Testimony of:

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Chairman Waxman, Ranking Member Davis, and Members of the Committee:

My name is Aaron Kesselheim. I am an Internal Medicine physician in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham & Women's Hospital in Boston and am an Instructor in Medicine at Harvard Medical School. I am also a lawyer and I spend most of my time conducting research on the ways that legal and regulatory issues affect medical practice, in particular related to uses of prescription drugs. It is an honor to have the opportunity to share my thoughts with you today about the important role litigation plays in the drug safety system.

The subject of the hearings today is federal preemption of lawsuits against pharmaceutical manufacturers, usually brought by injured patients or state attorneys general on behalf of their citizens. Most of the time, these lawsuits involve charges that the manufacturer failed to exercise proper care in warning about the risks of their drug products. Blocking such lawsuits, in my view, would do great harm to the public health. These lawsuits are important because in the current US regulatory system, a drug's manufacturer plays the central role in the development and dissemination of knowledge about its product, and therefore exerts considerable influence over what is known about its product and how it is used in the marketplace. When a drug is approved by the FDA, it is approved on the basis of a small number of studies in a modest number of subjects, some of whom may be healthy volunteers and many of whom are far healthier than the patients for whom we usually write prescriptions. Often, the effect that forms the basis of approval is improvement of a laboratory test rather than real clinical outcomes. Requiring a drug to be studied in tens or hundreds of thousands of patients over a number of years could delay important new products from entering the market. But as a result, when a drug is approved for marketing, the FDA cannot fully certify its ongoing safety. As many more patients are prescribed the drug in the post-approval setting, new data about adverse events often arise, and the FDA does not have the resources to fully monitor the uses and outcomes of all approved drugs. The drug's manufacturer is often in an excellent position to identify emerging safety problems with its own product, but has an inherent conflict of interest in that role. Manufacturers have a strong financial incentive to promote their drugs' effectiveness and increase sales of their products, but manufacturers may also sometimes be faced with their own safety-related data that suggest limiting use of their product, or withdrawing it from the market altogether.

In the past few years, we have seen how manufacturers faced with this conflict of interest can make poor decisions that adversely affect public health. First, manufacturers have misrepresented safety and efficacy findings in published medical literature in ways that favor their products.[1] For example, in the case of Vioxx, an early study organized by the manufacturer showing the drug's effectiveness was criticized because the authors did not accurately represent all the safety data regarding serious cardiovascular side effects available to them as the study was being reviewed by a leading medical journal.[2] The exclusion of that data minimized the appearance of the cardiovascular risks to physicians reading the study and using it as a basis for prescribing decisions.

Second, manufacturers have minimized safety signals in their reports to the FDA to avoid raising concerns from regulators about their products. Again using Vioxx as an example – although many others could be cited – the manufacturer conducted several randomized trials of its drug in patients with cognitive impairment. In analyses conducted by company biostatisticians, Vioxx was associated with an increased risk of mortality in two studies. Yet the manufacturer delayed communication of the findings to the FDA and ultimately reported it in a way that minimized the appearance of risk. When FDA regulators noted the increased mortality and raised questions about the ethics of continuing one of the studies, the manufacturer dismissed the findings as "chance fluctuations."[3] In the case of cerivastatin (Baycol), a cholesterol-lowering medication that substantially increases the risk of a rare form of muscle breakdown and kidney failure, the

manufacturer received reports suggesting this increased risk as early as 1999. A study of internal company documents indicated that the company did not conduct timely follow-up analyses or pass along internal analyses of drug safety signals to the FDA.[4] A company memorandum reportedly stated "If the FDA asks for bad news, we have to give, but if we don't have it, we can't give it to them."[5] These behaviors can impede the ability of the FDA to recognize early safety-related signals and be able to judge whether a drug is potentially dangerous.

At the same time, a drug's manufacturer manages how the drug is promoted to physicians and patients. Numerous studies show that these promotional messages are extremely powerful in influencing physicians' prescribing practices. However, like any sales messages, they also tend to inflate the benefits of a medication and downplay its risks. Vioxx's manufacturer continued actively promoting its wide use even after it reportedly knew about the drug's association with cardiovascular adverse events. Such promotional tactics included specific instructions to its detailers how to dodge questions from physicians concerned about these side effects.[6] Similar marketing tactics occurred in the case of Baycol, where one of the manufacturer's executives, aware of potential safety concerns about its product, instructed its marketing department to "promote the hell out of this product."[7]

The Vioxx and Baycol cases are just two recent examples illustrating how manufacturers' dual role as promoter of drug sales and collector of safety information led to decisions detrimental to the public health. In this context, litigation plays an important oversight role, aside from helping people injured by dangerous products obtain financial recoveries.[8] First, lawsuits can help bring important data to light so that physicians can make more well-informed prescribing decisions in the future. Second, lawsuits help reveal improper business tactics, punish such actions, and hopefully prevent similar behavior from occurring on other occasions in the future. Third, lawsuits can help reveal gaps in FDA policies and procedures in the oversight of drug safety.

In sum, FDA approval does not end the process of information development about drug risks and benefits that define the safety of a drug and how a drug should properly be used. In our research group at Harvard Medical School, we contribute to this process in a number of ways. We conduct research, sometimes at the request of drug manufacturers, looking at large databases of patient experiences with drugs in order to determine if there are associations between the drugs and important side effects that bear further investigation. We also educate physicians about how to make optimal drug use decisions through a process of academic detailing. But our work, and the work of similar drug safety researchers across the country, can be readily undermined if pharmaceutical companies manipulate or restrict access to patient safety data.[9]

Applying the principle of preemption in these cases would treat FDA approval and labeling decisions as the final word on knowledge about a drug's safety, when substantial experience shows that they are not. Preempting lawsuits against pharmaceutical manufacturers would remove a check on pharmaceutical manufacturers that is essential to prescription drug safety and the public health. Without the possibility of litigation against manufacturers and their executives, we are likely to see greater misrepresentation of safety-related data and more inappropriate use of potentially harmful medications. Manufacturers should not be absolved of blame when they inadequately evaluate or report their products' risks. Manufacturers continue to have a key role in the development and organization of efficacy and safety data about their products, but they also have an inherent conflict of interest when evaluating their own products. In my view, it is therefore important to continue to encourage manufacturers to act responsibly by subjecting their decision making to judicial review.

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