BY DENISE MYSHKO

FDA An Agency in Transition

IN THE PAST YEAR, THE FOOD AND DRUG ADMINISTRATION HAS BUILT SOME MOMENTUM IN SPEEDING DRUG DEVELOPMENT AND ADDRESSING PRODUCT SAFETY. **DESPITE THE PROGRESS MADE IN IMPROVING ITS INTERNAL STRUCTURE**, THE AGENCY IN THE COMING YEAR WILL CONTINUE TO FACE OBSTACLES.

ROBERT DELUCCIA
MacroChem

> A shifting political environment **WILL CHANGE THE THRUST** of what's going on at the FDA.

LAST YEAR, THE FOOD AND DRUG ADMINISTRATION WAS BUSY ISSUING AND LAUNCHING MORE THAN TWO DOZEN GUIDANCES AND INITIATIVES. From stricter enforcement efforts to the formation of task forces to the issuance of new and updated guidelines, the agency made significant progress in modernizing the drug-approval process. The agency beefed up its efforts to improve the safety and effective use of prescription drugs and made strides in addressing the advances in science and medicine that are likely to lead to innovative therapies. (See timeline on page 36 for more information and visit fda.gov for complete details.)

But much work still needs to be done. There looms in the next 12 months a possible battle in Congress about the renewal of PDUFA legislation, as well as continued discussion around the Institute of Medicine's (IOM) report for improving the safety of prescription drugs.

FDA officials say in 2007, the agency will continue work begun in April 2006 when it restructured the Center for Drug Evaluation and Research (CDER). The aim is to create improvements in regulatory and drug-development science and in how the agency evaluates and ensures the safety and efficacy of products. One of the goals of the restructuring was to sustain a multidisciplinary, cross-center approach to drug safety. The agency elevated the Office of Surveillance and Epidemiology (formerly the Office of Drug Safety) to report directly to the office of the center director. The FDA also appointed an associate center director for safety policy and communication.

Experts say the change in Congress, as a result of the 2006 election, will likely have an impact on the FDA, although it is too early to say how extensive the effects will be.

"Companies large and small need to be

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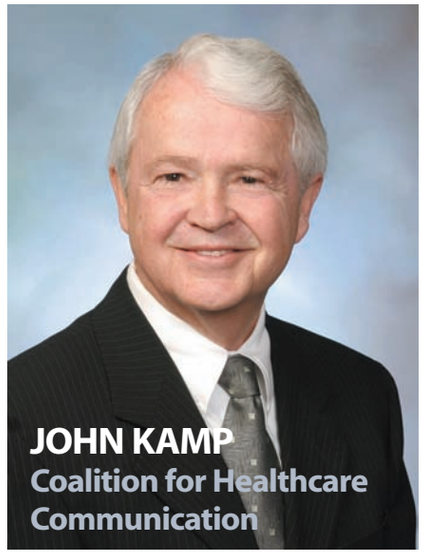


JOHN KAMP
Coalition for Healthcare Communication

ready to face continued scrutiny from the public and media," says Robert J. DeLuccia, president, CEO, and vice chairman of the board at MacroChem Corp. "I am reminded of the early 1990s when the pendulum of industry favor was swinging in a similar adversarial direction."

He warns that larger companies in particular are going to have to pay more attention to how they select and develop new drugs, as well as to their business practices.

"With respect to smaller, development-stage companies, such as MacroChem, there are opportunities for innovation but there are going to be many speed bumps along the way," Mr. DeLuccia says. "There likely will be more scrutiny of clinical trials and more emphasis on ensuring longer term safety for new chemical entities. Contrary to the effort to speed up clinical trials, there will be new pressures that will result in slowing down drug development. One key to future success will be to ensure an appropriate dialogue with the FDA during the drug-development process."

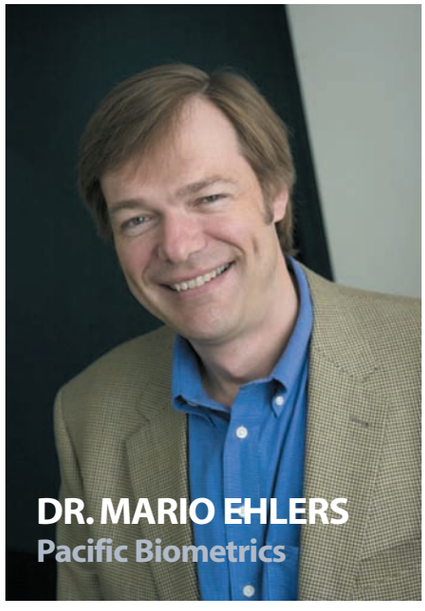
Despite the new challenges, Mr. DeLuccia is optimistic that companies will overcome such obstacles for the benefit of patients, the medical community, and the industry.

For Mario Ehlers, M.D., Ph.D., chief medical officer of Pacific Biometrics Inc., the concern is that the new Congress may be at odds with the current administration, which could stall progress.

"We might be entering a period where changes will not occur for several years until the political climate becomes clearer," he says. "As issues become politically sensitive, the natural reaction is for the FDA to become conservative."

ESTABLISHING AN AGENDA

But there are certain issues that just can't wait until the political climate settles. For instance, the Prescription Drug User Fee Act (PDUFA), which authorizes the FDA to collect user fees, expires in September 2007. Without further legislation, the FDA would be unable to collect user fees. Possible other sources of funding are reportedly being considered.



DR. MARIO EHLERS
Pacific Biometrics

> There is a disconnect between the leadership at the FDA and the rank and file in terms of how to proceed. **THE NEW COMMISSIONER HAS TO RE-ESTABLISH** a clear vision for the future of the agency.

For example, according to a recent article in *The Wall Street Journal*, the FDA is evaluating the possibility of screening television ads from drug companies alongside a separate five-year PDUFA accord. According to the article, companies would pay about $40,000 to $50,000 at the beginning of each year for each TV ad campaign they planned to air that year. The amount could be higher if not enough companies sign up and the agency faces a budget shortfall. The annual target is $6 million in fees, which would double in the first year to create a reserve fund. In return, the agency would try to review TV ads within 45 days.

The higher user fees would fund drug-safety initiatives, as well as add drug-review staff, develop new drug-development guidelines, improve IT systems, and help pay for the FDA's move to a new office building. Both the screening accord and PDUFA require HHS acceptance and approval by Congress.

> The basic rules and guidelines of the **FDA HAVE NOT CHANGED** appreciatively, but the requirements that device manufacturers have to meet are at a higher level.

DOUGLASS SIMPSON
Corgenix Medical

FDA Initiatives in 2006

Jan. 12 — FDA announces Exploratory IND Studies and INDs - Approaches to Complying with CGMP During Phase 1, a guidance to advance the earliest phases of clinical research in the development of innovative medical treatments.

Jan. 18 — FDA unveils a major revision to the format of prescription drug information, commonly called the package insert, to give healthcare professionals clear and concise prescribing information.

Jan. 20 — CDRH launches its Postmarket Transformation Initiative to better protect the public health by allowing the FDA to identify, analyze, and act on problems more quickly, including alerting the public sooner to potential medical-device issues.

Feb. 14 — FDA, NCI, and CMS form the Oncology Biomarker Qualification Initiative (OBQI) to improve the development of cancer therapies and the outcomes for cancer patients through biomarker development and evaluation.

March — OSE begins working with CDER's Quality Management Staff to improve and standardize the process used by safety evaluators in OSE's Division of Drug Risk Evaluation.

March 16 — FDA and C-Path form the Predictive Safety Testing Consortium to share laboratory methods to predict the safety of new treatments before they are tested in humans.

April — The agency elevated the Office of Surveillance and Epidemiology (formerly the Office of Drug Safety) to report to the center director.

April 18 — FDA creates a new position within CDER to provide oversight of drug-safety issues and policies and manage the staff who disseminate safety information through the FDA's Website.

April 19 — FDA adopts SNOMED as the standard computerized medical vocabulary system to be used to electronically code important terms in the highlights section of prescription drug labeling.

May 5 — CDER launches an internal assessment of its advisory committee meeting system to establish best practices.

May 22 — FDA launches the Medical Device Innovation Initiative to make new medical devices available more quickly for patients and expand the efforts of CDRH.

June 14 — FDA and the ISMP launch an educational campaign to reduce the number of common but preventable sources of medication mix-ups and mistakes caused by the use of unclear medical abbreviations.

In fiscal year 2007, the FDA is expected to receive upwards of $300 million in fees. The proposed agreement would increase the fees received by about one-third in fiscal 2008.

The use of the additional fees on safety evaluation falls in line with another one of the agency's priorities for this year, which is evaluating the long-term safety of products postapproval.

"The ability to monitor or to institute effective surveillance of approved drugs and the ability to take effective action should there be safety concerns has not been as tight as it should have been," Dr. Ehlers says. "Postapproval undertakings from companies to perform studies on long-term safety and Phase IV studies are often not met or are delayed. That has to improve." (See related article on page 20.)

The U.S. public, as well as Congress, are nervous about drug safety, says John Kamp, executive director of the Coalition for Healthcare Communication.

"There was an incorrect assumption by most people that all drugs, if approved by the FDA, were safe," he says. "We no longer have that illusion in this country. The question becomes: what is the continuing role of the FDA to ensure that drugs are as safe as possible?"

To address this need for postmarketing surveillance, CDER has formed a Process Improvement Team (PIT) that works with the National Institutes of Health's Office of Science Education (OSE) to develop standards for postmarketing safety. This team is documenting the roles and responsibilities for the Office of New Drugs (OND) and the OSE and is working closely with CDER to develop an overall, integrated system for tracking activities.

Dr. Ehlers says, however, this focus on safety could threaten the positive initiatives implemented by the FDA to address modernizing the drug-approval process.

"With so much pressure being put on regulators to tighten safety, it may force them into a conservative position," he says, "There may be a backslide on long-overdue initiatives to modernize the drug-development process. There is almost a disconnect between the leadership at the FDA and the rank and file within the FDA in terms of how to proceed. The new commissioner has to re-establish a clear vision for the future of the FDA."

Some experts say meeting the dual need for bringing safer drugs to the market faster will require more funding for the regulatory agency.

"The FDA has responsibility for almost 20% of the American economy, and it's running on a shoe string," Mr. Kamp says. "There hasn't been a significant increase in the agency's budget in almost 20 years."

PAY IT FORWARD

Some say there is broad recognition in Congress that if the agency is to expand its postmarketing responsibilities it will require more funding

Mr. Kamp says the IOM report is likely to be a starting point for discussions on Capitol Hill and a template for how the agency should act.

In September 2006, IOM released a report on improving the safety of prescription drugs. The report finds that there is a lack of clear regulatory authority, chronic underfunding, organizational problems, and a scarcity of postapproval data about drug risks and benefits.

The report contains 25 recommendations that cover the agency's resources, authorities, processes, science, and organizational culture.

There has been a great deal of pressure on the agency to address product safety in all areas it regulates, experts say.

For example, in November 2006, the FDA announced its plan for strengthening the way it monitors the safety of medical devices. And in 2005, the FDA's Center for Devices and Radiological Health (CDRH) completed a

June 26 — FDA announces the Human Subject Protection and Bioresearch Monitoring (HSP BIMO) Initiative to facilitate the modernization of the regulation of clinical trials and strengthen its oversight and protection of patients in trials.

July 20 — FDA creates a new position to oversee emerging and pandemic threat preparedness in CBER.

July 24 — FDA announces a plan to strengthen advisory committee processes, including providing greater clarity and transparency in the relationships that could present the appearance of conflicts of interest.

Aug. 9 — FDA forms a Nanotechnology Task Force charged with determining regulatory approaches that encourage the development of innovative, safe, and effective products that use nanotechnology materials.

Aug. 23 — FDA proposes the Electronic Drug Registration and Listing System to manage drug information more efficiently by automating the process by which drug firms register themselves and list their products with FDA.

Aug. 30 — FDA forms a multidisciplinary task force on human cell and tissue safety to assess the effectiveness of new tissue regulations, which went into effect in 2005.

Sept. 22 — IOM releases a report on improving the safety of drugs. The report contains 25 recommendations that cover the agency's resources, authorities, processes, science, and organizational culture.

Sept. 29 — FDA issues a final guidance on Quality Systems Approaches to Pharmaceutical CGMP Regulations, which provides manufacturers with the ability to make technological improvements more readily, with appropriate regulatory oversight.

Nov. 9 — FDA releases an action plan to strengthen the monitoring of medical devices after they reach the marketplace, including the creation of a cross-cutting organizational structure within the CDRH to better integrate premarket, postmarket, and enforcement efforts.

comprehensive assessment of the tools used to monitor the safety of medical devices after the agency approves them for marketing.

Douglass T. Simpson, president and CEO of Corgenix Medical Corp., says the agency has made tremendous strides to communicate better with device manufacturers, but regulators are asking for more data and better analysis.

"We have to have more clinical data," Mr. Simpson says. "The statistical information that we provide has to be much stronger, and there has to be more sophisticated statistical analysis."

Within the biologics arena, in August 2006, the FDA formed the Human Tissue Task Force (HTTF), which will be led by senior FDA officials from within the Center for Biologics Evaluation and Research (CBER) and the Office of Regulatory Affairs (ORA). The multidisciplinary team was established as part of the agency's efforts to strengthen its risk-based system for regulating human cells and tissue.

Another initiative is the Predictive Safety Testing Consortium, which was formed in March 2006 by the FDA and The Critical Path Institute (C-Path).

The consortium is between C-Path and five of America's largest pharmaceutical companies to share internally developed laboratory methods to predict the safety of new treatments before they are tested in humans. The goal of the consortium is to enable companies to share knowledge and resources and to determine which of the lab tests that they have developed individually should be recommended by the FDA.

At the same time, the agency also is moving forward with its Critical Path initiative to modernize the way it reviews new products, and there have been many efforts along this line as well as its initiatives to address new science. ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

Experts on this topic

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