

PREAMBLE PREEMPTION AND THE
CHALLENGED ROLE OF FAILURE TO WARN AND
DEFECTIVE DESIGN PHARMACEUTICAL CASES
IN REVEALING SCIENTIFIC FRAUD, MARKETING
MISCHIEF, AND CONFLICTS OF INTEREST

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I. INTRODUCTION

In January 2006, the Bush administration articulated a position in favor of a broad conflict preemption doctrine¹ that would immunize pharmaceutical manufacturers from civil liability when the Food and Drug Administration (“FDA”) had previously granted permission to place a prescription drug on the market.² This was accomplished through

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1. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922 (Jan. 24, 2006). Specifically, the comments on the product liability implications of the proposed rule (“the preamble”) state, *inter alia*, that “[s]tate law actions . . . threaten [the] FDA’s statutorily prescribed role as the expert Federal agency responsible for evaluating and regulating drugs.” *Id.* at 3935; *see also, e.g., In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 270 (E.D.N.Y. 2007) (discussing and quoting the preamble).

2. This dramatic departure from the former judicial and FDA recognition of state common law claims in the context of pharmaceuticals approved by the FDA, first manifested itself in *amicus* briefs in ongoing litigation prepared at the direction of the Bush administration’s former Chief Counsel Daniel E. Troy, supporting the manufacturers’ argument that federal law preempts state

a preamble to a new regulation in the Federal Register³ related to prescription drug labeling formats that declared compliance with FDA requirements for drug labeling preempts state tort law claims, without any notice and comment period for the public or interest groups to respond.⁴ If federal preemption was held to apply to pharmaceutical companies, a preemption defense could obliterate failure to warn or defective design drug cases.⁵ Because federal law does not recognize

common law claims. See Congressman Maurice Hinchey, *FDA Is Placing Corporations Above Public*, <http://www.house.gov/hinchey/issues/fda.shtml> (last visited Oct. 2, 2007). This web site lists documentation that shows Chief Counsel Troy's involvement with manufacturers, including a sworn affidavit discussing a speech that Troy made at a conference on drug and medical device defense attorneys in which Troy allegedly actively solicited cases where the agency might intervene to argue preemption and actively encourage defense attorneys to make preemption arguments in their cases. Beginning in 2002, the FDA filed several *amicus* briefs arguing that its decisions not to require suicide warnings preempted claims asserting a state-law duty to provide those same warnings. See *Amicus* Brief for the United States in Support of the Defendant-Appellee and Cross-Appellant, and in Favor of Reversal of the District Court's Order Denying Partial Summary Judgment to Defendant-Appellee and Cross-Appellant at 15-25, *Motus v. Pfizer, Inc.* (Roerig Div.), 358 F.3d 659 (9th Cir. 2004) (Nos. 02-55372, 02-55498); *Amicus* Brief for the United States, *Kallas v. Pfizer, Inc.* at 23-26 (D. Utah Sept. 15, 2005) (No. 04-CV-00998); Brief for *Amicus Curiae* the United States of America at 13-23, *Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514 (E.D. Pa. 2006) (No. 05-5500); Brief of United States as *Amicus Curiae* in Support of Defendants-Appellees at 16-30, *Colacicco v. Apotex, Inc.* (3d Cir. Dec. 4, 2006) (No. 06-3107). These briefs are available online at the web site of the American Enterprise Institute for Public Policy Research ("AEI"), pro-preemption organization. AEI, FDA Preemption and Pharmaceutical Product Liability, <http://www.aei.org/research/liability/subjectAreas/pageID.1378,projectID.23/default.asp> (last visited Oct. 2, 2007). The court in *Motus* avoided the preemption issue. 358 F.3d at 660. The *Kallas* litigation settled before there was any decision. The district court in *Colacicco* agreed with the FDA and found the SSRI claim preempted. 432 F. Supp. 2d at 538 (currently on appeal).

3. Specifically, the preamble states that "FDA approval of labeling [under the new labeling requirements] . . . preempts conflicting or contrary State law, regulations, or decisions of a court of law for purposes of product liability litigation." Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. at 3933-34. The FDA further stated that it was "the expert Federal public health agency charged by Congress with ensuring that drugs are safe and effective, and that their labeling adequately informs users of the risks and benefits of the product and is truthful and not misleading." *Id.* at 3934. The Bush administration has also been accused of attempting to bypass the courts and nullify state products liability and consumer protection law through other agencies adopting such regulatory preambles, including the National Highway Traffic Safety Administration and Consumer Product Safety Commission. See, e.g., Richard Frankel, *Undue Deference*, 42 TRIAL 30, 30-31 (Nov. 2006).

4. See, e.g., *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 274 (noting under 21 C.F.R. §§ 10.85(d)(1), (e), (g), this lack of notice and comment period suggests that the preamble is advisory, binding only on the agency and subject to limited deference); see also *Reno v. Koray*, 515 U.S. 50, 61 (1995) (limited deference when no notice and comment period).

5. The Bush administration's position has been described by several law commentators as contrary to the principles of federalism and as a "back-door" attempt to sidestep Congress and courts after the Bush administration failed to persuade either to adopt a preemption doctrine. See Jonathan V. O'Steen & Van O'Steen, *The FDA Defense: Vioxx and the Argument Against Federal Preemption of State Claims for Injuries Resulting From Defective Drugs*, 48 ARIZ. L. REV. 67, 92 (2006); see also *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 240 (noting that if preemption

private litigants with a cause of action, if the FDA or the manufacturer negligently fails to consider a potential danger posed by a pharmaceutical drug, it is the “injured consumer alone who will pay the price.”⁶ In addition, because the Supreme Court has found that product liability claims premised on fraud on the FDA are implicitly preempted,⁷ such implied preemption would mean that even if market approval was obtained through intentional misrepresentation on the part of the manufacturer, by, for example, failing to report studies indicating substantial risks, injured consumers cannot recover any compensation for their injuries when a plaintiffs’ theory of liability is solely based on fraud on the FDA.⁸ The position taken by the Bush administration in the 2006 preamble has been noted not only to be contrary to Congress’s intent in enacting the FDA⁹ and against well-established state and federal law,¹⁰ but also against the FDA’s prior position recognizing common law suits as protecting consumers.¹¹ This has resulted in

occurred, the manufacturer at most would be liable for injuries that occurred up to the first FDA approved warning label or the time the new label was worded, or perhaps the distribution of the “Dear Doctor” letters under circumstances of case).

6. *Riegel v. Medtronic, Inc.*, 451 F.3d 104, 129 (2d Cir. 2006) (Pooler, J., concurring in part and dissenting in part), *cert. granted*, 127 S. Ct. 3000 (June 25, 2007) (No. 06-179). While this statement was made in the context of a medical device case where the plaintiff was found by the majority of the court not to have a claim for failure to warn or defective design on preemption, the same result will hold true in pharmaceutical tort cases if the preamble is found to preempt private consumer failure to warn or defective design tort actions.

7. *See* *Buckman Co. v. Plaintiffs’ Legal Comm.*, 531 U.S. 341, 348 (2001). The United States Supreme Court has recently granted certiorari in *Desiano v. Warner-Lambert*, 467 F.3d 85 (2d Cir. 2007), to hear the narrow issue of whether “fraud on the FDA” claims are implicitly preempted. *See* *Warner-Lambert Co., LLC v. Kent*, No. 06-1498, 2007 WL 1420397 (U.S. Sept. 25, 2007); *infra* notes 14-19 and accompanying text.

8. *Buckman* did not involve a drug manufacturer, but a facilitator hired to negotiate the FDA process, and involved a whole theory of state law liability premised exclusively on FDA fraud. *Buckman Co.*, 531 U.S. at 348 (“[S]tate-law fraud-on-the-FDA claims conflict with, and are therefore impliedly pre-empted by, federal law.”). Thus despite manufacturers and some courts such as *Desiano* extending *Buckman* to apply in situations where fraud on the FDA is an element of proof, thus limiting the ability to get recovery even in the face of known misrepresentations made to the FDA, arguably *Buckman* does not extend that far.

9. *See, e.g.*, Brian Wolfman, *Why Preemption Proponents Are Wrong*, 43 TRIAL 20, 27 & n.39 (Mar. 2007) (noting that when Congress was considering the legislation that led to the enactment of the FDA, the end for a private federal cause of action for damages was explicitly rejected on the grounds that a common law right of action already existed).

10. *See, e.g.*, *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 271 (noting that “[n]early every court to have considered the issue of federal [FDA] preemption before the preamble was issued has rejected the FDA’s current position”). The FDA, in the preamble, claimed that these cases were based on a misunderstanding that the FDA labeling requirements only established a minimum safety standard, and not a ceiling. *See* 71 Fed. Reg. 3922, 3934 (Jan. 24, 2006).

11. *Id.* at 273-74 (citing prior agency positions in Federal Register where the FDA took a contrary stance). The Bush administration’s position has been described by several law

organizations such as the prestigious *New England Journal of Medicine* criticizing the Bush administration's "politicalization" of the FDA.¹² On June 25, 2007, the United States Supreme Court granted certiorari in *Riegel v. Medtronic*¹³ on the issue of whether FDA pre-market approval of a medical device preempts state-law tort claims relating to the safety or efficacy of the device. Then on September 25, 2007, the Court granted certiorari in *Warner-Lambert Co., LLC v. Kent*¹⁴ on the narrow issue of whether any reference to "fraud on the FDA," whether in state legislation or common law, is void as a result of implied preemption.¹⁵

commentators as contrary to the principles of federalism and as a "back-door" attempt to sidestep Congress and courts after the Bush administration failed to persuade either to adopt a preemption doctrine. See O'Steen & O'Steen, *supra* note 5, at 92-93; Catherine M. Sharkey, *Preemption by Preamble: Federal Agencies and the Federalization of Tort Law*, 56 DEPAUL L. REV. 227, 228 (2007) ("Federal agency momentum towards increased preemption—evidenced by clear statements in the preambles of issued regulations—fits the broader pattern of what [we] have termed 'backdoor federalization.'").

12. Gregory D. Curfman et al., Editorial, *Blueprint for a Stronger Food and Drug Administration*, 355 NEW ENG. J. MED. 1821 (2006). The Bush administration's appointees to the FDA have been accused of actively soliciting lawyers for the industries they are supposed to be regulating to offer up cases in which the FDA could file briefs in order to extend FDA preemption in support of the manufacturers. See, e.g., Thomas Frank, *Erasing the Rules*, NEWSDAY, Oct. 11, 2004, at A04; Michael Kranish, *FDA Counsel's Rise Embodies US Shift*, BOSTON GLOBE, Dec. 22, 2002, at A1; Anne C. Mulkern, *Watchdogs or Lap Dogs? When Advocates Become Regulators President Bush Has Installed More than 100 Top Officials Who Were Once Lobbyists, Attorneys or Spokespeople for Industries They Oversee*, DENVER POST, May 23, 2004, at A-01. In addition to this current threat of implied preemption through the Bush administration, perhaps realizing that they are on the losing end of the preemption debate, pharmaceutical companies are attempting to avoid the preemption debate altogether by lobbying state legislatures to pass state laws that preclude state tort actions against manufacturers of drugs approved for use by the FDA. See, e.g., O'Steen & O'Steen, *supra* note 5, at 69 (discussing the issue of pharmaceutical lobbying of state legislatures). In fact, one state, Michigan, passed a law that explicitly gives immunity to drug manufacturers for failure to warn if the medicine was in compliance with FDA regulations at the time of sale. MICH. COMP. LAWS § 600.2946(5) (2007). The constitutionality of this statute was upheld in *Taylor v. SmithKline Beecham Corp.*, 658 N.W.2d 127 (Mich. 2003). The only exception to this defense is if the company fraudulently withheld information that would have led the FDA to recall the drug or deny approval. MICH. COMP. LAWS § 600.2946(5)(a) (2007). This exception may be difficult for plaintiffs to use because in *Buckman*, the Supreme Court suggested that fraud on the FDA claims may be preempted from being litigated by entities other than the FDA, which would leave Michigan residents unable to recover under this exception. 531 U.S. at 344. The Michigan statute is currently under legislative challenge. See H.B. 4044, 4045, 94th Leg., Reg. Sess. (Mich., as passed by House, Feb. 22, 2007).

13. 127 S. Ct. 3000 (June 25, 2007) (No. 06-179).

14. *Warner-Lambert Co., LLC v. Kent*, No. 06-1498, 2007 WL 1420397 (U.S. Sept. 25, 2007); see *supra* note 7.

15. The Petitioner manufacturer framed the issues as being:

1. Whether, under the conflict preemption principles in *Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341 (2001), federal law preempts state law to the extent that it requires the fact-finder to determine whether the defendant committed fraud on a federal agency that impacted the agency's product approval, where the agency—which is authorized by

While the *Riegel* case can be clearly distinguished from pharmaceutical cases in that the pertinent federal statute involved¹⁶ contains an express preemption provision, and *Warner- Lambert Co., LLC v. Kent* deals with a narrow self-contained issue—essentially whether any reference to “fraud on the FDA” in state legislation or common law is void as a result of implied preemption¹⁷—these cases are certainly part of the broader debate over the extent to which the Bush administration and Congress may preclude the states from imposing consumer regulations that are more stringent than the federal government’s and viewed as pitting the states against the manufacturers.¹⁸ Given that federal circuit courts and state courts are split on this issue, no question exists that sooner or later the Supreme Court will hear the sister issue of whether pharmaceutical failure to warn or defective design lawsuits are preempted if a prescription drug has been approved by federal law.¹⁹

Congress to investigate and determine fraud—has not found any such fraud

2. Whether, [under *Buckman*], federal law preempts the provision in a Michigan statute that allows a product liability claim to be maintained against a manufacturer of an FDA-approved drug where, without an FDA finding of fraud on that agency, the fact-finder is required to make a finding under state law as to whether the manufacturer committed fraud-on-the-FDA and whether, in the absence of that fraud, the FDA would not have approved the drug.

Petition for a Writ of Certiorari, *Warner-Lambert Co., LLC v. Kent*, 2007 WL 1420562 (May 10, 2007) (No. 06-1498). Even if the Supreme Court found that *Buckman* implicitly preempts “fraud on the FDA” claims, arguably this would not mean that state tort law claims are barred but merely that state legislatures would have to rewrite state tort law so as to not refer to fraud on the FDA.

16. This case involved the Medical Device Amendments of 1976 (“MDA”), 21 U.S.C. § 360c *et seq.* (2000), to the Federal Food, Drug, and Cosmetic Act (“FDCA”), 21 U.S.C. § 301 *et seq.* (2000). The MDA contains an express preemption provision that forbids a state from adopting any requirement “which is different from, or in addition to, any requirement” in federal law and involved what is considered to be the most stringent pre-approval process compared to an earlier United States Supreme Court medical device case where no preemption was found. 21 U.S.C. § 360k(a) (2000). Earlier, federal courts that have heard this issue reached different results on the issue of the preemption of state statutory and common law claims. *See, e.g., Riegel v. Medtronic, Inc.*, 451 F.3d 104, 106 (2d. Cir. 2006) (summary judgment dismissal of the plaintiffs-appellants’ strict liability, breach of implied warranty, and negligent design, testing, inspection, distribution, labeling, marketing, and sale claims as to the Evergreen Balloon Catheter, a PMA-approved medical device); *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 270 (E.D.N.Y. 2007) (noting difference between FDCA and FDA preemption issues).

17. *See supra* note 8.

18. *See, e.g., Stephen Labaton, Supreme Court to Weigh Limits on Cases Involving Medical Devices*, N.Y. TIMES, June 26, 2007, at C3.

19. *See infra* note 112 and accompanying notes discussing *Levine v. Wyeth*, No. 2004-384, 2006 WL 3041078 (Vt. Oct. 27, 2007), which is the first top state court in which the United States Supreme Court has been asked by the manufacturer to consider granting certiorari on this issue. A number of cases rejected any argument of preemption based on the FDA preamble. *See, e.g., In re Vioxx Prods. Liab. Litig.*, No. MDL 1657, 2007 WL 1952964, at *8-9 (E.D. La. July 3, 2007); *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 270-78; *Perry v. Novartis Pharms. Corp.*, 456 F. Supp. 2d 678, 684 (E.D. Pa. 2006); *Adesina v. Aladan Corp.*, 438 F. Supp. 2d 329, 337-38

This Article is not intended to discuss the legal arguments against the preemption of state tort law claims for pharmaceutical manufacturers' failure to warn or defective design which has been discussed recently by a number of commentators²⁰ and courts,²¹ but weighs in on this preemption debate in a practical manner. We suggest that understanding lack of "adequacy and candor of representations to the FDA and of robustness of inquiry and decisions of the FDA"²² is important in understanding the crucial role that litigation plays in protecting the general public, and is critical given the current FDA preemption debate and efforts in Congress to reform the FDA postmarket drug decision making and oversight process.²³ First we discuss the important gaps in the ascertainment and reporting of adverse effects associated with prescription drugs.²⁴ We then discuss the critical role that state and federal common law litigation plays in protecting the general public from scientific fraud, marketing mischief, and conflicts of interest²⁵ in a world where pharmaceutical companies are estimated to spend as much as \$12 billion annually marketing to physicians through in-office promotion, hospital promotions, and journal advertising.²⁶ Finally, we return to the issue of preemption and ask whether the FDA

(S.D.N.Y. 2006); *Jackson v. Pfizer, Inc.*, 432 F. Supp. 2d 964, 968 (D. Neb. 2006) (rejecting FDA preemption); *McNellis v. Pfizer, Inc.*, No. Civ. 05-1286, 2006 WL 2819046, at *10 (D.N.J. Sept. 29, 2006) ("The Preamble, without more, does not signal to this Court Congressional intent to obviate state law."); *Laisure-Radke v. Par Pharm., Inc.*, 426 F. Supp. 2d 1163, 1172 (W.D. Wash. 2006) ("FDA regulations provide only the minimum requirements . . . compliance with those regulations does not necessarily establish that the warnings at issue were adequate."); *Deutsch v. Wyeth, Inc.*, HRT Mass Tort Case Code 266, MID-L-998-06 MT (N.J. Super. Ct. June 22, 2007) (order denying defendant's motion for partial summary judgment); Transcript of Oral Argument at 585:21-586:9, *Doherty v. Merck & Co., Inc.*, No. ATL-L-0638-05-MT (N.J. Super. Ct. June 9, 2006) (on file with author) (Judge Higbee stating on the record that the FDA's preemption preamble is "a political statement" that is "contrary to all the law on preemption"). A number of other cases adopted FDA preemption. *See, e.g., Colacicco v. Apotex, Inc.*, 432 F. Supp. 2d 514, 538 (E.D. Pa. 2006) (deferring to FDA preemption preamble).

20. *See, e.g., O'Steen & O'Steen, supra* note 5; Wolfman, *supra* note 9; Robert L. Rabin, *Poking Holes in the Fabric of Tort: A Comment*, 56 DEPAUL L. REV. 293 (2007) (discussing the implications of agency initiated preemption).

21. *See, e.g., In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d at 240-41.

22. *Id.* at 240.

23. For example, the FDA has recently announced a plan to do a comprehensive assessment of the safety of drugs eighteen months after introduction, but no starting date for this plan has yet been announced and the assessment will be due eighteen months after that. *See Gardiner Harris, F.D.A. Installs Drug Reviews at 18 Months; Critics Say More Changes Are Needed*, N.Y. TIMES, Jan. 31, 2007, at A17.

24. *See infra* Part II.

25. *See infra* Part III.

26. Stephanie Saul, *Doctors and Drug Makers: A Move to End Cozy Ties*, N.Y. TIMES, Feb. 12, 2007, at C10.

might possibly be retreating from its 2006 preamble preemption position, albeit in an impractical and unpredictable manner.²⁷ We conclude that the FDA current postmarketing scheme is incapable of protecting consumers from pharmaceutical manufacturer's misconduct, and that lawsuits brought by private litigants provide a vital and essential role in discovering the hidden dangers of drugs currently on the market.

II. IMPORTANT GAPS IN THE ASCERTAINMENT AND REPORTING OF ADVERSE EFFECTS ASSOCIATED WITH PRESCRIPTION DRUGS

In the past decade, and prior to that, several widely used prescription medications have been removed from the market either voluntarily, or pursuant to FDA request, upon reports that such medicines were causing life threatening adverse effects, and in some cases deaths.²⁸ Withdrawal is virtually never the result of the FDA initiating formal proceedings to remove a drug because, as the Director of New Drugs at the FDA, Dr. John Jenkins, recently acknowledged, in the context of an FDA expert advisory panel recommending an outright ban of over-the-counter pediatric cold products for children under the age of six, a forced withdrawal requiring a rule-making process could take "many years" to carry out.²⁹ The FDA has been criticized for taking "years to acknowledge risks to millions of patients that had been apparent to some researchers."³⁰ Judge Weinstein, in rejecting a pharmaceutical company's preemption defense noted that "[i]t is apparent . . . that the FDA's own research is limited and that it relies heavily on the self-motivated representations and studies by the pharmaceutical industry,"³¹ suggesting that the "lack of

27. See *infra* Part III.D.

28. For example, the FDA has already requested voluntary withdrawal of two drugs in 2007. Pergolide drug products used to treat Parkinson's disease, based on serious risk of damage to patients' heart valves on March 29, 2007. FDA, FDA Public Health Advisory: Pergolide (marketed as Permax), Mar. 29, 2007, <http://www.fda.gov/cder/drug/advisory/pergolide.htm>. It similarly requested the voluntary withdrawal of Novartis Pharmaceuticals Corporation's Zelnorm, used for the treatment of irritable bowel syndrome, based on identified increased risk of serious cardiovascular adverse events on March 30, 2007. FDA, FDA Public Health Advisory: Tegaserod maleate (marketed as Zelnorm), Mar. 30, 2007, <http://www.fda.gov/cder/drug/advisory/tegaserod.htm>. The FDA generally posts recalls, market withdrawals, and safety alerts of the last sixty days on its website at <http://www.fda.gov/opacom/7alerts.html>, with a complete list of recalls available on the FDA enforcement list at <http://www.fda.gov/opacom/enforce.html>.

29. Gardner Harris, *F.D.A. Panel Urges Ban on Cold Medicines for Child Colds*, N.Y. TIMES, Oct. 20, 2007, at A1.

30. Harris, *supra* note 23, at A17.

31. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 240 (E.D.N.Y. 2007).

adequate . . . [FDA] supervision of the pharmaceutical industry” is actually a factor to be considered in “the larger legal and factual context” in which the determination of fact and damages is made in pharmaceutical tort cases.³² The removal of drugs from the market almost uniformly shows that there are “often important gaps in the ascertainment and reporting of adverse effects associated with prescription drugs, and the balance of information presented to physicians about the risks and benefits of medications may understate the former and inflate the latter.”³³ The danger of hidden adverse drug effects is that even a relatively small risk of a serious adverse effect can translate into a high number of consumers killed or hurt by such adverse effects, due to the vast number of prescriptions written for popular drugs. For example, related to the selective COX-2 inhibitor drug Vioxx, at the time of its withdrawal, more than two million patients around the world were taking the drug, leading to an estimated 88,000 to 140,000 Americans suffering Vioxx-related heart attacks, strokes, and other serious medical problems.³⁴

*A. The Problem: Limited U.S. Food and Drug Administration
Post-Approval Authority Over Pharmaceuticals*

Once the FDA approves a drug, “the FDA [does] not have the explicit authority to require that drug sponsors take other safety

32. *Id.* at 239.

33. Aaron S. Kesselheim & Jerry Avorn, *The Role of Litigation in Defining Drug Risks*, 297 JAMA 308, 308 (2007); see also David B. Ross, *The FDA and the Case of Ketek*, 356 NEW ENG. J. MED. 1601, 1601 (2007).

34. See David J. Graham et al., *Risk of Acute Myocardial Infarction and Sudden Cardiac Death In Patients Treated With Cyclo-Oxygenase 2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs: Nested Case-Control Study*, 365 LANCET 475, 480 (2005); see also Memorandum from Rep. Henry A. Waxman to the Democratic Members of the Gov’t Reform Comm., Re: The Marketing of Vioxx to Physicians, at 4 (May 5, 2005), available at <http://oversight.house.gov/documents/20050505113149-41995.pdf> [hereinafter Waxman Report] (citing Carolanne Dai, Randall S. Stafford & G. Caleb Alexander, *National Trends in Cyclooxygenase-2 Inhibitor Use Since Market Release*, 165 ARCHIVES OF INTERNAL MED. 171, 171-77 (2005)). This Report has been described as “the most extensive account ever provided to Congress of a drug company’s efforts to use its sales force to market to physicians and overcome health concerns.” *Id.* at 1. Merck’s latest annual report estimated that 105 million prescriptions for Vioxx were written from May 1999 through August 2004 and states that Merck faces legal claims in 27,400 product liability suits, involving 46,100 plaintiff groups in the United States and also is a defendant in 264 class actions related to the use of Vioxx. Merck & Co., Inc., Annual Report (Form 10-K), at 5, 16 (Feb. 28, 2007). Merck has admitted that during 2006, “the Company spent \$500 million, including \$175 million in the fourth quarter, in the aggregate in legal defense costs worldwide” and recorded charges of \$673 million to increase the reserve solely for its future legal costs to \$858 million. *Id.* at 17.

actions”³⁵ and “has limited authority to require that sponsors conduct postmarket safety studies”³⁶ or ensure compliance with suggested changes in labeling or marketing practices.³⁷ The limited FDA post-approval authority was the subject of a 2006 Government Accountability Office (“GAO”) Report to Congress,³⁸ which reported a lack of coherent decision-making process for postmarket drug safety, the need for systematic tracking of postmarket drug safety issues, and explicitly recommended that the FDA be granted greater authority to order postmarketing studies by drug manufacturers.³⁹ In addition, a September 2006 extensive 350 page report by the Institute of Medicine of the National Academies of Science,⁴⁰ which is considered to be one of the most important medical advisory organizations in the country, criticized the FDA as being “rife with internal squabbles and hobbled by underfinancing, poor management and outdated regulations.”⁴¹ The Institute Report made twenty-five specific recommendations, many of which would require Congressional authorizations, including that new drugs should be approved for only five year periods so the FDA can thoroughly review postmarket safety questions; newly-approved drugs should display a black triangle on their label to warn consumers that the drug is new and that their safety is more uncertain than older drugs; drug

35. U.S. GOV'T ACCOUNTABILITY OFFICE, DRUG SAFETY: IMPROVEMENT NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS 10 (2006) [hereinafter 2006 GAO Report].

36. *Id.* at 11; *see also* Bruce M. Psaty & Curt D. Furberg, *Rosiglitazone and Cardiovascular Risk*, 356 NEW ENG. J. MED. 2522, 2523 (2007) (noting that while FDA frequently requires postmarket studies to address safety issues, only about a quarter of the *required* phase 4 postmarket trials were completed and noting the inadequate designs of such studies).

37. *See* Kesselheim & Avorn, *supra* note 33, at 308.

38. *See* 2006 GAO Report, *supra* note 35, at 9-12.

39. *See id.* at 5-6. While this may change as a result of new legislation, *see infra* note 45, until now the FDA has had limited authority to require drug manufacturers to conduct postmarket safety studies. It may impose such post market studies during the premarketing stage under 21 C.F.R. § 314.510 (2007) as a condition of accelerated approval of new drugs for serious or life-threatening illnesses to allow the FDA to more quickly approve potentially life-saving drugs. Second, under 21 C.F.R. § 314.610(b)(1) (2007), the FDA can require postmarket studies as part of pre-marketing approval where human efficiency studies are not ethical or feasible due to the nature of the drug. The only postmarket situation where the FDA can currently require that drug sponsors conduct postmarket studies is under the Pediatric Research Equity Act of 2003 when such studies are needed to provide adequate labeling to ensure the safe and effective use in children. *See* 21 U.S.C. § 355c(b) (2000). In addition, even when postmarket studies are ordered, the FDA has remarkably little enforcement authority to force a manufacturer to comply with such studies.

40. INSTITUTE OF MEDICINE, COMMITTEE ON THE ASSESSMENT OF THE U.S. DRUG SAFETY SYSTEM, THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC (Alina Baciu et al. eds., 2007), *available at* <http://search.nap.edu/nap-cgi/skimit.cgi?recid=11750&chap=1-14> [hereinafter INSTITUTE REPORT].

41. Harris, *supra* note 23, at A17.

advertisements should be banned during this initial period; the FDA should be given the authority to issue fines, injunctions, and withdrawals when pharmaceutical manufacturers fail to complete required safety studies—which the manufacturers often do.⁴² The Institute Report also recommends a six year term for the FDA commissioner—perhaps an implicit recognition of the problems caused when the FDA is politicized, as it has been under the Bush administration.⁴³ A January 2007 written response by the FDA to the Institute of Medicine’s report, however, has been described by an Institute author as being “disappoint[ing]” in terms of how it failed to adopt the Institute’s suggestion that the FDA be given greater authority to access the safety of drugs after they go on the market.⁴⁴ On September 27, 2007, President Bush signed into law the Food and Drug Administration Revitalization Act,⁴⁵ which is intended to strengthen the FDA’s ability to carry out these tasks. The law has been described as a “Christmas tree with more moving parts than you can imagine” by a former FDA general counsel.⁴⁶ At the time that this Article went to press, whether the new law will significantly address the issues brought up in the Institute Report and the 2006 GAO Report is unclear, in part because how the Act’s provisions will be implemented and their usefulness in protecting public health and safety depends on the writing of rules and regulations in the days to come. In the meantime, however, ample examples make clear “a drug’s label can vary in its completeness and balance and may not be updated in a timely way to reflect new data.”⁴⁷

B. Result: Lack of Manufacturer Incentive to Investigate or Report Potential Adverse Effects and Massive Settlements Which Results in Impaired Prescription Decisions

Virtually every major pharmaceutical manufacturer has either been caught concealing, or is currently accused of concealing, information related to either the safety or effectiveness of blockbuster prescription drugs. Some high visibility cases include: Baycol (cerivastatin) (manufacturer allegedly suppressed knowledge that patients were

42. See INSTITUTE REPORT, *supra* note 40, at 164-73.

43. See *id.* at 92-93.

44. See Harris, *supra* note 23, at A17.

45. See Jeffery M. Drazen, Stephen Morrissey & Gregory D. Curfman, Editorial, *Open Clinical Trials*, 357 N. ENG. J. MED. 1756 (2007).

46. Gardner Harris, *House Passes Bill Giving More Power to the F.D.A.*, N.Y. TIMES, Sept. 20, 2007, at A18.

47. Kesselheim & Avorn, *supra* note 33, at 308.

developing a potentially life-threatening muscle disease, and that the risk of such condition increased with higher dosages at the time the company was negotiating with the FDA for approval of the drug at higher dosages);⁴⁸ Bextra (valdecoxib) (\$1.2 billion in sales in 2004 allegedly achieved through Pfizer marketing drug as a “breakthrough” drug despite Pfizer’s knowledge of the drug’s lack of superiority and increased cardiovascular risks and potentially life-threatening skin reactions);⁴⁹ Ortho Evra (manufacturer currently accused of misrepresenting that birth control contraceptive patch was as safe as oral contraceptives even though it knew or should have known of excessive estrogen release);⁵⁰ Paxil (paroxetine) (manufacturer allegedly suppressed studies showing increased risk of suicidal behavior in children and adolescents taking antidepressant, while releasing the favorable exculpatory study resulting in \$55 million in sales related to mood disorders);⁵¹ Vioxx (rofecoxib) (manufacturer allegedly suppressed known cardiovascular dangers of drug and instead waged aggressive marketing campaign to increase use of drug);⁵² Zyprexa (olanzapine) (30,000 cases brought against manufacturer that allegedly suppressed knowledge that drug caused hyperglycemia, diabetes, and excessive weight gain and instead provided false data to physicians).⁵³

48. See *infra* note 55 and accompanying text. The authors’ firm has been involved in the Baycol MDL litigation in federal district court in Minnesota and the Pennsylvania state court.

49. See, e.g., *In re Bextra and Celebrex Mktg. Sales Practices and Prod. Liab. Litig.*, No. CV-05-1699, 2006 WL 2472484, at *2 (N.D. Cal. Aug. 24, 2006) (discussing allegations). The authors’ law firm is involved in this ongoing litigation and related litigation pending in the New York state court system. The web sites involving these litigations and supporting documents are at <https://ecf.cand.uscourts.gov/cand/bextra/> (California) (last visited Oct. 5, 2007), and <http://www.nypscbextracelebrex.com/Home.aspx> (New York) (last visited Oct. 5, 2007). New Jersey mass tort litigation related to this drug is also pending. See NJCourtsOnline.com, Mass Tort—Bextra/Celebrex, <http://www.judiciary.state.nj.us/mass-tort/bextra-celebrex/index.htm> (last visited Oct. 5, 2007).

50. See, e.g., Associated Press, *Birth Control Patch Linked to Higher Fatality Rate*, MSNBC.COM, July 20, 2005, <http://www.msnbc.msn.com/id/8565177/>; Associated Press & CBS, *Birth Control Patch Users Warned*, Nov. 11, 2005, http://www.cbsnews.com/stories/2005/11/11/earlyshow/health/health_news/main1037611.shtml. Multi-district litigation alleging that the patch was defectively designed and that users received inadequate warnings as to the product’s side-effects and safety profile is currently pending in the Northern District of Ohio. See *In re Ortho Evra Prods. Liab. Litig.*, 422 F. Supp. 2d 1379, 1381 (Jud. Pan. Mult. Lit. 2006). The authors’ firm is also involved in this litigation.

51. See Press Release, Office of the New York State Attorney General, Major Pharmaceutical Firm Concealed Drug Information: GlaxoSmithKline Misled Doctors About the Safety of Drug Used to Treat Depression in Children (June 2, 2004), available at http://www.oag.state.ny.us/press/2004/jun/jun2b_04.html.

52. See *infra* notes 88-90 and accompanying text.

53. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 236 (E.D.N.Y. 2007). The authors’ firm formerly has been involved in this litigation.

What these drugs' debacles convincingly demonstrate is that the current FDA scheme is not protecting public health and safety, leading to what one recent commentator recently noted would be "the serious concerns raised by a system that would tolerate both tort preemption and regulatory failure."⁵⁴ After all, what impact are multi-million dollar fines when a product is considered to be a potential blockbuster product, with global sales exceeding \$586 million in 2000, growth of 84%, and with forecast sales of \$1 billion for the next year?⁵⁵ Or when a product is by far a company's most profitable drug, with sales of \$4.2 billion a year?⁵⁶ In such situations, the effects of a product withdrawal can go beyond an immediate loss in product sales and impact the company's long term revenue potential.⁵⁷ From the authors' practical experience in involvement in numerous pharmaceutical cases over the years, the sad result is that corporate executives may continue aggressive marketing campaigns and negotiating with the FDA for approval of additional uses or higher approved dosages of blockbuster drugs at the time that internal documents show the company knew or should have known that patients are developing life-threatening conditions as a result of using a company's product. These executives' bonuses are tied to year-end revenues and they may very well be at another company by the time that the health concerns relating to a product come to light.

In addition, based on their personal experience, the authors of this Article believe that confidential settlements as a means of hiding manufacturer misconduct have long been a pervasive problem in mass tort pharmaceutical product liability cases, where the danger exists that a

54. Wolfman, *supra* note 9, at 27.

55. See *Bayer Reaches Settlement Over Drug Disclosure*, HOUSTON BUS. J., Jan. 23, 2007, available at <http://houston.bizjournals.com/houston/stories/2007/01/22/daily29.html> (discussing Baycol's \$8 million settlement involving thirty states); ResearchAndMarkets.com, *The Impact of the Baycol Withdrawal*, Sept. 2001, http://www.researchandmarkets.com/reportinfo.asp?report_id=1049 (discussing financial data related to Bayer's Baycol). The facts related to Eli Lilly's alleged misrepresentations and omissions related to this drug are discussed in a security class action lawsuit brought on the behalf of shareholders. See *In re Bayer AG Sec. Litig.*, 423 F. Supp. 2d 105, 107-10 (S.D.N.Y. 2005); *In re Bayer AG Sec. Litig.*, No. 03 Civ. 1546, 2004 WL 2190357, at *1-6 (S.D.N.Y. 2004).

56. See Alex Berenson, *Eli Lilly Said to Play Down Risk of Top Pill*, N.Y. TIMES, Dec. 17, 2006, at 1 (discussing how drug manufacturer Eli Lilly is accused of waging a decade-long effort to play down the health risks of Zyprexa, its best selling medication for schizophrenia, with sales of \$4.2 billion in 2006, based on hundreds of internal documents and e-mail messages among top company managers). The documents related to *The New York Times* article were recently found by a federal judge to be subject to a protective order and ordered to be returned to the defendant. See *In re Zyprexa Injunction*, 474 F. Supp. 2d 385, 397 (E.D.N.Y. 2007).

57. See ResearchAndMarkets.com, *The Impact of the Baycol Withdrawal*, Sept. 2001, http://www.researchandmarkets.com/reportinfo.asp?report_id=1049.

manufacturer facing a massive number of potential lawsuits will attempt to settle cases as quietly as possible in an effort to avoid confrontations with the FDA, bad publicity and attendant stock market changes and/or additional lawsuits by injured parties who were unaware that the drug may be the cause of their injury.⁵⁸ Despite how Rule 26(c) of the Federal Rules of Civil Procedure and similar state laws generally require a showing of “good cause” for restricting access to discovery documents when necessary “to protect a party or person from annoyance, embarrassment, oppression, or undue burden or expense,”⁵⁹ in most cases where the parties file settlement agreements that include a provision sealing the discovery documents, the requirement of “good cause” is ignored by the courts. Thus, “agreeing to a secrecy order may become a bargaining chip between the parties, with defendants agreeing more readily to an early settlement if the plaintiff agrees not to disclose the details of the case to the public.”⁶⁰ Such sealed orders create a difficult situation for the plaintiff’s lawyer whose ethical obligation lies in the best possible representation of existing client(s), whose interest often is obtaining an expeditious settlement versus the plaintiff attorney’s desire to expose important health information learned in litigation to protect the public or help other prospective plaintiffs. In reality, disclosure will often weaken the plaintiff’s bargaining position for securing the defendant’s acquiescence in discovery of certain materials, and also damage the plaintiff’s ability to maximize the settlement value. Ethical rules, however, are clear: The plaintiff’s attorney’s foremost duty is to act in the best interest of her existing client.⁶¹ Any question that such settlement agreements are not uncommon can be dispelled by simply reading the newspapers. For

58. See Andrew D. Goldstein, *Sealing and Revealing: Rethinking the Rules Governing Public Access to Information Generated Through Litigation*, 91 CHI.-KENT L. REV. 375, 375 (2006) (noting commonness of “umbrella” protective orders); Charles J. Reed, *Confidentiality and the Courts: Secrecy’s Threat to Public Safety*, 76 JUDICATURE 308, 308 (1993) (“As a preemptive measure at the beginning of the discovery process, defense attorneys insist that the plaintiff’s attorney agree to a protective order preventing communication with anyone regarding any information provided by the manufacturer.”).

59. See, e.g., Dorothy J. Clarke, *Court Secrecy and the Food and Drug Administration: A Regulatory Alternative to Restricting Secrecy Orders in Product Liability Litigation Involving FDA-Regulated Products*, 49 FOOD & DRUG L.J. 109, 114 & n.30 (1994) (listing state rules).

60. *Id.* at 114.

61. MODEL RULES OF PROF’L CONDUCT R. 3.6(a) (2004) (advising that a lawyer should not make extrajudicial statements that may be disseminated to the public if it will materially prejudice the adjudicative process); MODEL RULES OF PROF’L CONDUCT R. 1.7(a) (2004) (instructing that a lawyer should not represent a client if representation will be limited by the lawyer’s own or another client’s interests); see also MODEL CODE OF PROF’L RESPONSIBILITY Canon 7 (1983).

example, in January 2007, *The New York Times* reported that Eli Lilly agreed to a \$495 million confidential settlement with Zyprexa that covered more than 18,000 patient claims.⁶² An earlier \$700 million Zyprexa settlement dispensed with approximately 8000 claims.⁶³

The problem with this company inertia, deliberate concealment, and confidential settlement of potential dangers is that most physicians learn about prescription drugs from publications of clinical trials, promotional materials, or alert letters that are provided by pharmaceutical companies.⁶⁴ For example, drug industry financing of mandatory continuing medical education has reportedly nearly quadrupled since 1998, from \$302 million to \$1.12 billion with over half of all continuing medical education courses in the United States paid for by drug companies, resulting in a situation where pharmaceutical companies set much of the agenda for what doctors learn about drugs.⁶⁵ As noted by then-New York State Attorney General Elliot Spitzer in his complaint against GlaxoSmithKline for allegedly misrepresenting, concealing, or otherwise failing to disclose four studies related to the antidepressant Paxil: A physician cannot act in accordance with his professional obligation owed to the patient if the physician's prescribing decision is based on inadequate or biased information.⁶⁶ Or as recently noted by the Honorable Judge Weinstein: "But even fine doctors have to rely on, and could . . . [be] misled by . . . incomplete and possibly misleading information available to them as a result of lack of adequate warnings on the label and [the manufacturer's] overselling."⁶⁷ The current situation is such that physician reliance on pharmaceutical companies to provide adequate and accurate safety information has been likened by the Honorable Judge Richard Posner of the Seventh Circuit Court of Appeals as reliance on the proverbial fox guarding the henhouse.⁶⁸

62. Reuters, *Settlement on Zyprexa Hurts Results at Eli Lilly*, N.Y. TIMES, Feb. 1, 2007, at C3.

63. *Id.*

64. See Waxman Report, *supra* note 34, at 7-16; see also *infra* notes 84-90 and accompanying text.

65. Daniel Carlat, Op-Ed., *Diagnosis: Conflict of Interest*, N.Y. TIMES, June 13, 2007, at A21 ("Because pharmaceutical companies now set much of the agenda for what doctors learn about drugs, crucial information about potential drug dangers is played down, to the detriment of patient care.") (using Avandia and Vioxx as examples).

66. See *supra* note 51.

67. *In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 241 (E.D.N.Y. 2007).

68. Larrissa MacFarquhar, *The Bench Burner: How Did A Judge With Such Submissive Ideas Become A Leading Influence On American Legal Opinion?*, NEW YORKER MAGAZINE, Dec. 10, 2001, at 78, 80-81.

III. THE SIGNIFICANT ROLE THAT PRODUCT LIABILITY LITIGATION PLAYS IN SCIENTIFIC FRAUD, MARKETING MISCHIEF, AND CONFLICTS OF INTEREST

As shown above, the lack of postmarketing studies, likely concealing, underreporting or spinning of adverse reactions, confidential settlements, and pharmaceutical involvement in mandatory continuing medical education means that the pharmaceutical companies, not the FDA, are in effect controlling the flow of information to treating physicians and the public. This situation leads to three distinct patterns of manufacturer misconduct consistently discovered through pharmaceutical products liability litigation: scientific fraud, marketing mischief, and conflicts of interest. The discussion below is artificial in that each kind of fraud is focused on in isolation, whereas litigation demonstrates that pharmaceutical manufacturers may engage in overlapping combinations of abuses in order to obtain FDA approval and keep their product on the market.

A. *Scientific Fraud*

The most common kind of scientific fraud committed by manufacturers may be the withholding of relevant information from physicians, the public, and sometimes the FDA,⁶⁹ either by withholding or modifying research results, by spinning the data, by blaming exclusively other risk factors rather than acknowledging the multifaceted role of the drug superimposed on the underlying risk factor, or by failing to report potential adverse drug reactions timely as required by the FDA. Recent cases where pharmaceutical manufacturers were accused of either modifying scientific results or failing to timely report adverse reactions show that drug companies often downplay serious, if not potentially life-threatening, side-effects, while trying to expand the market for their product.

For example, Merck's best selling, non-steroidal, anti-inflammatory drug, Vioxx, was approved of by the FDA in May 1999 as a safer alternative for the management of acute pain and the treatment of

69. There is no question that in some circumstances, the FDA has access to adverse effects rates from competitors related to the same family of drugs, yet has been remarkably slow to act. In some recent situations, such as the SSRI antidepressants, the FDA had access to adverse effect rates from different clinical trials at different companies, and yet, as one commentator has noted, was simply slow to aggregate all the clinical data in order to examine the link between SSRIs and suicide more systematically. See JERRY AVORN, *POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS* 359-87 (2004).

osteoarthritis. “From that date through August 2004, 105 million Vioxx prescriptions were filled in the U.S. and an undetermined number were filled outside the U.S.”⁷⁰ “In 2003 alone, Merck’s worldwide Vioxx sales totaled \$2.5 billion.”⁷¹ Merck has been accused of knowing about the cardiovascular risks of this COX-2 inhibitor since the early development of this drug, including internal e-mails made public through litigation in which Merck officials successfully persuaded the authors of a company sponsored study in 1996-97 to soften their conclusions as to the potential risk for thrombus formation with this drug.⁷² Yet instead of studying cardiovascular outcomes, Merck disseminated pooled data from different small studies which falsely minimized cardiovascular risks to physicians in its “cardiovascular card” used by sales representatives with doctors, in an effort to promote Vioxx’s cardiovascular safety to physicians.⁷³ In January 1999, Merck launched its largest study yet of Vioxx, the so-called VIGOR gastrointestinal outcome research which was designed to compare the safety of Vioxx compared to a traditional NSAID naproxen related to rheumatoid arthritis by which the company hoped to expand the drug’s approved uses by the FDA.⁷⁴ Despite Merck’s own chief scientist Edward Scolnick stating in an internal e-mail that the results were a “shame” and indicated Merck employees/consultants being right about COX-2 inhibition possibly increasing cardiovascular risks,⁷⁵ the published VIGOR study in the *New England Journal of Medicine* emphasized the purported positive gastrointestinal efficacy results. The published VIGOR study, however, did not contain data on edema and fluid retention at all, despite physician concern related to these issues.⁷⁶ Even more significant, the study obscured the cardiovascular (CV) risk associated with Vioxx by including data from an interim analysis that used different endpoint data for cardiovascular and gastrointestinal events—counting gastrointestinal events for one month longer—a highly irregular procedure which was not reported in the publication and led to

70. W. John Thomas, *The Vioxx Story: Would It Have Ended Differently in the European Union?*, 32 AM. J.L. & MED. 365, 365-66 (2006).

71. *Id.* at 366.

72. See Harlan M. Krumholz et al., *What Have We Learnt From Vioxx?*, 334 BRITISH MED. J. 120, 120 (2007).

73. *Id.*

74. *Id.* at 120-21.

75. This e-mail and other e-mails related to the Vioxx litigations are currently available on the Internet. See *VioxxDocuments.com*, Krumholz Vioxx Documents, www.vioxxdocuments.com (last visited Oct. 6, 2007).

76. See Krumholz et al., *supra* note 72, at 121.

the cardiovascular risk being understated because three additional myocardial infarctions occurred in the Vioxx group the month after the researchers stopped counting the cardiovascular events, whereas none occurred in the control group.⁷⁷ In addition, the cardiovascular risk was further concealed by presenting the hazard of myocardial infarctions as if the naproxen group was the intervention group and without reporting the absolute number of cardiovascular events, even though all other results were reported appropriately with rofecoxib as the intervention group.⁷⁸ Finally, the VIGOR study suggested a “naproxen hypothesis” which suggested that the difference in cardiovascular events between the Vioxx group and naproxen group was because naproxen allegedly had a strong cardioprotective effect, despite there being no accepted medical evidence that naproxen was cardioprotective and despite the fact that Merck knew it was concealing data by using different data for cardiovascular events.⁷⁹ Sadly, Merck strongly promoted the VIGOR study—reportedly purchasing nearly one million reprints to circulate to doctors and other healthcare professionals.⁸⁰ Thanks to these revelations shown through discovery and litigation, the *New England Journal of Medicine* re-examined the VIGOR study it published in 2000, and took the unusual step of publishing an “Expression of Concern” where it concluded that the Merck-employed authors of the article edited the manuscript to delete data revealing heart attacks in three of the study participants.⁸¹ One of the authors, Dr. Alise S. Reicin served as Merck’s lead scientific witness in several of the trials.⁸²

B. Marketing Mischief

To make matters worse, when drug manufacturers are confronted with potential declines in sales due to negative publicity associated with

77. *Id.*

78. *Id.*

79. *Id.*

80. *Id.*

81. See Gregory D. Curfman, Stephen Morrissey & Jeffrey M. Drazen, *Expression of Concern: Bombardier et al., “Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis,”* 353 *NEW ENG. J. MED.* 2813 (2005); see also Associated Press, *Vioxx Editorial May Bolster Merck Suits*, CBSNEWS.COM, Dec. 11, 2005, <http://www.cbsnews.com/stories/2005/12/11/ap/health/printableD8EEB0HG0.shtml>.

82. See Thomas, *supra* note 70, at 365, 367 & n.20 (discussing Merck expert witness being VIGOR study author). As pointed out, none of the authors of the VIGOR study have publicly conceded error or taken responsibility for the biased VIGOR presentation, and in fact, two VIGOR authors continue to collaborate on high profile work with Merck. Krumholz et al., *supra* note 72, at 121.

potential negative adverse effects, manufacturers frequently respond by increasing advertising campaigns, including hiring doctors who are considered highly respected and influential “thought leaders” in the respective medical community to promote their drug, even when such physicians do not actively use the drug during their own practice,⁸³ and specifically training sales representatives how to respond to potential issues.

A good example of documented marketing mischief is a 2005 Congressional Report, which reviewed over 20,000 pages of Merck internal company documents and found that “[e]ven as evidence mounted that use of Vioxx was associated with heart attacks and strokes, physicians continued to prescribe Vioxx to millions of patients,” thanks at least in part to strategies that Merck used to market Vioxx to physicians.⁸⁴ These efforts included instructing highly trained representatives to show physicians a pamphlet—the so called “CV Card”—which was based on data that the FDA considered improper for a safety analysis that suggested “Vioxx might be 8 to 11 times safer than other anti-inflammatory drugs, prohibited the representatives from discussing contrary studies (including those financed by Merck) that showed increased risks from Vioxx, and launched special marketing programs—named ‘Project XXceleration’ and ‘Project Offense’—to overcome the cardiovascular ‘obstacle’ to increased sales.”⁸⁵ The sales representatives were trained to use “obstacle handlers” to persuade doctors that Vioxx is the drug of choice. The Report is worth reading for its insights into the lucrative hidden world of pharmaceutical sales representatives and how it shows the incredible lengths⁸⁶ that Merck

83. For an example of this from the authors’ firm’s own practice related to the Parlodel cases, discussed *infra* notes 98-107 and accompanying text, Dr. Ted King, the former chairman of the Johns Hopkins University OB/GYN Department from 1979 to 1983 and the former chair of the FDA OB/GYN Advisory Committee was hired by Sandoz to write an affidavit to submit to the FDA on the purported need for Parlodel and to travel and lecture on the need for Parlodel for a consulting honorarium of \$1500 daily (two decades ago). See Deposition of Theodore King at 13:2-13:8, 71:19-72:1, Dunn v. Sandoz Pharms. Corp., 275 F. Supp. 2d 672 (M.D.N.C. 2003) (No. 1:98 CV 00912) (on file with the Hofstra Law Review). Dr. King’s deposition reveals that he had never prescribed Parlodel to any of his patients and that he recognized that the reason that Sandoz wanted him involved was simply because it believed he was a leader in the OB/GYN community. *Id.* at 28:7-28:14, 30:3-30:13, 43:3-43:7, 49:24-50:17, 56:17-56:20. His affidavit on behalf of Parlodel, however, never stated that he did not prescribe the lactation agent, yet he agreed that physicians reading his affidavit could believe that he wrote the affidavit based on his own experience as an obstetrician. *Id.* at 60:5-60:15.

84. See Waxman Report, *supra* note 34, at 3.

85. *Id.*

86. Such instruction included training sales representatives on how to shake hands, eat bread, and other non-verbal clues. *Id.*

went to “exhaustively” train its sales representatives how to persuade physicians to prescribe Vioxx and other Merck products.⁸⁷

Significantly, however, the Report showed that after each development which suggested that Vioxx might pose a heightened risk of heart attacks and strokes, Merck sent special bulletins or special messages to its sales force, “directing them to use highly questionable information to assuage any physician concerns.”⁸⁸ After the February 2001 FDA Advisory Committee voted that doctors should be informed about data from the VIGOR study, instead of backing off from its marketing of Vioxx, Merck launched “Project A&A XXceleration” with the slogan “In It To Win It” with financial incentives for sales representatives who helped Merck meet its goal of an increased market share.⁸⁹ Similarly, after an August 22, 2001 study published in the *Journal of the American Medical Association (JAMA)* raised serious questions about the safety of Vioxx and the other COX-2 inhibitors, Merck launched “Project Offense” a major new marketing campaign with the continued goal of increasing Vioxx’s share of the market with the company again explicitly instructing its sales representatives how to deal with the cardiovascular safety concerns of Vioxx, including a decision tree called the “CV Obstacle Response” which again emphasized the CV Card as a way of assuring physicians about the

87. *Id.*

88. *Id.* Among examples of questionable practices, the Waxman Report noted:

After Merck’s VIGOR study reported increased heart attack risks, Merck directed its sales force to show physicians a “Cardiovascular Card” that made it appear that Vioxx could be 8 to 11 times safer than other anti-inflammatory drugs. *This card omitted any reference to the VIGOR findings and was based on data FDA considered to be inappropriate for a safety analysis.*

Id. at 4 (emphasis added).

After the FDA advisory committee voted that physicians should be informed about the risks found in the VIGOR study, Merck sent a bulletin to its sales force that advised: “DO NOT INITIATE DISCUSSIONS ON THE FDA ARTHRITIS COMMITTEE . . . OR THE RESULTS OF THE . . . VIGOR STUDY.” If physicians asked about the VIGOR study, Merck representatives were directed to respond, “*I cannot discuss the study with you.*”

Id. (emphasis added).

After the *New York Times* reported on the cardiovascular dangers of Vioxx, Merck instructed its field staff to tell physicians that patients on other anti-inflammatory medications were eight times more likely to die from cardiovascular causes than patients on Vioxx. The Merck bulletin told its sales force to show physicians the Cardiovascular Card and state: “Doctor, as you can see, Cardiovascular Mortality as reported in over 6,000 patients was Vioxx .1 vs. NSAIDS .8 vs. Placebo 0.”

Id.

89. *Id.* at 23.

cardiovascular risks and instructing sales representatives to emphasize allegedly new “efficacy” data.⁹⁰

C. Conflict of Interest: The Problem Of Pharmaceutical Funding of Private Research and Undisclosed Involvement of Defense Experts in Research

As already hinted above through the example of Merck pressuring authors of company-based studies to “soften” their conclusion about the possible cardiovascular effects of Vioxx, GlaxoSmithKline’s suppression of unfavorable Paxil studies that showed a possible link between suicide and SSRI anti-depressants in teenagers and children,⁹¹ and other numerous real-world examples, only a few of which are discussed here, the studies upon which a drug’s label is based may be compromised by industry research funding. Such private research funding may require contractual agreements that allow the company to delete information from publication or delay publication of results, put pressure on researchers not to publish negative studies, and, in extreme cases, wage campaigns to discredit negative studies and destroy the scientists who attempt to publish negative results.⁹² Given the enormous scale of research and educational grants given out by manufacturing companies, professional journals are noting that they are having a hard time finding experts in the field to review journal submissions who do not have industry ties, especially in situations where a particular company may have market dominance over a product.⁹³ Both legal and medical commentators have suggested that pressure exerted on researchers of sponsored research and sponsor control over data may be common “but because researchers so seldom stand up to their sponsors . . . ‘there is no way to know how many negative studies have been suppressed—or worse, how many negative studies were converted to positives.’”⁹⁴ Until September 2007, there was no requirement that pharmaceutical manufacturers disclose the results of all clinical trials

90. *Id.* at 25-26.

91. *See supra* note 51 and accompanying text.

92. *See* Drummond Rennie, *Thyroid Storm*, 277 JAMA 1238, 1238-43 (1997) (citing, among others, WESLEY COHEN ET AL., UNIVERSITY-INDUSTRY RESEARCH CENTERS IN THE UNITED STATES (1994)).

93. *Id.* at 1242.

94. Susan Haack, *Scientific Secrecy and “Spin”: The Sad, Sleazy Saga of the Trials of Remune*, 69 LAW & CONTEMP. PROBS. 47, 63 (2006) (quoting Marcia Angell, Editor-in-Chief of the *New England Journal of Medicine*). Haack suggests that “almost every day there is more reason to believe that the iceberg of corruption is sizable.” *Id.*

involving humans, although this was part of the FDA legislation which was recently passed in Congress.⁹⁵

An example of how conflict of interest is discovered in the course of product liability litigation is the Parlodel (bromocriptine mesylate) lawsuits. Numerous new mothers or their estates sued Sandoz Pharmaceuticals Corporation (now Novartis Pharmaceuticals Corporation) after they suffered hypertension, seizures, strokes, myocardial infarctions and death after their ingestion of Parlodel for the prevention of physiological lactation (lactation suppression).⁹⁶ The drug was routinely prescribed to mothers who chose not to breast-feed.⁹⁷

During the course of litigation,⁹⁸ the plaintiffs through discovery obtained a document titled *Postpartum Stroke—A Twenty Year Experience*, by Dr. Andrea Witlin, Farid Matter, and Dr. Baha M. Sibai, which had been submitted to and accepted by the prestigious *American Journal of Obstetrics and Gynecology* for publication.⁹⁹ Dr. Sibai was a defense witness in the case. The study, which claimed to be a twenty year *prospective* study of strokes in women following childbirth, exonerated Parlodel as the cause of strokes, reporting that of the alleged 40,000 women taking Parlodel, only one of these women suffered a stroke and that not only was Parlodel not a cause of strokes in the postpartum period, but was actually protective.¹⁰⁰

95. See Drazen et al., *supra* note 45, at 1756 (discussing soon to be enacted requirement for sponsors of all clinically directive therapeutic trials to register their studies at the inception, in comparison with the past where “a clinical trial could be conducted in secret. The trial’s sponsor, claiming proprietary rights, could keep all information about it, including its very existence, private. Thus, if a drug had important adverse effects, this information might never be made public.”).

96. For a review of how Sandoz Pharmaceuticals has been noted to have done everything it could to resist changes to labeling of Parlodel and its later removal from the market, see Margaret A. Berger & Aaron D. Twerski, *From the Wrong End of the Telescope: A Response to Professor David Bernstein*, 104 MICH. L. REV. 1983, 1987-88 (2006).

97. However, mother’s milk abates naturally in a few days if not stimulated, so in 1994 the FDA filed proposal to withdraw the approval of the lactation suppression indication. See Opportunity for a Hearing on a Proposal to Withdraw Approval of the Indication, 59 Fed. Reg. 43,347 (Aug. 23, 1994).

98. The authors’ firm was involved in the incident described.

99. The transcripts of the depositions of Drs. Sibai and Witlin related to this office are on file with the authors.

100. The original manuscript’s conclusion in full was that “[a]lthough bromocriptine [Parlodel] is no longer approved for use in postpartum lactation suppression . . . it does not appear to be etiologic for postpartum stroke as has previously been reported. . . . Indeed, one might argue that woman exposed to bromocriptine were at a lower risk . . .” Andrea G. Witlin, Farid Mattar & Baha M. Sibai, *Postpartum Stroke: A Twenty-Year Experience* 13 (unpublished manuscript, on file with the Hofstra Law Review); see generally Deposition of Dr. Baha M. Sibai, *Siharath v. Sandoz Pharms. Corp.*, 131 F. Supp. 2d 1347 (N.D. Ga. 2001) (testifying as to his findings regarding the relationship between bromocriptine and postpartum stroke) (on file with the Hofstra Law Review).

Depositions taken by plaintiffs' attorneys of the study's authors, Drs. Witkin and Sibai, however, revealed the serious conflicts of interests in the study—including that Dr. Sibai had been a paid expert witness for Sandoz in several lawsuits involving Parlodel and admitted his payments averaged \$10,000 to \$20,000 per year.¹⁰¹ They further revealed the study's obvious flaws including that (1) although the manuscript described the study as a prospective compilation in a database of clinical data on women who suffered strokes, no prospective database ever existed;¹⁰² (2) no written criteria was set for the inclusion/exclusion of patients in the study, much less any clear definition of "stroke";¹⁰³ and (3) the manuscript was allegedly based on a single spreadsheet that consisted of thirty-three columns of information for each of the twenty women identified as having a stroke, yet many of the columns were missing information, including that in the "postpartum medications" column which formed the basis for the Parlodel conclusions, no information was available for half of the women with respect to their use of postpartum medicines.¹⁰⁴ As a result, the plaintiffs' attorneys wrote a detailed letter to the *American Journal of Obstetrics and Gynecology*,¹⁰⁵ which resulted in further review of the paper. It was then significantly revised so that the study was now identified as being retrospective, not prospective (which is significant in that prospective studies are considered to have greater scientific weight and be less subject to the reviewer bias phenomenon). Even more significant, unlike the conclusion of the earlier-accepted manuscript, which had explicitly stated that Parlodel "does not appear to be etiologic for postpartum stroke," the final version of the study entirely omitted any discussion of Parlodel.¹⁰⁶

101. This Parlodel saga is written about in JEROME P. KASSIRER, ON THE TAKE: HOW MEDICINE'S COMPLICITY WITH BIG BUSINESS CAN ENDANGER YOUR HEALTH 42-44 (2005) (concluding that after reviewing the doctor's depositions that "some of the data were incomplete, unreliable, unverifiable, and nonreproducible" and "[c]learly the research of Drs. Sabai [sic] and Witlin was not only flawed, but contaminated by Dr. Sabai's [sic] financial conflict of interest").

102. See, e.g., Deposition of Andrea Witlin at 48:6-50:2, 50:20-51:6, 99:4-99:13, Brasher v. Sandoz Pharms. Corp., 160 F. Supp. 2d 1291 (N.D. Ala. 2001) (on file with the Hofstra Law Review).

103. See, e.g., *id.* at 59:21-69:17, 75:6-75:19, 76:40-76:25, 92:7-92:19.

104. See *id.* at 76:14-76:19, 88:7-88:8, 92:7-93:12, 94:5-95:23.

105. Letter from Jerry Kristal to Frederick P. Zuspan, M.D., Editor-in-Chief, *American Journal of Obstetrics and Gynecology* (Aug. 6, 1999) (on file with author).

106. The conclusion of the earlier-accepted manuscript explicitly stated that Parlodel "does not appear to be etiologic for postpartum stroke." See Witlin, Mattar & Sibai, *supra* note 100, at 13. Unlike the earlier manuscript, the conclusion in the published version was simply that "postpartum stroke remains an uncommon, multifactorial, and nonpreventable complication of pregnancy We found an association between postpartum stroke and hypertensive disorders of

The key is that if Drs. Witlin and Sibai had not been deposed and asked the questions they were asked, the conflict of interest and the numerous defects in the study would never have been discovered. The original study that exonerated Parlodel would have been published by this well-respected journal and would have been used in the Parlodel litigation or even by Novartis to try to bring the product back on the market. Despite their violations of the *American Journal of Obstetrics and Gynecology's* policies on conflicts of interest and the implicit acknowledgment of the flaws as mandated by the re-write of the manuscript omitting the Parlodel conclusion, Drs. Sibai and Witlin have continued to publish in the *American Journal of Obstetrics and Gynecology* without any apparent censure, although Dr. Sibai has recently been censured by the journal for his involvement in another study in which a study was misrepresented as a randomized trial when it was submitted and accepted by the journal and when it was presented at the journal's annual meeting.¹⁰⁷

*D. A Quick Note: Is The FDA Retreating from Its
Preemption Position?*

In an amicus letter brief filed in *Perry v. Novartis Pharmaceutical Corporation* in the United States District Court for the Eastern District of Pennsylvania on September 21, 2006, the FDA, while continuing to assert that “state tort claims premised on the defendants’ failure to provide a warning that FDA had specifically considered and rejected as scientifically unsubstantiated during the relevant period,”¹⁰⁸ expressly disclaimed any intention to “occupy the field.”¹⁰⁹ The FDA further made clear that failure to warn claims that do not directly conflict with the FDA regulatory decisions remain viable, noting that “federal regulations explicitly recognize that manufacturers can, and in some limited instances must, modify their labels to add new warnings of hazards associated with the drug without awaiting prior FDA approval.”¹¹⁰ Thus,

pregnancy and cesarean delivery” Andrea G. Witlin, Farid Mattar & Baha M. Sibai, Postpartum Stroke: A Twenty-Year Experience, 183 AM. J. OBSTETRICS & GYNECOLOGY 87 (2000). Instead of mentioning Parlodel, the study found that there was “no association [between] conductive anesthesia” and postpartum stroke. *Id.* (emphasis added).

107. Editorial, *Announcement of Inappropriate Acts in the Publication Process*, 195 AM. J. OBSTETRICS & GYNECOLOGY 886, 887 (2006).

108. See Brief of United States as *Amicus Curiae* in Support of Defendants at 1, *Perry v. Novartis Pharms. Corp.*, 456 F. Supp. 2d 678 (E.D. Pa. Sept. 21, 2006), available at <http://www.aei.org/research/liability/subjectAreas/pageID.1378,projectID.23/default.asp>.

109. *Id.*

110. *Id.* at 10.

this letter made clear that failure to warn claims that do not directly conflict with FDA regulatory decisions remain viable and can be interpreted to be consistent with the argument that there can be only conflict preemption (a direct and positive conflict) when the FDA has been asked to consider a warning, reviewed all the data, and rejected it, that is, a case-by-case approach to preemption.¹¹¹ The *Perry* amicus letter, however, raises more questions than it answers in that the FDA typically does not reject warnings, but just determines that data is either conclusive or inconclusive about the need for a warning at a given point in time. Moreover, labeling gets “negotiated” between the FDA and the manufacturer, and thus decisions can be made for reasons distinct from the merits, as can happen in any negotiation. Further, would this result in perpetual debate about what the FDA would or would not do? Would this limited *Perry* preemption result in a situation where the FDA will step in and specifically provide the answer in individual litigations? It would seem that the current Bush administration FDA is unlikely to flatly say, no, we would have not rejected a specific warning and thus plaintiff may proceed. In arguing against *Perry* preemption, plaintiffs should argue that the pharmaceutical company has the continuous duty, even after receiving market approval, to ensure the safety of its products on the market, and as such, the pharmaceutical company has the burden of showing that it proposed a warning or new warning or label change, submitted all relevant clinical data, and that the FDA explicitly rejected this clinical data. Plaintiffs should also argue these are factual issues that cannot be decided on summary judgment or Federal Rule of Civil Procedure 12(b)(6) motions.

The evolving position of the FDA may be important as to the outcome in a pending certiorari petition concerning the preamble preemption issue. The Vermont Supreme Court, the country’s first highest state court to address the claims that the FDA preamble preempts failure to warn pharmaceutical litigation, handily dismissed such claims

111. This limited view of preemption was adopted by the *Perry* court. *See Perry*, 456 F. Supp. 2d at 684-85; *see also In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 277 (E.D.N.Y. June 11, 2007) (“FDA would consider preempted *only* those state-law adequacy of warning claims which seek to impose liability for failure to include labeling language already rejected by the FDA.”) (emphasis added). For an old but relevant law journal article on the topic of limited preemption, see Margaret Jane Porter, *The Lohr Decision: FDA Perspective and Position*, 52 FOOD & DRUG L.J. 7, 11 (1997) (discussing the Supreme Court’s decision in *Lohr*, including how the FDA’s position in *Lohr* recognized that “[r]egulation cannot protect against all possible injuries that might result from use of a device over time. Preemption of all such claims would result in the loss of a significant layer of consumer protection”).

as being without merit in *Levine v. Wyeth*.¹¹² The drug manufacturer Wyeth filed a petition for certiorari, last term, and the Supreme Court, on May 21, 2007 expressly invited the Solicitor General to file a brief in this case expressing the views of the United States. No brief has been filed to date. If a brief is filed, and the Supreme Court grants certiorari and defers to the administration view, the landscape of drug safety and victim's rights may be detrimentally altered given the current administration's anti-consumer stance.

IV. CONCLUSION

We believe that American consumers possibly may be using a number of medications that have serious risks, due to the inability of the current FDA scheme to meaningfully police pharmaceutical manufacturer misconduct. To end the vital role that litigation plays in uncovering hidden drug dangers and providing some recompense to injured consumers would be an unnecessary end to the prominent role of the states as the prime protector of their citizens' health and safety.¹¹³ As potentially recognized by the FDA's possible retreat from its earlier position, Congress, in enacting the consumer protection statutes did not and could not have intended the nightmare that will result if FDA preemption of private common law pharmaceuticals cases occurs.

112. No. 2004-384, 2006 WL 3041078 (Vt. Oct. 27, 2006). Petition for Certiorari Filed, 75 USLW 3500 (Mar. 12, 2007) (No. 06-1249).

113. *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 475 (1996) (noting "prominence of the States in matters of public health and safety").