



## Healthy for Life Newsletter

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I am a person of Faith, but not blind faith. When it comes to anything except God, I ask a lot of questions before I entrust myself to someone or something. Particularly when it comes to prescription drugs, I find myself asking more and more questions. The answers I find continue to shake my confidence in the drug industry and the FDA. **Most people assume that the prescription drugs they take are very safe, thinking they having gone through rigorous and thorough testing by the Food and Drug Administration. But is that the case?** Is the FDA doing its job in protecting the public from potentially harmful drugs? Understanding how the FDA works might shake your faith a bit, as have the recent events surrounding the drug **Vioxx**.

On September 30, 2004, Merck withdrew their very popular Cox-2 inhibitor and arthritis medication Vioxx from the market. After years of building controversy and concerns over safety, Vioxx was pulled from the market because of solid evidence that **the risk of heart attack and stroke doubled in patients who were taking Vioxx long-term.** This set off an immediate flurry of concern within the media and medical community about the safety of other similar drugs like Celebrex, Bextra, and Mobic. Hearings were started by the US Senate chaired by Senator Charles Grassley from Iowa.

Immediately, the concerns spread to other drugs like the use of the anti-depressant drug Prozac in children, which increases the risk of suicide, and the use of the cholesterol-lowering drug Crestor, which increases the risk of muscle and liver damage. The question everyone is asking is this: **“If the FDA is supposedly doing its job, why**

**are so many drugs being taken off the market after being approved?”** While researching and writing my book *Death by Prescription*, I found a lot of answers, and raised many concerns of my own about the way drugs are being approved in the US today.

#### The Great Clinical Trial—You

**When the FDA first approves a medication for use by the public, they know less than half of the serious adverse drug reactions of that drug.** That is a fact. They know less than half of the adverse drug reactions of a particular medication at the time that the drug is approved. The clinical trials that are done by the pharmaceutical industry prior to approval are relatively small and short-term. Once a drug is released onto the market, millions of scripts may be written and less frequent; however, maybe even more serious side effects may occur. There is no way these pre-clinical trials can elicit all the potential problems that a drug may have. How do they find out the other half of these adverse drug reactions? The answer is very simple—YOU! **You are the “Great Clinical Trial.” You are the “human guinea pigs” they use to discover adverse reactions of the new drugs that are put on the market.**

Once a new drug is released to the public, there is a *voluntary* reporting system back to the FDA. As a doctor, if I observe an adverse drug reaction in one of my patients, I am *not required* to report this to the FDA. It is strictly voluntary. It's not surprising that **less than 1% of the adverse drug reactions are ever reported back to the FDA.**

Even when adverse drug reactions are reported back to the FDA, they are given to a department that has absolutely no authority except to gather

the data. Once enough red flags are raised about the potential new risk of a drug that is already on the market, they refer their concern back to the committee that originally approved the drug. Normally, the only thing that happens is a new warning added to the package insert or drug label. But it gets worse: **In order to put new warnings on a drug, the FDA must get permission from the company that makes the drug!** In the case of Vioxx, the FDA had wanted stronger warnings added to the drug label two years before this drug was pulled from the market. However, this change to the drug label was never accomplished because Merck did not approve of this action.

**This is a serious and obvious problem.** Voluntary reporting and inefficient bureaucracy keep dangerous drugs on the market too long, and many drugs that do stay on the market do so with warnings that don't reflect the risks that have been discovered as the drugs have been tested on you.

## The Deadly Partnership

But how do these questionable drugs make it on the market in the first place? In 1992, under pressure from the public and the pharmaceutical industry, **Congress passed the “drug user fee act” which required the pharmaceutical companies to pay a fee to the FDA, which would be used to help the FDA approve drugs much faster.** A pharmaceutical company actually pays the FDA a “user fee” of \$250,000 each time they submit a New Drug Application to the FDA. This fee was to be used strictly to move this approval process along. Additional pressure in this legislation forces the FDA to cooperate with the pharmaceutical industry to get their drugs approved much faster.

The legislation has been effective. The time to get a drug approved has dropped from an average of 24 months down to 12 months. Fast-track drug approvals have dropped from 12 months down to 6 months. **Drugs are now being**

**approved at an unprecedented rate, far more quickly than at any time in the history of the FDA.**

What is even more concerning is the fact that today **over 50% of the FDA's budget now comes from the pharmaceutical companies** via these “user fees.” The industry that the FDA is supposed to be governing is now its primary source of funds. The FDA has had a definite change in attitude. **Instead of determining if a drug should be approved, the FDA is now concerned with how to get a drug approved and quickly.**

Furthermore, the “user fee” money can only be used for the approval process of new drugs. This raises major concerns about the safety of these drugs because the post-marketing surveillance division of the FDA (the department responsible for evaluating the seriousness of the adverse drug reactions after a drug has been released to the public) has not had any significant increase in funding. **Therefore, more and more drugs are being approved faster and faster, which is placing a greater burden on an underfunded, under-staffed safety department.**

## The Vioxx Story

Vioxx along with the other Cox-2 inhibitors (Celebrex, Bextra, and Mobic) were heralded as a major breakthrough in the treatment of arthritis.

**Prior to these drugs, most people turned to NSAIDS (non-steroidal anti-inflammatory drugs) like Motrin and Aleve.** These drugs block both the Cox-2 and the Cox-1 enzymes in an attempt to decrease inflammation and improve the symptoms of arthritis. But Cox-1 enzymes are critical in protecting the lining of the stomach. When they are blocked, you may decrease inflammation in the joint; however, you also may create a problem of decreasing the protective lining of the stomach, which can lead to bleeding from the stomach. In fact, the **NSAIDS had been**

**shown to be responsible for over 100,000 admissions to the hospital each year in the US alone because of stomach bleeding. Over 16,000 of these patients actually died each year as a result of this bleeding.**

That didn't appear to be the case with Vioxx. The Cox-2 inhibitors primarily blocked only the Cox-2 enzymes and left the Cox-1 enzymes alone. As a result, they were initially shown to significantly decrease the risk of bleeding from the stomach. **These newer Cox-2 inhibitors took the marketplace by storm and quickly became the most prescribed arthritis drugs in the world. An estimated 80 million people had taken Vioxx by the time it was withdrawn. Annual sales of the drug exceeded \$2.5 billion.**

But shortly after Vioxx was released, a major study was reported in the *Journal of the American Medical Association* (2001). **Serious evidence was mounting that the patients who were taking Vioxx had a significantly greater risk of having a heart attack or a stroke.<sup>1</sup>** The evidence continued to grow, but the slowness of the post-marketing surveillance division of the FDA kept the truth from getting out quickly, and of course Vioxx was unwilling to place stronger warnings on its product. As the system faltered, millions continued to take the drug in good faith, too often learning the dangers the hard way. In the end, Dr. Graham, a senior official of the FDA's Office of Drug Safety, estimated that **since the introduction of Vioxx into the market in 1999, it has been responsible for an estimated 88,000 to 140,000 excess cases of heart attacks and strokes, many of which were fatal.**

We know the problem now. If only the Cox-2 enzyme is blocked, there quickly becomes an imbalance in the body between the Cox-2 and Cox-1 enzymes. This leads to an increase in the level of other inflammatory products called

thromboxane A2. These cause increased clotting due to abnormal platelet aggregation which can cause a heart attack or stroke. Other side effects cause increased hardening of the arteries which, in turn, contributes to coronary artery disease. Even the decrease in stomach bleeding has been called into question with the Cox-2 inhibitors... But we didn't know any of that until they tested it on you.

Dr. David Graham testified during the Congressional hearings that the FDA's failure to protect the public health in the case of Vioxx was **"a profound regulatory failure."** In the October 21, 2004 *New England Journal of Medicine*, Dr. Topol wrote a very strong editorial criticizing the FDA's role in never mandating a post-market trial of Vioxx and similar Cox-2 inhibitors. **Vioxx was never tested, after its release, to see if it really was a serious risk for heart attacks and strokes in spite of the mounting medical evidence that this was happening. Rather than fund a study, Merck had spent millions of dollars trying to convince physicians and the public that these concerns had absolutely no validity.**

## What to Do

Every drug has an inherent risk of producing adverse drug reactions. Drugs create a pharmacological effect by blocking certain normal enzymatic reaction or reactions to create a desired result. In the case of NSAIDS and Cox-2 inhibitors the result is decreased inflammation in the joints. However, these same enzymatic reactions are necessary for other beneficial functions in the body. When they are blocked, it can lead to very undesirable effects. In the case of NSAIDS, it can lead to stomach bleeding. In the case of Vioxx, it can lead to an increased risk of heart attacks or strokes.

<sup>1</sup> Mukherjee D, Nissen SE, Topol EJ. "Risk of cardiovascular events associated with selective Cox-2 inhibitors. *JAMA* 2001;286:954-959

Finally, it was determined that risks involved in taking Vioxx were greater than the benefits. Therefore Merck removed Vioxx from the market

worldwide on September 30, 2004. **Celebrex, Bextra, and Mobic are now under increased scrutiny** because they potentially could have the same problems as Vioxx. Again, thousands may die taking these drugs for an illness that is never life threatening.

At this point, **I'm encouraging everyone to switch to other arthritis medications which are in the NSAID class.** At least, we know that the main problem they have is upper GI bleeding. **If you have to take Celebrex, Bextra or Mobic, I would strongly recommend that you ask your doctor if you could take a low dose aspirin (81 mg daily) along with it.** This can at least possibly reduce the increased risk of a heart attack and stroke as further studies are finally being done to determine the safety of these other Cox-2 inhibitors.

**In next month's newsletter, I will discuss the natural remedies that are available today which can improve your arthritis. These remedies have no side effects and require only a little bit of faith to try.**

If you are interested in finding out more about the dangerous world of prescription drugs, go to my web site ([www.raystrand.com](http://www.raystrand.com)) and order your personal copy of my book, *Death by Prescription* (Thomas Nelson 2003). It is now in paperback and is available for a cost of \$12.95 plus shipping. If you order 2 or more books, the price is \$9.95 each plus shipping. **Take advantage of this special offer and learn how you can protect yourself and your loved ones from being injured or dying from the 3<sup>rd</sup> leading cause of death in this country—adverse drug reactions.**

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