

Scientific Integrity Recommendations for the Food and Drug Administration

Problem: For too long, top FDA officials have put politics and the priorities of commercial interests above public health and safety. This has harmed thousands of Americans and shaken the public's faith. In 2006 nearly 1000 scientists responded to a survey conducted by UCS. 69 FDA scientists (9 percent) said they "have been asked, for non-scientific reasons, to inappropriately exclude or alter technical information or my conclusions in an FDA scientific document," and 378 FDA scientists (39 percent) disagree that the "FDA is acting effectively to protect public health." 311 scientists (32 percent) disagree that the "FDA routinely provides complete and accurate information to the public. (The full report is at www.ucsus.org/surveys.)

Solving these problems will require a concerted effort by the next FDA Commissioner, the new FDA chief scientist, and FDA managers. They must fully implement and build on reforms enacted by the 110th Congress. They must use their leadership to reduce the politicization of the regulatory process, make agency decision making more transparent, protect FDA scientists from reprisals, and reform FDA advisory committees.

"Scientific discourse is strongly discouraged when it may jeopardize an approval... Whenever safety or efficacy concerns are raised on scientific grounds...these concerns are not taken seriously."

—A scientist from the Food and Drug Administration

Solutions:

Agency Regulatory Reform

The FDA was slow to recognize serious side effects of popular drugs such as the diabetes drug Avandia, the painkiller Vioxx, and the antibiotic Ketek. As a result, thousands of Americans lost their lives or were seriously harmed. These incidents prompted the passage of the Food and Drug Administration Amendments Act (FDAAA) of 2007. The act requires that the FDA make a drug approval "action package" publicly accessible on its web site. That package must include drug review documents, and a summary that describes the views of all reviewing disciplines about the drug. Disclosure must also include a description of any disagreements among the drug review team, and how they were resolved. In addition, the new law stipulates that a scientific review of a drug application is considered the work of the reviewer, and shall not be altered. To fully implement this law and go beyond its modest reforms, FDA must:

- ✓ **Publish a summary statement discussing the scientific basis for any regulatory decisions informed by science.** The statement should be available in a timely fashion, and clarify how officials made the final decision given the evidence. The statement should include: (1) the rationale for the decision, including all scientific documents and data used to make it, (2) a minority report including any dissenting opinions and how the agency resolved such differences of opinion, and (3) identification by name of each official and employee who participated in the decision.
- ✓ **Make it easier for the public to access and understand drug approval packages.**



- ✓ **Disclose all scientific studies in the FDA’s possession related to a proposed regulation**, regardless of whether the study was directly cited or whether it directly informed the final decision.
- ✓ **Make clear that the agency’s first priority is public safety**, and that its “clients” are American families, not drug companies.
- ✓ **Strengthen the role of the FDA chief scientist** to be a champion for scientific integrity at the agency. Appoint a widely respected expert to this position.

Greater Transparency at the FDA

After facing years of attempts to censor, alter or suppress their work, FDA scientists must receive a clear message from the next FDA Commissioner, chief scientist, and senior managers that the culture has changed. FDA leadership must:

- ✓ **Permit FDA scientists to present their findings before FDA advisory committees.** Exceptions should be rare and part of the public record.
- ✓ **Issue a memo to all FDA employees declaring that the FDA will strive to be as transparent as possible and conduct its operations in a “fishbowl.”** In 1983, to restore the credibility of the Environmental Protection Agency (EPA) after multiple scandals, then EPA Administrator William Ruckelshaus issued such a memo—a move that should be replicated at FDA.
- ✓ **Institute a transparency policy for official meetings with outside entities.** This policy should require that the FDA post on its website a complete record of all meetings with outside entities including for-profit and not-for-profit organizations, other agencies, and individuals.
- ✓ **Implement an FDA-wide policy that seeks to ensure free and open communication between scientists and researchers, and the media, policy makers, and the public.** This policy should explicitly state that (1) FDA scientists may freely express their personal views provided they make it clear they are not speaking on behalf of the agency, and (2) FDA scientists have the right to review, amend and comment publicly on the final version of any document that significantly relies on their research, identifies them as an author or contributor, or purports to represent their scientific opinion.
- ✓ **Provide training on the provisions of the FDAAA** and its rules concerning publication in peer-reviewed journals. The new law permits scientists who have asked for permission to publish their work in peer-reviewed journals, and who have not heard back from the FDA after 30 days, to publish with a disclaimer that they are not speaking for the agency.

Protecting FDA Scientists

Over the past five years, FDA scientists who questioned the safety of the drugs such as Avandia, Vioxx, and Ketek not only were ignored but were also intimidated and censored. In each case, their concerns were ultimately proven right, but only after thousands of patients died or suffered serious harm.

- ✓ **The FDA Commissioner should instruct his management staff to refrain from retaliating against whistle-blowers through reassignments, demotions or terminations.**
- ✓ **The FDA Commissioner should issue a statement that encourages staff to speak out internally about concerns and communicate that the agency values their input.**
- ✓ **FDA staff members should feel empowered to report not just waste, fraud and abuse, but also instances where science has been manipulated, suppressed or distorted.**
- ✓ **FDA should proactively educate its scientists and researchers regarding their rights and protections.** These efforts should include mandatory briefings for new hires, requirements for posting educational information in workplaces, and in-service trainings.

Reforming FDA Advisory Committees

The FDA's drug and device advisory committees often include participants who have significant financial ties to special interests that will benefit from the committee's decisions. The FDAAA makes very modest changes to the FDA advisory system. It directs the agency to increase efforts to recruit non-conflicted experts and establishes some limits on the aggregate use of waivers for members with conflicts. Nevertheless, the current FDA advisory committee process continues to permit those with financial ties to a drug or device that will benefit from an advisory panel's review to have an unacceptable level of influence on the findings of advisory committees.

Studies of the FDA advisory committee system have revealed a flawed process. Between January 1, 2001, and December 31, 2004, an analysis of 221 FDA advisory committees found that conflicted experts were the norm, not the exception. In more than 20 percent of meetings, half the membership of an FDA advisory committee had a conflict of interest.ⁱ And in more than eight out of ten meetings reviewing a specific drug product, there was at least one member with a conflict of interest.ⁱⁱ

The votes of conflicted experts can make a difference in the final outcomes of advisory committee recommendations. In 2005, for example, 10 of the 32 advisors on FDA panels considering whether painkillers Bextra, Vioxx and Celebrex should remain on the market had financial ties to the makers of the drugs. The vote to continue the marketing of Bextra was 17 to 13; nine of the conflicted experts voted yes. The vote to continue marketing Vioxx was 17 to 15, with nine conflicted experts voting yes.ⁱⁱⁱ

The FDA must vigorously commit itself to reforming its advisory committee process, and to ultimately eliminating conflicted experts on its panels. FDA leadership must:

- ✓ **Specify which advisory committees are expressly scientific and which are designed to gather stakeholder input.** For committees whose mission is purely to provide objective scientific advice (as opposed to committees designed to gather input from stakeholders), committee members should be appointed as "special government employees."
- ✓ **Adopt strict conflict of interest rules** with a goal of completely phasing out significant financial conflicts of interest among scientific advisory committee members. Lower the threshold for allowable cumulative financial ties to all companies whose products may be affected by a panel review (current FDA policy is \$50,000).

- ✓ **Aggressively recruit new committee members** by looking to universities and medical schools. Use of conflicted committee members is rarely necessary. The FDA has 30 advisory committees and 18 device panels, requiring the services of 463 members, while the pool of qualified, non-conflicted physician-scientists and other experts is over 120,000 individuals.^{iv} (The FDAAA directs the FDA to do more recruitment, and gradually limits the use of conflicted experts over several years.)
- ✓ **Permit experts with conflicts to present** at scientific advisory committees, and to answer questions, but do not allow them to participate in panel discussions or votes.
- ✓ **Take concrete steps to ensure that inappropriate criteria such as party affiliation and political opinions are never a part of the process for selecting members of scientific committees.** The FDA should select advisory committees members based solely on their experience and technical qualifications in the topic the committees will address.
- ✓ **Scientists who have taken public positions on issues should not be excluded from an advisory committee because of concerns about bias.** Having a point of view does not preclude an objective assessment of the information presented to a committee. A scientist's membership in a scientific association should not be considered evidence of bias, even if that association has a stated policy agenda.

For more recommendations from the Scientific Integrity Program, please see our report, *Federal Science and the Public Good*, available at:

www.ucsus.org/federalscience



Union of Concerned Scientists, December 2008

ⁱ Peter Lurie, 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*, 26 Apr. 2006.

ⁱⁱ Ibid.

ⁱⁱⁱ Gardiner Harris and Alex Berenson, “10 Voters on Panel Backing Pills Had Industry Ties,” *The New York Times*, 25 Feb. 2005.

^{iv} Data provided by Susan F. Wood, Ph.D., the former Assistant Commissioner for Women's Health at the Food and Drug Administration.