

ADVERSE EVENT REPORTS IN CONTEXT

Part 1: Prescription drugs: How safe is safe enough?

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Adverse Event Reports for drugs are being taken more seriously by more people since the Vioxx recall in September 2004. At a November 17th hearing, Sen. Charles Grassley (R-Iowa), Chairman of the Finance Committee, proposed a new board of drug safety independent from the FDA.¹ The Vioxx recall has also triggered opposition to a medical malpractice bill which has passed the House but not the Senate. The bill includes a provision for liability protection for pharmaceutical companies against punitive damages.²

At the Senate committee hearing, Dr. David Graham of the FDA's Office of Drug Safety (ODS), Dr. Gurkirpal Singh of the Stanford University School of Medicine, and Dr. Bruce Psaty of the University of Washington all testified that Vioxx had been approved too quickly, in spite of danger signs.³

The exact number of heart attacks, strokes and deaths caused by Vioxx will never be known, because doctors report adverse drug reactions to the drug companies on a voluntary basis.

Drug approval process

Within the FDA, the (ODS) is part of the Center for Drug Evaluation and Research (CDER) which also includes the Office of New Drugs (OND). According Dr. Raymond Woosley, Vice President for Health Sciences at the University of Arizona, drug companies are required to carry out, or sponsor, tests on about 3,000 people prior to FDA approval.⁴ The fast-track approval process takes only months. Dr. Graham testified that the OND "unrealistically maintains a drug is safe unless reviewers establish with 95 percent certainty that it is not."⁵ Vioxx is one of over a dozen prescription drugs recalled since 1997.⁶

According to Dr. Graham, since the passage of the 1992 Prescription Drug User Fee Act the OND gets "new drug application fees of more than \$500,000 per application."⁷ The ODS, with no independent source of funding and no regulatory authority of its own, has to compete with the industry-funded OND for influence within the CDER⁸,

Post-market analysis

Drug companies are required to compile and analyze the adverse event reports receive from doctors and

submit the data to the FDA. The FDA's "MedWatch" system requires manufacturers to submit adverse event reports within 15 days, and the FDA also requires post-market statistical studies.⁹

Is Merck liable?

As early as 1999, FDA scientists suspected increased risk of heart attacks and strokes from Vioxx, but the drug was approved anyway.¹⁰ The FDA first required a warning on Vioxx labels in April 2002.¹¹ Merck voluntarily withdrew Vioxx from the market on Sept. 30, 2004.¹²

Merck CEO Raymond Gilmartin¹³ and Dr. Sandra Kweder, of the OND¹⁴ both affirm that Merck appropriately complied with the requirement to publish test results, although Merck had not published preliminary reports received about a year earlier.¹⁵ Merck's defense lines up with drug company arguments in favor of exemption from punitive damages in cases like the Vioxx, as long as they have complied with the letter of the law.

With law firms soliciting Vioxx clients on the Internet, Merck is facing up to \$15 billion worth of litigation.¹⁶

Once a drug is on the market, it is prescribed to a patients with a wider age-range and a broader spectrum of health conditions. If post-market analysis reveals an alarming pattern of adverse events, the FDA may issue statements warning that the drug should not be taken with specific medications or by patients with specific conditions. The FDA may also recommend additional long-term research, as in the issue of anti-depression and suicide.¹⁷ Even when a manufacturer fails to carry out recommended research, as with Serevent, the FDA rarely orders a mandatory recall for pharmaceutical drugs. (Serevent is still on the market after a long-term trial (with 90 percent certainty) showed it to cause deaths.¹⁸

Conflicts of interest

At the FDA, conflicts of interest involve two areas of concern: conflicts between competing drug
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