



May 21, 2007

Division of Dockets Management (HFA-305)
US Food and Drug Administration
5630 Fishers Lane
Rm 1061
Rockville, MD 20852

Regarding: docket number 2007D-0101

Subject: OMB Watch comments on the U.S. Food and Drug Administration's draft guidance, "Procedures for Determining Conflict of Interest and Eligibility Participation in FDA Advisory Committees."

On March 21, 2007, the U.S. Food and Drug Administration (FDA) released draft guidance on "Procedures for Determining Conflict of Interest and Eligibility Participation in FDA Advisory Committees." OMB Watch appreciates FDA's thoughtful efforts in developing this draft guidance as well as the opportunity for public input. OMB Watch is pleased to comment on the draft guidance today.

OMB Watch is a nonprofit, nonpartisan research and advocacy center promoting an open, accountable government responsive to the public's needs. Founded in 1983 to remove the veil of secrecy from the White House Office of Management and Budget, OMB Watch has since then expanded its focus beyond monitoring OMB itself. We currently address four issue areas: right to know and access to government information; advocacy rights of nonprofits; effective budget and tax policies; and the use of regulatory policy to protect the public.

Our interest in the new FDA guidance stems from our concern about the great influence regulated industry has on, among other things, FDA's drug approval process. Recent history is replete with examples of drugs that have come to market before they have been determined to be safe. As part of the rush to market these drugs, industry scientists are permitted to play active roles on FDA advisory committees and may be exerting undue influence on the agency's final decisions about marketing these products resulting in real threats to consumer health and safety.

We believe that there should be a strong presumption against having any members with conflicts serve on FDA's advisory committees absent strong evidence that other qualified professionals without conflicts are unable or unwilling to serve. Allowing agency personnel to waive conflicts undermines the original criteria for determining financial conflicts of interests. Conflicts either exist or they do not. Mitigating the severity of a conflict of interest should be an option only in the rarest of cases.

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Should FDA choose to maintain, finalize and implement many of the provisions detailed in the draft guidance, we urge FDA to eliminate certain loopholes currently present in the draft guidance. Our comments address these loopholes.

Addressing Industry Influence

FDA should be applauded for addressing the increasing problem, actual and perceived, of the influence of regulated industries in agency proceedings. OMB Watch has analyzed the increasing scrutiny of FDA practices, particularly the FDA drug approval process.¹ Both the media and the United State Congress have recently paid great attention to the agency's drug approval process.² Their critiques have been largely negative. FDA's draft guidance is an important first step in addressing the problems about which the American public is increasingly concerned.

OMB Watch hopes FDA will pursue further measures to stem industry influence in agency proceedings. Congress, FDA, industry, and the American public should be engaged in vigorous debate as to the ways in which industry influence can be minimized to the fullest extent possible. The reauthorization of the Prescription Drug User Fee Act, as well as the need for regulatory policy in regard to the burgeoning fields of organics and cloning, provide opportunities for such debate. Industry influence compromises the integrity of FDA. It is not in the best interest of the American public for the nation's premiere consumer product regulator to be in any way influenced or governed by those it regulates.

FDA Advisory Committees

Financial conflicts of interest on FDA advisory committees are of real concern. An investigative report in the Sept. 25, 2000 edition of *USA Today*³ found at least one member to possess a financial conflict of interest in 92% of advisory committee meetings related to drug approval.

Furthermore, evidence exists to show these conflicts of interest effect voting habits. A 2006 study⁴ published in the *Journal of the American Medical Association* (JAMA) found "the overall amount of conflict in a meeting could have an influence on overall voting behavior." The study finds in hearings held on specific drugs, where the advisory committee contains members with a financial interest in the approval of the drug, the committee is likely to recommend approval. This supports arguments for limiting to the fullest extent possible the number of members with any degree of conflict.

The \$50,000 Threshold

FDA's draft guidance establishes \$50,000 as the threshold for exclusion from advisory committee membership. Potential members with financial conflicts of interest of \$50,000 or less would be permitted to serve, but prohibited from voting.

¹ OMB Watch. "FDA Drug Approval Process under Scrutiny," Feb. 21, 2007. Available at: <http://ombwatch.org/article/articleview/3728>.

² For a media example, see *The Washington Post*, "FDA Rules Override Warnings About Drug," March 4, 2007. Available at: <http://www.washingtonpost.com/wpdyn/content/article/2007/03/03/AR2007030301311.html>.

For examples from Congress, see two hearings from the House Energy and Commerce Committee subcommittee on Oversight and Investigations, *The Adequacy of FDA Efforts to Assure the Safety Efforts of the Drug Supply*, Feb. 13, 2007 and March 22, 2007

³ Cauchon, Dennis. "FDA Advisers Tied to Industry," *USA Today*. Sept. 25, 2000.

⁴ Lurie, Peter, MD, MPH, et al. "Financial Conflict of Interest Disclosure and Voting Patterns at Food and Drug Administration Drug Advisory Committee Meetings." *Journal of the American Medical Association*. Vol. 295 No. 16, April 26, 2006.

OMB Watch is concerned \$50,000 is not a strict or effective enough threshold. The JAMA study found – for advisory committee members whose financial interest was created by consulting – only two percent of the study sample received payments amounting to greater than \$50,000. The study’s authors called financial interests of even \$10,000 “large,” and urged those members not to serve. The \$50,000 threshold is excessive and should be significantly decreased.

Similarly, a recent investigation by the Center for Science in the Public Interest (CSPI) found the new guidelines would have minimal impact on reducing conflicts. CSPI’s investigation shows the guidance “would eliminate just one of every ten panelists who currently gets a waiver.”⁵ Again, we argue for lower thresholds. However, regardless of the threshold FDA ultimately chooses, OMB Watch encourages FDA to include its rationale for the threshold in the final guidance.

Identifying Financial Conflicts of Interest

The process detailed in the draft guidance for identifying financial conflicts of interest is simpler than the current framework. This simplification is an improvement, in that it is likely to allow agency personnel to more quickly and accurately identify potential financial conflicts of interest.

The draft guidance includes simple methods for meeting statutory requirements related to financial conflicts of interest. In steps 4a and 4b of the algorithm included in the draft guidance, provisions pursuant to 18 U.S.C. 208(b)(1) and 21 U.S.C. 355(n)(4) clearly meet statutory requirements. These provisions should allow agency personnel to quickly and accurately make decisions reflecting the intent of the law. The provisions also properly provide the rights to grant waiver requests exclusively to the FDA commissioner.

The draft guidance also includes provisions which exceed statutory requirements. The draft guidance is clear in stating that potential members possessing any financial conflict of interest, even if allowed to serve on an advisory committee, should serve as non-voting members. The draft guidance also includes criteria for identifying financial interest held within the preceding year, and instructs agency personnel to treat these interests in the same way as currently held financial interests. These are welcome steps by FDA because, as the draft guidance points out, “the public has a particular interest in and high expectations for FDA’s process.”

Determining Exemptions in Regard to the Need for an Individual’s Service

OMB Watch is concerned the draft guidance creates loopholes and does not reflect the spirit of impartiality in regard to the identification of the need for a unique individual to serve on an agency advisory committee. Pursuant to 18 U.S.C. 208(b)(1), step 5 of the algorithm included in the draft guidance includes provisions for the determination of whether “financial interest is not so substantial as to be deemed likely to affect the integrity of the services provided by that individual.” These provisions apply to potential members who are government employees. Pursuant to 18 U.S.C. 208(b)(3), step 5 of the algorithm includes provisions for the determination of whether “the need for the individual’s services outweighs the potential for a conflict of interest.” These provisions apply to potential members who are not considered government employees, but who would become “special government employees” (SGEs) in serving on an agency advisory committee.

Certain factors would justify service exemptions for potential members. The following apply to government employees and/or SGEs:

⁵ Center for Science in the Public Interest, Integrity in Science Watch. “Few Waivers Eliminated by FDA’s Proposed Guidance,” May 14, 2007. Available at: <http://www.cspinet.org/integrity/watch/index.html#3>.

- “The type of financial interest that is creating the disqualification;”
- “The relationship of the person whose financial interest is involved to the member;”
- “The dollar value of the disqualifying financial interest; and”
- “The extent to which the disqualifying financial interest could be affected by the actions of the advisory committee”

For both government employees and SGEs, the draft guidance instructs agency personnel to consider factors that qualify criteria initially found to substantiate a financial conflict of interest.

The qualifying factors essentially contradict the criteria FDA has set forth in identifying financial conflicts of interest. For example, the possession of a financial interest by a potential member’s spouse should not be used to substantiate a conflict of interest but then used to minimize that same conflict thus allowing participation. Likewise, a financial interest of \$51,000 should not be used to waive the non-participation threshold of \$50,000 simply because the difference is negligible. This type of situation points out the arbitrariness of the financial threshold.

There are additional factors in the proposed guidance that would justify service exemptions related to the uniqueness of an individual’s expertise. The following apply to government employees:

- “The nature and importance of the employee’s role in the matter; and”
- “The need for the employee’s services in the particular matter.”

The following apply to SGEs:

- “The uniqueness of the individual’s qualifications,”
- “The difficulty of locating a similarly qualified individual without a disqualifying financial interest.”

OMB Watch is concerned that opening the door for such exemptions will subvert the intent of the draft guidance. Expertise on a subject matter is valuable and in some instances rare. However, when that expertise is acquired by industry-funded means, it will include inherent and intractable bias. Impartiality and expertise should be viewed as a package, the total value of which should often exceed that of biased expertise. The final guidance should include language to reflect such an aggregated valuation of expertise and impartiality.

Furthermore, allowing exemptions when there is “difficulty locating similarly qualified individuals without a disqualifying financial interest” is not a great enough expectation. OMB Watch is concerned agency personnel may use lack of time and resources or political motives as excuses to apply this factor. In a Sept. 25, 2000 *USA Today* article, then FDA senior associate commissioner Linda Suydam states, “The best experts for the FDA are often the best experts to consult with industry.” Suydam’s comments indicate a dangerous presumption which OMB Watch is concerned may still exist in FDA: that scientists working alongside industry managers in the development of a drug are most qualified to determine the drug’s safety. Such an expectation is unacceptably low.

Agency personnel should search exhaustively for unbiased experts. Exemptions for expertise should be granted in only the rarest of cases. Language to this effect should be strengthened in the final guidance. We urge FDA to disclose publicly the extent of the search for unbiased expertise by documenting the results of that search and providing a clear rationale for choosing those who have conflicts.

The final guidance should also include a clearer identification of which agency personnel are to be responsible for applying exemptions and/or determining the need for an individual's service. Full disclosure allows Congress and the public to more effectively hold decision makers accountable.

However, FDA should not rely on Congress and the public to ensure integrity in granting exemptions for service. The agency should make sure to police itself in such matters. In the final guidance, FDA should detail the recourse it may take if agency personnel violate statutory requirements in granting waivers.

Conclusion

The draft guidance provides a much needed framework for ensuring impartiality on FDA advisory committees. However, the proposal also includes several loopholes which could allow agency personnel to advance a political agenda and sacrifice scientific integrity in the process. If FDA closes these loopholes, this conflict of interest guidance may set a course for other agencies to follow.

Sincerely,
Rick E. Melberth, PhD
Director of Regulatory Policy
OMB Watch