FDA Reform, Clinical Trial Design Changes Urged

BY MARY ELLEN SCHNEIDER
New York Bureau

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 the 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.

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 a series of steps over the last 2 years to try to improve the 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 that physicians can quickly see the key information they need to make 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.

However, 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.

Nevertheless, the FDA also should improve its postmarketing surveillance, said panelist Dr. John D. Abramson, a clinical instructor in 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 primarily 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 companies 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, adding that 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." ■