



May 21, 2007

COMMENTS: "DRAFT GUIDANCE FOR THE PUBLIC, FDA ADVISORY COMMITTEE MEMBERS; AND THE FDA STAFF ON PROCEDURES FOR DETERMINING CONFLICT OF INTEREST AND ELIGIBILITY FOR PARTICIPATION IN FDA ADVISORY COMMITTEES

Submitted by the Union of Concerned Scientists

DOCKET NUMBER: 2007D-0101

The Food and Drug Administration has taken an important first step in increasing the FDA's accountability and integrity by acknowledging the public's concerns about the large number of scientists with conflicts of interest on its advisory committees. As the Draft Guidance points out, the public has high expectations for the advisory committee process. Any use of scientists with ties to companies with a stake in the outcome of a committee's deliberations undermines the public's faith in the process. Conflicts of interest can have serious consequences for drug safety. For example, ten of the 32 scientists on the February 2005 advisory committee that considered the safety of Cox-2 inhibitors, including Vioxx, had ties to the drug companies that made the products. The scientists voted to permit the companies to continue marketing the drugs, even though Vioxx had already been withdrawn from the market and had been implicated in tens of thousands of deaths.

While your Draft Guidance acknowledges the current process needs improvement, the proposal is at best a minimal first step toward developing a new committee formation process that will serve both the public interest and the FDA's ability to obtain the best available advice.

Reduced to its essence, the Draft Guidance:

1. Forbids the use of scientists with conflicts of interest if those financial arrangements amount to more than \$50,000 in the year prior to the meeting;
2. Prohibits any scientist who receives a waiver for lesser conflicts from voting at the conclusion of the meeting; and
3. Presumes there are cases where the need for an individual scientist's expertise outweighs any conflict of interest under \$50,000 because no one with comparable expertise can be found.

The Union of Concerned Scientists has a number of objections to the Draft Guidance:

- As a practical matter, only about a tenth of scientists currently receiving waivers will be prohibited from serving on FDA advisory committees because of these proposed guidelines. Of the 169 waivers granted at 41 meetings between September 2006 and

May 2007, just 18 involved conflicts of interest greater than \$50,000, according to waiver documents available on the FDA website.

- By limiting the “look-back” period to one year, which may be shorter than the current look-back period, the number excluded may be even lower. A one-year look-back period is a completely inadequate standard for evaluating conflicts of interest. Many major medical journals consider conflicts of interest going back at least three years for purposes of disclosure accompanying published articles. A recent guideline from Blackwell Publishing, which publishes over 800 journals, established a three-year look-back period as a minimum. We suggest the FDA adapt a three year look-back period for the purposes of its guidance.
- The agency’s most recent report to Congress (“Fifth Report on FDA Efforts to Identify Qualified Persons for Appointment to FDA Advisory Committees,” Conference report 109-255, Jan. 31, 2007), showed that one in every four special government employees chosen for FDA advisory committees has been issued waivers. This proposal raises the possibility that non-voting members will comprise a majority of some future advisory committees, a circumstance that would further undermine the public’s confidence in the deliberations of the agency.
- Any cutoff (other than zero) will be very difficult if not impossible to implement. While it is fairly easy to measure the current value of stock in a publicly traded drug company owned by a committee member, how does one evaluate the current value of a January 2007 stock option given to the committee member by a drug company to buy a specified number of shares at a specified price at any time in the next five years? What is the current value of a two-year contract signed in January 2007, renewable at the option of the drug company, that says the physician will be paid \$5,000 for each speech given to other physicians and that the number of such speeches will be jointly determined by the company and the physician? How does one evaluate a February 2007 contract between the drug company and the physician or scientist whereby the company agrees to pay \$500 per hour for each hour of consulting over the next three years? These are all situations where the advisory committee member could benefit substantially from his or her influence at the FDA meeting.

Our Proposal:

Because this Draft Guidance is aimed at the professional staff that creates and manages the advisory committees, we believe it should articulate a set of goals at its outset and outline a set of procedures that should be followed to achieve those goals. This Comment offers our proposed set of goals and procedures. Then the Comment proposes a limited circumstance that could justify the use of waivers, one that will insure the FDA can gain access to the best scientific advice that this nation has to offer in all instances.

Goal 1:

The Guidance should establish at its outset that it is the policy of the Food and Drug Administration to create outside advisory panels that are free from conflicts of interest.

Granting scientists with conflicts of interest waivers to serve on advisory committees can defeat the reason for excluding them in the first place, even if they don't have a vote. The time has come to end the participation of all scientists with conflicts of interest on FDA advisory committees, even in a non-voting capacity. Most votes are unanimous or nearly unanimous. Since many committee members are relatively inactive participants, one or two outspoken members of an Advisory Committee can have a disproportionate influence on the discussion as well as the outcome of the vote, even if they themselves don't get to vote. Indeed, busy professionals are unlikely to participate as non-voting members unless they believe they can influence the outcome through discussion. Having non-voting members who are actively trying to influence the outcome of the meeting would negate the policy of not allowing them to vote.

Goal 2:

The Guidance should require the staff to choose a range of scientists for each advisory committee. It should include experts that can address all the issues of concern to both the agency and the public. Many current advisory panels lack balance even though it is a requirement of the Federal Advisory Committee Act. Most advisory committees are biased towards physicians and academic physician-researchers who treat patients for the specific conditions that fall under the purview of the specific committee. The committees frequently lack experts in population health and public health protection. Those with expertise in biostatistics, pharmaco-epidemiology, epidemiology, pharmaco-vigilance, drug safety and risk management as well as non-physician health professionals are underrepresented.

Goal 3:

The Guidance should address transparency in the advisory committee process by creating mechanisms that give the public greater and more timely access to the information that is presented to the Food and Drug Administration's outside advisers. There is substantial room for the FDA to improve the transparency of the advisory committee process. The advisory committee roster and any limited waivers (see below) should be released to the public at least 15 days before any advisory committee meeting. Briefing documents should be made available for public inspection at least one week before a meeting, not one day as is now the case. This will allow the public, patient advocates and independent researchers much-needed time to analyze this information before testifying at the public portion of the meeting.

Procedure:

To find outside experts without conflicts of interest, the FDA staff should follow the following procedures (the algorithm).

1. Once a year, the staff should carry out a systematic informational and recruiting outreach campaign to identify scientists who may serve on its scientific advisory panels who do not have conflicts of interest. The letters should include a detailed description of the types of expertise needed on FDA advisory committees and the requirement that the scientists have no conflicts of interest. This outreach campaign should include letters of inquiry to:
 - a. medical, scientific and professional societies;
 - b. the deans of the nation's medical schools; pharmacy schools and schools of public health;
 - c. the Office of Women's Health, the Office of Orphan Product Development, and the Office of Pediatric Therapeutics of the Food and Drug Administration;
 - d. the 27 heads of the institutes and centers at the National Institutes of Health;
 - e. the Centers for Disease Control; and
 - f. the Agency for Healthcare Research and Quality.
2. Once a year, the staff should carry out a systematic informational and recruiting outreach campaign to identify qualified members of patient organizations who could serve as patient representatives without conflicts of interest on advisory committees;
3. The staff should follow up on those letters as necessary to compile a roster of experts without conflicts of interest who are available for and interested in serving on advisory committees. The staff should regularly communicate with members of this roster regarding the reasons for their inclusion on the list, including their lack of conflicts of interest, and provide them with regular updates on the likelihood of their being included in an upcoming advisory committee meeting.
4. Upon being notified of an upcoming meeting, the staff should consult the roster and recruit non-conflicted experts as needed.
5. Should a committee need a particular expertise not available on the roster generated by the initial outreach campaign, the staff should contact at least ten (10) institutions from the initial outreach list that have the greatest likelihood of housing a scientist with the required expertise and solicit participation.

The Limited Exemption:

If the staff believes an expert with conflicts of interest is necessary for a complete airing of all issues involving a particular new drug, biologic or device, it may hire that expert as a special government employee to provide expert testimony as long as that expert does not vote and does not participate in the intra-committee discussions prior to the vote.

If the above process has been exhausted and does not generate a sufficient number of experts for an advisory committee or has excluded an expert deemed vital to the deliberations of the committee, the staff may hire a special government employee(s) with conflicts of interest to serve as a non-voting, non-discussant expert. This scientist can make a presentation to the

committee and/or answer questions. This person(s) presentation should be distinct from and independent of either the sponsor's or FDA's presentation at the meeting.

Even if the staff has created an advisory committee without conflicts of interest with all the expertise required to render a judgment, nothing in this algorithm prevents the FDA staff from hiring a scientist with conflicts of interest to provide testimony and/or answer questions from the advisory committee if the staff believes that presentation will add value to the meeting.

In no case, however, shall a scientist with conflicts of interest hired in this capacity be allowed to vote at the advisory committee meeting or be allowed to take part in discussions among members of the advisory committee prior to the vote.

Conclusion:

The Union of Concerned Scientists believes the time has come to end the participation of scientists with conflicts of interest on FDA advisory committees. This will help ensure that the Food and Drug Administration's assessment of the safety and efficacy of drugs is not inappropriately influenced by scientists with ties to the drug companies affected by an FDA approval decision. The integrity of science is vital to ensuring that decisions by federal policymakers benefit the public, and not the agendas of special interests. We at the Union of Concerned Scientists are working to ensure that federal scientists, and those who advise federal agencies, are free to do their work without interference. Prohibiting conflicts of interest will be a constructive step in addressing the pervasive problem of political interference in government science and help restore the public's faith in the ability of the agency to carry out its mission.

Sincerely,

A handwritten signature in black ink that reads "Francesca Grifo". The signature is written in a cursive, flowing style.

Francesca T. Grifo, Ph.D.
Senior Scientist and Director
Scientific Integrity Program
Union of Concerned Scientists