FDA Revamps Committee Conflict-of-Interest Rules

The U.S. Food and Drug Administration is overhauling the process for vetting conflict of interest among its advisory committee members, an effort that has been widely called for but is unlikely to assuage most of the agency’s critics.

In July, the FDA revealed plans to create new guidelines overseeing conflict of interest among its advisory committee members and outlining when the agency can grant waivers. The policies were last updated in 2000. “There have been changes in the marketplace and in people’s work that have happened since then, and there have also been changes in our thinking as an agency,” FDA Deputy Commissioner Scott Gottlieb, M.D., said during a forum on conflict of interest held the same day the revisions were announced. “And so we’re going to ask a lot of hard questions about whether or not certain relationships should still even require a waiver and whether or not certain relationships should even be granted a waiver.”

He admitted that the current policies have been applied unevenly and often out of public view. The new guidelines, which the agency plans to draft over the next few months, should bring more clarity to which financial relationships warrant a conflict-of-interest waiver and which do not. They will also be used to determine how and when those waivers are revealed publicly.

Ultimately, the decision to grant waivers is expected to be based on several factors: the total dollar amount involved; the nature of the relationship (whether the experts consults for, conducts research for, or owns stock or stock options in a company); whether the conflict is with the sponsor of a drug under review or a competing company; and whether the tie to industry is a direct one or through the expert’s institution.

However, revising these guidelines does not go far enough, according to critics who have called on the agency to expunge the advisory committees of all conflicts.

“If you’re acting as an agent for a company, then, fundamentally, you shouldn’t be judging that company’s drugs. That’s just common sense, and that’s what we’ve got to get to,” said Steve Nissen, M.D., whose term as chair of the FDA’s Cardiovascular and Renal Drugs Advisory Committee ended last year. “And, unfortunately, the policy in the past has been very erratic, hard to follow, and, frankly, has led to a lot of conflicted panels.”

Researchers who conduct clinical trials do have a choice, Nissen said during the same forum at which Gottlieb spoke. “I don’t take the money.” Similar calls are also coming from Capitol Hill.

“The FDA continues to demonstrate a lack of commitment to ensuring that all of its advisory panels are filled with members who have no conflicts of interest with the drug or device being reviewed,” Rep. Maurice Hinchey (D-N.Y.), said in a statement responding to the agency’s announcement. Hinchey has authored a measure attached to the spending bill that funds the FDA that would bar the agency from granting any waivers for members with reported conflicts of interest.

**Internal and External Conflicts**

According to critics, there is substantial evidence that the FDA’s current policy granting waivers to members with conflicts of interest is inadequate.

In 2002, the FDA held 221 advisory committee meetings; there was a statement of a financial conflict of interest for at least one member disclosed at 73% of them. Across all of those meetings, 28% of members had some conflict of interest, such as owning stock in or consulting for either the maker of the drug under review or a competitor. But only 1% were recused by the FDA, according to a study by Citizen’s Health Research Group published in the *Journal of the American Medical Association*.

Although empaneling a conflict-free advisory committee is a nice ideal, it just won’t work for the FDA, Gottlieb said. “We don’t convene meetings around specific issues as they come up, so we don’t have the luxury of being able to select people based on their lack of certain associations. We have standing advisory committees, and we can’t foresee what issues are going to come before those committees,” he said.

In the process of weeding out conflict of interest, you also run the risk of weeding out expertise, said Silvana Martino, D.O., who recently ended her stint as the chair of the Oncologic Drug Advisory Committee.

“That goal [of no conflict of interest] is logical; it’s understandable. But it is a difficult goal,” she said in an interview. “You want people on these committees that have been around for a while. People who have experience.
People with a certain background to their years of service to the medical profession. You don’t get to that level without having had some contact, some exposure in the research world. And the research world does expose you to various companies and representatives of those companies.”

However, Martino also said that it would be fair to have any potential conflict of interest publicly aired before a committee meeting. That idea has been proposed by lawmakers but privately opposed by FDA officials, according to watchdog groups.

Gottlieb has said that inviting even more scrutiny to what is already a public position for many academic scientists could have a chilling effect on the FDA’s ability to recruit outside experts.

According to the announcement in July, the agency will issue new guidelines specifying when and how much information on conflict-of-interest waivers will be released to the public. Currently, those waivers are available only through a freedom of information act request.

**Too Cozy With Industry?**

But critics say the agency’s refusal to ban all conflicts of interest, combined with its inappropriate coziness with industry, has allowed several unsafe drugs to enter the market.

A recent survey by the Union of Concerned Scientists (UCS) found that many of the FDA’s own scientists have lost confidence in the agency’s ability to clamp down on industry when needed. The UCS also cataloged a series of failures over the past few years that have led to unsafe drugs entering the market, including the highly publicized cases of COX-2 inhibitors and the antibiotic Ketek, which more recently has begun to raise concerns among lawmakers who oversee the agency.

“The allegations of misconduct in this case are as bad as I’ve heard yet,” Sen. Chuck Grassley (R-Iowa) said in a statement accompanying a letter to the FDA requesting a detailed accounting of how and why a Ketek study that agency scientists had raised questions about was presented without caveat to the advisory committee that recommended the drug’s approval.

“It looks like the FDA caught the drug company red handed and let them get away with it. On top of that, the FDA failed to set the record straight and, in fact, continues to cite a discredited safety study as a principal reason to feel OK about using this drug,” he said.

Such slipups have helped to erode public confidence. According to a Wall Street Journal Online/Harris Interactive poll conducted in May, 58% of those contacted said the FDA does a fair or poor job of ensuring the safety and efficacy of new drugs, whereas 36% said the agency does a good or excellent job. That is a flip from just 2 years ago when 56% thought the FDA did a good or excellent job and 37% thought the agency did a fair or poor job.

“Unfortunately, we’re in an era when public trust in the FDA is at an all-time low and so the appearance of conflict of interest is as serious as the conflict itself because it undermines the public trust,” said Nissen.

However, concerns about conflict of interest may go deeper than the membership of the advisory committees themselves. As the UCS’s confidential survey shows, the agency staff reported that by the time study information makes it to committee meetings, the data may have already been tainted by political or industry pressures.

That bias comes through loud and clear, according to Nissen, who said it was sometimes obvious to him which way the FDA wanted the panel to vote by the way studies were presented.

But there is a public misperception that the most important thing that comes out of a committee meeting is whether the agency should approve a drug, said Gottlieb.

“That’s not to suggest that the panel’s answer to the question of whether or not a product should be approved is extremely important to the agency, and it’s not to say that sometimes the panel can change the agency’s mind,” he said. “But I think we lose sight of some of the real value that we get out of the advisory panels, which is the very subtle questions around the scope of the prescribing of the drug.”

Martino said the Oncologic Drug Advisory Committee may have been different from other committees, but its members often struggled with difficult questions over whether to approve the drugs presented to them.

“There is a weight to your decisions, which you appreciate more and more as your 4 years go by. … The FDA makes most of its decisions without anyone from outside advising them. It is really the most contentious, difficult applications and also the new agents where one doesn’t have a world of experience,” she said.

That’s why Martino is troubled that the FDA allows ad hoc members to vote. The agency often uses these consultants to augment the expertise of the standing advisory committees. According to the JAMA study, 86% of committee meetings include at least one voting consultant, and more than half of those consultants have a conflict of interest.

“Most often those are people who are well known in their field but who really are not experienced in the job of the committee. Yet here they are today sitting with us and they get to vote,” Martino said. “… That vote is a very critical one and unless you have been on the committee and understand the fullness of the weight of your vote, it just makes me uncomfortable.”

—Joel B. Finkelstein