, at C4 (describing a settlement with GlaxoSmithKline and citing New York Attorney General Eliot Spitzer’s threat to pursue similar actions against Eli Lilly, Johnson & Johnson, and Merck).

163. See Glaxo Complaint, *supra* note 92, at 1; Barbara Martinez, *Spitzer Charges Glaxo Concealed Paxil Data*, WALL ST. J., June 3, 2004, at B1. The complaint against GSK was brought under a New York statute authorizing the Attorney General to enjoin fraudulent or illegal business acts. See N.Y. EXEC. L. § 63(12) (McKinney 2002).

promoted the off-label use of paroxetine in children while simultaneously concealing negative information.¹⁶⁴ Significantly, much of the negative information impacted efficacy (or the lack thereof) as opposed to safety. A subsequent inquiry was initiated against Forest Labs regarding the marketing of its antidepressants Lexapro and Celexa.¹⁶⁵

The results of the New York actions were swift and significant. The initial litigations quickly settled with powerful consent decrees requiring much broader disclosure of clinical trials.¹⁶⁶ Several other companies under scrutiny announced the initiation of their own websites to list clinical trials and results in order to ward off litigation.¹⁶⁷ The information provided is not necessarily comprehensive as manufacturers may choose slightly different levels of disclosure; nor is it convenient since it rests on several Internet locations instead of a central database.¹⁶⁸ But the response certainly worked to create greater access to clinical study data, complementing the efforts of private tort litigation as well as regulatory and scientific incentives.

The New York Attorney General's Office essentially created a model for other states by undertaking such an aggressive and creative role in the information-disclosure controversy. Many state statutes lend themselves to an action similar to New York's.¹⁶⁹ When another controversy erupts regarding an alleged failure to disclose information, the call for reparations may come from one or many of these jurisdictions. Given the success of New York, the chances of such litigation are increased.

The combination of online registries, publication rules, and new government action may render the secret clinical study a thing of the past. Although initial public statements of companies suggest eager compliance with the new transparency regime,¹⁷⁰ their actual response may be less than desired. Assuming the existence of the same practice-based tort disincentives described above, a rational company must consider the costs of increased information disclosure. Greater opportunities for the production of negative information will lead to more litigation risk, which in turn

164. Glaxo Complaint, *supra* note 92, at 7–11.

165. See Press Release, Office of N.Y. Att'y Gen., Forest Labs to Establish Clinical Trials Registry (Sept. 7, 2004), available at http://www.oag.state.ny.us/press/2004/sep/sep7b_04.html (noting that a settlement with Forest resulted from a June 2004 inquiry by the Attorney General's Office).

166. See, e.g., *id.*; Consent Order & Judgment, New York v. GlaxoSmithKline, PLC, No. 04-CV-5304 MGC (S.D.N.Y. Aug. 26, 2004), available at http://www.oag.state.ny.us/press/2004/aug/aug26a_04_attach1.pdf.

167. See Sabine Vollmer, *Some Pharmaceutical Firms to Begin Posting Results of Clinical Trials Online*, NEWS AND OBSERVER (Raleigh, N.C.), Sept. 29, 2004, at 1.

168. See Berenson, *supra* note 6 (contrasting the comprehensive efforts of Eli Lilly to post trials with the paltry efforts of Pfizer and Merck).

169. The best evidence of this comes again from the tobacco company litigations. Forty-six state attorneys general were able to use their enforcement powers to pursue companies for, inter alia, their concealment and suppression of the true health effects of tobacco. See, e.g., Margaret A. Little, *A Most Dangerous Indiscretion: The Legal, Economic, and Political Legacy of the Government's Tobacco Litigation*, 33 CONN. L. REV. 1143, 1156–61 (2001) (quoting a tobacco company lawyer describing, somewhat derisively, the causes of action involved in the cases).

170. See Berenson, *supra* note 6 (noting Eli Lilly's promise to disclose all results for all drugs it sells, but suggesting other companies are less forthcoming).

increases the marginal costs of information production (see figure 2, curve MC_T). That should reset the cost-benefit equilibrium point such that information will be produced at a lower level (Q_{I_T}).

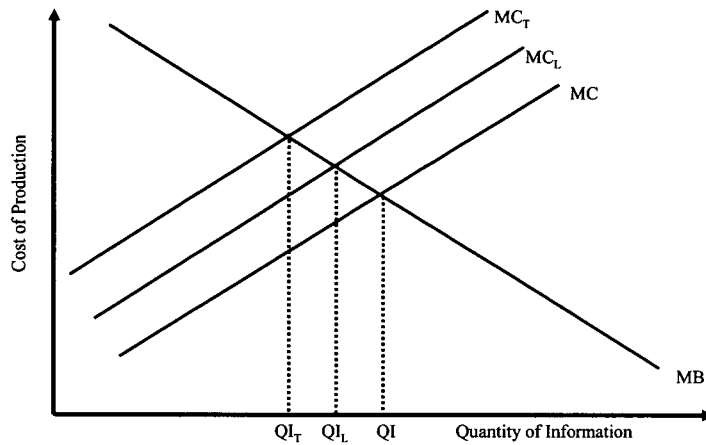


Figure 2. Impact of Increased Transparency. The marginal cost curve MC_T reflects the increased costs of ex post liability transfer stemming from a more transparent information regime. The additional costs further reduce the quantity of information produced to Q_{I_T} levels.

Thus, increased transparency would be expected to result in a more dangerous information environment unless some means of absorbing the additional costs is employed.

In fact, cost absorption is a realistic solution to the problem, and there are several possible routes to achieving this. The most effective will utilize the power of the market and expertise of the firm, but any measure would have a more favorable impact than increasing only transparency without regard to production.

III. EMPLOYING ADDITIONAL INFORMATION-CREATION INCENTIVES TO RESOLVE THE PARADOX

To optimally induce the production of safety and efficacy information, one must reduce or eliminate the impact of tort disincentives without wiping out all of the beneficial effects of products liability law. One can envision a number of possibilities for enhancing minor parts of the existing environment. But to ensure significant and lasting impact, there are essentially two distinct courses from which to choose. One is a market-based solution that will make use of the diffuse knowledge that is in the hands of industry. This article proposes such a mechanism and suggests that it is the best option due to the political desirability and economic efficiency of increasing the incentives for a private company to conduct clinical studies on its own initiative. A more heavy-handed and direct approach would be to connect the FDA's assessment to tort duties by preempting state product liability law when a valid federal approval is obtained. Additionally, one could undertake detailed regulatory revision to provide the FDA with the power to demand additional clinical trials when it deems necessary or to preempt the costs of state liability through its review. Both are second best options that will have lesser benefits in terms of information creation than a market-based solution.

Because to a great extent the two courses for reform are mutually exclusive—many aspects of regulatory revision will eliminate market-based incentives—a choice must be made. Given the recent forward momentum of regulatory revisions, it is important to act quickly and decisively if market-based options are to prevail.

A. Market-Based Optimization: Immunize Timely Disclosure

The idea of a market-based incentive is to encourage a firm to use its knowledge and expertise in the medical product in question to determine what studies will be most likely to provide important safety and efficacy information. The need to identify and avoid future harm as early as possible provides the economic impetus; since some such studies will not occur due to tort liability disincentives, a market-based approach seeks to remove these barriers.

Reducing tort disincentives involves, first and foremost, absorbing the additional marginal costs of transparency by limiting the viability of certain product liability cases. In other words, a type of limited tort reform must be employed. Through this mechanism, the costs of *ex post* practice-based tort liability are effectively transferred back to those allegedly harmed. To be sure, it is a public policy choice—one that places greater value on society's increased access to information over the benefits plaintiffs and their attorneys derive from litigation uncertainty. The net societal gains in terms of the ability to rationally assess medical treatments would seem to outweigh the benefits of retaining the status quo.

Since some tort liability is important to induce a company to internalize the costs of future harm by producing information, complete immunity is not a reasonable option; one must be more circumscribed. Rather, a very narrow legal revision must be adopted that specifically links the desired information with a liability limitation. The limitation need not go beyond ensuring that a manufacturer that acts in a manner that benefits society will not face liability as a result.

The notion of an information-linked tort liability limitation has been articulated before.¹⁷¹ Most prominently, the ALI's 1991 Study on Enterprise Responsibility for Personal Injury suggests the adoption of a regulatory compliance defense that could encompass information disclosure beyond that which is required by the FDA.¹⁷² According to the study, this would address information shortfalls resulting from "regulatory lag or other causes [that] leave risks unregulated; where regulation is purely nominal; or where regulation is compromised [due to information asymmetries]."¹⁷³ However, the ALI report acknowledges that such immunity could be overbroad, permitting a company to continue to market in the face of agency inaction, with tort immunity.¹⁷⁴ Additionally, such a proposal would not preclude secrecy; a firm is permitted to determine after the information is created whether the disadvantages of

171. See, e.g., Salbu, *supra* note 126, at 223–26 (discussing such a limitation in the context of pharmaceutical advertising for off-label use); Stewart, *supra* note 10, at 2179–81 (advocating the adoption of the ALI study's notion of tort preclusion in exchange for full regulatory disclosure).

172. ALI REPORTERS' STUDY, *supra* note 57, at 97.

173. *Id.*

174. *Id.* at 97 n.31. ("While courts might be uneasy with this result, they must not ignore the institutional uneasiness that stems from allowing individual juries to second-guess a specialized agency's reluctance to tighten its existing regulations.").

disclosure outweigh the advantages of tort immunity (or to wait until the equation favors disclosure and then obtain immunity).

A better model for addressing the disadvantages of blanket immunity is the familiar tort concept that restricts evidence of subsequent remedial measures, embodied most familiarly in Rule 407 of the Federal Rules of Evidence.¹⁷⁵ The rule states that evidence of subsequent measures that, "if taken previously, would have made the injury or harm less likely to occur," are not admissible to prove "negligence, culpable conduct, . . . a defect in a product's design, or a need for a warning or instruction."¹⁷⁶ The purpose of the rule is to encourage remedial acts a defendant might not otherwise undertake because such acts could increase liability by establishing that a problem existed at the time of the plaintiff's injury.¹⁷⁷ It has been applied to pharmaceutical products liability cases that involve desirable remedies such as post-injury changes to package inserts.¹⁷⁸ In practice, the rule is less than perfect as an evidentiary barrier due to the many exceptions that nevertheless permit remedial measures to be introduced.¹⁷⁹ However, it can still serve an important purpose in focusing the trier of fact on the specific use of the evidence rather than its tendency to indicate fault.¹⁸⁰ Rule 407 and the many analogous state rules are significant because they are prominent real life embodiments of the aforementioned public policy decision to transfer the liability costs of socially beneficial behavior back to plaintiffs.

Although structural similarities between an information production incentive and existing subsequent remedial measure evidence rules are appropriate, the two must necessarily be subtly different in the behavior they encourage. The object of a production incentive is to induce action—the undertaking of voluntary studies—prior to any knowledge of harm. Rule 407, on the other hand, addresses acts that take place after the harm, when the appropriate remedial act is clear. To the extent that both relate to future loss avoidance, the goals are otherwise the same. Most important to parallel is the use of a limited evidentiary preclusion as a means for preserving the advantages of tort liability.

Applying the notion of a limited exception to information incentives, the first step is to articulate the particular type of information that requires encouragement. In the context of medical treatments and devices, this is most certainly a controlled clinical

175. FED. R. EVID. 407. Most states have similar provisions. See Thomas M. Fleming, Annotation, *Admissibility of Evidence of Repairs, Change of Conditions, or Precautions Taken After Accident—Modern State Cases*, 15 A.L.R. 5th 119, 159 (1993) (noting that only one state has abandoned the rule).

176. FED. R. EVID. 407.

177. See 2 CHRISTOPHER B. MUELLER & LAIRD C. KIRKPATRICK, FEDERAL EVIDENCE § 127 (2d ed. 1994).

178. See BECK & VALE, *supra* note 71, § 11.01[2][a]–[b] (listing pharmaceutical cases using the subsequent remedial measures rule in both state and federal jurisdictions).

179. The rule itself states that it "does not require the exclusion of evidence of subsequent measures when offered for another purpose, such as proving ownership, control, or feasibility of precautionary measures, if controverted, or impeachment." FED. R. EVID. 407. This can be a fairly wide opening. See MUELLER & KIRKPATRICK, *supra* note 177, § 127, at 26 (suggesting that the rule invites courtroom games in an attempt to introduce the evidence).

180. See MUELLER & KIRKPATRICK, *supra* note 177, § 127, at 26 ("[T]he principal impact of FRE 407 is not so much in keeping evidence out altogether as it is in limiting the uses to which the evidence may be put.").

trial to investigate either efficacy or safety. More specifically, the important trials to incentivize are those agreed-upon or voluntary studies that occur after FDA approval, when the public is at most risk but the FDA has a weakened ability to persuade. Secondly, the optimal timing of information creation and disclosure must be considered. Early production and disclosure should be rewarded, while delayed acts should receive no special treatment. Finally, one must address the particular liability that creates the disincentive. As described above, liability is generally for a failure-to-warn product defect case that is premised on the argument that a manufacturer failed in its duty to communicate the problem before a given injury occurred.¹⁸¹

Putting it together, one could design a rule such that if a manufacturer follows a specific, expeditious creation and disclosure path, it could count on avoiding a particular type of tort liability. Generally, the liability limitation should be constrained to studies conducted by the manufacturer as opposed to government or academic researchers. This ensures that a manufacturer has a strong incentive to invest in discovering the information first, as another's discovery of the same product defect will not affect tort liability.

To cement the tort limitation into law and provide the necessary predictability, it should be adopted as a statutory exception to a state's existing tort regime and/or as a federal evidentiary law.¹⁸² Although appropriate wording is flexible, it is possible to imagine a basic template. The exception should address a clinical study's role in establishing a warning defect in later-filed cases:

- (a) When a postmarketing study, conducted by or on behalf of a manufacturer and initiated after [the date of this law's enactment], is fully disclosed through registration and the reporting of all outcomes, it may not be used as evidence in a design defect, a failure -to -warn defect, or a negligent failure-to-warn case filed after the disclosure.

The exception should also separately address the fact that clinical studies are used to retrospectively suggest knowledge of a defect:

- (b) Additionally, said study shall provide a rebuttable presumption that a manufacturer was not knowledgeable before the study's conclusion as to any problem discovered as a result.

181. *See supra* notes 101–118 and accompanying text. The exact tort cause of action could differ from state to state, depending on how it has been developed in a given jurisdiction. Some jurisdictions could refer to this as a negligence case and some as strict liability, while states within those groups could differ as to whether the failure to warn makes a product defective or is, in and of itself, actionable. *See* BECK & VALE, *supra* note 71, § 2.02; PRODUCTS LIABILITY, *supra* note 63, § 4.12. Semantics aside, the basic liability that must be circumscribed is apparent.

182. Enacting an evidentiary limitation into federal law may have an effect on state product liability cases via diversity jurisdiction. Generally, state law controls when it provides the substantive rule of decision. *See* *Erie R.R. Co. v. Tompkins*, 304 U.S. 64 (1938). Some federal jurisdictions view Rule 407 as subordinate to this doctrine and some find that the rules preempt conflicting state law. *See* MUELLER & KIRKPATRICK, *supra* note 177, § 133, at 70–71.

To take advantage of this important evidentiary exclusion and presumption, a manufacturer will be encouraged to address safety and efficacy issues as soon as possible, certainly before a third party does. And as is appropriate for a market-based incentive, the stronger the sales and wider the patent population, the more powerful the incentive will be.

Of course, a tort liability limitation as stated above is not without drawbacks. While the provisions are narrowly tailored to preserve most of the incentive in product liability cases, they may end up restricting some cases with merit. This should be acceptable as long as the overarching goal of greater information production is satisfied. Additionally, one must recognize that other disincentives that accompany the disclosure of negative information will not be avoided. For example, the economic loss a company will suffer from pulling a high-profit product from the shelves¹⁸³ will still act as a force against creation and disclosure. Also, one could argue that companies will be likely to manipulate research in order to obtain the tort advantage (at least until a disinterested third party uncovers the truth).¹⁸⁴ However, on balance, the greater incentives lie with undertaking an investigation, and doing it early to gain tort immunity, rather than focusing on strategies to generate short-term sales.

B. Second-Best Options: Regulatory Revisions

Given the existing power and expertise of major regulatory agencies such as the FDA, it is reasonable to consider whether such government authority can be better leveraged to address the likely information shortfall. At least two possible avenues for regulatory revision are apparent. One would simply tie a manufacturer's obligation in tort to the requirements for regulatory approval; satisfying the regulators would preempt additional state tort law. Another would be to increase the FDA's ability to demand information, particularly post-approval. Both would probably be effective in increasing the amount of information produced, but are likely to be less efficient and effective than a market-based approach for a variety of reasons.

1. FDA Preemption and the Decrease in the Marginal Benefits of Production

Whether complying with FDA regulations should satisfy state common law tort duties,¹⁸⁵ or indeed, should preempt them, has long been a popular topic among legal commentators.¹⁸⁶ Clearly, manufacturers face stringent FDA production and disclosure requirements on the road to approval and thereafter. In many cases, manufacturers may also be limited in undertaking certain acts by regulatory law, such as disseminating

183. See *supra* note 82.

184. Former medical journal editor Marcia Angell suggests that the danger of allowing medical product companies to control clinical trial research is so great that the system should be completely revamped to provide for strong federal oversight and administration. See ANGELL, *supra* note 51, at 244–45.

185. Note that noncompliance with FDA regulations could be the basis of a negligence per se action. PRODUCTS LIABILITY, *supra* note 63, § 4.22 at 194; see also David G. Owen, *Proving Negligence in Modern Products Liability Litigation*, 36 ARIZ. ST. L.J. 1003, 1008–09 (2004) (describing the requirements for a negligence per se case generally and noting that a violation of a statute or regulation must be proven).

186. See *supra* note 10.

certain information to the public without FDA review and approval.¹⁸⁷ This tight control over the information environment may be appropriate for a primarily or exclusively federal legal landscape.

In theory, Congress could have carved out an explicit preemption scheme for the regulatory regime articulated by the Food, Drug, and Cosmetic Act (FDCA)¹⁸⁸ and the Medical Device Amendments Act (MDA).¹⁸⁹ However, in the context of the MDA, the Supreme Court has ruled that congressional intent does not suggest the elimination of all state product liability law as a remedy for manufacturer disclosure issues.¹⁹⁰ Additionally, several courts and commentators have recognized the lack of any explicit preemption in the FDCA as applied to prescription drugs.¹⁹¹ To the extent there is a case for preemption, it appears that implied conflict preemption¹⁹² is the essential

187. For example, sample labels must be included with the drug applications. 21 U.S.C. § 355(b)(1)(F) (2000 & Supp. IV 2004); 21 C.F.R. § 314.120 (2004). Additionally, all safety and effectiveness claims made in prescription drug promotion must be based on substantial evidence or substantial clinical experience, and cannot be false or misleading. 21 U.S.C. § 352(q) (2000 & Supp. IV 2004); § 355(d)–(e); 21 C.F.R. § 202.1(e) (2004).

188. § 355(d)(5).

189. 21 U.S.C. § 360(b) (2000 & Supp. IV 2004). There is, in fact, limited statutory preemption for FDA regulations in the context of nonprescription drugs. *See* 21 U.S.C. § 379r (2000) (No state may establish requirements that are “different from or in addition to, or that [are] otherwise not identical with, a requirement under this chapter, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 et seq.), or the Fair Packaging and Labeling Act . . .”). An even more limited provision exists for medical devices. *See* 21 U.S.C. § 360k (2000) (No state may establish requirements that are “different from, or in addition to, any requirement applicable under this chapter to the device . . .”). Additionally, in 2005 the House of Representatives passed a bill that would grant immunity for punitive damages related to safety, labeling, or packaging for companies that comply with FDA standards. Help Efficient, Accessible, Low-cost, Timely Healthcare (HEALTH) Act of 2005, H.R. 5, 109th Cong. § 7(c) (2005). The bill did not emerge from the Senate and has not been reintroduced in the 110th Congress.

190. *See* *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 491 (1996) (“[Section] 360(k) [of the MDA] simply was not intended to pre-empt most, let alone all, general common-law duties enforced by damages actions.”).

191. *See, e.g.,* *Motus v. Pfizer Inc.*, 127 F. Supp. 2d 1085, 1092 (C.D. Cal. 2000) (“[M]ost courts have found that FDA regulations as to design and warning standards are minimum standards which do not preempt state law defective design and failure to warn claims.”) (citing, among others, *Hill v. Searle Labs.*, 884 F.2d 1064, 1068 (8th Cir.1989); *Mazur v. Merck & Co.*, 742 F. Supp. 239, 247 (E.D. Pa.1990); *Kociemba v. Searle & Co.*, 680 F. Supp. 1293, 1299 (D. Minn.1988)), *aff’d on other grounds*, 358 F.3d 659 (9th Cir. 2004); James T. O’Reilly, *A State of Extinction: Does Food and Drug Administration Approval of a Prescription Drug Label Extinguish State Claims for Inadequate Warning?* 58 *FOOD & DRUG L.J.* 287, 289–90 (2003) (noting the lack of preemption for prescription drugs). The lack of a preemption clause may be due to the fact that the FDCA was adopted before state tort law became such a powerful force. *See* David R. Geiger & Mark D. Rosen, *Rationalizing Product Liability for Prescription Drugs: Implied Preemption, Federal Common Law, and Other Paths to Uniform Pharmaceutical Safety Standards*, 45 *DEPAUL L. REV.* 395, 397 (1996).

192. Many types of preemption are theoretically possible in the context of a regulatory compliance defense. *See generally* Viet D. Dinh, *Reassessing the Law of Preemption*, 88 *GEO. L.J.* 2085 (2000) (reviewing traditional and suggesting novel categories of preemption, including explicit, conflict, and field). But the fact that federal FDA law is generally presumed

question, which must be determined on a case-by-case basis.¹⁹³ The Supreme Court has stated that the decision to preempt has been delegated in part by Congress to the FDA, to be accomplished through regulation.¹⁹⁴ Although the FDA has traditionally been reticent to issue rules that explicitly preempt state law,¹⁹⁵ it has recently made some very strong moves in this direction.

The first steps taken by the FDA in asserting a more strict preemption doctrine involved the increasing use of amicus briefing in medical product liability cases.¹⁹⁶ By far the most significant push for preemption is manifested in the FDA's 2006 drug labeling rules.¹⁹⁷ The new rules are mundane in most respects, the product of typical notice and comment rulemaking. However, in response to comments received related to preemption, the FDA included some rather extreme language that purports to articulate the agency's official position: "[The] FDA believes that under existing preemption principles, FDA approval of labeling under the act, whether it be in the old or new format, preempts conflicting or contrary State law."¹⁹⁸ The statement caught many observers off guard, as the preamble to the originally proposed rule specifically stated that it was *not* intended to preempt existing state law.¹⁹⁹ In a subsequent lengthy

to coexist with state tort law leads to the conclusion that conflict preemption is the only important form.

193. See *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 347–48 (2001) (finding implied preemption for a state tort action based on fraud on the FDA, as the entire interaction occurred only because of FDA law); *Hurley v. Lederle Labs. Div. of Am. Cyanamid*, 863 F.2d 1173, 1179 (5th Cir.1988) (suggesting, in dicta, that preemption could occur in failure to warn cases based on labeling). Given the similarities of standards and level of review, there does not appear to be any reason to treat drugs and biologics differently from medical devices in terms of preemption analysis. See, e.g., *Green & Schultz*, *supra* note 10, at 2123–24.

194. *Medtronic, Inc.*, 518 U.S. at 496 ("Because the FDA is the federal agency to which Congress has delegated its authority to implement the provisions of the [Medical Device Amendments statute], the agency is uniquely qualified to determine whether a particular form of state law [is an obstacle and] therefore, whether it should be pre-empted.") (citation omitted).

195. See *Noah*, *supra* note 10, at 2158 (describing the FDA's lack of opposition to judicial second-guessing as "difficult to fathom").

196. See, e.g., *Hom v. Thoratec Corp.*, 376 F.3d 163, 177 (2004) ("The FDA conceives of Hom's state common law claims as imposing a 'requirement' which is 'different' from that imposed by the FDA in the PMA process, and thus requiring preemption."); Amicus Brief for the U.S. in Support of the Defendant-Appellee & Cross-Appellant, & in Favor of Reversal of the Dist. Court's Order Denying Partial Summary Judgment to Defendant-Appellee & Cross-Appellant, *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2002) (Nos. 02-55372, 02-55498), 2002 WL 32303084; Amicus Curiae Brief of the U.S. in Support of Defendants/Respondents *Smithkline Beecham Consumer Healthcare LP, et al., Dowhal v. Smithkline Beecham Consumer Healthcare, LP*, 88 P.3d 1 (Cal. 2004) (No. S109306), 2003 WL 23527781; *Plaintiff, Device Maker Differ on Significance of Government's New Stand on Preemption*, 32 *Product Safety & Liability Rep. (BNA) No. 24*, at 567 (June 21, 2004) (noting that the FDA interpreted device preemption more expansively in a brief submitted in a federal appeals court case); Gary Young, *FDA Strategy Would Pre-Empt Tort Suits*, NAT'L L.J., Mar. 1, 2004, at 1.

197. See *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products*, 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006) (to be codified at 21 C.F.R. pts. 201, 314, and 601).

198. *Id.*

199. See *Requirements on Content and Format of Labeling for Human Prescription Drugs and Biologics*, 65 Fed. Reg. 81,081, 81,103 (proposed Dec. 22, 2000) (to be codified at 21 C.F.R. pt. 201) ("Accordingly, FDA has determined that this proposed rule does not contain

discussion that responded to comments made about the proposed rule, the FDA argued against the notion that labeling requirements are a safety “floor” over which state tort law may build a higher duty of care.²⁰⁰ According to the agency, the rules are intended to be comprehensive.²⁰¹ Because the FDA controls so completely the labeling requirements, it argues that state tort law decisions that require any different or additional warnings are in dangerous conflict.²⁰² At this point, it is unclear what effect the new labeling rule would have on the viability of failure-to-warn tort cases²⁰³ or even whether it will endure.²⁰⁴

policies that have federalism implications or that preempt State law.”). A particularly vociferous objection was raised by the National Conference of State Legislatures over this policy change. *See* Letter from Sen. Steven J. Rauschenberger, President, National Conference of State Legislatures, to Hon. Mike Leavitt, Secretary, U.S. Dep’t of Health and Human Servs. (Jan. 13, 2006), *available at* <http://www.ncsl.org/statefed/FDArule.htm>.

200. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3934–35.

201. *Id.* at 3935.

202. The FDA’s strongly worded position appears to argue against the basic utility of state tort law in addressing pharmaceutical information disclosure:

Given the comprehensiveness of FDA regulation of drug safety, effectiveness, and labeling under the act, additional requirements for the disclosure of risk information are not necessarily more protective of patients. Instead, they can erode and disrupt the careful and truthful representation of benefits and risks that prescribers need to make appropriate judgments about drug use.

Id.

203. Recent district court rulings on preemption that consider the FDA’s comments have been decidedly mixed. At least three courts have found that the language in the preamble preempts state tort law in the context of a pharmaceutical failure-to-warn case. *Ackerman v. Wyeth Pharm.*, No. 4:05CV84, 2006 WL 2591078, at *7 (E.D. Tex. Sept. 8, 2006), *withdrawn*, 2006 WL 3780913 (Dec. 20, 2006); *In re Bextra & Celebrex Mktg. Sales Practices & Prod. Liab. Litig.*, No. M:05-1699 CRB, 2006 WL 2374742, at *9–*10 (N.D. Cal. Aug. 16, 2006); *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 537–38 (E.D. Pa. 2006). On the other hand, at least five other courts have found under similar circumstances that it does not. *Perry v. Novartis Pharma Corp.*, 456 F. Supp. 2d 678, 683–84 (E.D. Pa. 2006); *McNellis v. Pfizer, Inc.*, No. Civ. 05-1286, 2006 WL 2819046, at *8–*10 (D. N.J. Sep. 29, 2006); *Alaska v. Eli Lilly & Co.*, No. 3:06-CV-88 TMB, 2006 WL 2168831, at *3–*4 (D. Alaska July 28, 2006) (federal jurisdiction only); *In re Prempro Prods. Liab. Lit.*, Nos. 4:03CV1507-WRW, 4:05CV00497, 2006 WL 3806391, at *1 (E.D. Ark. Dec. 27, 2006); *Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d 964, 968 (D. Neb. 2006). The Second Circuit considered the preemptive effect of the FDA’s new position in dicta and indicated that it seriously questioned the agency’s power to make such a determination. *Desiano v. Warner-Lambert & Co.*, 467 F.3d 85, 97 n.9 (2d Cir. 2006).

204. The FDA itself concedes at the conclusion of the comments that “FDA’s regulation of drug labeling will not preempt all State law actions.” Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3936. Courts will be left to determine whether any company in compliance with FDA rules can fail with respect to disclosing information to the public. For example, a regulatory defense to a failure-to-warn claim may be thwarted if the use of the medical product is a foreseeable one that is outside the scope of FDA approval. This is particularly important in the context of drugs, wherein “off-label” uses are an extremely common U.S. medical practice. *See James O’Reilly & Amy Dalal, Off-Label or Out of Bounds? Prescriber and Marketer Liability for Unapproved Uses of FDA-Approved Drugs*, 12 ANNALS HEALTH L. 295, 298 (2003) (noting the prevalence of off-label prescriptions and quoting an AMA study that found forty to sixty percent of U.S. drug

Even if the FDA's position on preemption were to be reversed or toned down, it is possible to achieve the same effect through action by the States. In the context of product liability cases, state courts may (and do) defer in differing degrees to FDA requirements when assessing a manufacturer's compliance with tort law obligations. For example, a court may consider disclosures to the FDA as evidence of due care in satisfying the duty to warn.²⁰⁵ In many instances regulatory compliance may be sufficient, but the facts of the individual case must be assessed on the merits.²⁰⁶ A few states possess a common law or statutory presumption that compliance with FDA rules demonstrates that a warning is sufficient²⁰⁷ or at least limits damages.²⁰⁸ Often, the presumption may be rebutted by evidence that either the regulations or agency review was insufficient to provide safety.²⁰⁹ This approach has been part of the growing tort reform movement²¹⁰ and was largely embraced by the *Restatement (Third) on Torts*.²¹¹

prescriptions are for offlabel uses); James M. Beck & Elizabeth D. Azari, *FDA, Off-Label Use, and Informed Consent: Debunking Myths and Misconceptions*, 53 FOOD DRUG L.J. 71, 80 (1998). And Congress could, of course, resolve any ambiguity by rewriting the applicable statutes to explicitly reject or adopt and delineate the FDA's preemption doctrine. See, e.g., *Schism v. United States*, 316 F.3d 1259, 1289 (Fed. Cir. 2002) ("Congress may ratify agency conduct 'giv[ing] the force of law to official action unauthorized when taken.'") (citing *Swayne & Hoyt v. United States*, 300 U.S. 297, 302 (1937)). For a period of time, it could even reject the rule under the provisions of the Congressional Review Act. 5 U.S.C. §§ 801-808 (2000).

205. See PRODUCTS LIABILITY, *supra* note 63, § 4.22, at 193-94.

206. *Id.*; BECK & VALE, *supra* note 71 § 2.04[2].

207. California is one example of a state with at least some semblance of a common law defense based on the adequacy of administrative review. See *Ramirez v. Plough, Inc.*, 863 P.2d 167, 172 (Cal. 1993). Several states apply a statutory presumption of adequacy based on FDA approval, specifically. See MICH. COMP. LAWS § 600.2946(5) (1995); N.J. STAT. ANN. § 2A:58C-4 (West 2000); TEX. CIV. PRAC. & REM. CODE ANN. § 82.007(a) (Vernon 2003). A few states apply a presumption to products in compliance with government codes, regulations, etc. See ARK. CODE ANN. § 16-116-105(a) (1999); COLO. REV. STAT. § 13-21-403 (1991); IND. CODE § 34-20-5-1 (1999); KAN. STAT. ANN. § 60-3304 (1994); N.D. CENT. CODE § 28-01.3-09 (2003); OHIO REV. CODE ANN. § 2307.75(B)(4) (Anderson 2001); TENN. CODE ANN. § 29-28-104 (2005); UTAH CODE ANN. § 78-15-6(3) (2005); WASH. REV. CODE ANN. § 7.72.050(1) (West 1992).

208. At least five states apply a statutory limitation on punitive damages. ARIZ. REV. STAT. ANN. § 12-701 (2003); COLO. REV. STAT. § 13-64-302.5(5) (1991); OHIO REV. CODE ANN. § 2307.80(C) (LexisNexis 2001); OR. REV. STAT. § 30.927 (2003); UTAH CODE ANN. § 78-18-2 (2005).

209. See David G. Owen, *Special Defenses in Modern Product Liability Law*, 70 MO. L. REV. 1, 21 (2005) (citing examples of product liability cases won because the plaintiff was able to show FDA review to be inadequate).

210. Perhaps the strongest limitation on state tort law is Michigan's statute on product liability reform, enacted in 1995, see 1995 Mich. Pub. Acts 249, *relevant section codified at* MICH. COMP. LAWS § 600.2946 (2000), and upheld as constitutional by the Michigan Supreme Court in 2003. *Taylor v. Smithkline Beecham Corp.*, 658 N.W.2d 127, 137 (Mich. 2003) (finding that MICH. COMP. LAWS § 600.2946(5) was not an unconstitutional delegation of legislative power to the FDA). The relevant section applies to drugs, specifically, and states, in part,

In a product liability action against a manufacturer or seller, a product that is a drug is not defective or unreasonably dangerous, and the manufacturer or seller is not liable, if the drug was approved for safety and efficacy by the United States food and drug administration, and the drug and its labeling were in compliance

Whether preemption of state tort law is achieved directly at the federal level or through state-specific tort reform, one might think that the elimination of liability would fully address the practice-based information disincentives described above. Without the burden of speculative mass torts, a manufacturer would be free to engage in full prospective loss avoidance. But such strong measures may be less than optimal, significantly underperforming compared to market-based incentives. The natural limitations of a large bureaucracy are to blame.

For FDA approval, due process and basic administrative procedure dictate the use of general rules and guidelines.²¹² Through the mandated formality of industry-agency interactions, a bureaucratic disconnect can form which may not incorporate all of the relevant knowledge possessed by a firm.²¹³ Such a structure is inherently less flexible than a company using proprietary information and its own best judgment as to when an investment in greater knowledge is appropriate. As a result, some products may be suboptimally regulated.²¹⁴ A rational company will meet only the minimum requirements necessary for the FDA seal of approval. Additionally, an agency composed of a small and somewhat uniform set of actors would be expected to be less efficient in conducting essential information tasks than an agency-industry collaborative effort that utilizes the diverse research elements of private companies.²¹⁵ In fact, a prominent review of FDA culture and authority issued by the National Academies' Institute of Medicine in 2006 found that the agency suffers from "organizational dysfunction" that "may directly or indirectly affect [its] handling of drug safety concerns."²¹⁶ Requesting the right information, analyzing it correctly, and determining how best to disseminate it to the public are critical to information flow,

with the United States food and drug administration's approval at the time the drug left the control of the manufacturer or seller.

MICH. COMP. LAWS § 600.2946(5) (1995).

211. See RESTATEMENT (THIRD) OF TORTS: PRODUCT LIABILITY § 6(d)(2) cmt. e ("When the content of the warnings is mandated or approved by a governmental agency regulation and a court finds that compliance with such regulation federally preempts tort liability, then no liability under this Section can attach.").

212. For example, FDA employees in the Center for Drug Evaluation and Research use a standard Manual of Policies and Procedures (MaPP) to guide appropriate agency-industry interactions. See FDA, CDER MANUAL OF POLICIES AND PROCEDURES (MAPP), <http://www.fda.gov/cder/mapp.htm> (last visited Oct. 30, 2006); see also Jon D. Hanson & Kyle D. Logue, *The Costs of Cigarettes: The Economic Case for Ex Post Incentive-Based Regulation*, 107 YALE L.J. 1163, 1339 n.724 (1998) (describing, in the context of the tobacco litigations, the problems of "command-and-control regulation" by the FDA and noting that it is constrained by the Administrative Procedures Act).

213. See Ernst R. Berndt, Adrian H.B. Gottschalk & Matthew W. Strobeck, *Opportunities for Improving the Drug Development Process: Results from a Survey of Industry and the FDA* 22-26 (NBER Working Paper No. 11425, 2005), available at <http://www.nber.org/papers/w11425> (referring to survey results of FDA personnel and individuals at companies regulated by the FDA demonstrating that communications between the two are not always good, and more communications would be perceived as valuable by both sides).

214. It has been suggested that suboptimal regulation exists as a general matter with respect to medical devices as compared to drugs. Green & Schultz, *supra* note 10, at 2145.

215. ALI REPORTERS' STUDY, *supra* note 57, at 97 (acknowledging that agency regulation can fail in instances wherein "the agency does not have material information about risk and its assessment or control, but regulated firms do").

216. IOM REPORT, *supra* note 40, at 79-90.

and private actors should be provided with the incentives to contribute. Finally, blanket tort immunity or preemption may encourage gaming of the regulatory process.²¹⁷ The FDA is often accused of acting in an overly industry-friendly manner,²¹⁸ and given the powerful incentives of tort immunity for regulatory compliance, the benefits in exerting undue influence on the agency only increase.

Where the regulatory process falls short, state tort law could provide a useful supplement. But in a preemption world, the regulatory schema becomes both the baseline and the ceiling for firm behavior. A firm derives no benefit from acting beyond the regulatory rules because it will face no liability costs. And if the regulatory rules operate at any point below that to which a cost-internalizing company might otherwise aspire, the marginal benefits of information production will be reduced as compared to the market-based ideal (see figure 3, curve MB_p).

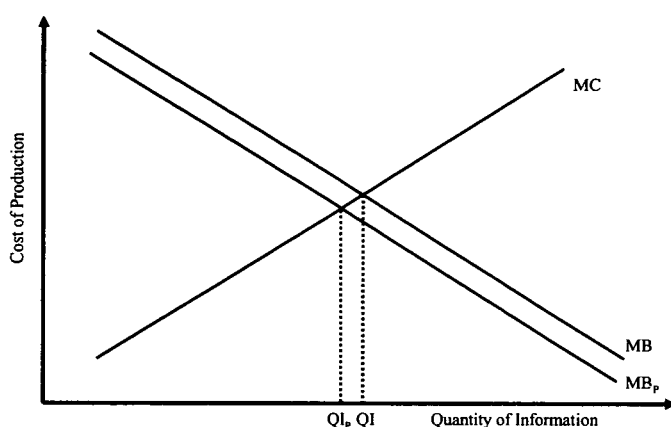


Figure 3. Impact of FDA Preemption. FDA preemption permits a company to avoid some liability for future harm through FDA compliance. Thus, the marginal benefits curve MB_p reflects the decreased benefits for uncovering defects due to this incomplete internalization as compared to MB . The reduction in benefits can be expected to reduce the quantity of information to QI_p .

Information production may be significantly better under a preemption/immunity scheme than a bare transparency scheme—particularly if FDA requirements are reasonably close to the cost-internalizing idea. That makes preemption a second best solution, and perhaps one that is a useful placeholder until a market-based approach can be implemented.

217. See, e.g., Rabin, *supra* note 10, at 2076–79; Thomas O. McGarity, *Beyond Buckman: Wrongful Manipulation of the Regulatory Process in the Law of Torts*, 41 WASHBURN L.J. 549, 558–70 (2002) (describing, in the context of medical devices, strategies to mislead the FDA and suggesting that the agency is unable to respond).

218. See IOM REPORT, *supra* note 40, at 70, 74–75 (describing various investigations into the question of undue industry influence on FDA decision making); Steenburg, *supra* note 33, at 338 (suggesting that pharmaceutical companies have, in the past, used political and social pressure to encourage the FDA to make concessions on approval and postapproval requirements).

2. Increased FDA Power to Compel Information in View of the Disadvantages of Central Control

Employing a regulatory option to address clinical study production disincentives seems straightforward. Nominally, it involves nothing more than increasing the FDA's authority to require postmarketing studies. This would effectively eliminate much of the need for companies to voluntarily fill in the information gaps. Since this power already exists in a limited context,²¹⁹ this appears to be simply a matter of broadening the statute. Bills have actually been introduced in the 110th Congress to do just that, either directly²²⁰ or through the establishment of a "Center for Postmarket Drug Evaluation and Research."²²¹ However, the regulatory empowerment fix is likely to be more problematic than this suggests. Ultimately, the details of empowering the FDA in this manner may make this regulatory option less attractive.

The primary problem is the FDA's general inexperience with identifying and structuring appropriate postmarket clinical trials.²²² Existing FDA authority to require such trials is limited to two instances in which clearly identified categories of clinical trials, normally conducted preapproval, are deferred for postmarketing testing: (1) when a drug is approved under accelerated approval conditions,²²³ and (2) when drugs are planned for use in pediatric populations but the studies of some subpopulations are deferred.²²⁴ However, in those cases, the FDA is not actually responding to a problem or encouraging a general program of long-term testing. For studies conducted in connection with accelerated approval, the FDA is doing little more than moving the approval date forward to get the drug on the market sooner; the usual number of traditional clinical studies are still conducted in approximately the same amount of time.²²⁵ Deferred pediatric studies permit a manufacturer to obtain an approval for

219. See 21 U.S.C. § 356 (2000 & Supp. IV 2004); 21 C.F.R. §§ 314.55, 314.510, 601.27, 601.41 (2004).

220. The SAFE Drug Act gives the Secretary of Health and Human Services the power to order manufacturers of approved drugs to conduct postmarketing studies "after receiving evidence of a significant issue regarding the safety or lack of effectiveness of an approved drug." H.R. 1165, 110th Cong. § 2 (2007).

221. The Food and Drug Administration Safety Act of 2007 gives the director of a proposed Center for Postmarket Drug Evaluation and Research—an internal FDA entity that would continually assess risk for approved drugs—the power to require postmarketing studies. S. 486, 110th Cong. § 2 (2007) (detailing a proposed § 507(e) revision to the FDCA). A substantially similar bill was introduced in the House of Representatives. See Food and Drug Administration Safety Act of 2007, H.R. 788, 110th Cong. The Enhancing Drug Safety and Innovation Act of 2007, S. 484, 110th Cong. § 101, takes a slightly different approach by incorporating the power to require postmarketing studies into a "risk evaluation and mitigation strategy" tailored to particular drugs.

222. Currently, oversight of postmarketing commitments is not a top priority at FDA. See DEP'T OF HEALTH AND HUMAN SERVS., OFFICE OF THE INSPECTOR GEN., MONITORING OF POSTMARKETING STUDY COMMITMENTS 17–18 (2006) [hereinafter OIG REPORT].

223. 21 U.S.C. § 356 (2000 & Supp. IV 2004); 21 C.F.R. §§ 314.510, 601.41 (2004).

224. 21 C.F.R. §§ 314.55, 601.27 (2004).

225. 21 C.F.R. § 314.510. *But see* STAFF REPORT, CONSPIRACY OF SILENCE: HOW THE FDA ALLOWS DRUG COMPANIES TO ABUSE THE ACCELERATED APPROVAL PROCESS (June 1, 2005) [hereinafter CONSPIRACY OF SILENCE], available at http://markey.house.gov/docs/health/iss_health_rep050601.pdf (suggesting that many of these studies are not, in fact, completed).

general application while continuing to work to establish safety and efficacy in children.²²⁶ Again, such studies are not a higher-level inquiry into a medical treatment that has been red flagged, but rather a standard undertaking to gather evidence for a specialized group spread out over a different timeline.

A better analogy to the kind of analysis the FDA would be conducting with the expanded clinical trial authority is that which is undertaken for determining when “agreed upon” studies are appropriate.²²⁷ In such cases, the FDA or a company believes there may be a possible safety or efficacy issue, but not one great enough to delay approval, and they agree on a study that will provide additional information.²²⁸ However, one would expect that the atmosphere is a bit more conciliatory during preapproval negotiations than after a drug has been on the market, generating potentially billions of dollars in sales each year.²²⁹ Postapproval, companies clearly have much more incentive to oppose the FDA. In the face of firm opposition, giving the FDA the legal authority to undertake an action may stop somewhat short of real-world power.

The FDA’s power to punish firm behavior, even in the face of a possible safety issue, is somewhat limited. Actually removing a drug, biologic, or medical device from the market is especially difficult.²³⁰ First, as a doctrine of enforcement, an FDA initiated “recall” of an approved treatment or device is extremely rare.²³¹ The agency almost always prefers to encourage the manufacturer to voluntarily remove the medical product from the market.²³² In fact, the FDA has no authority to order a mandatory

Accelerated approval may result in an additional number of total studies, when those conducted using a surrogate endpoint are added to the required postmarketing studies.

226. 21 C.F.R. §§ 314.55, 601.27 (2004).

227. See 21 U.S.C. § 356b (2000 & Supp. IV 2004); 21 C.F.R. § 314.81(b)(2)(vii) (2004).

228. See FDAMA 130 GUIDANCE, *supra* note 37, at 3.

229. See CONSPIRACY OF SILENCE, *supra* note 225, at 24.

From a financial perspective, post-marketing confirmatory studies are very expensive and the completion of the study does nothing to increase profits. . . . Under the current system there are few benefits and numerous risks associated with conducting post-marketing studies, so it is to companies’ advantage to delay their completion indefinitely.

Id.

230. See IOM REPORT, *supra* note 40, at 157 & n.1 (“After approval . . . FDA’s regulatory and enforcement options generally lie at the ends of the spectrum of regulatory actions: do nothing or precipitate the voluntary withdrawal of the drug.”).

231. See 21 C.F.R. § 7.40 (2004) (describing voluntary and FDA initiated recall requests, and stating that “[a] request by the Food and Drug Administration that a firm recall a product is reserved for urgent situations”).

232. See *id.* (stating that, in the context of drugs and biologics, “[r]ecall is generally more appropriate and affords better protection for consumers than seizure, when many lots of product have been widely distributed”). Media reports often inaccurately suggest that the FDA forces manufacturers to involuntarily recall marketed treatments when a safety issue arises. In fact, in almost every case, the manufacturer actually agrees to withdraw the product. For example, a recent New York Times article carried the headline “F.D.A. Orders Recall of Intravenous Pumps” and referred to the recall of 206,000 Baxter International pumps that deliver medicines intravenously to patients. Gardiner Harris, *F.D.A. Orders Recall of Intravenous Pumps*, N.Y. TIMES, July 22, 2005, at A12. However, the FDA press release on the recall states that Baxter initiated the recall and that it had “voluntarily stopped shipping” the product. Press Release, FDA, FDA Announces Class I Recall of Baxter Healthcare’s Colleague Volumetric Infusion

recall of drugs and biologics—only medical devices.²³³ Second, if the FDA does decide to revoke the marketing approval of a drug or device on its statutory authority, the execution is no simple flipping of a switch.²³⁴ Such a proceeding is nominally an administrative procedure, and as an agency subject to the Administrative Procedure Act (APA),²³⁵ the FDA must provide opportunities for manufacturer responses and possibly even hearings.²³⁶ The arduous nature of such an act renders much less potent its power to induce an unwilling manufacturer to produce information.²³⁷ This inability to employ a big regulatory stick apparently extends to situations in which FDA rules are actually violated. For example, the FDA reports that forty-seven percent of NDA holders with postmarketing commitments and half of BLA holders did not comply with the annual reporting requirements in 2005.²³⁸ Additionally, an independent analysis, conducted by Representative Edward Markey, of industry compliance with

Pumps (July 21, 2005), available at <http://www.fda.gov/bbs/topics/NEWS/2005/NEW01209.html>.

233. If a manufacturer refuses to cooperate with an FDA-requested drug or biologic recall, the FDA's only recourse is technically referred to as seizure, not recall. *See, e.g.*, 21 U.S.C. § 332 (2000) (seizure of products under the Food, Drug and Cosmetic Act for misbranding or adulteration); 21 C.F.R. § 7.40(c) (2004) ("Seizure, multiple seizure, or other court action is indicated when a firm refuses to undertake a recall requested by the Food and Drug Administration, or where the agency has reason to believe that a recall would not be effective, determines that a recall is ineffective, or discovers that a violation is continuing."). However, the FDA has clear authority to order a mandatory recall of medical devices. 21 U.S.C. § 360(h)(e) (2000 & Supp. IV 2004); 21 C.F.R. § 810.10 (2004).

234. *See* IOM REPORT, *supra* note 40, at 168–69 ("[Any grant of FDA authority] must be accompanied by administrative procedures that protect the due process rights of affected parties.").

235. Pub. L. No. 79-404, 60 Stat. 237 (1946) (codified at 5 U.S.C. §§ 551–559, 701–706 (2000)).

236. 21 U.S.C. §§ 355(e), 360e(e) (2000 & Supp. IV 2004); 21 C.F.R. §§ 16.1, 810.11 (2004).

237. *See* Steenburg, *supra* note 33, at 337–38 (referring to the "toothless threat of withdrawal" as an obstacle to enforcing compliance with phase IV clinical trial agreements). Of course, most companies would be much better off complying with FDA requests rather than opposing them, given the potential liability that could follow from marketing a product deemed unsafe by the agency. Some suggest that this provides FDA with a great deal of power compared to other agencies. *See, e.g.*, Lars Noah, *Administrative Arm-Twisting in the Shadow of Congressional Delegations of Authority*, 1997 WIS. L. REV. 873, 892–93 (1997). While this may be true, it is still less power than most believe the FDA possesses, and perhaps not enough to effectively police violations of FDA rules. *See* William W. Vodra & Arthur N. Levine, *Anchors Away: The Food and Drug Administration's Use of Disgorgement Abandons Legal Moorings*, 59 FOOD & DRUG L.J. 1, 3–4 (2004) (describing the FDA's limited remedies for manufacturers' violations of rules, consent decrees, and injunctions when product withdrawal is off the table).

238. The FDA indicated that forty-seven percent of postmarketing commitments attached to approved NDAs or abbreviated new drug applications (ANDAs) and fifty percent of postmarketing commitments attached to BLAs had no annual report submitted within sixty days of their anniversary dates. *See* Report on the Performance of Drug and Biologics Firms in Conducting Postmarketing Commitment Studies, 71 Fed. Reg. 10,978, 10,978–79 (Mar. 3, 2006); *see also* Steenburg, *supra* note 33, at 362–69 (describing phase IV noncompliance data and the lack of available enforcement tools). According to the HHS Inspector General's Office, the FDA does not have the ability to track postmarketing study timeliness or progress toward completion. OIG REPORT, *supra* note 222, at 11.

postmarketing commitments raised similar concerns.²³⁹ For the accelerated approval program, specifically, it found that half the outstanding studies had not even been started (even though the drug was marketed), and forty-six percent of the commitments made since 1992 are not complete.²⁴⁰ Despite these incidents of noncompliance, no drug has disappeared from the market as a consequence.

There may be additional political issues that hamper this solution. In the eyes of the public, an FDA order to conduct further clinical studies on a currently marketed product could appear to be a tacit admission that the product is not safe.²⁴¹ Given the recent attacks on the FDA's ability to safeguard the nation's drug and device markets, the agency may be loath to encourage the suggestion that it failed in its job to fully review the product in question before approval.²⁴² Additionally, there may be internal pressure within the FDA against imposing greater scrutiny. A 2002 survey of almost four hundred FDA scientists found that almost one-fifth claimed to have been pressured to recommend approval of a new drug despite the existence of safety, efficacy, or quality questions.²⁴³ Additionally, the *IoM Report* noted that the agency's heavy reliance on user-fees for funding exacerbates the concern regarding industry influence.²⁴⁴ As a result of FDA culture, far fewer studies may be ordered than would be optimal in view of the evidence, making this option less effective overall than a market-based incentive.

CONCLUSION

While the recent attempts to improve transparency in the medical products industry have a laudable goal, they risk creating a more dangerous environment than currently exists. Greater disclosure of industry-sponsored testing could lead to a reasonable, if disappointing, decision to minimize tort and consumer protection risks by generating less information. As a result, important information flowing from voluntary clinical trials could dry up under this new regime. Revelations like those that impacted the safety-efficacy profiles of drugs such as Vioxx might never occur.

To unravel the paradox of greater future disclosure resulting in less information, the source of the disincentive must be explicitly addressed. The rules must be rearranged to produce a *creation* incentive as well as a disclosure incentive. Due to the advantages of full firm participation in information creation, the optimal structure is a market-

239. CONSPIRACY OF SILENCE, *supra* note 225, at 10–11.

240. *Id.* at 10–11.

241. In the same vein, an approval conditioned on further study could be an acknowledgement that the application did not contain adequate tests to demonstrate safety under the conditions described on the label. Steenburg, *supra* note 33, at 359–60. The FDA is careful, semantically, to avoid this perception. *Id.*

242. See Elizabeth C. Price, *Teaching the Elephant to Dance: Privatizing the FDA Review Process*, 51 FOOD & DRUG L.J. 651, 654–59 (1996) (describing the FDA's culture of risk aversion). However, one could also argue that the same tendency toward risk aversion would induce the FDA to request more tests. *Id.*

243. See Marc Kaufman, *Many FDA Scientists Had Drug Concerns, 2002 Survey Shows*, WASH. POST, Dec. 16, 2004, at A1 (quoting an HHS survey in which 63 of 360 respondents said “they had been pressured to recommend approval of a new drug despite reservations about its safety, effectiveness or quality”).

244. IOM REPORT, *supra* note 40, at 73.

based incentive that attenuates tort exposure from product liability litigation in response to positive information disclosures through an evidentiary limitation. However, a structure that utilizes blanket preemption in exchange for regulatory compliance or simply increases the authority of the FDA to require clinical trials will at least partially resolve the transparency paradox. As such, regulatory revision proposals should be considered second-best solutions to the information production problem. Through the proper balance of information creation and disclosure incentives, the highly positive contributions of medical products to health care in the United States and throughout the world can be maintained, and hopefully improved.

