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The Change in Knowledge Proposal: Repairing Preemption Doctrine in Medical Products Liability

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Abstract:

This Article proposes a new rule that would allow the FDA to achieve the best balance of medical product availability and safety without interference from tort law when the agency has adequately reviewed the safety science. After an analysis of the FDA’s competency to review, and manufacturers’ ability to hide, safety concerns, this Article argues that FDA review is adequate during the initial approval process, but the agency cannot adequately respond to newly acquired safety information that arises post-market. To take advantage of this finding, the change in knowledge proposal would require tort plaintiffs to show a change in the state of safety knowledge from FDA approval to the time of the injury.
The Change in Knowledge Proposal: Repairing Preemption Doctrine in Medical Products Liability

I. INTRODUCTION 3

II. FDA COMPETENCY AND INDUSTRY INTERESTS 6

A. The competencies of the Food and Drug Administration 6
   i. Premarket approval process 7
   ii. Concerns about agency capture 10
   iii. Postmarket monitoring 13

B. Ability of the medical products industry to hide safety data 19
   i. Premarket actions 20
   ii. Postmarket inactions 21

III. OTHER PREMISES 25

A. No substantively correct answer for whether a medical product should be on the market 26

B. FDA is better than courts for deciding the balance of availability and safety in the approval context 28

C. Tort liability disrupts the FDA’s balance of availability and risk 29

IV. THE CHANGE IN KNOWLEDGE PROPOSAL 32

A. Rule 32

B. Application 36
   i. Defective design 36
   ii. Failure to warn 38
   iii. Daubert Inquiry and Limiting Frivolous Claims 39

C. Benefits 41

D. Response to Counterarguments 44
   i. Manufacturers will have the same disincentive to discover safety data postmarket 44
   ii. Federalism concerns with implementation 45

E. Generic products 47

V. CONCLUSION 49
I. Introduction

The reality of medical products is that it is impossible to see all the risks at the time of market approval. And while the epistemic risk of undiscovered harms decreases as the size, length, and number of pre-approval clinical trials increase, requiring more testing by the manufacturer is expensive and could unnecessarily delay the release of products. So is there anyone to blame when there are lawsuits against Merck for the harmful side effects of Vioxx, against Wyeth for the risks of hormone replacement therapy, or Johnson & Johnson for the risks of heart stents? Do we fault the Food and Drug Administration (hereinafter FDA or Agency) for sleeping on the job, the manufacturer for putting profit above patient safety, or personal injury lawyers for bringing frivolous suits? Our sense of who is blameworthy informs our perceptions of preemption doctrine in medical products tort law and the role FDA and courts should play in the regulation of public health.

Tort liability and FDA regulation have a long history together of imposing significant costs on drug and medical device manufacturers. This relationship between tort and regulatory law is defined by the doctrine of preemption; that is, whether the decisions of the FDA immunize manufacturers from state tort liability. Recently, the Supreme Court has waded into medical products preemption jurisprudence with Riegel v. Medtronic, Wyeth v. Levine, and Pliva v.  

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3 552 U.S. 312 (2008).

Mensing. These cases have established the rule that certain failure-to-warn claims against the most dangerous medical devices are preempted by FDA approval, but that the same claims against prescription drugs are not preempted, except when the claim is against a generic manufacturer. Ostensibly, the Court reached these holdings on the basis of statutory interpretation of the Food and Drug Commercialization Act (FDCA), and subsequent Medical Device Regulation Amendments of 1976 (MDA) and Hatch-Waxman Act. Yet, the decisions also suggest that the Court was also compelled by adequacy of FDA review. This Article expands on this concern about FDA competency to recommend the change in knowledge proposal for medical product tort law.

In Part II, this Article surveys the competency and interests of the two most important actors in medical products research: the FDA and the manufacturer. During the FDA approval process, the agency is able to collect and process all relevant clinical information, engage in productive dialogue with the manufacturer, and wield powerful and flexible regulatory authority. In this context, additional tort liability has little benefit and can upset the FDA’s balance of availability and safety. But the FDA’s capabilities are greatly weakened for products already on

5 131 S.Ct. 2567 (2011).
6 The holdings are discussed in more detail infra.
10 In Riegel, the Court spends two pages discussing the adequacy and “rigor” of FDA review. Riegel, 552 U.S. at 1004-05. The Levine decision described FDA’s limited resources for postmarket monitoring and the manufacturers’ superior access to information about emerging risks. Levine, 129 S. Ct. at 1202 and n. 11. Moreover, a successful failure-to-warn claim in Riegel could only lead to the conclusion that the FDA made an incorrect decision despite reviewing all the relevant clinical trial data during its approval process; while the successful failure-to-warn claim in Levine instead signaled the jury’s determination that the FDA did not have enough resources to adequate review new safety concerns discovered postmarket. Compare Riegel v. Medtronic, Inc., No. 99-CV-0649, 2003 WL 25556778 at *4, *7 (N.D.N.Y., Dec. 2, 2003) (finding that plaintiff’s use of the device was contraindicated in the original labeling, based on premarket studies) with Levine, 129 S. Ct. at 1192 (finding that plaintiff relied on risks of amputation that came to light after the product was on the market). Professor Metzger makes a similar claim that Levine was decided not solely on statutory interpretation grounds, but instead should be read as fundamentally concerned with improving federal administration and the potential for federal agency failure. Gillian E. Metzger, Federalism and Federal Agency Reform, 111 COLUM. L. REV. 1, 5 (2011). Professor Sharkey argues judicial preemption outcomes can be best explained through an “agency reference model” that examines the adequacy of federal agency review before finding preemption of state laws. See Sharkey, supra note 64, at 453, 502-520.
the market. The agency allocates significantly less funding for postmarket monitoring, and the manufacturer becomes averse to cooperating with the FDA after a medical product is already approved. In the postmarket context, tort liability acts as an important regulatory and monitoring supplement for safety concerns.

In Part III, this Article establishes other premises necessary to argue that tort regulation of medical products is only appropriate for new safety information that arises post-market: First, there is no substantively correct answer for whether a medical product should be on the market. Second, an adequately informed FDA is better than the courts at weighing the clinical benefits of a medical product against the known risk of adverse effects. And finally, tort liability necessarily disrupts the FDA’s balance of availability and risk.

In Part III, I detail the change in knowledge proposal for tort claims. Capitalizing on the switch in FDA competency and manufacturer interest pre- and post-market, the change in knowledge rule would require that plaintiffs show a change in the state of safety knowledge from the time of FDA approval to the time of the injury. Only after showing that there was a change in knowledge because of information discovered postmarket can plaintiffs then argue that the manufacturer inadequately responded to the changed safety concerns. The change in knowledge rule would not allow courts to interfere with the FDA’s judgment when the agency is at its highest competence, but it would still allow tort law to serve as a supplemental regulator when the FDA has inadequate resources to review products already on the market.

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II. FDA Competency and Industry Interests

There are two opposing views on the question of FDA adequacy and medical product preemption. One view is that tort liability should be preempted because courts do not have the expertise to impose liability on manufacturers for medical products that the FDA has already signed off on. The opposing view is that tort liability is a necessary backstop regulator because the FDA may be captured by industry and does not have the resources to monitor all the drugs on the market effectively. This Article tries to reconcile these views by arguing that both are correct, but at different stages in a medical product’s life-cycle. Through an evaluation of the FDA’s competency and manufacturers’ ability to hide safety data, I argue that only the FDA’s decisions at the time of initial market approval should have preemptive effect; thus, market approval can serve as an effective heuristic for reconciling two opposing views of medical product preemption.

A. The competencies of the Food and Drug Administration

The FDA was created in 1939 in response to growing concerns about unsafe drugs and fraudulent marketing. After its enactment, medical product manufacturers had to seek FDA approval to sell their products. This licensing ability is the central element of FDA’s regulatory authority, and the agency devotes the majority of its resources to premarketing clinical

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12 See infra notes 115-120 and accompanying text.
14 See infra footnotes 51-81 and accompanying text; see also Bates v. Dow Agrosciences LLC, 544 U.S. 431, 451 (2005) (discussing the benefits of tort actions because they “may aid in the exposure of new dangers associated” with the product and even help the agency to “decide that revised labels are required in light of new information that has been brought to its attention.”); Struve, supra note 2, at 612 (“The tort system should remain free to redetermine product safety in the light of information developed during litigation, because the FDA may not always uncover relevant safety information and may not act quickly enough upon the information that it does receive.”).
assessment. But this budget allocation also means that the postmarket monitoring department of the agency has to keep an eye on 11,000 drugs that are already on the market with limited resources. Consequently, the FDA’s current regulatory authority is most effective at evaluating drugs during the initial approval process, but the agency lacks the resources needed to effectively monitor all the drugs already on the market.

i. Premarket approval process

The current approval process for medical products is exhaustive and involves extensive dialogues between the FDA and industry representatives.\textsuperscript{17} The manufacturers of the riskiest class of medical devices (Class III)\textsuperscript{18} and prescription drugs submit comprehensive clinical data to the FDA. For Class III medical devices, a manufacturer must usually submit a multivolume application.\textsuperscript{19} The application includes results of all studies and investigations of the device’s safety and effectiveness that have been published or should reasonably be known to the applicant, a “full statement” of the device’s “components, ingredients, and properties and of the principle or principles of operation,” “a full description of the methods used in, and the facilities and controls used for, the manufacturer, processing, and, when relevant, packing and installation of, such device,” samples or device components required by the FDA, and a specimen of the proposed labeling.\textsuperscript{20} The FDA spends an average of 1,200 hours reviewing each application\textsuperscript{21} and grants market approval if it finds there is a “reasonable assurance” of the device’s “safety and effectiveness”.

\textsuperscript{17} David A. Kessler & David C. Vladeck, \textit{A Critical Examination of the FDA’s Effort to Preempt Failure-to-Warn Claims}, 96 Geo. L.J. 461, 470-471 (2008); see also Medtronic, Inc. v. Lohr, 518 U. S. 470, 477 (1996) (describing premarket approval as a “rigorous” process).

\textsuperscript{18} “A device is in class III if insufficient information exists to determine that general [or special] controls are sufficient to provide reasonable assurance of its safety and effectiveness … and if, in addition, the device is life-supporting or life-sustaining, or for a use which is of substantial importance in preventing impairment of human health, or if the device presents a potential unreasonable risk of illness or injury.” 21 C.F.R. § 860.3(c)(3).


\textsuperscript{20} 21 U.S.C. §360e(c).

\textsuperscript{21} \textit{Lohr}, 518 U.S. at 477.
effectiveness.” 22 The agency must “weig[h] any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.” 23

The review is equally rigorous for prescription drugs, and the manufacturer submits multiple applications at each stage of drug development and clinical testing. The manufacturer must submit an Investigational New Drug application (IND) before new drugs substances can be shipped across state lines for research. 24 To receive an IND, the manufacturer must detail information concerning the plan for human investigations; this would include chemical and toxicology data; clinical trial protocols; safety and efficacy data in humans; and information about the manufacturing process. 25 Only after approval of an IND can the manufacturer begin multi-step clinical trials on humans for efficacy and safety. 26 These clinical trials typically involve thousands of patients on the drug for multiple years. 27 Typically after years of collecting clinical data, the manufacturer can submit a New Drug Application (NDA) to the FDA for approval. The NDA will contain many of the same materials as the Class III medical product application discussed already.

Throughout the approval process, there is extensive dialogue between manufacturers and the FDA to determine what needs to be in the application and what results are expected for approval. 28 Moreover, the FDA may request additional data from the manufacturer at any time. 29

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23 Id. §360c(a)(2)(C).
24 21 C.F.R. §§ 312.1, 312.2(a).
25 Id. at §312.23.
26 The IND establishes safety and efficacy targets for clinical trials. The data must meet those targets for the FDA to grant New Drug Application (NDA) approval. Id. at § 312.22.
So in a sense, the FDA is a de facto co-designer of the clinical trials and target parameters even before the start of clinical studies. This is an important characteristic of the approval process because the FDA, unlike the manufacturer, has no financial incentive to get medical products onto the market quickly by allowing lax clinical studies or setting low efficacy targets. In fact, the FDA has an incentive to make clinical targets unduly hard as a way to decrease the risk of a potential public relations backlash from missing serious adverse events.\(^{30}\)

Not only does the FDA have a lot of flexibility in determining the specifics of the clinical trials needed for approval, the agency can also triage the length of the review process based on unmet need in the patient community. For example, the FDA could require lengthy clinical studies if a manufacturer wanted to market another heartburn medicine without significant advantage over the heartburn drugs already on the market. On the other end of the spectrum, the FDA could, and has, fast tracked the approval process for new drugs that “treat[] a serious or life-threatening condition and . . . demonstrate [] the potential to address unmet medical needs for such a condition,”\(^{31}\) allowing more urgently needed drugs to go through the review process faster. Take the example of fast-track approval for AIDS medication. In 1985, the FDA approved an experimental new AIDS treatment called azidothymidine (AZT). Patients on AZT significantly improved during intermediate and small clinical trials.\(^{32}\) On this basis, AZT was rushed through the FDA approval process in record time; some advocates hailed AZT’s approval

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\(^{30}\) One of the many examples is the public fallout over FDA’s inadequate regulation of Vioxx. See, e.g., Gardiner Harris, F.D.A. Official Admits ‘Lapses’ on Vioxx, N.Y. TIMES, March 2, 2005, available at http://www.nytimes.com/2005/03/02/politics/02fda.html. There is more discussion of the FDA’s motivations in subsection A.ii infra.

\(^{31}\) 21 U.S.C. § 356(a)(1) (2006). For drugs that receive fast track evaluation, the agency may also impose safety restrictions on the distribution and use of the drug, and may require postmarket studies. Id. § 314.520, 314.510.

\(^{32}\) A phase II clinical trial found a substantial difference in six-month morbidity rates between patients in the control and drug groups.
an example of what the agency could accomplish by prioritization and early consultation with pharmaceutical manufacturers.\textsuperscript{33}

Another area for flexibility is the FDA’s authority over labeling.\textsuperscript{34} The premarket approval process includes review of the device’s proposed labeling, which includes a product’s indications, warnings and precautions, contraindications, black box warning, dosage, drug interactions, etc.\textsuperscript{35} The FDA has the flexibility to decide which safety concerns are severe enough to qualify as black box warnings and which ones are mild enough to be included in the general warnings and precautions. The agency can approve one dosage of a drug while denying approval of another dosage that may not have enough clinical data. The label is important not only because it is the crux of a failure-to-warn tort claim, but also because manufacturer can only promote within the prescription label. So the FDA has significant flexibility in approving only certain uses of a product and qualifying approval with strong warnings through the label.\textsuperscript{36}

\textbf{ii. Concerns about agency capture}

Agency-capture is a serious concern that deserves a separate discussion. When discussing the adequacy of FDA review, there is a worry is that the FDA may not be making decisions based solely on the expert opinions of scientists and doctors,\textsuperscript{37} and instead is motivated or

\begin{footnotes}
\footnote{\textsuperscript{33} Michael D. Greenberg, \textit{AIDS, Experimental Drug Approval, and the FDA New Drug Screening Process}, 3 J. LEG. & PUB. POL’y 295, 312-313 (2000). The Phase II clinical trial had problems such as un-blinded methodology, low completion rates, and lack of a diverse study population. Greenberg, supra, at 313.}
\footnote{\textsuperscript{34} For the sake of brevity, I will not discuss the many other ways that the agency has flexibility in its approval authority, such as expanded access during clinical trials, parallel tracking, generics, treatment and “compassionate use” investigational drug exemptions, and the personal use import exemption. Greenberg, supra note 33, at 301.}
\footnote{\textsuperscript{36} The FDA evaluates safety and effectiveness under the labeled uses, and determines whether the proposed labeling is false nor misleading. 21 U.S.C. §360c(a)(2)(B); 21 U.S.C. §360e(d)(1)(A).}
\footnote{\textsuperscript{37} MCGARITY & WAGNER, \textit{supra} note 13, at 43.}
\end{footnotes}
influenced by political considerations, interest groups, or industry capture. For example, the HIV/AIDS interest groups criticized the FDA for unreasonably long approval processes; eventually, interest groups got legislation to expedite the approval of drugs for life-threatening diseases and expanded clinical trial access for patients with limited treatment options. The financial worry is alleviated by the agency’s conflict of interest policy requiring financial disclosures for safety research conducted by private parties in support of an approval application.

Notably, there is empirical evidence that public health primarily motivates regulatory behavior in the FDA. In 1995, Professor Mary Olson found evidence that among new brand-name drugs approved between 1971 and 1991, the FDA placed more emphasis on safety than industry financial interests and the preferences of political overseers. This is understandable. The agency was created because of drug-related tragedies (e.g., Thalidomide), creating a bias toward delay in the approval of new products. The professional concerns of the regulators point towards protecting public health. The reputations of FDA regulators may influence their career

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38 See generally WILLIAM A. NISKANEN, BUREAUCRACY AND REPRESENTATIVE GOVERNMENT (1971); Barry Weingast & Michael Moran, Bureaucratic Discretion or Congressional Control: Regulatory Policymaking by the Federal Trade Commission, 91 J. POLITICAL ECONOMY 765 (suggesting that regulatory agencies will reflect the preferences of their political overseers to avoid political sanctions); McGarity & Wagner, supra note 13, at 181-189. Of course, political pressure is not necessarily inappropriate in the FDA’s risk management process. But ideologically-driven positions that are at odds with scientific data is problematic.


40 See generally McGarity & Wagner, supra note 13.

41 Greenberg, supra note 33, at 308-315.

42 McGarity & Wagner, supra note 13, at 95, 189.

43 Mary K. Olson, Regulatory Agency Discretion among Competing Industries: Inside the FDA, 11 J. LAW, ECONOMICS, & ORGANIZATION 379 (1995); see also Mary K. Olson, Managing Delegation in the FDA: Reducing Delay in New-Drug Review, 29 J. Health Pol. Pol’y & L. 397, 400-401 (2004) (explaining that consumer safety motivates the FDA because the agency is often publicly criticized when individuals are harmed by drugs; in contrast, failure to approve beneficial drugs has not produced the same type of backlash).

prospects. Since drug-related tragedies may damage professional reputations, these concerns contribute to caution in new-drug review. An internal FDA survey conducted in 2004 also suggests FDA scientists approve medical products on the basis of in-depth, science-based reviews.

More recently, there is concern that Prescription Drug User Fee Act (PDUFA) has tainted the approval process by allowing unsafe drugs into the market. PDUFA allows manufacturers to pay application fees in exchange for earlier review and a potential faster approval. The Act did not, on its face, change FDA's standard for safety and effectiveness. Since its enactment in 1992, PDUFA fees have paid for a 60-percent increase in staff in the agency’s new drug application department. Because of the increase in staff, the average time from submission to approval has dropped from about 30 to 12 months. Importantly, an empirical study showed that even though drugs are being approved faster post-PDUFA, the Act has not decreased the successfulness of identifying safety risks. Thus, it appears that PDUFA is not having a perverse consequence on the FDA review of safety risks.

Thus, the agency has the ability to review applications adequately during the approval process because it has absolute licensing authority and does not appear to be perversely

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45 MURRAY J. HORN, THE POLITICAL ECONOMY OF PUBLIC ADMINISTRATION: INSTITUTIONAL CHOICE IN THE PUBLIC SECTOR 58 (1995) (noting that government officials who earn reputations for “vigorous prosecution” improves after-agency job prospects; other the other hand, they may have incentives to take positions that favor their future private-sector employers).
46 Quirk, supra note 44.
47 FDA Survey, supra note 28 (finding that 82% of respondents believed that “the NDA review process allows for in-depth, science-based reviews”).
49 Comparisons of drugs approved during the 1990s to those approved before PDUFA show that the rate of market withdrawals for safety reasons has remained relatively unchanged. Risk Management Report, supra note 2, at 13. In fact, the study found that rates of serious adverse events identified postmarketing were lower for drugs reviewed under PDUFA. Risk Management Report, supra note 2, at 52. Other studies have confirmed that PDUFA has not caused an increase in adverse events. Henry Grabowski & Y. Richard Wang, Do Faster Food and Drug Administration Drug Reviews Adversely Affect Patient Safety? An Analysis of the 1992 Prescription Drug User Fee Act, 51 Journal of Law & Economics 377 (2008). But see Carpenter, supra note 48 at 1359 (finding that the rate of postmarket safety-related events were higher for drugs approved two months before PDUFA deadlines).
influenced by industry interests. But the initial approval process is only a portion of the FDA’s responsibilities and the agency’s role in preemption of tort law. The next subsection discusses the FDA’s competency in monitoring medical products already on the market, and argues that the FDA is an inadequate regulator in this context.

iii. Postmarket monitoring

The importance of postmarket monitoring to detect previously unforeseen safety issues cannot be overstated. During pre-approval clinical testing, products are tested on relatively small populations of patients for limited durations. Thus, pre-approval testing generally is poor for detecting adverse effects that occur infrequently, have long latency periods, or affect subpopulations not included or inadequately represented in the studies (for example, the elderly, ethnic minorities, and pregnant women). It would be impossible to get statistically significant efficacy and safety data on all subgroups prior to market approval because of the limited numbers enrolled in the clinical trials. As the FDA’s former Deputy Commissioner of Policy put it, a clinical study “can detect drug-related injuries that occur at a rate of between one in 500 and one in 1,000. Yet, if the drug is used by 200,000 people, a serious adverse event appearing in as few as one in 10,000 people is very significant, since it would occur 20 times.” These rare reactions can be identified only after a drug has been widely used in the population.

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50 See also FDA Survey, supra note 28 (in a survey of 400 FDA regulators, 75% responded that there was enough time during the approval process to conduct an in-depth, science-based review; and 82% believed that “the NDA review process allows for in-depth, science-based reviews”; but see id. (reporting that 18% have felt pressured to approve or recommend approval for an NDA despite reservations about the safety, efficacy, or quality of the drug.).
51 Kessler & Vladeck, supra note 17, at 471. Risk Management Report, supra note 2, at 48 (stating that the differences between the real population and clinical trial include size, heterogeneous patients, less stringent diagnosis criteria, and that clinical trial patients are closely monitored).
53 Michael D. Green, Statutory Compliance and Tort Liability: Examining the Strongest Case, 30 U. MICH. J.L. REFORM 461, 496 (1997) (stating that the approval trials are unable “to identify all of the risks associated with use of a drug”).
example, Vioxx was used by an estimated 20 million patients.\textsuperscript{54} Thus, even if the FDA correctly balances availability and safety with all the available clinical trial data it deems relevant, the product’s approval does not mean that it will not have serious adverse effects that could necessitate further restrictions in the real world. The question then becomes, who should be responsible for “detect[ing] adverse events not previously observed, improv[ing] understanding of the potential severity of previously unanticipated risks, detect[ing] events resulting from drug interactions or drug effects in particular populations, and assess[ing] the potential for causal relationships.”\textsuperscript{55}

On paper, it would seem that the FDA has the regulatory authority to take on this responsibility and adequately supervise all the drugs on the market. The FDA has the de jure authority to employ several different methods, including reporting systems, medical databases, and studies and registries focused on specific issues to evaluate products on the market.\textsuperscript{56} In 2005, the FDA established the Drug Safety Oversight Board (DSOB) to better monitor drugs on the market.\textsuperscript{57} And a 2007 Amendment provided the agency with additional new resources to monitor the safety of drugs on the market:\textsuperscript{58} the agency could require manufacturers to undertake postmarket safety studies,\textsuperscript{59} and the agency could force manufacturers to make label changes,\textsuperscript{60} and the Amendment diverted greater resources to monitor direct-to-consumer advertising.\textsuperscript{61} The agency may conditionally approve a drug subject to future performance standards, restrict sales,

\textsuperscript{54} In re Vioxx Prods. Liab. Litig., 501 F. Supp. 2d 776, 779 (E.D. La. 2007).
\textsuperscript{55} Risk Management Report, supra note 2, at 52.
\textsuperscript{56} Risk Management Report, supra note 2, at 54.
\textsuperscript{57} FDA, About Drug Safety Oversight Board, http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm082129.htm (last visited November 9, 2011).
\textsuperscript{59} Id. tit. IX, sec. 901(a), § 505(o)(3), 121 Stat. 823, 923-24.
\textsuperscript{60} See id. tit. IX, sec. 901(a), § 505(o)(4), 121 Stat. at 924-26.
and impose device-specific restrictions by regulation. The agency can withdraw approval if presented with new data and must withdraw approval if it determines that a product is unsafe under its labeled use.

Despite these regulatory tools, however, many critics have correctly voiced serious concern that the FDA has a huge enforcement void in the postmarket process. For instance, the FDA requires postmarket monitoring studies in nearly three-quarters of drug approvals, but less than one-quarter of these postmarket studies have ever been completed. And if the FDA does not make ex-ante requirements such as postmarket monitoring studies, then the monitoring process becomes dependent on voluntary reporting by healthcare providers and on industry self-reporting. Healthcare professionals can notify the FDA directly through the MedWatch program or indirectly by notifying the manufacturer. These systems, however, are plagued by underreporting. For instance, healthcare providers may notice unexpected harms in a few

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63 21 U.S.C. §360(e)(1); see also 21 U.S.C. §360h (e) (recall authority).
64 See, e.g., US House of Representatives, Committee on Oversight and Government Reform, FDA Career Staff objected to Agency Preemption Policies, at i, available at http://cdn.levinlaw.com/pdf/Waxman%20FDA%20preemption%20report.pdf (2008) [hereinafter “COGR Report”] (stating that FDA regulators “know that many current approved drug labels are out of date and in many cases contain incorrect information (e.g., the overdose section) … [I]t is unwise to suggest that FDA approved labeling is always up-to-date and always contains a full and complete listing of all pertinent risk information.”); Catherine M. Sharkey, Products Liability Preemption: An Institutional Approach, 76 GEO. WASH. L. REV. 449, 497-498 (2008) (noting the “enforcement void” of regulation). This is in stark contrast to the approval process, where the FDA is not so understaffed. See Friedman, supra note 28, at 7 (stating that FDA’s most comprehensive reviews are made at the time of initial product approval, and postmarket review can be relatively inconsistent).
65 Gao Drug Safety, U.S. Gov’t Accountability Office, Drug Safety: Improvement Needed in FDA’s Postmarket Decision-making and Oversight Process 28, available at http://www.gao.gov/new.items/d06402.pdf (last visited November 9, 2011); see also Office of Inspector Gen., U.S. Dep’t Health & Human Servs., HHS Survey (2002), http://www.peer.org/docs/fda/12_14_04_FDA_survey.pdf [hereinafter “Internal Survey”] (finding that 34% of FDA regulators said they were mostly or completely confident that the agency adequately monitored the safety of prescription drugs on the market.).
68 The manufacturer is required to report to the FDA incidents in which the product may have caused or contributed to death or serious injury. 21 C.F.R. §803.50(a).
patients, but they are unable to know if the harm came from the drug or a patient idiosyncrasy. Healthcare providers also may be unwilling to report events that might get them into trouble. The prevalence of off-label use exacerbates this problem, as healthcare providers do not want to risk potential liability when harms occur because they have prescribed off-label use. Reporting of unrelated harmful events is a problem for FDA analysis as well. The MedWatch system generates some 22,000 reports each year, and of these, a substantial number may not involve a causal link between the product and the injury. Other critics have also suggested that the agency lacks the resolve to investigate postmarket safety issues aggressively because doing so may show that their co-workers in the FDA approved the product incorrectly.

This enforcement void is also a product of inadequate resources and monitoring structure within the agency. The majority of the FDA’s funding goes to pre-approval evaluation and so...
resources are constraint in the agency's post-marketing surveillance efforts.\textsuperscript{75} The FDA's Office of New Drugs, which conducts premarket approval review, has “more than 1,000 employees work to review a few dozen new drugs each year.”\textsuperscript{76} In contrast, the department charged with postmarket monitoring only has approximately 100 employees.\textsuperscript{77} Many academic commentators and independent commissions have echoed this notion that the FDA is understaffed and under-funded, especially in the postmarket monitoring process.\textsuperscript{78} Even “FDA doctors and scientists share this view: 70% believe that the FDA lacks sufficient resources to protect the public health, and two-thirds worry that the FDA is not adequately monitoring the safety of drugs once they are on the market.”\textsuperscript{79}

An example of the agency’s inadequate mechanisms of monitoring is the Vioxx debacle. The cardiovascular side effects of Vioxx were clinically proven not because of MedWatch reports or FDA-mandated postmarket safety trials; instead, Merck only reported a significant increase in cardiovascular events when it began to conduct trials to gain new indication approval in the area of colon cancer.\textsuperscript{80} The FDA’s monitoring system failed to detect the safety issues and, had the manufacturer not voluntarily started new clinical trials, the dangers of using the drug in

\textsuperscript{75} This imbalance in funding is in large part due to PDUFA, and its stipulation that industry fees are only used to increase staffing on initial approval reviews.  
\textsuperscript{76} Ensuring Drug Safety: Where Do We Go From Here?: Hearings Before the S. Comm. on Health, Educ., Labor and Pensions, 109th Cong. 4-6 at 42 (2005) (statement of Dr. Bruce Psaty).  
\textsuperscript{77} Kessler & Vladeck, supra note 17, at 485.  
\textsuperscript{78} See, e.g., Kessler & Vladeck, supra note 17, at 465 (“The reality is that the FDA does not have the resources to perform the Herculean task of monitoring comprehensively the performance of every drug on the market.”); The National Academies, Institute of Medicine, The Future of Drug Safety: Promoting and Protecting the Health of the Public 193–194, available at http://www.nap.edu/openbook.php?record_id=11750&page=193 (2007) (“The [FDA] lacks the resources needed to accomplish its large and complex mission . . . . There is widespread agreement that resources for post-marketing drug safety work are especially inadequate and that resource limitations have hobbled the agency’s ability to improve and expand this essential component of its mission.”).  
\textsuperscript{79} Kessler & Vladeck, supra note 17, at 485.  
\textsuperscript{80} The FDA recalled Vioxx because of a 2000 Merck trial; the trial was designed to study the protective effects of Vioxx in preventing colon polyps, but patients unexpectedly experienced an increase in heart attacks or strokes. See Press Release, Merck & Co., Merck Announces Voluntary Worldwide Withdrawal of VIOXX (Sept. 30, 2004), available at http://www.vioxx.com/vioxx/documents/english/direct_purchasers.pdf; Amanda J. Dohrman, Rethinking and Restructuring the FDA Drug Approval process in Light of the Vioxx Recall, 31 J. CORP. L. 203, 205 (2005).
the general population might not have been discovered. Even after concerns about Vioxx’s safety started to arise, the FDA was slow to react. The agency took over a year before adding heart attack and stroke warnings to Vioxx's label.81 Furthermore, the warning label was weaker than what the agency originally desired.82 This difficulty of negotiating with manufacturers after a drug is already on the market is unsurprising. Once new risk data of an already approved drug starts to mount, the manufacturer has a strong financial incentive to resist adding a new warning to the label or removing the drug from market, both of which would abruptly decrease the revenue stream.

To sum up, the agency in the preapproval context has time to evaluate safety data and the competency to balance the efficacy and safety of products. The agency is adequately staffed, and has enough time to conduct an in-depth scientific review. Once a product is on the market, however, the FDA loses its powerful and flexible approval authority. No longer does the FDA have the luxury of time to evaluate efficacy and safety data in a manner of its choice because the longer it takes the FDA to act, the more people get hurt. The agency is constrained by inadequate resources and there is no longer the mandatory dialogue with industry that enabled the FDA to gather and analyze all the necessary data during approval. These resource and mechanism gaps in the FDA’s monitoring ability undermine the argument for preemption in the postmarket context. Thus, tort law is a necessary regulatory supplement for FDA’s decisions, of lack thereof, in the postmarket context. But there is another, perhaps even more important reason that

81 The FDA was unable to effectively force the manufacturer to revise its label in a complete and quick manner. “[T]hey rejected many of our proposals,” Dr. Kweder, Deputy Director of the FDA’s Office of New Drugs, told the Senate. “[W]e don’t have the authority to tell a company, this is how your label has to look . . . [w]e have to negotiate with the company the specific language of how things should be worded, the placement, those kinds of things, after talking to them.” FDA’s Drug Approval Process: Up to the Challenge?: Hearing Before the S. Comm. On Health, Educ., Labor and Pensions, 109th Cong. 10 (2005) (joint statement of Sandra Kweder, Deputy Dir., Office of New Drugs, FDA and Janet Woodcock, Acting Deputy Comm’r for Operations, FDA) at 23.
preemption should not be extended to the postmarket context: the manufacturer has the financial incentive and ability to turn a blind-eye to new adverse events.

**B. Ability of the medical products industry to hide safety data**

The medical products industry spends a lot of money and time on research and development to bring a product to market. As discussed above, each potential drug goes through extensive studies, with one compound in 25,000 selected for clinical trials and one in three of those compounds gaining FDA approval.\(^83\) The average cost to bring a drug to market is around a billion dollars.\(^84\) Nevertheless, drugs have the potential to be blockbusters with sales over a billion dollars a year.\(^85\) It is understandable, then, that manufacturers have a very strong financial incentive to maintain revenue for drugs already on the market.

This creates a switch pre-and post-market in the manufacturer’s incentive to generate new clinical data. Before approval, there is a financial interest to fund clinical studies in order to satisfy the FDA and gain approval. After approval, the greatest financial return is instead to spend money on marketing campaigns to increase use of the product.\(^86\) Before approval, the manufacturer has a financial incentivize to cooperate with the FDA and submit to all their requests. After FDA approval, without the threat of legal liability\(^87\) and given the FDA’s

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\(^{83}\) Friedman, *supra* 28, at 560-62.


\(^{86}\) The drug industry spends between $22 billion and $57 billion a year on marketing. Jesse C. Vivian, 33 U.S. PHARM. 44 (Sept. 18, 2008), available at http://www.uspharmacist.com/content/d/pharmacy_law/c/10978/.

\(^{87}\) As this Article will discuss *infra* in sections III.B.i and ii, tort liability current imposes obligations under theories of design defect and failure to warn, among others, for prescription drugs. Under the most common “failure to warn” theory of liability, “a prescription drug or medical device is not reasonably safe due to inadequate instructions or warnings if reasonable instructions or warnings regarding foreseeable risks of harm are not provided.” Third Restatement of Product Liability.
enforcement void, the manufacturer has very little incentive to conduct new research or analyze clinical data for fear of uncovering undiscovered risks.

**i. Premarket actions**

The manufacturer is as important, and perhaps more important, than the FDA in foreseeing, detecting, and responding to safety concerns about a product. The manufacturer is intimately familiar with the product and its patient population. The manufacturer funds and conducts nearly all the scientific and clinical data at all stages of in-vitro, animal, and human studies; the manufacturer’s clinicians and scientists are therefore very familiar with the scientific profile and clinical data of each product. The manufacturer’s marketing department has already decided which patient population to target and the expected use of the product prior to FDA approval. Thus, even before the drug is approved, the manufacturer is in the best position to foresee what safety issues could arise with expected use in the general population.

But even if the manufacturer has serious concerns about the safety of an experimental medical product because of previously conducted structure, in-vitro testing, or animal studies, the manufacturer still has a strong financial incentive to conduct clinical trials in order to get efficacy data and satisfy the FDA. So in the premarket context, the manufacturer must conduct the necessary clinical trials. It is extremely difficult and unlikely that a manufacturer could report only efficacy and omit safety data from the FDA during a clinical approval trial.\(^{88}\)

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\(^{88}\) The manufacturer must submit all scientific and clinical data to the FDA to gain approval; this requirement includes the obligation to inform the FDA of new clinical investigations or scientific studies concerning the product which the applicant knows of or reasonably should know of. 21 CFR §814.84(b)(2). “All the primary clinical information about the subjects, such as pathology reports, x-rays, blood reports, etc., is made available for FDA review.” Friedman, *supra* note 28, at 564. The agency may also review individual results and conduct on-site inspections. Friedman, *supra* note 28, at 564. It is extremely unlikely that a manufacturer could purposely omit safety data in its application to the FDA. MCGARITY & WAGNER, *supra* note 13, at 71-72.
Moreover, the manufacturer designs clinical studies jointly with the FDA, so the manufacturer cannot blatantly design studies that will not uncover safety risks.\(^89\) Of course, the manufacturer just wants to squeak by the FDA in the approval process and has no incentive to actually figure out the risks of the product. This task falls largely on the FDA once it has all the raw data.\(^90\) Still, tort liability is not needed in the preapproval stage to encourage the manufacturer to conduct clinical trials and generate new data.

This is in stark contrast to the postmarket context. After a product is on the market, tort liability is needed as a supplemental regulator because the manufacturer has many strategies to hide bad clinical data from the FDA while still following the letter of the law.

**ii. Postmarket inactions**

After a product is on the market, the manufacturer is still in a better position than FDA to collect, generate, and analyze clinical data. The infrastructure for manufacturers to collect safety data in the real world is already in place: at its disposal are help-lines for doctors to report to, large staffs of medical liaisons that travel to clinics and hospitals throughout the nation educating physicians on the product, and a sales force that engages in face-to-face visits several times a day. The manufacturer is also in the best position to analyze new data for a few reasons: First, the scientists and clinicians funded or employed by the manufacturer are likely to be the most knowledgeable about the product. Second, the manufacturer not only has unlimited access to the scientific and clinical trial data, but it also has marketing and sales data to show how the drug is being prescribed. And third, the manufacturer has the money to conduct these new analyses.

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\(^{89}\) *See supra* notes 25-30 and accompanying text. *But see* McGarity & Wagner, *supra* note 13, at 66-71 (discussing how manufacturers bias their drug studies protocol in advance of seeking FDA approval).

\(^{90}\) As Section II.A, *supra*, shows, the FDA has tremendous authority and resources to ensure that the review is adequate.
But after a product is on the market, because of inadequate FDA monitoring, tort liability is needed to counteract the manufacturer’s financial aversion to generate safety data. After approval, the manufacturer is under a legal obligation only to gather and send to the FDA those adverse events reported by patients and practitioners. And the manufacturer only sponsors postmarket clinical trials when it is trying to increase use of the product or is required to do so by the FDA. This is understandable because uncovering additional safety data can only decrease sales once that news is shared with healthcare providers and investors. Given that manufacturers have invested approximately a billion dollars to develop each product, instances of falsification and concealment of safety data by manufacturers is lamentable, but predictable.\textsuperscript{91} For example, New York brought a civil action against GlaxoSmithKline, alleging that the company fraudulently withheld studies showing that its drug increased the risk of suicide in children and young adults.\textsuperscript{92} The company told its employees to “manage the dissemination of data in order to minimize any potential negative commercial impact” while also encouraging its sales representatives to say that “Paxil demonstrates remarkable efficacy and safety in the treatment of adolescent depression.”\textsuperscript{93}

Instances of pharmaceutical manufacturers hiding safety data also highlight the dangers of relying solely on FDA regulation without tort liability. This is especially acute in the postmarket context, where the FDA has a huge enforcement void because of resource deficiencies and a lack of adequate monitoring infrastructure. Because of this, manufacturers are not faced with enough regulatory liability to incentivize them to reasonably collect, generate,

\textsuperscript{91}Michael D. Green, \textit{Statutory Compliance and Tort Liability: Examining the Strongest Case}, 30 U. Mich. J.L. Reform 461, 488 (1997) (noting that “the pharmaceutical industry’s history is littered with instances of deliberate or negligent withholding of information from the FDA in the new drug approval process”).
\textsuperscript{92}Gardiner Harris, \textit{Spitzer Sues a Drug Maker, Saying It Hid Negative Data}, N.Y. Times, June 3, 2004, at A1.
\textsuperscript{93}Id.
analyze, or disclose safety data.\textsuperscript{94} For instance, litigation uncovered that Pfizer had an unpublished study showing that its drug increased heart attacks but waited two years before submitting the study to the FDA. Even more significant, Pfizer waited until after the FDA held a meeting to consider whether similar drugs, such as Vioxx, should carry warnings for heart attack and stroke before giving the agency its postmarket study.\textsuperscript{95} It is unsurprising that after the meeting, the agency recommended a warning be added to the labeling for Vioxx, Celebrex’s main competitor, but not Celebrex.\textsuperscript{96} Next, I illustrate three types of actions that the manufacturer can take in the postmarket context to avoid FDA regulatory oversight.\textsuperscript{97}

The first way to hide potential safety issues is intentional ignorance.\textsuperscript{98} As already discussed, federal law imposes significant reporting duties on manufacturers to report deaths and serious injuries to the FDA. Yet, this reporting requirement is passive because there is no affirmative duty placed on manufacturers to solicit safety data.\textsuperscript{99} Manufacturers can take advantage of this passive requirement by adopting policies of willful ignorance for their medical liaisons and sales representatives. There could be directives to the manufacturer’s field personnel, whether clinicians or salespeople, to avoid topics that could result in an adverse event report.\textsuperscript{100} A telling example of this kind of conduct occurred with the antipsychotic medication olanzapine. Litigation revealed that the manufacturer of olanzapine recognized that the drug was linked to

\textsuperscript{94} See Thomas Scarlett, The Relationship Among Adverse Drug Reaction Reporting, Drug Labeling, Product Liability, and Federal Preemption, 46 FOOD DRUG COSM. L.J. 31, 35 (1991) (“there are severe regulatory and other penalties” for violating FDA rules but “product liability pressure” is necessary to complement).

\textsuperscript{95} See Alex Berenson & Gardiner Harris, Pfizer Says 1999 Trials Revealed Risks with Celebrex, N.Y. TIMES, Feb. 1 2005, at C1. The studies in question were concluded after market approval.

\textsuperscript{96} Id.

\textsuperscript{97} McGARTY & WAGNER, supra note 13 (describing in much greater detail these tactics and more for all administrative agencies that deal with scientific risks).

\textsuperscript{98} McGARTY & WAGNER, supra note 13, at 104-106.

\textsuperscript{99} This has led to estimates that only ten percent of all adverse drug experiences are actually reported, with some studies indicating the actual rate of reporting is far lower. Michael A. Friedman, What is the Value of an FDA Approval in a Judicial Matter?, 12 J.L. & Pol’y 559, 570-571 (2004).

\textsuperscript{100} See, e.g., Dohrman, supra note 80, at 207 (describing how Merck trained its sales representatives to avoid questions about potential cardiovascular risks with Vioxx in a document called “Dodge Ball Vioxx”).
weight gain and diabetes but did not warn prescribers about the risks. During litigation, documents revealed that the manufacturer had long downplayed the studies showing weight gain and high blood sugar, informing the sales representatives: “Don't introduce the issue!!!”

Another way to hide potential safety issues is inadequate follow up to potential safety concerns. An example of this is Vioxx. There were indications that Merck was aware of, and tried to suppress, potential problems with Vioxx before it withdrew the drug from the market. For example, there are documents where Merck executives discussed a link between Vioxx and heart risks years before the company publicly admitted the harm. Another report stated that Merck was aware that Vioxx had no benefits for a certain class of patients and never planned to follow up with additional testing. FDA regulations only require that manufacturers notify the FDA and revise their warning labels when there is “reasonable evidence of an association of a serious hazard with a drug.” But by not conducting further studies, manufacturers can plausibly argue that there is inadequate data to warrant new safety warnings.

102 Id.
103 Gardiner Harris, F.D.A. Failing in Drug Safety, Official Asserts, N.Y. TIMES, Nov. 19, 2004, at A1. See also Anna Wilde Mathews & Barbara Martinez, Warning Signs: E-mails Suggest Merck Knew Vioxx's Dangers at Early Stage, Wall St. J., Nov. 1, 2004, at A1 (stating that “internal Merck e-mails and marketing materials as well as interviews with outside scientists show that the company fought forcefully for years to keep safety concerns from destroying the drug's commercial prospects”).
104 Barry Meier, Questions Are Seen on Merck's Stance on Pain Drug's Use, N.Y. TIMES, Nov. 24, 2004, at A1 (finding that “as far back as 2001,” Merck knew that Vioxx might not provide benefits for older users taking aspirin, and that Merck “never followed up with a plan in 2001 to run a definitive test about the drug's advantages, if any, to aspirin users”).
105 21 CFR §201.57(e) (interpreting 21 U. S. C. §352(f)(2), which provides that a drug is “misbranded . . . unless its labeling bears . . . adequate warnings against . . . unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users.”). The change-being-effected (“CBE”) process permits drug manufacturers to “add or strengthen a contraindication, warning [or] precaution” when there is “sufficient evidence of a causal association with the drug.” 21 C.F.R. § 314 (2006); 73 Fed.Reg. 49603, 49604 (2008) (“Expressly requiring that a CBE supplement reflect newly acquired information and be based on sufficient evidence of a causal association will help to ensure that scientifically accurate information appears in the approved labeling for such products.”).
Another way to hide potential safety issues is intentional inertia. The prime example of this comes from the *Levine* case. There, Wyeth first notified the FDA after the first arm amputation came to their attention in 1967. The FDA did not require a change in the label and amputations continued to occur in later years. Wyeth could have analyzed the accumulating data and added a stronger warning about IV-push administration of the drug, but did not. This is unsurprising because there was no incentive for Wyeth to do more than simply relay reports from practitioners to the FDA.\(^{107}\) In fact, there was a financial disincentive for Wyeth to reanalyze the data for statistical significance, dig deeper into the adverse occurrences, or press the FDA to approve greater warnings on its label.

Tort liability, therefore, is acutely needed in the postmarket context to hold manufacturers to a reasonable standard and prevent, or at least expose, manufacturer-created roadblocks to adequate safety monitoring.\(^{108}\)

### III. Other premises

In the previous Part, this Article established the most important premises of the change in knowledge proposal: that the FDA is able to adequately balance safety and efficacy during the initial approval process, but cannot adequately monitor products already on the market. Before introducing the change in knowledge proposal, some other premises need to be established: First, there is no substantively correct answer for whether a medical product should be on the market. Second, the FDA is better than courts at making judgments on the balance of availability and safety in the approval context. And third, that tort liability necessarily disrupts the FDA’s

\(^{107}\) See Richard A. Nagareda, FDA Preemption: When Tort Law Meets the Administrative State, 1 J. TORT L., Issue 1, Art. 4, at 45 (2006) (“At present, the pharmaceutical industry stands to reap nothing but benefit from FDA inaction, once the FDA has permitted a new device or drug to reach market.”)

\(^{108}\) See *Levine*, 129 S.Ct. at 1202 (“State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly”).
balance of availability and safety by decreasing the availability of medical products. If these premises are accurate, then the change in knowledge proposal – which preempts tort liability based on pre-approval data, but not post-market data – would set a better balance of availability and safety at the approval stage while still imposing duties to monitor on the manufacturer.

A. No substantively correct answer for whether a medical product should be on the market

One premise is that there is no substantively correct answer to whether a medical product should be on the market. Regulation of new medical products is “ultimately a function of scientific procedures and risk management techniques, as well as of policy decisions concerning the limits of personal autonomy and free market commercialism in a field characterized by imperfect information, iatrogenic [] effects, and externalities . . . .”109 Many risks are unamenable to quantitative evaluation.110 Knowledge about a product will always be limited at the time of approval. Rare side effects and long-term outcomes may not be known when a product is approved because of the relatively small size and short duration of clinical trials.111 Even after long use of a product, uncertainties will remain.

Even if epistemic risks did not exist and all the harms and benefits were known for a particular product, there still would not be a substantively correct answer to the question of whether that product should be on the market. It would be impossible to quantify the benefits and

109 Greenberg, supra note 33, at 329, 337 (noting that “FDA regulation of new drug development is at its heart an exercise in risk management.”).
110 Greenberg, supra note 33, at 299 (noting that “serendipitous undiscovered benefits (e.g., differential utility for particular patient populations or therapeutic uses beyond those under clinical trial), or calamitous undiscovered risks (e.g., obscure toxicities by interaction or long-term carcinogenicity)” always remain after product approval.).
111 See supra note 2.
harm in a way that allows for a proportioned balancing on a national scale.\textsuperscript{112} Take the example of prescription drugs. All FDA-approved drugs show statistically significant benefits. But all drugs have side effects. Rarely, if ever, are the beneficial effects the same type as the main side effect; for example, a cough medicine will not have coughing as the most prevalent side effect. Moreover, all drugs have multiple side effects. So taking the example of cough medicine again, the FDA is not weighing the benefits of cough-relief against the adverse effect of more cough; instead, the FDA is weighing the benefits of cough-relief against the adverse effects of drowsiness, stomach pain, and heart palpitations at varying levels of prevalence.\textsuperscript{113} Also complicating this balancing test is the statistical threshold of error used for FDA approval. The current threshold for clinical tests to show statistical significance (the alpha) is five percent. That is, the FDA makes the judgment that a medical product’s benefit exists even if based on all available clinical data, there is a five percent chance that the benefit is does not exist. There is, of course, no substantively correct answer for whether this five percent threshold is the right criteria for approval of medical products; instead, it is a policy judgment by the FDA to use that statistical threshold.

Thus, the optimal balance of availability and risk has no substantively correct answer, but instead is a policy judgment\textsuperscript{114} made by the most competent actor. The next subsection will establish that FDA is a more competent actor than courts for deciding whether a product should be approved based on pre-approval data.

\textsuperscript{112} There is no substantively correct amount of utility or disutility to assign for each health benefit or aliment on a national scale. Individually, of course, a patient could weigh the pros and cons of a particular treatment.


\textsuperscript{114} Greenberg, supra note 33, at 299 (noting that political values are most apparent when an administrative agency struggles with decisions when risks are not defined or estimable).
B. FDA is better than courts for deciding the balance of availability and safety in the approval context

Another premise – that the FDA is better than courts for making judgments on the balance of availability and safety in the approval context – is based on the FDA’s medical and epidemiological expertise advantage over courts, the agency’s flexibility in tailoring its remedy, and because the agency is accountable for its decisions. The FDA is comprised of scientific and clinical experts,\textsuperscript{115} has a broad view of the medical needs of current and future patients, is familiar with currently available and soon-to-be available products, has a self-preservation incentive to take a cautious approach to drug approval,\textsuperscript{116} and has the capability of tailoring the response to inadequate data.\textsuperscript{117} The courts and jury, on the other hand, need the advice of expert witnesses,\textsuperscript{118} are susceptible to hindsight bias, are narrowly focused on the injured plaintiff before them, only have the blunt remedy of declaring a product reasonable or unreasonable, award excessive punitive damages, and are narrowly focused on the medical product before them.\textsuperscript{119} Tort litigation also leads to litigation science, that is, biased scientific research and analysis commissioned solely for the purpose of advancing a party’s interest in private litigation.\textsuperscript{120}

\textsuperscript{115} A typical agency drug review team includes chemists, pharmacologists and toxicologists, physicians, clinical pharmacologists, statisticians, microbiologists. Risk Management Report, \textit{supra} note 2. An expert-driven approach has traditionally been viewed as better for risk regulation and cost-benefit analysis. See \textsc{Stephen Breyer}, \textsc{Breaking the Vicious Circle: Toward Effective Risk Regulation} 78 (1993) (“Regulatory agencies are equipped to make the risk comparisons on which all progressive transformation of the risk environment must be based.”). \textit{But see} Govind C. Persad, Article, \textit{Risk, Everyday Intuitions, and the Institutional Value of Tort Law}, 62 \textsc{Stan. L. Rev.} 1445 (arguing that lay intuitions about risk are important).

\textsuperscript{116} See \textit{supra} notes 43-47 and accompanying text.

\textsuperscript{117} See \textit{supra} notes 28-36 and accompanying text.

\textsuperscript{118} Greenberg, \textit{supra} note 33, at 298 (noting that lay juries are incapable of understanding the complex scientific and statistical evidence relevant to product safety).

\textsuperscript{119} Struve, \textit{supra} note 2, at 587.

\textsuperscript{120} \textsc{McGarity & Wagner}, \textit{supra} note 13, at 32 (noting that litigation science has become both an annoyance to the judicial system and a threat to the legitimacy and respectability of its judgments). The change in knowledge proposal
This analysis suggests that the FDA is the better evaluator than courts of when a product should be on the market. Of course, this comparison is only true if the FDA and courts have access to the same safety information and adequate time to review. That is what the change in knowledge proposal endeavors to accomplish, because this rule only applies to premarket information known to the FDA during market approval. Consequently, as the next subsection will explain, the decision of the FDA during the approval process should “preempt” tort liability because tort liability necessarily second-guesses the FDA’s balance of availability and safety.

C. Tort liability disrupts the FDA’s balance of availability and risk

The final premise—that tort liability necessarily second-guesses the FDA’s balance of availability and safety by decreasing the availability of medical products—is based on the notion that litigation liability based on preapproval data imposes additional or longer safety trials, less research and development money for other products, or some combination of the two scenarios. Whenever a court imposes tort liability on a medical product based on preapproval data, the court is necessarily disagreeing with the FDA’s decision to allow that product into the market. Tort law acts as a distinct regulator because it imposes costs separate from those alleviates this problem by forcing the litigants to use existing data at the time of approval, thereby freezing the state of knowledge. Nor would the change in knowledge proposal prevent Daubert hearings to change the admissibility of the manufacturer’s expert testimony. McGarity & Wagner, supra note 13, at 94.

121 I use quotation marks here because the change in knowledge proposal is not preemption in the traditional sense, as explained in the next Part.

122 Indeed, this is just a narrow application of the broad theory of the “standard Law and Economics account of tort law as a regulatory tool or system of deterrence, that is, as a means of giving regulated parties the optimal ex ante incentives to minimize the costs of accidents.” Kyle D. Logue, Coordinating Sanctions in Tort, 31 Cardozo L. Rev. 2313, 2313, 2319-31 (2010).

123 Or, as in the case with failure-to-warn liability, state tort claims can impose additional warnings can lead to labeling that does not accurately portray what the FDA deemed to be the product’s risks, thereby potentially discouraging FDA-approved use. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3935 (Jan. 24, 2006)
required by the FDA. To account for the costs of tort litigation, the manufacturer can increase product prices, decrease expenses such as research and development, or conduct additional safety research – that would otherwise be unnecessary to pass FDA evaluation – to refute tort claims.

In all these scenarios, the medical product’s availability is decreased by increased prices, decreased number of products in development, or delay in release of the product to market. Thus, whenever tort law imposes liability based solely on safety information already known to the FDA, it necessarily disrupts the FDA’s balance availability and safety.

For example, commentators found that fear of potential liability decreased research investment for the development of an AIDS vaccine. Another example is the infamous Bendectin litigation, which forced Merrill Dow Pharmaceuticals to remove the product from the U.S. market for economic reasons despite strong evidence that there was no causal link between the drug and birth defects. Bendectin had been on the market since 1956 to treat morning

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124 A disadvantage of tort law acting as a regulator in the approval context is that courts can only punish for too much risk; tort law cannot increase the availability of a product. So tort law would not be able to correct unreasonable agency inaction at the approval stage. See Amy Widman, *Advancing Federalism Concerns in Administrative Law through a Revitalization of State Enforcement Powers*, 29 YALE L. & POL’Y REV. 165, 167 (2010); Richard A. Epstein, *The Case for Field Preemption of State Laws in Drug Cases*, 103 NW. U. L. REV. 463, 469 (2009).

125 This does not necessarily mean that the manufacturer always consciously conducts frivolous research for the sole purpose of escaping tort liability. It does not have to be that black-and-white of a choice. The manufacturer could be uncertain about how future courts may view the adequacy of their research and decide the risk-avoiding route of extending the trial longer or conducting a separate safety trial in a different population before releasing the product. Put another way, without precluding tort claims that rely solely on approval data, the manufacturer would not have a predicatable picture of what safety data is adequate to prevent future liability. The manufacturer cannot have a dialogue with a future court or jury in the same way that it can with the FDA about the adequacy of their clinical trials.

126 This sentiment is shared by the Supreme Court and the reason for holding tort claims against medical devices preempted. See *Riegel*, 128 S. Ct. 999, 1007-1011 (holding that common-law tort claims impose “requirement[s]” on manufacturers the same way that FDA’s regulations do).


sickness. In the 1970’s, more than 300 lawsuits were filed against the manufacturer for birth defects. In 1980, the FDA conducted review of available data and found that no association between Bendectin and birth defects.\textsuperscript{129} Nevertheless the manufacturer withdrew Bendectin in 1983 after a jury awarded $750,000 to a family of a deformed child.\textsuperscript{130} According to the manufacturer, their decision was made not because the drug had been proved hazardous, but because their insurance premiums soared to $10 million a year.\textsuperscript{131} It was not until 1993 that the Supreme Court concluded that these plaintiffs suing the manufacturer were relying on junk science.\textsuperscript{132} As a result of the Bendectin experience, drug companies have stayed away from developing medications for pregnant patients.\textsuperscript{133} And there is currently no FDA approved drug available in the U.S. to combat nausea in pregnancy.

To sum up the premises, requiring more safety data does not mean better patient outcomes; there is no correct answer to how much safety data is needed before releasing a product onto the market.\textsuperscript{134} Instead, if we conclude that the FDA is better at balancing availability and safety, and the agency has adequately reviewed the relevant safety data, then the best outcome for patients is not to allow courts to disrupt the FDA’s decision.\textsuperscript{135} If courts were

\textsuperscript{129} Merrell Dow Pharm., Inc., 959 F.2d 1349, 1353 (referring to 35 epidemiological studies clearly demonstrating no causal relation between birth defects and the use of Bendectin).
\textsuperscript{130} Brody, supra note 128.
\textsuperscript{131} Brody, supra note 128 (quoting the company’s director of professional communications as saying "We were forced for business reasons to take a safe and effective medication off the market.").
\textsuperscript{132} Daubert v. Merrell Dow Pharmaceuticals, 509 U.S. 579 (1993)
\textsuperscript{133} See Deborah Ann Wing, et al., U.S. Food and Drug Administration Drug Approval: Slow Advances in Obstetric Care in the United States, 115 OBSTETRICS & GYNECOLOGY 825 (2010). Only two medications have been approved between 1962 and 2010 for obstetrical indications by the FDA.
\textsuperscript{134} It is dissimilar from civil engineers routinely building redundancy into safety systems precisely because they sometimes fail.
\textsuperscript{135} Other scholars have echoed this notion that tort preemption is warranted when the agency’s regulatory review is considerable. Catherine M. Sharkey, What Riegel Portends for FDA Preemption of State Law Products Liability Claims, 103 NW. U. L. REV. 437, 440–62 (2009) ("preemption is warranted in certain narrow contexts, such as
able to disrupt the FDA’s approval of a product, as they must do if tort liability is imposed, then courts undermine the FDA’s determination of when a product should be on the market. This same reasoning for limiting tort liability in the pre-approval context should not apply for safety concerns arising postmarket. Postmarket, we worry that the FDA has not adequately evaluated the safety data because of its enforcement gap and changed manufacturer interest, so tort liability is needed to second-guess the FDA’s decisions, or lack thereof.

IV. The Change in Knowledge Proposal

A. Rule

Under the change in knowledge proposal, plaintiffs filing a tort action could only support their claim by showing 1) that there was a change in knowledge of safety data after FDA approval and 2) that the manufacturer’s response to this change was inadequate.

The plaintiff could only show change by comparing the state of scientific knowledge at the time of the injury with safety information that was known to the FDA at the time of approval. The state of scientific knowledge is not a new concept in tort liability. In Carlin, the California Supreme Court attempted to fine tune the definition of the “knowability” threshold, explaining that a pharmaceutical company would have a duty to warn only of “reasonably scientifically knowable risks.” Long-standing case law has required manufacturers to keep

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136 While the initial burden would be on the plaintiff, a defendant manufacturer could raise a defense by arguing that the state of knowledge at the time of the injury was not different than the FDA’s understanding of the safety risks at the time of approval.

137 Carlin v. Superior Court, 920 P.2d 1347, 1349 (Cal. 1996) (“[W]e have expressly and repeatedly applied a strict liability standard to manufacturers of prescription drugs for failure to warn of known or reasonably scientifically knowable risks.”). Other courts have similarly concluded manufacturers have no duty to warn of unknowable risks.
themselves informed of scientific developments. The court in Carlin suggested that the inquiry would focus on how a reasonable “scientist conducting state-of-the-art research” would interpret a body of data.

In contrast, FDA knowledge of safety risk would be limited to actual knowledge, and not constructive knowledge. This would include all clinical data on the product that was submitted to the FDA by the manufacturer during the approval process. Importantly, it would not encompass safety risks that existed, but were unknown to the FDA at the time of approval.

This Article’s change in the state of scientific knowledge inquiry is similar to the regulatory definition of “newly acquired information” in the FDA’s change-being-effected (“CBE”) process. The CBE regulation permits drug manufacturers to “add or strengthen a contraindication, warning, [or] precaution,” based on “newly acquired information” with

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See id. at 1353 (“[W]hen a plaintiff's claim is based on an allegation that a particular risk was ‘reasonably scientifically knowable,’ an inquiry may arise as to what a reasonable scientist operating in good faith should have known under the circumstances of the evidence.”).

Thus, the change in knowledge proposal would not preclude plaintiffs from using discovery tools to uncover a manufacturer’s misrepresentations to the agency regarding a device’s safety or effectiveness. FDA regulation defines misrepresentation in 21 C.F.R. § 814.3(i) (“A false affirmation or silence or an omission that would lead a reasonable person to draw a particular conclusion as to the safety or effectiveness of a device also may be a false statement of material fact, even if the statement was not intended by the person making it to be misleading or to have any probative effect.”). Nor would the change in knowledge proposal prevent plaintiffs from discovering safety data that has been excluded from the FDA’s knowledge by confidentiality agreements and as business secrets. McGarity & Wagner, supra note 13, at 97, 109-110 (noting that the problem of manufacturers hiding safety data through “contractual provision forbidding scientists who sign the contract to disclose the results of scientific studies without the approval of the sponsor or employer” in employment contracts and research contracts).


“sufficient evidence of a causal association with the drug.” In turn, “newly acquired information” is defined in the final rule as “data, analyses, or other information not previously submitted to the [FDA], which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.” This Article’s change in the state of scientific knowledge inquiry is broader than the FDA’s “newly acquired information” definition because it includes changes in the entire disease category. For example, a later-developed treatment option would qualify as a change in the state of scientific knowledge, but not as “newly acquired information” under the FDA’s regulation. One illustrative example is the case of the antihistamine Terfenadine. Terfenadine was the first in its class to relieve symptoms of allergic rhinitis without causing drowsiness, and it received FDA approval despite known risks of cardiac arrhythmias. A few years later, safer antihistamines in the same class, including a metabolite of Terfenadine, were developed. The newer drugs arguably made Terfenadine unreasonably unsafe under tort law, but would not qualify as “newly acquired information” under the FDA regulation because the known safety profile of Terfenadine did not change.

Nevertheless, the FDA “newly acquired information” definition is helpful because it highlights that new safety concerns arise not only out of new kinds of adverse events, but also changes in the type, severity, or frequency of adverse events. For example, if pre-approval clinical trials did not show any incidence of brain hemorrhage, then even one postmarket report of brain hemorrhage should be considered to change the state of knowledge for that product. On

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143 See 21 C.F.R. §§ 314, 601, 814; see also Wyeth, supra, at 568.  
144 21 C.F.R. § 314.3.  
the other hand, if brain hemorrhages occurred with ten-percent frequency during clinical trials, then the plaintiffs have the burden of showing that postmarket data of brain hemorrhage changes the state of knowledge at the time approval; for example, the plaintiff may be able to do this by arguing that the frequency or severity of hemorrhaging differs from those seen during clinical trials, or that the patients in the real world are different than those used for clinical trials. The FDA’s “newly acquired information” definition is also helpful because it highlights that the source of new safety concerns can be derived from re-analysis of old data. This accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments. For example, in August 2001, Dr. Eric Topol published a meta-analysis in the Journal of the American Medical Association entitled “Risk of Cardiovascular Events Associated with Selective COX-2 Inhibitors” that served as a strong warning to physicians about the risks of Vioxx.146

As a second step to establish tort liability, the plaintiff must argue that the manufacturer responded inadequately to this change in knowledge. For instance, in a jurisdiction that applied a strict-liability failure-to-warn standard,147 the plaintiff could not win by showing an increase in the expected incidences of upset stomach only to argue that it was inadequate for the manufacturer not to have a stronger warning that the product caused death due to gastric bleeding. In order to argue that the manufacturer should have a stronger mortality warning, the plaintiff would have to show that there was postmarket data suggesting that the incidences of mortality were higher than predicted at the time of market approval for that product. As discussed in Section VI.B. infra, the adequacy of manufacturer’s response will depend on what

146 Dohrman, supra note 80, at 208-209.
147 See, e.g., California Civil Jury Instructions 1205, Strict Liability – Failure to Warn – Essential Factual Elements (requiring that the manufacturer failed to adequately warn of known or knowable risks).
theory of product liability was claimed, such as defective design or failure to warn, and that jurisdiction’s liability standard, such as strict liability or negligence.

**B. Application**

In the following sections, I will discuss the current jurisprudence of medical product liability and explain how the change in knowledge proposal would change these doctrines.  

**i. Defective design**

States have set a high hurdle for plaintiffs claiming defective design. The Restatement (Second) of Torts asserted that many products, such as prescription drugs, are “unavoidably unsafe” and that those manufacturers should not incur strict liability in the absence of manufacturing defects or inadequate warnings. The Third Restatement was similarly unwelcoming of defective design claims; it stated these claims can be sustained only when “the foreseeable risks of harm posed by the drug or medical device are sufficiently great in relation to its foreseeable therapeutic benefits that reasonable health-care providers, knowing of such

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148 I discuss the most commonly-used theories of defective design and failure to warn. I forego discussing liability under manufacturing defect theory because these claims involve postmarket evidence that would be unaffected by the change in knowledge proposal. *See* Restatement (Third) of Torts: Prod. Liab. § 2 (1998). A manufacturing defect theory of liability is truly strict in the sense that the manufacturer will compensate people injured using the product as long as the product caused the harm, regardless of foreseeability or utility-risk balance. *See* Kessler & Vladeck, *supra* note at 479 n. 77; Transue v. Aesthetech Corp., 341 F.3d 911, 917–20 (9th Cir. 2003) (holding that the trial judge erred in failing to use a strict liability instruction on a manufacturing defect claim involving silicone-gel breast implants). Nor will I discuss negligent marketing claims, which would also likely involve postmarket information unaffected by the change in knowledge proposal.

149 Restatement (Second) of Torts Sec. 402A comment k (1965) (“there are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs.... Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it unreasonably dangerous.”). Some courts hold that a manufacturer may be liable under a negligence cause of action even if the product is unavoidably unsafe. *See*, e.g., Stone v. Smith, Kilne & French Lab., 447 So. 2d 1301, 1303 (Ala. 1984) (noting that after comment k removes a drug from strict liability, the principles of negligence apply); Toner v. Lederle Lab., 732 P.2d 297, 310 (Idaho 1987) (“[W]hen comment k applies, the plaintiff still may allege negligence.”), cert. denied, 485 U.S. 942 (1988); Johnson v. American Cyanamid Co., 718 P.2d 1318, 1324-25 (Kan. 1986) (holding that when strict liability is prohibited under comment k the plaintiff may plead a design defect theory on the basis of negligence); *see also* Richard L. Cupp, *Rethinking Conscious Design Liability for Prescription Drugs: The Restatement (Third) Standard versus a negligence approach*, 63 GEO. WASH. L. REV. 76 (describing how a negligence standard would keep the reasonable alternative and conscious design inquiries).
foreseeable risks and therapeutic benefits, would not prescribe the drug or medical device for any
class of patients.” \(^{150}\) Most jurisdictions purport to follow the Restatements’ language. Many
courts engage in a case-by-case risk-benefit analysis to determine whether a particular drug or
device is “unavoidably unsafe.” \(^{151}\) Other courts have precluded a design defect theory of liability
by concluding that all medical products should be viewed as unavoidably unsafe. \(^{152}\)

The change in knowledge proposal would not force a change in jurisdictions that
currently preclude the theory of design defect liability. \(^{153}\) For jurisdictions that still conduct the
risk-benefit analysis, the plaintiff’s defective design claim would have to shift its focus to the
change in safety knowledge since the product was first approved for marketing; so a plaintiff
could not solely use evidence of the product’s known clinical profile at the time of approval to
support a defective design claim. A plaintiff can no longer argue that the product was
unreasonably designed when first approved by the FDA; instead, the plaintiff would have to
claim that the manufacturer should have removed the product from the market because
postmarket information, such as newly discovered safety risks \(^{154}\) or better alternatives, \(^{155}\) showed
that it was unreasonable for the product to be used by anyone. \(^{156}\)

\(^{150}\) Restatement (Third) of the Law of Torts: Products Liability § 6(c); see generally James A. Henderson & Aaron D.
Twerski, Drug Designs Are Different, 111 YALE L.J. 151, 152 (2001) (“Plaintiffs may establish defectiveness by
showing that safer alternative drugs were available on the market that reasonable health care providers would have
prescribed in place of a defendant’s drug for all classes of patients.”).

\(^{151}\) See, e.g., Freeman v. Hoffman-La Roche, Inc., 618 N.W.2d 827, 840 (Neb. 2000) (holding that comment k will
provide an affirmative defense “when it is shown that (1) the product is properly manufactured and contains
adequate warnings, (2) its benefits justify its risks, and (3) the product was at the time of manufacturer and
distribution incapable of being made more safe”); Tansy v. Dacomod Corp., 890 P.2d 881, 886 (Okl. 1994)
(applying a similar test for medical devices).

\(^{152}\) See, e.g., McDaniel v. McNeil Lab., Inc., 241 N.W.2d 822, 828 (Neb. 1976) (holding that an unavoidably unsafe
prescription drug should be considered safe unless there is a showing of fraud); Leibowitz v. Ortho Pharmaceutical
Corp., 307 A.2d 449, 458 (Pa. Super. Ct. 1973) (holding that a prescription drug is a reasonably safe product and
that any tort claim must prove an impurity or an inadequacy in labeling).

\(^{153}\) This would ease some federalism concerns, discussing in more detail infra in Part III.C.

\(^{154}\) Under the Third Restatement standard, the plaintiff would have to show that a reasonable physician would not
use that product on any patient because of postmarket acquired information. Many drugs that have been subject
to FDA recall would fit this criterion. See, e.g., Gardiner Harris, Studies Lead to Withdraw of Drug for Bowel Ailment,
ii. Failure to warn

The majority of tort claims against pharmaceutical manufacturers proceed under “failure to warn” theories of liability. The Third Restatement’s section on warning defects states that: “a prescription drug or medical device is not reasonably safe due to inadequate instructions or warnings if reasonable instructions or warnings regarding foreseeable risks of harm are not provided.” A failure to warn claim can be based in negligence or strict liability. In the typical failure-to-warn case, the plaintiff alleges that the product’s label failed to adequately warn of risks that were evident at the time the plaintiff was injured. Under the change in knowledge proposal, failure-to-warn claims could not challenge the FDA’s decision to approve the label at the time of initial approval. Instead, failure-to-warn claims would challenge the

155 For example, the antihistamine Terfenadine, discussed supra, arguably should have been removed – and eventually was removed by the FDA – once safer antihistamines in the same class were developed. FDA, FDA Talk Paper, FDA Approves Allegra-D Manufacturer to Withdraw Seldane from Marketplace, http://www.scienceblog.com/community/older/archives/M/1/fda0452.htm.
156 Removal from market is necessary because a medical product’s design can no longer be changed after the point of approval. As the Supreme Court proclaimed, changing the label is different than a change to the drug. Levine, 129 S.Ct. at 1197 (“But strengthening the warning about IV-push administration would not have made Phenergan a new drug.”); Restatement (Third) of the Law of Torts: Products Liability § 6(c).
158 Restatement (Third) of the Law of Torts: Products Liability § 6(d).
159 Because inquiries into reasonableness, foreseeability, and adequacy are present even in a strict liability failure-to-warn context, the difference between traditional strict liability and negligence doctrine are minimal. See, e.g., Gonzalez v. Volvo of America Corp., 752 F.2d 295, 300 (7th Cir. 1985) (holding that language and concepts of reasonableness in strict liability failure-to-warn cases under Indiana law are the same as negligence cases); Bernier v. Raymark Industries, Inc., 516 A.2d 534, 538 (Me. 1986) (reasonableness of defendant's conduct is a factor); Feldman v. Lederle Laboratories 479 A.2d 374, 385 (N.J. 1984) (same); Bilotta v. Kelley Co., Inc., 346 N.W.2d 616, 622 (Minn. 1984) (holding that strict liability-failure-to-warn claims based on negligence concepts); see generally, Henderson & Twerski, Doctrinal Collapse in Products Liability: The Empty Shell of Failure to Warn, 65 N.Y.U. L. REV. 265, 271–273 (1990); Prosser & Keeton, The Law of Torts § 99, p. 95, fn. 21 (1988 supp.); Bromberg, The Mischief of the Strict Liability Label in the Law of Warnings, 17 CONN. L. REV. 256, 534–535 (1987). But at least one state court has attempted to articulate a difference between failure-to-warn claims based on negligence and strict liability. Anderson v. Owens-Corning Fiberglas Corp., 53 Cal.3d 987, 1003 (stating that there would be a difference in outcome if “a reasonably prudent manufacturer might reasonably decide that the risk of harm was such as not to require a warning as, for example, if the manufacturer's own testing showed a result contrary to that of others in the scientific community”). In both strict-liability and negligence, the jury is asked to evaluate the same risk-risk tradeoffs as the FDA.
160 Most jurisdictions have applied a negligence standard for failure-to-warn claims against medical products manufacturers, thus requiring that the safety concerns were known or knowable to the manufacturer.
manufacturer’s failure to revise or update its warning label in response to postmarket information. Thus, the plaintiff could use evidence of risks discovered after approval that were unknown at the time the drug was approved, or known risks that turn out to be more serious.

iii. *Daubert* Inquiry and Limiting Frivolous Claims

Even a small change in the state of knowledge is sufficient to satisfy the first prong of the change in knowledge proposal. Thus, one argument against this Article’s proposal might be that it would not limit tort litigation (compared to no preemption) because it is too easily satisfied. My response is that the change in knowledge proposal allows judges to dismiss frivolous claims earlier in litigation through two means: a *Daubert* examination of the plaintiff’s expert testimony and the relational aspect of the second prong.

The first prong in the change in knowledge proposal—whether there has been a change in safety knowledge from what the FDA knew at the time of approval—will be a tool for judges to dismiss a tort claim through a *Daubert* examination of the plaintiff’s expert witness testimony. If the change in knowledge proposal were implemented, the two opposing parties would necessarily use medical and statistical experts to argue that state of knowledge has or has not changed from what the FDA knew at the time of approval. The easy case of showing a change in the state of knowledge would be postmarket incidence of a previously unknown adverse effect caused by the product. In that case, the judge must decide under a *Daubert* inquiry that sufficient, reliable evidence of a new adverse effect caused by the product existed. A *Daubert* inquiry of evidence of previously unknown adverse effects depends on whether the new adverse

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161 Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993). The *Daubert* inquiry into the adequacy of expert testimony allows judges as gatekeepers to exclude testimony that is not the product of sound scientific methodology. The relevant factors for making that determination include: empirical testing, peer review, error rate, standards and controls, and general acceptance by a relevant scientific community. See id. at 592-595.
162 Here is where adverse event reporting can have an impact. While the system is statistically flawed – such reporting can raise red flags about new adverse events previously unassociated with a product.
effect can be attributed to that product. If the effect appeared in a controlled clinical trial setting, then a court can be confident there was a causal relationship. On the other hand, if there’s only a single MedWatch report without a lot of background information, then the chances of a causal relationship are low.

The harder case would be if the plaintiff’s expert argued that there was a greater incidence of a particular adverse effect than was already known to the FDA at the time of approval. Take the example of selective serotonin reuptake inhibitor antidepressants (SSRIs) and teenage suicide. Before the introduction of SSRIs, adolescents with depression were at a greater risk of suicide than was the general population. After SSRIs were approved in adolescents, there were, of course, still incidences of suicide and suicidal ideations.163 But given the infrequency of suicide and suicidal ideations, it was not possible during the clinical trial stage to compare the active ingredient and placebo groups adequately.164 It would therefore be nearly impossible to conclude on the basis of adverse event reporting that SSRIs caused an increased incidence of suicidal ideations. Under a Daubert standard, a judge would likely need more than just incidence reporting to conclude that there was a change in safety knowledge from what the FDA knew at the time of approval.165 That does not mean that the change in knowledge proposal requires conclusive evidence of increased incidence of suicidal ideations associated with SSRI use in adolescents. In the case of SSRIs, epidemiological studies or meta-analysis of several different

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165 Under a Daubert inquiry into potentially increased incidence of a known adverse effect, the reliability of the evidence would depend on how the incidence rate was discovered. For example, the rate of adverse effects seen in randomized controlled clinical trials would be most reliable while MedWatch report would be least reliable. In Daubert, the Court dismissed on summary judgment plaintiffs’ product liability claims because their expert evidence suggesting that Bendectin could cause birth defects was inadequate. Plaintiff’s expert testimony was based on in vitro and in vivo animal studies, pharmacological studies, and reanalysis of other published studies; however, the Court decided that these types of studies had not adequately established causation. See Daubert, 509 U.S. at 583.
trials was sufficient to suggest an increased incidence of suicidal ideations to the FDA even though causation was not completely clear. Thus, the first prong is satisfied by even a slight change in the state of safety knowledge as long as the postmarket evidence is based on studies that can pass the Daubert inquiry.

The relational aspect of the second prong also addresses concerns about how easy it would be to trigger the first prong. Even if one argues that the first prong is too easily satisfied by a small change in the state of knowledge, the second prong only authorizes liability when the manufacturer inadequately responds to the seriousness of the change. So if the change in the state of safety knowledge is very incremental, an adequate response in a jurisdiction applying a failure-to-warn standard would be small or even nothing at all. For example, even if a plaintiff was able to satisfy the first prong by showing that aspirin use in children caused hair loss, there is probably not much more the manufacturer could do to address the new discovery adequately because aspirin is already contraindicated for use in children because of Reye’s Syndrome. Thus, a judge could dismiss the plaintiff’s suit as a matter of law because no reasonable jury would agree that there should be a warning on aspirin’s label about hair loss in children.

C. Benefits

The primary purpose, and benefit, of the change in knowledge proposal is to set a better balance of availability and safety for medical products. As discussed previously, the optimal balance will be achieved by placing that decision in the most qualified and informed actor, not by having multiple actors attempting to find a substantively correct answer about whether a

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167 Without reliable expert testimony that the state of safety knowledge has changed since approval, the change in knowledge proposal would necessitate dismissing plaintiff’s claims as a matter of law. In this way, the Daubert inquiry acts as a gate against frivolous tort litigation even in the pretrial context, such as on a motion to dismiss.
168 Under a failure-to-warn test, an additional warning of “children’s hair loss” is likely not required for a product that already clearly forbids use in children because of deadly Reye’s Syndrome.
product should be approved or not. The change in knowledge proposal uses the point of initial market approval as an effective heuristic of when the FDA should be deemed adequate to regulate and when it should not be. By requiring the plaintiff to show that there was a change in knowledge from the time of FDA approval, the change in knowledge proposal allows courts to dismiss tort claims that attempt to redo the FDA’s decision. And by changing the tort standard to testing the reasonableness or adequacy of the manufacturer’s response to newly acquired postmarket information, the change in knowledge proposal requires states to respect the FDA’s decision on data that the agency has adequately reviewed.

Another scholar, Professor Catherine Sharkey, similarly argues that the FDA’s decision should preempt state tort claims when the FDA has made a decision after careful review of all relevant data. Professor Sharkey’s “agency reference model” depends on courts to scrutinize the FDA review process and evaluate the reasons set forth by the agency for their decisions before deciding the preemption issue.\textsuperscript{169} Under the agency reference model approach, the key inquiry facing courts is the extent to which the FDA had considered and issued a conclusive determination as to the risk at issue in the state tort claim.\textsuperscript{170} The change in knowledge proposal differs in that it does not require courts to review the adequacy or extent of FDA review because a clear “preemption” line is drawn at the time of initial market approval. Instead, courts determine whether the state in scientific knowledge has changed from what the FDA knew at the time of approval.\textsuperscript{171} Moreover, the change in knowledge proposal would not foreclose tort claims based on adverse events arising after initial product approval, even if the FDA had reviewed the

\textsuperscript{169} See Sharkey, \textit{supra} note 64, at 514 (“Courts should scrutinize the regulatory process itself, relying on the FDA as a source of relevant information regarding the precise contours of the risks that it has considered.”).

\textsuperscript{170} See Sharkey, \textit{supra} note 64, at 517.

\textsuperscript{171} The subtle difference is that under the change in knowledge proposal, courts would assume that the FDA knew everything that was submitted to them at the time of approval, whereas under the agency reference model, courts would scrutinize the regulatory record to determine whether FDA review of a particular safety concern was adequate.
postmarket adverse events. The reason for this is manufacturers still have ways to hide safety concerns despite careful FDA review of available adverse event reporting. Another difference is that even if the tort law is not “preempted,” the plaintiff is limited to arguing that the manufacturer’s response to the newly acquired postmarket information was unreasonable or inadequate.

Another benefit of the change in knowledge proposal is that it incentivizes manufacturers to uncover and disclose more safety data to the FDA during the approval process in order to decrease future tort liability. This is because a single preliminary, but apparently incriminating, study can precipitate mass litigation against a manufacturer. Of course, there is a point at which the manufacturer would want to balance the incentive to secure a safe harbor against the risk of disclosing so much that approval is denied altogether. Nevertheless, the change in knowledge proposal would still create an incentive – compared to the status quo – to uncover and disclose safety concerns to the FDA when the agency is most competent.

When FDA monitoring is inadequate – in the postmarket context – tort law remains available to hold manufacturers liable for “hiding” safety concerns. Aside from tort law’s regulatory function, courts also have a supposed advantage over the FDA because of their ability to discover new safety data, increased accessibility for people with limited resources, and

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172 Professor Sharkey makes a similar claim in her “agency reference model.” See Sharkey, supra note 64, at 519 (“[the agency reference model” provid[es] manufacturers with incentives to go to the FDA upon discovery of new risks” . . . “only a specific FDA determination that claims of danger are unsubstantiated would insulate a drug manufacturer from liability, thus providing drug companies with a tremendous incentive to ensure the FDA has whatever information it needs to make a cognizable determination.”)

173 McGarity & Wagner, supra note 13, at 28.


175 See, e.g., Alexandra B. Klass, Tort Experiments in the Laboratories of Democracy, 50 WM. & MARY L. REV. 1501, 1509-10, 1564-75 (discussing views of tort law as private law, serving the interests of corrective justice and means by which state citizens obtain redress for private wrongs); McGarity & Wagner, supra note 13, at 287.
relatively insusceptibility to capture.\textsuperscript{176} As discussed previously, the change in knowledge proposal would not preclude the plaintiff from using discovery tools to uncover safety data unknown to the FDA because of misrepresentation or confidential business agreements.\textsuperscript{177} Nor would the change in knowledge proposal preclude access to courts because it does not eliminate tort liability, but only redirects the court’s consideration to the postmarket context.

\textbf{D. Response to Counterarguments}

\textbf{i. Manufacturers will have the same disincentive to discover safety data postmarket}

One possible counterargument to the change in knowledge proposal is that it would disincentivize manufacturers from continuing to perform clinical studies themselves, as they may uncover results that change the state of knowledge. One response to this concern is that there is no incentive currently, with or without tort liability, for manufacturers to perform clinical studies for the sole purpose of discovering new safety concerns. Indeed, the only way to increase manufacturers’ monitoring programs, including beginning new clinical studies, through the tort system is to impose a theory of product stewardship.\textsuperscript{178} As described by Professor Noah, product stewardship would add affirmative obligations on manufacturers postmarket, such as penalizing

\textsuperscript{176} \textsc{McGarity} \& \textsc{Wagner}, \textit{supra} note 13, at 260-261. For more detailed discussion of agency capture, see \textit{supra} notes 37-50 and accompanying text.

\textsuperscript{177} \textit{See supra} subsection III.B. However, for safety concerns arising postmarket, tort liability is still needed to uncover safety data because of the inadequacies of the FDA’s postmarket monitoring abilities and the manufacturer’s switched incentives. \textit{See supra} subsection II.B.ii.

\textsuperscript{178} \textit{See generally} Lars Noah, \textit{Platitudes About “Product Stewardship” in Torts: Continuing Drug Research and Education}, 15 Mich. Telecomm. \& Tech. L. Rev. 359 (2009). Currently, the way for manufacturers to avoid liability is not to uncover the risks and either warn or recall, but to stay willful ignorant and not uncover risks.
them for not adopting risk management plans. The courts have been resistant to such claims precisely because they place additional affirmative duties on the manufacturer. While I do believe that the tort system can be used for the purpose of product stewardship, the change in knowledge proposal does not require this expansion of tort duties that do not already exist. Put another way, if there is not enough tort incentive for manufacturers to monitor or study their products postmarket, the change in knowledge proposal would not fix this nor make it worse.

Currently, once a product is on the market, the only financial incentive to conduct new clinical studies is to gain additional uses for that product. It is unlikely that the implementation of the change in knowledge proposal would change this dynamic. Without preemption, the manufacturer has increased tort liability for newly discovered risks, the same as under a change in knowledge regime. With complete preemption, the tort liability for discovering new risks on an already marketed product may weigh against the financial incentive of conduct new clinical studies gaining a new indication. But tort liability is needed in the postmarket context to prevent manufacturers’ from “hiding” new safety information. Because the FDA is inadequate to effectively and promptly monitor products postmarket, the best outcome for public health is to have additional safeguards, such as tort liability, to respond to new safety concerns.

**ii. Federalism concerns with implementation**

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180 See e.g. *Swayze v. McNeil Laboratories*, Inc. 807 F.2d 464, 469 (5th Cir. 1987) (rejecting claim that the manufacturer should have restricted sales “to hospitals which establish and enforce appropriate procedures to assure that [the drug] is prescribed and administered in compliance with state law” because of it knew of widespread inappropriate use).

181 However, it is possible that courts would naturally gravitate towards placing additional obligations on the manufacturers in the postmarket context because the change in knowledge proposal has limited their liability for conduct pre-approval.
Although the change in knowledge proposal is principally a change in substantive tort law, there are, of course, strong federalism themes because regulations from a national agency are precluding certain state tort claims. Implementing the change in knowledge proposal is tricky because current preemption doctrine in medical product tort claims is muddled and different for medical devices and prescription drugs.

The Court in Riegel v. Medtronic held that certain state tort claims against medical devices were preempted. The Court interpreted MDA’s section 360k as preempting state requirements, including state tort laws, that are "different from, or in addition to, any requirement applicable ... to the device."\(^{182}\) The facts in Riegel made clear that FDA decisions during the initial approval process, such as approval and the initial label, will preempt state tort claims based on the same information.\(^{183}\) But what remains unclear is whether tort claims based newly acquired safety data may be litigated under state tort claims.\(^{184}\) Tort claims based on newly acquired information may not be preempted under section 360k because tort liability cannot be different from FDA regulation because the agency has not examined that information.

The Court in Wyeth v. Levine held that the CBE process allowed the manufacturer to update its label with new safety warnings without prior FDA review, and thus tort liability did not conflict with FDA approval.\(^{185}\) The Court suggested that if the manufacturer produced "clear evidence" that the FDA would not have approved the CBE request, then the manufacturer could not be found liable under state tort liability for not changing its label under the CBE

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\(^{182}\) 21 U.S.C. § 360c et seq.


\(^{184}\) See id. at 1013 n.1 (Ginsburg, J., dissenting) ("The Court's holding does not reach an important issue outside the bounds of this case: ... where evidence of a medical device's defect comes to light only after the device receives premarket approval."); see also Sharkey, What Riegel Portends, at 451 & n.67 ("The majority opinion is silent here- although several of the Justices took an interest in this issue during oral argument, see Riegel Oral Argument, at 26-27 (Roberts, C.J.); id. at 27-28 (Kennedy, J.); id. at 28 (Stevens, J.); id. at 29 (Souter, J.)--so perhaps the most that can be said is that this is an open (and sure to be heavily litigated) issue.").

regulation.\textsuperscript{186} To implement the change in knowledge proposal, courts could decide that all risk data already considered by the FDA during the approval process satisfies that “clear evidence” hurdle and preempts state tort claims.

Federalism concerns would arise if the United States Congress or the U.S. Supreme Court imposed the change in knowledge proposal on state tort law. Presumably, since Congress currently has the authority to preempt state tort claims completely, it could narrow the FDCA to preempt merely those tort claims that rely solely on data already reviewed by the FDA at the time of market approval.\textsuperscript{187} As discussed in the previous sections, the change in knowledge proposal would not change current state standards, such as strict liability or negligence, used under theories of defective design or failure to warn. Implementing the change in knowledge proposal through judicially created common law would be messier. For example, federal courts could find implied conflict preemption of premarket safety data for FDA-approval decisions. It is not unprecedented for federal courts to change substantive tort law using federal law doctrines.\textsuperscript{188}

\textbf{E. Generic products}

The Supreme Court recently decided that state tort actions against generic manufacturers are preempted if the generic manufacturers use the same warning label as their brand-name counterparts. Generic products are approved by showing equivalence to a reference listed drug that has already been approved by the FDA.\textsuperscript{189} Because there is no requirement to independent

\textsuperscript{186} Id. at 1198.
\textsuperscript{187} Typically, preemption statutes are too broad for this purpose. See Sharkey, supra note 64, at 450 (“Legislative pronouncements on preemption (or nonpreemption) are sledgehammers where sharp scalpels are more appropriate. Products liability is a realm in which Congress typically either says everything—coupling broad preemption provisions that would seem to wipe out competing state tort claims with broad “savings clauses” that would seem to preserve those same actions—or nothing at all.”).
\textsuperscript{188} The United States Supreme Court could change substantive tort law, as it has been accused of doing in \textit{State Farm v. Campbell}. 538 U.S. 408 (2003) (suggesting that the Due Process Clause imposes a multiplier-of-ten cap on punitive tort damages).
conduct clinical trials showing efficacy and safety, generic manufacturers can develop generic
drugs inexpensively. A generic drug must have the same safety and efficacy labeling as the
brand-name drug.”

In *Pliva Inc. v. Mensing*, the brand-name drug in question, Reglan, was approved in
1980, with generic products, metoclopramide, approved five years later. The label warnings
about tardive dyskinesia, the adverse effect experienced by the plaintiffs, did not change despite
mounting postmarket evidence that long-term metoclopramide users were at a much greater risk
of movement disorders than indicated by the drug’s label. Plaintiffs assert under a failure-to-
warn claim that generic manufacturers would have taken steps to enhance the warnings. The
FDA interpreted the CBE regulation to allow changes to generic drug labels only when a generic
drug manufacturer changes its label to match an updated brand-name label or to follow the
FDA’s instructions. The Court held conflict preemption due to impossibility applied,
precluding state tort claims against the generic manufacturer.

The Court’s decision goes against the policy considerations of the change in knowledge
proposal. Under the change in knowledge proposal, generic manufacturers would have a tort
duty to respond to new safety information discovered after FDA approval of the brand-name
product. As discussed *supra*, the FDA cannot adequately monitor adverse events after a product

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192 Mensing v. Wyeth, Inc., 588 F.3d 603, 606 (8th Cir. 2009), petitioner for certiorari approved as Pliva Inc. v.
193 Mensing, 588 F.3d at 607.
194 Id.
195 131 S.Ct. at 2580-81. The FDA also argued that Dear Doctor warning letters qualified as “labeling.” U. S. Brief
18; see also 21 U. S. C. §321(m); 21 CFR §202.1(l)(2). Thus, any such letters must be “consistent with and not
contrary to [the drug’s] approved . . . labeling.” 21 CFR §201.100(d)(1), 131 S.Ct. at 2581-82.
196 131 S.Ct. at 2584-85.
is on market. Tort regulation is needed to prevent manufacturers, even generic manufacturers, from “hiding” safety concerns.

Even safety data that emerges during the period between brand-product approval and generic-product approval should be considered postmarket information that can be used to show a change in knowledge. This is because the generic approval process is not an evaluation of efficacy and safety like the brand-name product approval process. Generic products are approved under an abbreviated application with efficacy and safety data. And in fact, the FDA is prohibited from doing more than asking for bioavailability studies. Therefore, the approval of a generic product cannot be interpreted as the FDA’s decision that the efficacy of the product outweighs its safety concerns. Pliva Inc. would have to be overruled to implement the change in knowledge proposal on generic manufacturers.

V. Conclusion

This Article has argued for a new rule that allows the FDA to achieve a better balance of medical product availability and safety without interference from tort law when the agency has adequately reviewed the safety science. The change in knowledge proposal would recognize that FDA review is adequate premarket and inadequate postmarket, and fine-tune medical product liability doctrine instead of using broad preemption tools. Under the change in knowledge proposal, courts could dismiss attempts to redo the FDA’s decisions, and juries would be asked to respect the agency’s decisions regarding premarket data.