Conflicts cause FDA to review advisory committees

Critics have lately cast the US Food and Drug Administration (FDA)'s scientific advisory panels as little more than partially owned subsidiaries of the pharmaceuticals industry. In fact, one influential US Congressman is so outraged by the degree to which panels are replete with scientists who sport financial conflicts of interest that for the second consecutive year, he has successfully attached a rider to the FDA budget that would prohibit the agency from using panelists so conflicted.

Facing a political firestorm stoked by conflicting studies[1] and a barrage of negative publicity,[2–5] the FDA in May announced a major internal review of its Advisory Committee Meeting system, its typical means of garnering expert advice on scientific issues around drugs. Roughly 20% of the 35–40 new "chemical entities" approved by the FDA each year are subject to external panel review.

Among aspects of this major review are an examination of the FDA's appointment process for the members of its 16 drug committees and 32 other advisory panels, and whether it needs to modify its practices for handling conflicts of interest among panelists.

Currently, the FDA allows conflicted scientists to apply for a "waiver" that permits them panel membership on the grounds that their individual expertise outweighs the seriousness of the conflict. Health Canada allows similar exemptions, although without a formal waiver process. Rather, conflicts are publicly declared or limits are placed on an individual "in the development of the panel's advice through a variety of mechanisms under the direction of the panel chair," says spokesperson Carole Saindon. She adds that Health Canada's approach to conflicts of interest is more rigorous than that of similar organizations in other nations, since "candidates who could receive direct financial benefit from a regulatory decision [such as company shareholders] are excluded from panel membership."

Such an automatic prohibition does not appear to be the goal of the FDA review. Spokesperson Crystal Rice says that the agency has no intention of changing its policies to prohibit conflicted scientists from serving on a panel, but will examine "our processes and procedures for implementing the current laws."

That, however, is unlikely to satisfy critics, led by Congressman Maurice Hinchey (Democrat–NY), a member of the influential House Appropriations Committee, who hold that such conflicts completely compromise the value of scientific advice. Last fall, Hinchey convinced the US House of Representatives to deny budget appropriations to the FDA unless it discontinued its practice of granting waivers. But in a subsequent political compromise with the Senate, reached during the budget process, the rider was lifted on the proviso that the FDA disclose potential conflicts and post them on its Web site 15 days before each meeting. The issues of an outright prohibition of participation by conflicted scientists and FDA's use of waivers were referred to the powerful Government Accountability Office for review.

Since then, a new study[1] found that in 2001–2004, the FDA recused less than 1% of conflicted scientists; and that, of the roughly 3000 advisory committee members who participated in the FDA's 221 drug-review meetings, some 28% had a conflict of financial interest with the affected company or product competitors within the preceding year. In the wake of that report, Hinchey again mustered enough political support to attach an identical rider in May to the FDA budget covering the 2006/07 fiscal year.

Although many laud the openness and transparency of the FDA's advisory committee system as an example to the world, the betting is that the agency's international reputation will not permit it to escape politically imposed change, especially after its recent avalanche of controversies. One was the study published in April by Peter Lurie (deputy director of the Washington-based consumer-advocacy Public Citizen's Health Group) and colleagues,[1] which found that conflicts of interest are rampant within FDA drug panels: in 2001–2004, a financial conflict of interest with the affected company was had by one or more panelists in 73% of the 221 drug reviews conducted by the FDA's 16 advisory committees. Only 1% of members were recused, although many conflicts were substantial: some 30% involved investments exceeding US$25 000; another 23%, grants or contracts topping $100 000. Lurie and colleagues nevertheless concluded that the outcomes of votes by the Center for Drug Evaluation and Research advisory committee essentially were uncompromised: excluding conflicted panelists would not have changed outcomes, but only reduced the vote margins.[1]

Another controversy involves an examination by the Center for Science in the Public Interest (CSPI),[2] at the request of the *New York Times*, of a 32-member panel that had studied the cardiovascular risk of COX-2 inhibitors,

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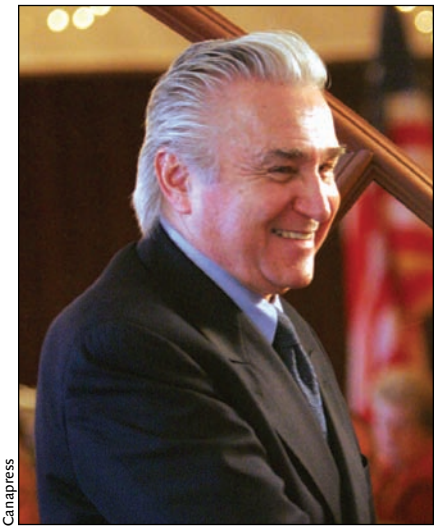

Canapress

US Congressman Maurice Hinchey (Democrat–NY), critic of the Food and Drug Administration.

controversial painkillers that include celecoxib (Celebrex), refecoxib (Vioxx) and valdecoxib (Bextra). Its widely publicized conclusion was that the panel would have voted differently on whether the drugs should be on the market if the 10 members with direct financial interests in the drug manufacturers had been excluded from participation.

Another storm began in March of this year when David Graham, Director for Science and Medicine of the Office of Drug Safety (and an FDA whistleblower), told the National Press Club that the Office of New Drugs (OND)'s authority over FDA advisory committees is heavily biased in industry's favour. In calling for structural reforms to provide more separation between the drug safety and drug review functions of the FDA, Graham said the OND had too much control over panel appointments, the assignment of drugs to specific committees and what information is presented to panelists. He also criticized the FDA's financial disclosure rules as being lax.

Other conflict allegations have been made about the advisory panels studying silicone breast implants,[3] the labelling of high-blood-pressure drugs[4] and of Tysabri,[5] a drug to treat multiple sclerosis. Much of the ensuing debate has focused on whether prohibiting conflicted scientists from sitting on a panel would, because the pool of available experts is limited, compromise the quality of scientific advice ultimately received. Merrill Goozner, CSPI Director of Integrity in Science, dismissed that notion as disingenuous, calling it offensive to suggest that only the best and brightest work for industry. There is a plethora of qualified and nonconflicted experts, he says, and the FDA is reluctant to expand panel membership to include more epidemiologists. "This should be turned into more of a deliberative body without a stake in the outcome, rather than a kind of good-old-boy network of people whose primary interest is to get their hands on a new therapy, either to test or for [their own] patients."

Peter Lurie is convinced that the FDA must move to broaden committee composition and adopt more stringent standards for determining when waivers will be granted, rather than automatically rubber-stamping them, as now appears the case. "A person goes on an advisory committee and they don't know what votes are going to come up in the future," he points out. "To ensure [a panel] without conflict of interest is either to recuse absolutely everybody, no matter how remote the conflict of interest, or to never allow anybody who's ever had any investment, of any kind, on the committee in the first place, in the possibility that a drug in which they've been involved might later come up." Because that is simply impractical, he adds, "there needs to be more hard-and-fast rules about who will be recused — and the barriers should be set lower."

Yet, change is unlikely to come from within the FDA, Lurie forecasts. "The most striking thing about this … is that the FDA thinks that an internal committee to review an external advisory committee process is the way to go. It's just totally illogical, and it really raises questions about the sincerity of the effort."

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