Experts Urge Reform of FDA Clinical Trial Rules

BY MARY ELLEN SCHNEIDER
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BOSTON — Any proposals to reform the Food and Drug Administration should meet the test that the changes would have prevented the arthritis drug Vioxx from getting to the market, Dr. David J. Graham said at the annual meeting of the American Public Health Association.

Dr. Graham, an FDA scientist who testified before Congress in 2004 about the unwillingness of FDA officials to recognize safety problems with Vioxx (rofecoxib), was among a panel of experts who called for changes at the FDA and reforms in the way that pharmaceutical companies design clinical trials.

The criticism comes on the heels of a report from the Institute of Medicine that recommends significant reforms at the FDA, including establishment of performance goals for safety.

The FDA has been "captured" by the industry and has taken on the value system of the pharmaceutical companies, said Dr. Graham, of the FDA Office of Surveillance and Epidemiology, who was speaking as an individual and not on behalf of the agency.

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FDA officials now see their jobs as getting drugs on the market as fast as possible, Dr. Graham said. "We have at FDA a lack of checks and balances."

FDA leadership was quick to rebut those charges. The vast majority of physicians, scientists, and staff members at the FDA reject the concept that the agency is beholden to the drug industry, Dr. Steven Galson, director of the Center for Drug Evaluation and Research (CDER), said in an interview.

In light of calls for reform, FDA officials have already taken steps in the last 2 years to try to improve processes within the agency, Dr. Galson said. For example, the agency has created a new drug safety oversight board that includes individuals from the FDA and other government agencies to provide advice on drug safety issues, and it has increased the number of staff working in the postmarketing safety area. FDA officials have also redesigned the drug label so physicians can quickly see key information needed for prescribing decisions. And the agency has a long to-do list of reforms aimed at promoting early detection of safety problems and improving communication with physicians and patients.

But the biggest advances in drug safety are more likely to come from basic science advances, he said. These advances, which the FDA is trying to foster through its Critical Path Initiative, will help scientists better predict which drugs in development will run into safety problems later.

"The best way to improve drug safety is by improving the science of drug development," Dr. Galson said.

But the FDA also should improve its postmarketing surveillance, said panelist Dr. John D. Abramson of the department of ambulatory care and prevention at Harvard Medical School, Boston. The current system—in which physicians voluntarily report drug-related adverse events—does not work, because it's passive, he said. The FDA could instead be doing epidemiologic studies to monitor side effects in the entire population taking a drug.

Panelists also took aim at how the pharmaceutical industry designs clinical trials. Drug trials are conducted mainly to maximize return on investment to shareholders by emphasizing benefits of the drug and minimizing risks, Dr. Abramson said.

Drug companies used to simply provide financial support for studies, but they now also design the study and keep the research, said panelist Dr. Marcia Angell, former editor-in-chief of the New England Journal of Medicine and a senior lecturer on social medicine at Harvard. "The researchers are treated like hired hands."

One possible way to limit the influence of pharmaceutical firms in study design would be to create an arm of the National Institutes of Health that would oversee the design of trials, Dr. Angell said. Such a body could be wholly or partially funded by industry. Registration of clinical trials at their inception should be a requirement to enroll human subjects, she said.

The panel also criticized the FDA statute that requires new drugs to show effectiveness compared with placebo, but does not require a new drug to be better than existing medications on the market. This leads to approval of drugs with limited benefits and unknown risks, Dr. Angell said. "That's the combination we're getting."

She cited Vioxx as an example of a drug that should never have been approved because it had only marginal benefits over existing drugs. In Dr. Angell's opinion, any FDA reform should require that approval of a new drug be based on comparison with existing medications to treat the same condition. Such a change would force drug companies to spend more time on innovative drugs and less time developing "me too" products, she said.

In an interview, CDER's Dr. Galson agreed that there needs to be more innovation coming from pharmaceutical companies, but said that Congress must be careful to ensure that any additional regulatory authority doesn't hamper innovation. "There's a balancing act there," he said.

Members of Congress also will have a chance to weigh in on FDA reform when the Prescription Drug User Fee Act (PDUFA) comes up for reauthorization in 2007. The PDUFA law, originally passed by Congress in 1992, set up a system in which the pharmaceutical industry pays user fees to the FDA in exchange for the agency's agreeing to meet certain deadlines in the review of drug applications. ■

POLICY & PRACTICE

Von Eschenbach Confirmed for FDA

Almost 9 months after he was first nominated to be Food and Drug Administration commissioner, Dr. Andrew von Eschenbach was finally confirmed by the Senate by an 80-11 vote in the wee hours of the 109th Congress. Confirmation came after an 89-6 vote to limit debate on his nomination. The naysayers included Sen. Chuck Grassley (R-Iowa), one of Dr. von Eschenbach's most vocal critics. As Finance Committee chairman, Sen. Grassley and his staff have been investigating what they call an inappropriate approval of Ketek (telithromycin). Sen. Grassley maintains that Dr. von Eschenbach has stonewalled committee investigators, and in an agitated floor statement during the nomination vote, he accused the nominee of hiding documents and intimidating FDA employees who dissented. Sen. Grassley warned his colleagues that Dr. von Eschenbach was a prime illustration of concerns about the lack of Senate oversight of the Bush administration. "I believe we need to send a message to the executive branch that it's not okay to impede congressional investigations. It's not okay to limit the Senate's access to documents, information, and employees of the executive branch," the senator said.

AMA Joins Washington Lawsuit

The American Medical Association has joined six Washington state physicians and the Washington State Medical Association in a lawsuit against Regence BlueShield asserting that the insurer used faulty internal quality data in excluding nearly 500 physicians from a new network that Regence is developing. "This lawsuit has repercussions far beyond Washington state as more health insurers impose financial disincentives which threaten to disrupt patients' longstanding relationships with physicians they know and trust," AMA Past President Edward J. Hill commented in a statement. The lawsuit, filed Sept. 21, stems from Regence's decision to create a "select network" of physicians who deliver "high quality, efficient care" to serve mainly Boeing Co. engineers. The lawsuit contends that the methodology Regence used to calculate performance failed to consider the population of patients seen by the physicians; used small samples and inaccurate records; and included patients who should have been excluded "because of their personal medical histories."

Med School Enrollment on Rise

The Association of American Medical Colleges reports that U.S. medical school enrollment for 2006 increased by just over 2% to 17,370. Some schools posted even greater gains, among them: Florida State University (36% increase), Brown University (25%), Boston University (15%), Saint Louis University (15%), Pennsylvania State University (13%), Wayne State University (11%), West Virginia University (11%), Drexel University (10%), and the University of Alabama, Birmingham (10%). There was an almost 5% increase in applicants in 2006, to 39,109. There were almost equal numbers of male and female applicants (19,812 and 19,297, respectively) and enrollees—8,924 men and 8,446 women. There was a 9% increase in the number of accepted black applicants and an 8% increase in the number of black enrollees. "With the looming doctor shortage, these results are good news indeed, and we hope this encouraging trend continues," said Dr. Darrell G. Kirch, AAMC president.

Health IT Have-Nots

The adoption gap in health information technology continues to widen, with physicians in smaller practices being left behind, according to a report from the Center for Studying Health System Change (HSC). Compared with 2000 and 2001, in 2004 and 2005 physicians in all types of practices increased their use of health IT for accessing patient notes, generating patient reminders, exchanging clinical data, accessing guidelines, and writing prescriptions. However, practices with 1 or 2 physicians increased their use of health IT for writing prescriptions by 5%, compared with 28% among practices with more than 50 physicians. The gaps are likely because of the greater financial and administrative resources of larger practices and economies of scale. Large practices also may have an advantage in adoption because they have more active physician leaders who are promoting IT and quality improvement, according to the report. The data in the report are from the HSC Community Tracking Study Physician survey, a nationally representative telephone survey of physicians who are involved in direct patient care in the United States. "Larger practices appear to be gaining critical mass in adopting IT for patient care, but the smallest practices, which account for more than half of all practicing physicians, appear to be at risk of being left behind," Joy M. Grossman, senior health researcher at HSC, said in a statement. The report is available online at www.hschange.org/CONTENT/891.

Omnicare Settles Drug Overcharges

Covington, Ky.–based Omnicare, which provides pharmacy services to nursing homes, has agreed to pay the federal government and 43 states $49.5 million to settle claims that the company overcharged Medicaid. The suit was filed by two whistle-blowers, who alleged that from 2000 to 2005, Omnicare was switching patients from cheaper to more costly versions of three drugs—ranitidine, fluoxetine, and buspirone—to inflate profits. In most cases, the company was substituting capsules for tablets or vice versa. Physicians either weren't aware of the switches or were falsely told that the substitution would cost less. The settlement was filed in U.S. District Court for the Northern District of Illinois in Chicago; Omnicare admitted no wrongdoing.

—Alicia Ault

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