Two-Thirds at FDA Call Safety Guards Inadequate

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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.

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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 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. 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 is presented to us and … you can tell where the agency wants you to go," said Dr. Nissen. "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, said Dr. Gottlieb. "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. ■

POLICY & PRACTICE

Part D Premiums Hold Steady

Premiums under Medicare's Part D drug benefit will remain stable in 2007, according to figures released last month by the Centers for Medicare and Medicaid Services. Officials at CMS estimate that the average monthly premium paid by Medicare Part D beneficiaries will be around $24 in 2007, about the same as in 2006. "Competition and choice in health care are working," Dr. Mark McClellan, CMS administrator, said during a press conference. In addition to holding consumer costs steady, CMS officials reported that the national benchmark that determines Medicare's subsidy of drug coverage will decline next year. The competitive bids for both the stand-alone drug plans and the Medicare Advantage managed-care prescription drug plans came in with lower-than-expected bids, according to CMS. The open enrollment period for 2007 will begin on Nov. 15.

Mixed Reviews for Merck

The most recent Vioxx court cases have produced mixed results for the drugmaker Merck & Co., Inc. In August, a Los Angeles jury ruled in the company's favor, finding that the Vioxx (rofecoxib) was not responsible for the heart attack of Stewart Grossberg, who had been taking the drug intermittently. Merck argued successfully that Vioxx was not responsible for Mr. Grossberg's heart attack because he has high cholesterol levels, atherosclerosis, and a family history of cardiac problems. But about 2 weeks later, a federal jury in New Orleans found Merck liable for $51 million in damages in the 2002 heart attack of Gerald Barnett, a 62-year-old retired special agent of the FBI. The company is currently exploring grounds for appeal including insufficient evidence and the application of incorrect legal standards, according to Merck. The company was also dealt another blow in August, when a New Jersey judge decided to set aside a 2005 jury verdict that had been in the Merck's favor. The judge ordered a new trial to take place early next year. The judge cited a December 2005 New England Journal of Medicine editorial expressing concerns about Vioxx-related study data as the basis for throwing out the jury verdict (N. Eng. J. Med. 2005;353:2813-4).

In the Dark on EC

Despite the controversy surrounding the proposal to provide Plan B emergency contraception without a prescription, only about one-quarter of Americans in a recent survey said they had heard a lot about the debate. And nearly an equal number said they had heard nothing about the politically charged issue. The survey was commissioned by the Pew Research Center for the People & the Press and the Pew Forum on Religion & Public Life. The survey also found that about 48% of those surveyed favored selling emergency contraception without a prescription, whereas about 41% opposed the idea. The national telephone survey was conducted in July among more than 2,000 U.S. adults.

Uninsured Figures Climb

The number of people in the United States without health insurance edged higher in 2005, fueled in part by a drop in employer-sponsored health insurance, according to figures released in August from the U.S. Census Bureau. In 2005, 46.6 million people were uninsured, up from 45.3 million the year before. The percentage of people covered by employer-sponsored health insurance dropped from 59.8% to 59.5% between 2004 and 2005, while the percentage covered by government insurance stayed the same, according to the Census figures. The new figures, compiled as part of the Current Population Survey, showed that the number of uninsured children also increased. Between 2004 and 2005, the number of uninsured children rose from 7.9 million to 8.3 million. And children living in poverty were the most likely to be uninsured, with the uninsured rate at 19% for children living in poverty compared with 11.2% of children overall in 2005. The American Medical Association issued a statement calling for action to address the uninsured problem. "The AMA plan for reducing the number of the uninsured advocates expanded coverage and choice through a system of refundable tax credits based on income, individually selected and owned health insurance, and market reforms that will enhance new, affordable insurance options," Dr. Ardis Hoven, an AMA board member, said in a statement.

Drug Code Directory Incomplete

The Department of Health and Human Services' Office of Inspector General has found that the Food and Drug Administration's National Drug Code Directory is incomplete and inaccurate, largely as a result of drug companies' failure to submit required data, though the FDA shares some blame. The NDC Directory is supposed to be a current compendium of marketed drug products. The FDA relies on internal reports and on submissions from pharmaceutical manufacturers, which must report when a new product is introduced or withdrawn. The OIG report is a snapshot of the NDC Directory as of February 2005. At that time, there were 123,856 products with unique NDCs. The OIG found that the FDA's listing left off just more than 9,000 drug products. For about 16%, the drug maker either had not submitted required forms or the agency had not appropriately processed them. Listings for about 5,100 products had been held up because the companies had failed to provide needed information. Finally, the OIG found that 34,000 products listed were either no longer marketed or their entries contained erroneous information, mostly because drug makers had not told the FDA that the products were discontinued. In a comment submitted with the report, the FDA acknowledged many of the failures, but also said there was a decrease in the percentage of missing products since 1990.

—From staff reports