FDA Losing Credibility With Public, Own Staff

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WASHINGTON — Members of the scientific community have raised a red flag over the apparent increasing influence of money and politics on what are supposed to be the independent and unbiased internal workings of the Food and Drug Administration and other federal watchdog agencies.

In a recent confidential survey of staff scientists in the FDA's Center for Drug Evaluation and Research, 19% reported being pressured to push through a drug about which they had reservations, and 66% said that they were less than wholly confident that the FDA adequately monitors the safety of drugs after they reach the market.

Across the agency, 50% of respondents said they did not believe that the FDA was headed in the right direction, according to the survey by the Union of Concerned Scientists and Public Employees for Environmental Responsibility.

In the words of one staff scientist: "The FDA is presently being stacked at every management level, including the lowest levels, based on those who will support the big companies' agenda, and the implications for safety and efficacy will be felt long into the future."

Such influences have led to a "crisis in public confidence," according to Dr. Steven Nissen, who until last year chaired the FDA's Cardiovascular and Renal Drugs Advisory Committee. "We have to work a lot harder now … to keep the politicians out of the science as much as possible and to keep the commercialization of science from coloring everything we see and hear of scientific value," he said at a panel discussion on conflict of interest on government science panels sponsored by the Center for Science in the Public Interest. CSPI is a nonprofit consumer organization focused on food, nutrition, and health issues; it is perhaps best known for its efforts to disclose the nutritional content of fast-food products.

Dr. Nissen criticized the agency's top leaders for "whining incessantly" to Congress about the burden of regulation rather than asking for more authority.

"While the American people worry about the safety of drugs, the top FDA leadership tells us we need fast drug approval," he said.

Dr. Nissen said the appointments of Lester Crawford, D.V.M., Ph.D., and Dr. Andrew von Eschenbach as acting FDA commissioner and Dr. Scott Gottlieb as FDA deputy commissioner for policy also have raised some troubling questions about conflict of interest with the agency, he said. (Dr. Crawford eventually gained Senate confirmation to his position, but resigned shortly thereafter.)

"In his role as director of the National Cancer Institute, [acting commissioner von Eschenbach] must seek FDA approval for human testing or approval of new

Advisory Process Undergoes Facelift

The FDA recently announced several steps it will take to codify the processes for bringing in expert voices and managing the agency's advisory committees.

"There are places where we can bring more consistency potentially to our processes. There are places where we can bring more transparency to the work we do. We know that and we feel that doing so is important to inspiring confidence in the process," Dr. Gottlieb said.

Those changes are to include:

- ► Revamped guidance identifying more clearly the conditions under which conflict-of-interest waivers are granted.
- ► New guidance specifying when those waivers will be disclosed to the public and what information will be made available.
- ► New guidance specifying when briefing materials used by advisory committees will be made available to the public.
- ► Broader dissemination of advisory committee schedules through mailings to public groups and electronic notifications through FDA listservs and the Web site.
- ► A streamlined approach to the appointment of members to drug-related advisory committees.

cancer drugs, an obvious conflict of interest. Even worse, the administration has appointed Scott Gottlieb as deputy commissioner, who came to this job with no regulatory experience, directly from Wall Street where he served as a biotech analyst and stock promoter," Dr. Nissen said.

Also speaking as part of the panel, Dr. Gottlieb refused to address those charges, but defended FDA policy that allows the agency leeway in impaneling advisory committee members who have financial ties to industry. The advice the FDA receives from advisory committees must span the breadth of both clinical research and clinical practice, he said. "That's the kind of advice that you can only get from people who are heavily engaged in clinical trials."

Dr. Gottlieb also announced FDA plans to revamp the advisory committee guidelines, including updated rules that determine whether members need to be recused due to a potential conflict of interest. (See box.) However, it is unclear how those changes will relieve the concern, both inside and outside the agency, that these panels are being manipulated.

"I've observed that [FDA] management and [drug and device manufacturing] companies have found ways to manipulate this process in favor of approval. These methods are very subtle and would not easily be recognized," recounted one respondent to the survey by the Union of Concerned Scientists. The anonymous respondent went on to describe these techniques.

Within the FDA, scheduling conflicts can be used to exclude a committee member who is expected to oppose a drug's approval, and managers have been known to massage the presentations to the committee to soften damaging findings. Drug companies have also learned that by hiring experts as consultants, they can deny FDA access to them, and that by hiring committee members themselves, they can force them to be excluded from voting on a company's drug.

"As advisers, we get the data that [are] presented to us and … you can tell where the agency wants you to go," Dr. Nissen said. "The material you get has to be unbiased, and I'm worried that it might not be."

It is easy to overlook the more subtle value that advisory committees can provide, Dr. Gottlieb said.

"The advice we are getting is not necessarily in many cases whether or not a drug can make it to market, but the contours of the approval, what the language should look like, what indications this drug should be approved for, should it be restricted, what is an appropriate postmarket monitoring plan," he said. ■