Written testimony before the

United States House of Representatives
Committee on Oversight and Government Reform

In Public Hearings on

FDA Preemption of State Tort Liability Lawsuits on FDA-Regulations Drugs and Devices

Wednesday, May 14, 2008

John E. Calfee, Ph.D.
email: calfeej@aei.org – tel: 202-862-7175

American Enterprise Institute
1150 17th St., NW
Washington, D.C.

I am honored to testify in these hearings on FDA preemption of state product liability lawsuits relating to FDA-approved drugs and medical devices. I will focus mainly on pharmaceuticals. In doing so, I will address the practical consequences of FDA preemption of liability litigation, and will largely ignore the complex legal issues to be discussed by other witnesses. By way of background, I am an economist who has specialized in government regulation, tort liability, information, and FDA regulation, beginning with my experience in the Bureau of Economics at the Federal Trade Commission in the 1980s.

The central issue in these hearings is whether state tort litigation against FDA-approved drugs and devices – especially lawsuits alleging failure to warn – should be preempted by FDA regulation including the content of the labels that accompany all approved drugs and devices. A current case now before the Supreme Court, *Wyeth v. Levine*, may strongly affect the role, if any, of preemption.

A commonly held view is that state tort liability litigation can do much good and little harm because such litigation provides added protection to patients and consumers through compensation for injury, better information in the form of new warnings and disclosures, and improved drug safety (e.g., Kennedy 2008; Glantz and Annas 2008). I believe these views are largely unsupported, however. Economic reasoning and historical experience strongly suggest that FDA preemption, if it becomes standard law, would actually tend to improve patient welfare.

Tort Liability Suits as a Compensation Mechanism

The original function of the tort liability system was to deter unsafe activity by causing firms and others to internalize the full costs of their actions. Since the 1960s, compensation has come to play an equal or perhaps predominant role. In the meantime, punitive damages, once rare, have assumed a crucial role in liability litigation, especially in shaping the many settlements through which most liability suits are resolved (Priest

1991; Rubin, Calfee, and Grady 1997; Moore and Viscusi 2002). Punitive damages are of course paid in addition to compensatory damages.

A substantial stream of research demonstrates that liability litigation is an extraordinarily inefficient tool for compensating patients. In asbestos litigation, which has been studied more than any other kind, plaintiffs have received only about forty percent of total damages payouts. Transaction costs including attorney and expert fees accounted for the rest (Hensler 1993). Some of the research critical of tort liability as a compensation mechanism has appeared in medical journals, sometimes accompanied by proposals to replace some components of the liability system (Studdert and Brennan 2001). An additional problem is the increasing role played by damages for pain and suffering (i.e., nonpecuniary losses). Here, the problem is that systematic use of pain and suffering damages amounts to a form of mandated insurance. There are compelling arguments that such insurance is often not worth its cost to consumers (Calfee and Winston 1993). The problem is worse for products (including virtually all pharmaceuticals) that usually prevent far more harm than they cause. Burdening pharmaceutical manufacturers with full compensation for apparent harm from their products would dramatically increase prices, transferring the burden to patients and payers generally. This can work to suppress even very valuable products, as recognized by former FDA Commissioner Mark McClellan (McClellan 2003). That this is more than a theoretical possibility became clear when liability engulfed the child vaccine market in the 1980s. As it became clear that the extra insurance bundled with childhood vaccines was worth far less than its cost, shortages ensued and manufacturers abandoned the market. The situation was resolved by replacing the liability system altogether (Manning 1994, 1996, 1997).

Information and Preemption

Much if not most litigation subject to FDA preemption involves allegations of failure to warn. The effects of preemption on drug information are therefore a central issue. It would be a mistake to assume that because liability suits would induce

pharmaceutical manufacturers to provide additional information and warnings, litigation is bound to improve information for patients and physicians. Experience has provided little reason to expect this kind of improvement in the wake of liability litigation. For example, a detailed and largely favorable assessment of the role of litigation in pharmaceutical markets noted that Vioxx litigation has done little or nothing to improve knowledge about that drug (Bernstein 2007, p. 1055). Even in the case of massive litigation sponsored by state governments and non-profit organizations – that relating to tobacco – there little if any evidence that public knowledge of the health effects of smoking was improved even though cigarettes are among the least regulated products (while pharmaceuticals are arguably the most regulated) (Schuck 2008, n. 104, citing Rabin 2001, p. 201).

Given that we cannot assume that tort liability litigation will improve product information, we must pay attention to how it actually works in pharmaceutical markets, where regulation is already exceptionally strong. In *Wyeth v. Levine*, for example, the dispute was essentially over whether Wyeth should have strengthened the warning for the drug Phenergan in order to contra-indicate a specific way to administer this drug in emergency situations. It seems clear from the record that the FDA itself had issued detailed warnings about administration but had also declined to contra-indicate this particular method because physicians would probably decide it was in fact the best method in some circumstances.

Rather than focusing narrowly on the debate over one particular contra-indication, however, we must pay attention to the larger effects limiting or prohibiting FDA preemption. An unwise contra-indication is an example of the more general problem of over-warning. It has become clear that liability worries encourage manufacturers to propose very detailed warnings and even to resist emphasis on relatively greater dangers for fear of being held accountable for downgrading rarer but still dangerous risks. Some of this was described in a series of *Wall Street Journal* articles that noted, for example, that the three erectile dysfunction drugs on the market each carried labels more than 20

pages long (Hensley 2005a, 2005b). The FDA has for many years sought to modify and improve drug labels while avoiding the constant danger of over-warning (Galson 2005).

Many new warnings and contra-indications are bound to be considered for a wide variety of drugs and devices. In the absence of preemption, firms will know that they (and physicians) may be subject to large damages verdicts at the will of juries that necessarily focus on a highly specific personal tragedy rather than on societal trade-offs. This applies with particular force to possible contra-indications. Physicians are likely to treat contra-indications as outright bans because to prescribe in the face of a labelled contra-indication is to court a malpractice lawsuits and punitive damages if anything goes wrong no matter how extensive the warnings might be. The result is that patients who would have benefitted from the contra-indicated use will be denied those benefits even if the expected net benefit greatly exceed the likelihood of harm.

If the FDA tended to provide too little in the way of warnings and contra-indications, one might doubt that preemption would serve a useful role. But there no reason to expect this problem. The FDA is legendary for its detailed probing and assessment of nearly anything related to drug safety, and does this under intense scrutiny from Congress, medical academia, the public press, and many others (cf. Schuck 2008, p. 14-15). It clearly seeks to balance the costs and benefits of information provided on drug labels and through other means. In fact, the agency probably tends to require too much of this kind of information. For example, the label for Rotateq, the rotavirus vaccine, was recently amended to include a warning against intestinal blockage, a rare but genuine problem with an earlier rotavirus vaccine since removed from the market. It did so even though extremely large clinical trials involving tens of thousands of subjects had revealed no excess likelihood of blockage for the vaccine compared to a placebo (*Wall Street Journal*, May 2, 2008).

Perhaps the most vigorous wave of criticism of the agency for inadequate warnings in recent years arose in connection with "suicidality" (roughly speaking, suicidal thinking) among youthful users of the SSRI class of antidepressants. Facing relentless criticism from litigators, politicians, popular press editorialists, and elite

medical journals, the FDA implemented its strongest "black box" warning for all antidepressants, not just SSRIs (because there was little reason to think that older drugs, which can cause fatal overdoses, are safer). Subsequent research taking a variety of approaches has found that SSRI use is strongly associated with lower, not higher, suicide rates, and that the highly publicized warnings probably did more harm than good by reducing antidepressant use. In particular, a series of reports has found that there is a striking, inverse relationship between SSRI prescriptions and youth suicides in a variety of data sets and that the imposition of new FDA warnings (beginning with public health alerts) is strongly associated with reduced antidepressant prescribing for children (and younger adults) and higher suicide rates (Shogren 2004; McKeown, Cuffe, and Schulz 2006; Ludwig, Marcotte, and Norberg 2007; Brent 2007; Gibbons et al. 2007; Lubell et al. 2007; Bridge et al. 2007; Pfeffer 2007).

The reasons why FDA is more likely to lean toward over-warning rather than under-warning become clearer when one looks at drug safety itself.

Drug Safety and Preemption[1]

Those who oppose FDA preemption of tort liability lawsuits for failure to warn and other reasons often seem to assume that the FDA has tolerated an unduly low level of drug safety (Glantz and Annas 2008). There is essentially no systematic evidence for this view. In its widely cited 2006 report on drug safety, the Institute of Medicine began by noting, "The committee did not attempt to document whether or not a drug safety crisis exists, and this report should not be interpreted as commenting on that claim one way or the other" (p. 1-1). Even when looking at the leading anecdotes that have aroused intense criticism of drug safety in the past few years, there is little reason to think drugs have become less safe or are unduly unsafe. I have already mentioned antidepressants. Also informative is the lengthy and exhaustively studied series of events that began with the

[1] This section draws upon my written testimony in the Feb. 27, 2008 hearings on drug safety and the FDA before the House Committee on Appropriations, Subcommittee on Agriculture and FDA.

withdrawal of the arthritis pain reliever Vioxx at the end of September 2004. As the FDA presciently pointed out at the time, it was far from clear that Vioxx or its competing Cox-2 inhibitor, Celebrex, was significantly riskier than the much older non-steroidal anti-inflammatory drugs (NSAIDs) they replaced, given that these older drugs had never been subjected to rigorous clinical trials like the one that brought Vioxx down. Subsequent research has largely vindicated that view, with the entire class of NSAIDs (old and new, Cox-2s or not) now bearing heart attack warnings (Calfee 2005; Kearney et al. 2006; Warner and Mitchell 2008).

This is hardly surprising. Even for products that are subject to far less regulation, no systematic evidence has emerged that the U.S. liability system in the U.S. improves safety (Moore and Viscusi 2002; Rubin and Shepherd 2007). In fact, there are compelling reasons to think that in balancing safety against the benefits of new drugs, the FDA tends to give too much weight to safety and not enough to benefits. The reasons lie in the biased incentive structure facing the FDA staff. The unrelenting criticism visited on the FDA since the Vioxx withdrawal illustrates a profound disparity how the public penalizes two different kinds of regulatory error. When FDA staff members decide whether the benefits of a proposed new drug exceed its risks, they know that if they commit what is often called a Type I error – the approval of a drug that turns out to be insufficiently safe once marketing begins – their error will usually become known (a "public error"). This can and often does lead to impassioned criticism of the agency and to correction of the error (although more often than not, critics fix upon something that was probably not an error at all). On the other hand, a Type II error – the failure to permit marketing of a drug that would in fact provide benefits in excess of harms – is typically detected by relatively few people (a "private error"), and its deleterious effects can persist more or less indefinitely.

The effect is to bias even the most conscientious FDA regulators toward exercising excessive caution and requiring excessive drug testing. This first became apparent in a stream of research on the "drug lag" of the 1960s and 1970s, when FDA approvals trailed far behind those in European nations. This research revealed no

consumer benefit in terms of safer drugs, yet similar approval lags continued for years afterward (Peltzman 1973, 1974; Wardell and Lasagna 1975; Katin and Brown 1995). Yet slow drug approvals here did not bring extra safety. An analysis of the United States, Spain, and the United Kingdom yielded essentially identical drug-withdrawal rates despite the more rapid drug-approval timelines in the European countries (Bakke, et al. 1995). Also, research has made clear that the advent of user-fee funding via the 1992 Prescription Drug User Fee Act has worked to the benefit of patients by accelerating the arrival of new drugs (Philipson, et al., 2005).

There is anecdotal evidence that soon after the Vioxx withdrawal and ensuing criticism, the FDA began to be even more cautious in approving new drugs and new indications (Harris 2005). Last year, for example, the FDA refused to approve the pain reliever Arcoxia and the weight-loss drug Accomplia even though both had been approved by the European Union and many other nations (Gottlieb 2007; Wadman 2007). The FDA has also been unreceptive to some promising new drugs for advanced cancer, including Provenge, Genasense, and others (Usdin 2007a; Miller and Henderson 2007; Miller 2007; Pardoll and Allison 2004). The 2007 FDAAA legislation, which is rooted in the view that the FDA staff has consistently neglected drug safety, has probably reinforced the FDA's innate tendency toward over-caution (Calfee 2007).

Finally, too little attention has been paid to another potent force: market-driven manufacturer incentives to maintain drug safety. Such incentives operate with powerful effect in far less regulated high-tech industries such as automobiles, petroleum, and electronics. As in other industries, pharmaceutical manufacturers rely heavily upon maintaining their reputation among customers (especially physicians) for product safety and efficacy. Post-approval clinical trials play a central role in this process. These trials are undertaken to expand markets, but they necessarily open the door to new and possibly alarming (as well as reassuring) safety information. Often, post-approval trials are bigger, longer, and more informative than the trials undergirding drug approvals. Often, they force revisions in accepted views of such basic matters as, for example, the benefits of

lowering serum cholesterol or the safety of all NSAID pain relievers (Topol 2004a; Wadman 2007).

Conclusions

The question of whether FDA regulatory rulings should preempt state or common law tort liability litigation for failure to warn and similar allegations turns on the question of whether such litigation would improve the pharmaceutical market in terms of compensation, information, and product safety. For three reasons, the absence of preemption is likely to worse markets and harm patients on the whole. First, the liability system is an extraordinarily inefficient mechanism to achieve compensation for harms from pharmaceuticals. The attempt to provide compensation through comprehensive liability litigation is likely to burden pharmaceuticals with excessive costs that would raise prices and tend to discourage the use of valuable drugs.

Second, the absence of preemption would make it far easier for litigation to induce new contra-indications and other warnings that on the whole are more likely to cause over-warning and under-use of essential drugs instead of improving the pharmaceutical information environment. One reason is that the pressure for excessive warnings is sufficiently intense that the FDA is unlikely to forego useful warnings, and will sometimes mandate excessively detailed warnings. And third, there is little reason to think that drug safety has suffered in recent years or that FDA incentives are such as to cause the agency to slight drug safety. Indeed, strong forces exert pressure to give too much weight to safety in comparison to approving new drugs and new indications. Further growth in liability litigation would reinforce these tendencies, to the disadvantage of patients, while preemption can provide a valuable check on these adverse consequences of litigation.

References

Bakke, Olav M., Michael Manocchia, Francisco de Abajo, Kenneth I. Kaitin, and Louis Lasagna (1995) "Drug Safety Discontinuations in the United Kingdom, the United States, and Spain from 1974 through 1993: A Regulatory Perspective," 58 *Clinical Pharmacology and Therapeutics*, v. 58, p. 108-117.

Bernstein, Anita (2007) "Enhancing Drug Effectiveness and Efficacy Through Personal Injury Litigation," *Journal of Law and Policy*, v. v 15, p. 1051-1078.

Brent, David (2007) "Editorial: Antidepressants and Suicidal Behavior: Cause or Cure?," *American Journal of Psychiatry*, v. 164, p. 989-991 (July).

Bridge, Jeffrey A., Satish Iyengar, Cheryl B. Salary, Rémy P. Barbe, Boris Birmaher, Harold Alan Pincus, Lulu Ren, and David A. Brent (2007) "Clinical Response and Risk for Reported Suicidal Ideation and Suicide Attempts in Pediatric Antidepressant Treatment: A Meta-analysis of Randomized Controlled Trials," *Journal of the American Medical Association*, v. 297, n. 15, p. 1683-1696 (Ap. 15).

Calfee, John E. (2005) "The Vioxx Fallout," AEI Health Policy Outlook, Sept.-Oct. 2005.

Calfee, John E. (2007) "Reform Without Reason," *Health Policy Outlook*, American Enterprise Institute, Washington, D.C., September 2007. Available at http://www.aei.org/publications/pubID.26859/pub_detail.asp. Accessed February 24, 2008.

Calfee, John E., and Paul Rubin (1992) "Some Implications of Damage Payments for Nonpecuniary Losses," *Journal of Legal Studies*, v. 21, n. 2, p. 371-411 (June).

Calfee, John E. and Clifford Winston (1993) "The Consumer Welfare Effects of Liability for Pain and Suffering: An Exploratory Analysis," *Brookings Papers on Economic Activity: Microeconomics*, n. 1, p. 133-174.

Galson, Steven (2005) "Drug Safety in Controversy: FDA Actions," presentation at the Johns Hopkins Bloomberg School of Public Health, March 15, 2005. Available at http://www.fda.gov/cder/present/galson/2005/JohnsHopkinsSchoolofPublicHealthMarch%2005.pdf. Accessed May 13, 2008.

Gibbons, Robert D., C. Hendricks Brown, Kwan Hur, Sue M. Marcus, Dulal K. Bhaumik, Joëlle A. Erkens, Ron M.C. Herings, and J. John Mann (2007) "Early Evidence on the Effects of Regulators' Suicidality Warnings on SSRI Prescriptions and Suicide in

Children and Adolescents," *American Journal of Psychiatry*, v. 164, p. 1356-1363 (Sept.).

Glantz, __ and Annas 2008

Gottlieb, Scott (2007a) "Drug Danger," *Wall Street Journal*, April 17.

Harris, Gardiner (2005) "F.D.A. Responds to Criticism With New Caution," *New York Times*, August 6.

Hensler, Deborah (1993) "Reading the Tort Liability Tea Leaves: What's Going On in the Civil Liability System?" *The Justice System Journal*, v. 16, n. 2, p. 139-154; reprinted by Rand Institute for Civil Justice.

Hensley, Scott (2005a) "Long Labels Help Drug Firms, But Can Obscure What Matter," *Wall Street Journal*, June 28, 2005.

Hensley, Scott (2005b)"Liability Worries Cloud Drug Labels: In Bloated Package Inserts, Fine Print Can Overshadow Facts of Most Use to Doctors," *Wall Street Journal*, July 5, 2005.

Institute of Medicine (2006) *The Future of Drug Safety: Promoting and Protecting the Health of the Public.*

Kaitin, Kenneth, and Jeffrey Brown (1995) "A Drug Lag Update," 29/2 *Drug Information Journal* 361-374.

Kearney, Patricia M, Colin Baigent, Jon Godwin, Heather Halls, Jonathan R Emberson, and Carlo Patrono (2006) "Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomised trials," *British Medical Journal*, v. 332, p. 1302-1308 (June 3).

Kennedy, Donald ___ (2008) "Editorial: ___," *Science*, v. __

Lubell, K.M., S.R. Kegler, A.E. Crosby, and D. Karch (2007) "Suicide Trends Among Youths and Young Adults Aged 10--24 Years – United States, 1990-2004," *Morbidity and Mortality Weekly Reports*, v. 56, n. 35, p. 905-908 (Sep. 7).

Ludwig, Jens, Dave E. Marcotte, and Karen Norberg (2007) "Anti-depressants and Suicide," NBER Working Paper No. 12906.

Manning, Richard L. (1994) "Changing Rules in Tort Law and the Market for Childhood Vaccines," *Journal of Law and Economics*, v. 37, n. 1, p. 247-286.

Manning, Richard L. (1996) "Is the Insurance Aspect of Producer Liability Valued by Consumers? Liability Changes and Childhood Vaccine Consumption," *Journal of Risk and Uncertainty*, v. ___.

Manning, Richard L. (1997) "Products Liability and Prescription Drug Prices in Canada and the United States," *Journal of Law and Economics*, v. 40, n. 1, p. ___ (April).

McClellan, Mark (2003) "Remarks before the Physician Insurers Association of America, May 24, 2003."

McKeown, Robert E., Steven P. Cuffe, and Richard M. Schulz (2006) "U.S. Suicide Rates by Age Group, 1970–2002: An Examination of Recent Trends," *American Journal of Public Health*, v. 96, n.10, p. 1744-1751.

Miller, Henry I., and David R. Henderson (2007) "Governmental Influences on Drug Development: Striking a Better Balance," *Nature Reviews Drug Discovery*, v. 6, p. 532-539 (July).

Miller, Richard (2007) "Cancer Regression," *Wall Street Journal*, Aug. 1, 2007.

National Academy of Sciences, Institute of Medicine (2006) *The Future of Drug Safety: Promoting and Protecting the Health of the Public.*

Moore, Michael, and W. Kip Viscusi (2002) *Product Liability Entering the Twenty-First Century: The U.S. Perspective*. AEI-Brookings Joint Center for Regulatory Studies.

Pardoll, Drew, and James Allison (2004) "Cancer Immunotherapy: Breaking the Barrers to Harvest the Crop," *Nature Medicine*, v. 10, n. 9, p. 887-892 (Sept.).

Peltzman, Sam (1973) "An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments," *Journal of Political Economy*, v. 81, n. 5., p. 1049-1091 (Sept.-Oct.).

Peltzman, Sam (1974) *Regulation of Pharmaceutical Innovation: The 1962 Amendments*, Washington DC: American Enterprise Institute for Public Policy Research.

Pfeffer, Cynthia R. (2007) "Editorial: The FDA Pediatric Advisories and Changes in Diagnosis and Treatment of Pediatric Depression," *American Journal of Psychiatry*, v. 164, p. 843-846 (June).

Philipson, Tomas J., Ernst R. Berndt, Adrian H. B. Gottschalk, and Matthew W. Strobeck (2005) "Assessing the Safety and Efficacy of the Fda: the Case of the Prescription Drug User Fee Acts," NBER Working Paper 11724.

Priest, George L. (1991) "The Modern Expansion of Tort Liability: Its Sources, Its Effects, and Its Reform," *Journal of Economic Perspectives*, v. 5, n. 3, p. 31-50.

Rabin, Robert L. (2001) "The Third Wave of Tobacco Tort Litigation," in R. Rabin & S. Sugarman, eds., Regulating Tobacco (Oxford U.P. 2001).

Rubin, Paul H., John E. Calfee, and Mark F. Grady (1997) "*BMW vs Gore*: Mitigating the Punitive Economics of Punitive Damages," *Supreme Court Economic Review*, v. 5, p. 179-216.

Rubin, Paul H., and Joanna M. Shepherd (2007) "Tort Reform and Accidental Deaths," *Journal of Law and Economics*, v. 50, n. 2, p. 221-238 (May).

Schuck, Peter H. (2008) "FDA Preemption of State Tort Law in Drug Regulation: Finding the Sweet Spot." Available at ssrn.com.

Shogren, Elizabeth (2004) "FDA Sat on Report Linking Suicide, Drugs: Officials ordered more studies after their own expert found children on antidepressants were twice as likely to show suicidal behavior," *Los Angeles Times*, April 6.

Studdert, David M., and Troyen A. Brennan (2001) "No-Fault Compensation for Medical Injuries: The Prospect for Error Prevention," *Journal of the American Medical Association*, v. 286, p. 217-223.

Topol, Eric (2004a) "Intensive Statin Therapy: A Sea Change in Cardiovascular Prevention," (editorial), *New England Journal of Medicine*, early release April 8, 2004, v. 350, n. 15, p. 1562-1564 (April 8).

Usdin, Steve (2007) "Blockbusted at ODAC" *BioCentury*, May 14, 2007, p. A1.

Wadman, Meredith (2007) "The Pain Game," *Nature*, v. 448, p. 400-401 (July 26).

Wall Street Journal, May 2, 2008, p. B8, "Label on Merck Vaccine To Disclose a Death."

Wardell, William M., and Louis Lasagna (1975) *Regulation and Drug Development*, American Enterprise Institute.

Warner, Timothy D., and Jane A. Mitchell (2008) "Viewpoint: COX-2 selectivity alone does not define the cardiovascular risks associated with non-steroidal anti-inflammatory drugs," *Lancet*, v. 371, p. 270-273.