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February 28, 2005

Lester M. Crawford, D.V.M, Ph.D
Acting Commissioner
US Food and Drug Administration
U.S. Department of Health and Human Services
Parklawn Building
5600 Fishers Lane, Room 15-47
Rockville, MD 20857

Dear Dr. Crawford:

On February 25, 2005, the New York Times reported that the members of the FDA advisory committee reviewing the safety risks of the cox-2 inhibitors were not obligated to disclose their potential conflicts of interest. Apparently the FDA determined that because of the general nature of the issues at hand, the members were not subject to the standard rules regarding conflicts of interest.

However, an investigation by the Center for Science in the Public Interest and the New York Times revealed that 10 of the 32 members who sat on the Cox-2 inhibitors advisory panel had ties to the pharmaceutical industry. According to the New York Times, if the 10 members of the panel had recused themselves from voting, then Bextra would have been withdrawn (12 to 8) and Vioxx would not have been allowed to return to the market (14 to 8).

I am concerned that the integrity of the review process may have been compromised by not following standard procedures regarding conflicts of interest and that the outcome of this advisory committee meeting may have been different if only those who were independent of industry had voted.

According to 18 U.S.C. § 208, if a person “participates personally and substantially as a Government officer or employee, through decision, approval, disapproval, recommendation, the rendering of advice, investigation, or otherwise, in a judicial or other proceeding, application, request for a ruling or other determination, contract, claim, controversy, charge, accusation, arrest, or other particular matter in which, to his knowledge, he, his spouse, minor child, general partner, organization in which he is serving as officer, director, trustee, general partner or employee, or any person or organization with whom he is negotiating or has any arrangement concerning prospective employment, has a financial interest...” then he/she “Shall be subject to the penalties set forth in section 216 of this title.”

These penalties do not apply if the person “makes full disclosure of the financial interest and receives in advance a written determination made by such official that the interest is not so substantial as to be deemed likely to affect the integrity of the services which the Government may expect from such officer or employee” or “in the case of a special Government employee serving on an advisory committee within the meaning of the Federal Advisory Committee Act (including an individual being considered for an appointment to such a position), the official responsible for the employee’s appointment, after review of the financial disclosure report filed by the individual pursuant to the Ethics in Government Act of 1978, certifies in writing that the need for the individual’s services outweighs the potential for a conflict of interest created by the financial interest involved.”

The Times reported that before each of the FDA advisory committee meetings, a secretary from the FDA read a statement to absolve the committee members of any potential conflicts of interest. The FDA secretary said that the agency "acknowledges that there may be potential conflicts of interest, but because of the general nature of the discussions before the committee, these potential conflicts are mitigated."

It is my understanding that if the FDA had determined that topic (the benefits and risks associated with Vioxx, Bextra, Celebrex and other cox-2 inhibitors) was specific in nature, the members of the committee would have been required to disclose their potential conflicts of interest and perhaps obtain waivers in order to participate in the meeting.

I am curious about FDA’s determination in this matter. It seems to me that the issues discussed were very specific and had enormous consequences for the two companies that make Vioxx and Bextra: Merck and Pfizer. Although the panel was not approving new drugs, they were trying to decide whether to recommend revoking approval of a drug. This could arguably have more impact on the reputation and financial well-being of a company than an approval. The fact that Merck and Pfizer’s stock increased significantly the day after the decision demonstrates that these decisions had significant financial implications.

Even if the conflicts of interest did not influence the panel’s decisions, the fact that potential conflicts of interest were not disclosed leads the public to question the integrity of the review process. For the past several months consumers have been left without real guidance on the risks and benefits of the cox-2 inhibitors. This meeting was supposed to provide the public with unbiased answers to these difficult questions. In order for the public to trust the recommendations of the FDA advisory committee, they need to know that patient well-being is their only concern and they are not being influenced by any financial or other relationships with the pharmaceutical industry.

It is critical that the people who are charged with making these important recommendations reveal any potential conflicts of interest to the public and recuse themselves from the process if there are any concerns about their ability to objectively evaluate the evidence and make an unbiased decision.

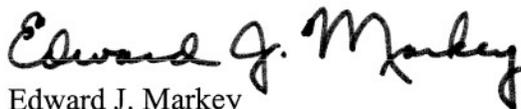
I respectfully request that the FDA conduct a review of any potential conflicts of interest, make a determination as to whether any conflicts of interest exist, and then make those determinations

public. Further, I also request your assistance in providing answers to the following questions:

1. Do you believe that conflicts of interest were not relevant for the purposes of this advisory committee hearing? If so, why?
2. After conducting a review of the potential conflicts of interest for all of the members on the advisory committee examining cox-2 inhibitors, did you find any conflicts of interest? If so, please include that information.
3. Do you believe that any of the conflicts of interest could have affected members' recommendations?
4. Does the FDA have any concerns about the final decision of the panel, in light of your review of the potential conflicts of interest? If so, do you plan to re-examine the safety of cox-2 inhibitors and specifically Bextra and Vioxx with members who do not have any conflicts of interest?
5. If the FDA is concerned about potential conflicts of interest in the case when a drug is being approved, then why is the FDA not concerned about these same potential conflicts of interest when the panel is considering withdrawing an approval?
6. Do you agree that the decision to either keep Bextra on the market, or withdraw the approval could have a significant financial impact on Pfizer? Do you agree that the decision to either allow the return of Vioxx to the market, or prevent the return could have a significant financial impact on Merck?
7. Does the FDA have any plans to make any changes in its ethics rules to ensure that all potential conflicts of interest are disclosed to the public prior to advisory committee meetings regardless of whether the issue is general or specific?

Thank you for your attention to this important issue. I respectfully request a response by March 14, 2005. If you have any questions regarding this request, please do not hesitate to contact Ms. Katharine Reinhalter or Mr. Jeffrey Duncan on my staff at 202-225-2836. I look forward to your prompt reply.

Sincerely,



Edward J. Markey
Member of Congress