Cleveland — After three years of denying that the arthritis drug Vioxx could induce heart attacks and strokes, this week Merck bowed to reality: it withdrew Vioxx from the market.

The impact of this decision is far-reaching, and not only because tens of millions of people have tried Vioxx. It also highlights the absence of Food and Drug Administration oversight of the pharmaceutical industry as well as the lack of comprehensive long-term studies of not only Vioxx but its entire class of arthritis drugs.

In 2001, I was part of a team from the Cleveland Clinic that published a paper demonstrating the significant heart attack risk of Vioxx. Our research, published in The Journal of the American Medical Association, found that compared to naproxen, a commonly used over-the-counter anti-inflammatory drug with similar benefits, Vioxx has a five times greater heart attack risk. In response, Merck claimed that early conclusions about the risk were flawed, and attributed the comparatively high heart attack rates to an unproven protective effect of naproxen. Our study was followed by several others demonstrating Vioxx's dangers. Each time Merck had a similar reply: the study was “flawed.”

Merck finally had to acknowledge the truth, but only by accident. The company undertook a large, randomized trial of 2,600 patients with colon polyps in hopes of proving that Vioxx could help their condition. In the process, though, Merck discovered that 3.5 percent of patients taking Vioxx suffered heart attacks or strokes as against 1.9 percent taking a placebo. Merck at last did the right thing by voluntarily and abruptly taking Vioxx off the market.

There are two important issues to consider here. First, the risk of heart attack or stroke found in the Merck study, at 15 cases per 1,000 patients, may be greatly underestimated. Merck’s trial did not include anyone with known heart disease - patients who might be expected to have the highest risk.

And the problem may extend beyond Vioxx and its users. While it’s true that when compared to the other Cox-2 inhibitors, Vioxx has repeatedly carried a far greater risk of heart attack and stroke, none of the manufacturers of Vioxx’s class of drugs, called Cox-2 inhibitor agents, have studied patients who already have heart disease. The number of patients who may have sustained heart attack or stroke as a result of using these drugs could be tens of thousands. It would be premature to conclude that the other drugs still on the market, like Celebrex and Bextra, do or do not carry some risk of heart attack until sufficient testing is done.

While we remain in this zone of uncertainty, people with arthritis should remember that conventional over-the-counter agents like naproxen (as in Aleve) or ibuprofen (as in Advil) work extremely well, are much cheaper than the Cox-2 agents, and are not known to have any risk of heart attacks. In addition, one of the most-cited benefits of the Cox-2 agents - that they are less likely to cause stomach ulcers than over-the-counter drugs - may be grossly exaggerated.

Second, and what may be more alarming, is that despite studies showing the magnitude of the public health problem, for several years Merck did nothing to investigate. This surely represents a conflict between the interests of the public and the interests of a company with a blockbuster drug that had sales of $2.5 billion in 2003.

Instead of doing the requisite research in patients with heart disease - who frequently have arthritis as well and are thus prime users of anti-inflammatory medicines - the company undertook studies that avoided them. At the same time, Merck spent at least $100 million a year for direct-to-consumer Vioxx advertising, while the company's employees and their consultants published several papers in medical journals rebutting studies reporting Vioxx's heart attack risk. The Food and Drug Administration could have forced Merck to do the appropriate research studies, but instead it was a bystander.

As the Vioxx debacle shows, we have a long way to go in this country to get on track with prescription medications. Most important, we need a stronger regulatory agency to compel pharmaceutical companies to do the proper studies and force these companies to stop direct-to-consumer advertising unless a drug has major benefits for patients and negligible increased risk of heart attacks and strokes.

Our two most common deadly diseases should not be caused by a drug.

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