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United States Senate

COMMITTEE ON FINANCE

WASHINGTON, DC 20510–6200

September 30, 2004

Via facsimile and USPS mail: (202) 690-7380
Via facsimile and USPS mail: (301) 827-1960

The Honorable Tommy G. Thompson
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, D.C. 20201

Dr. Lester M. Crawford, D.V.M.
Acting Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Dear Secretary Thompson and Dr. Crawford:

Today, Merck & Co., Inc. (Merck) announced a voluntary world-wide withdrawal of its arthritis and acute pain medication, Vioxx; a highly unusual move by a major drug manufacturer. According to media reports, the reason for this withdrawal stems from data of a three-year study intended to show that Vioxx prevents the reoccurrence of polyps in the colon and rectum. The data, recently reviewed by Merck, also demonstrated that there was an increased risk of heart attack and other cardiovascular complications beginning 18 months after patients started taking Vioxx.

The real news for me today is not so much why Merck pulled Vioxx off the shelves—we know that is because it causes heart attacks. The question in my mind is: Where has the Food and Drug Administration (FDA) been on Vioxx?

The FDA approved Vioxx in 1999. Since 1999, there have been many non-FDA conducted studies showing an increased risk in cardiovascular complications among those taking Vioxx. Specifically, in November 2000, Merck sponsored a study named VIGOR. In that study, Merck determined that there were more serious cardiovascular events occurring in patients taking Vioxx compared to patients taking naproxen, another anti-arthritic drug. This study was reviewed and discussed at the FDA's Arthritis Advisory Committee Meeting (Advisory Committee) on February 8, 2001. An FDA Talk Paper, dated April 11, 2002, approved a new indication for Vioxx and new labeling changes. The labeling changes advised patients and doctors of the potential cardiovascular risks and benefits associated with using Vioxx. However, a careful

reading of that label appears to be at best non-committal and provides no guidance to physicians and to the public.

In 2002, another study was published by Dr. Wayne Ray on Vioxx. This study found a two-fold increase in heart attack and sudden death associated with high dose Vioxx. In May 2004, Dr. Solomon of Harvard found both low dose and high dose Vioxx increased the risk of heart attack. Indeed, Dr. Solomon's study was startling because he found a 21% increase for heart attacks with low dose Vioxx and a 70% increased risk of heart attack with high doses of Vioxx as compared to a rival drug, Celebrex.

On or about August 25th, the FDA presented its own study on Vioxx. That study was conducted by Dr. David Graham, an FDA epidemiologist. Dr. Graham's study for the FDA study found that patients taking low dose Vioxx have a 50% greater chance of suffering a heart attack and sudden cardiac death than patients using Celebrex. In addition, Dr. Graham noted that the risk of heart attack and sudden cardiac death in those patients taking the highest recommended daily dose of Vioxx was three times that of patients taking standard painkillers.

Astonishingly, on or about September 8th, 2004, two weeks after Dr. Graham's study, the FDA approved Vioxx for use in children with juvenile rheumatoid arthritis, despite the fact that Dr. Graham's study showed there was a very high risk of sudden cardiac death and heart attacks in adults taking Vioxx. Why would the FDA approve Vioxx for use among children with Dr. Graham's study in hand? Frankly, it seems counter-intuitive. Why is the FDA approving new indications for Vioxx, especially for children, when shortly thereafter Merck is pulling the drug from the world-wide market?

Once again, the FDA has remained on the sidelines while life-threatening issues threatened the American public. Why has the FDA blindly dismissed a wealth of data showing serious cardiovascular side effects occurring in patients using Vioxx since the drug was approved in 1999? It appears that the FDA has yet again erred on the side of providing less information about the dangers associated with yet another drug, to the detriment of the American public. Because of these new developments, and the fact that the FDA recently approved Vioxx for children, I request that the FDA respond to the following questions and requests by October 25, 2004.

1. Describe in detail what action(s), if any, the FDA has taken since VIGOR to examine, address, or study the adverse affects of Vioxx. In preparing responses to this question, please be sure to identify these actions by date and please identify the FDA employee(s) by name and title who were involved in these actions.

2. Describe in detail the results of all pre-marketing clinical studies conducted on the use of Vioxx.

3. Provide copies of all FDA documents and materials relating to Vioxx and the risk of cardiovascular complications including all papers, drafts, e-

mails, agency evaluations, and any other documents relating to the use of Vioxx and the risk of cardiovascular complications.

4. Please make Dr. Graham available for an interview with my staff in the immediate future to discuss his Vioxx study, among other related matters.

When preparing responses to the questions identified above, please re-state the question and follow it with a detailed response. In the event that documents or other materials are requested, please be sure to mark them accordingly. Please be on notice that this is an active congressional inquiry. Accordingly, I request that you notify FDA employees, representatives and/or agents to preserve all documents and materials relating either directly or indirectly to this inquiry.

Thank you in advance for having your staff coordinate with my staff about this letter by October 6, 2004. And please provide the requested information, explanations and documents by October 25, 2004, unless it is available sooner. Should you have any questions regarding this letter, please do not hesitate to contact Emilia DiSanto or Michelle Anderson at (202) 224-4515. *All formal correspondence should be sent via facsimile to (202) 228-2131 and original by U.S. mail.* Please do not hesitate to contact me if you have any concerns.

Sincerely,

Chuck Grassley

Charles E. Grassley
Chairman