BY DENISE MYSHKO

THE FDA

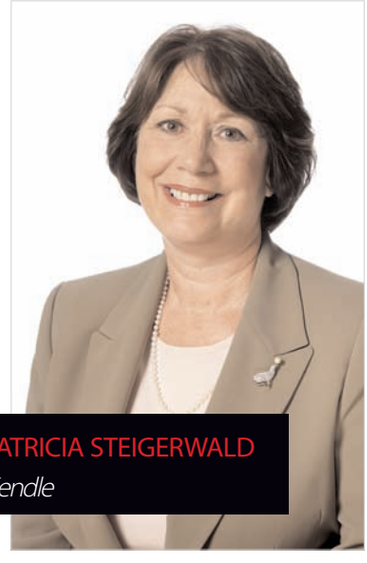
Tightening the Regulatory Reins

THE NEW LAW PASSED IN SEPTEMBER 2007 is expected to have an immediate and significant impact on the Food and Drug Administration's authority over manufacturing and marketing.

Right off the bat, pharmaceutical manufacturers and marketers of prescription drugs will face tougher regulations in 2008. On Sept. 27, 2007, President George W. Bush signed into law H.R. 3580, the Food and Drug Administration Amendments Act of 2007 (FDAAA). Among the many components of the law, the Prescription Drug User Fee Act (PDUFA) and the Medical Device User Fee and Modernization Act (MDUFMA) have been reauthorized and expanded.

The law, which is effective fiscal year 2008 to fiscal year 2012, enhances the FDA's authority to regulate marketed drugs, establishes a surveillance system to monitor and assess the safety profile of drugs on the market, reauthorizes and modifies programs that evaluate the use of drugs and devices by children, and expands federal databases that track information on certain clinical trials.

The new law also alters the process for submitting petitions to the agency by the public regarding certain drug applications, and it modifies procedures relating to that petition process.



PATRICIA STEIGERWALD
Kendle

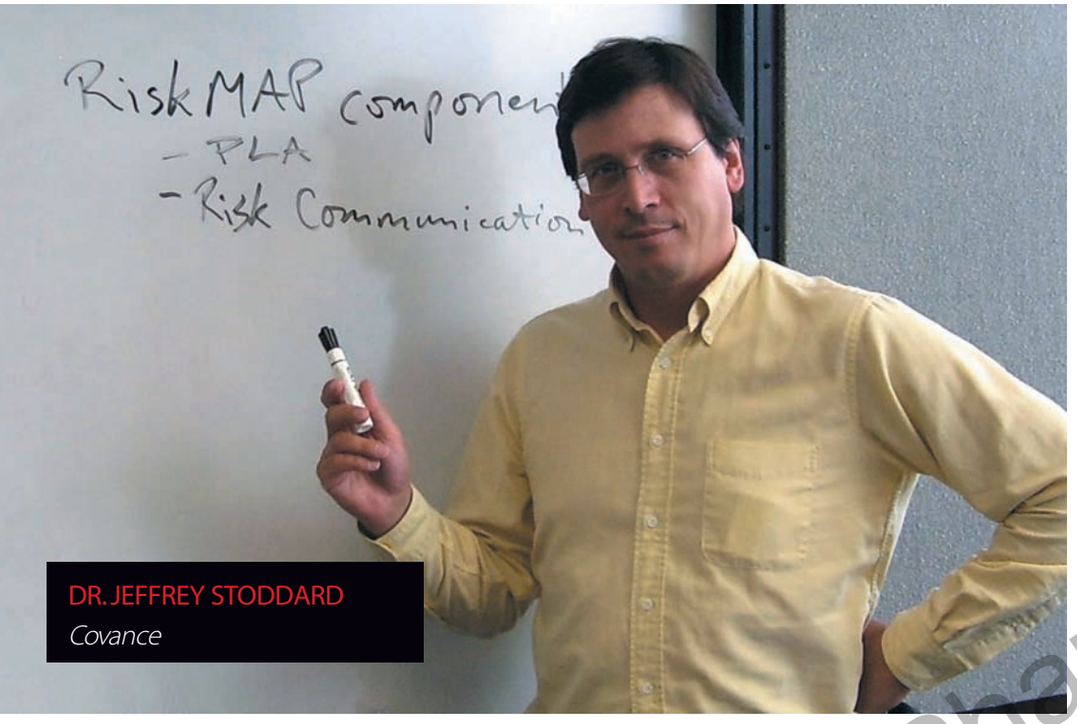
BIOPHARMACEUTICAL COMPANIES WILL NEED TO CONSIDER having a postapproval plan defined and ready to submit along with IND data.

"The FDAAA is the most comprehensive reform of prescription-drug regulation in decades," says Jeffrey J. Stoddard, M.D., VP of medical and scientific affairs, risk management and postmarketing programs, at Covance Inc. "There are few areas of drug development that are not touched by this reauthorization — many areas have been overhauled — and the new authority granted to the FDA under this legislation is noteworthy."

He says the impact of this legislation on the pharma/biotech industry will be substantial in many ways.

"Most notable among the gamut of affected areas will be pediatric research, labeling rules, postmarketing surveillance requirements, risk evaluation and mitigation, and direct-to-consumer advertising and marketing," Dr. Stoddard says.

Specifically, Dr. Stoddard says, the impact of these new provisions will include but not be limited to: increased costs of drug development, particularly with respect to increased post-approval expenditures; more stringent requirements to obtain patent extensions for approved products based on pediatric trials; increased



DR. JEFFREY STODDARD
Covance

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requirements for safety assessment, pharmacovigilance, risk evaluation, and risk mitigation/minimization; broadened access to clinical-trial data by the public; constrained ability to make marketing claims resulting from more restrictive labeling and tighter review of promotion; and tighter regulation of DTC messaging.

"In all likelihood, the FDAAA will translate into shifting of resources away from traditional 'powerhouse' departments of clinical development and marketing/commercialization toward drug safety, pharmacovigilance, risk management, epidemiology, medical affairs, and other key stakeholders engaged in postmarketing safety surveillance and research," he says. "Regulatory affairs and legal departments in pharma and biotech are likely also to swell."

Barton Cobert, M.D., VP of global regulatory initiatives and pharmacovigilance at Medidata Solutions Worldwide, says even though the impact will be significant it will be manageable.

"There will be more information and data available online," he says. "Companies will have to be more transparent, especially with regard to safety matters. Some of the safety decisions on which trials run and how labeling is written will now be controlled much more forcefully by the FDA. This will raise costs to the companies in the short run but may, in the long run, allow safety problems to be discovered earlier, thus decreasing patient morbidity and mortality as well as corporate pain and costly withdrawals and litigation."

Dr. Cobert says the regulatory world will become more complex, and more bureaucratic requirements will result.

"The net effect will probably slow new approvals down a bit and make approvals, when they do occur, somewhat more contin-

Experts

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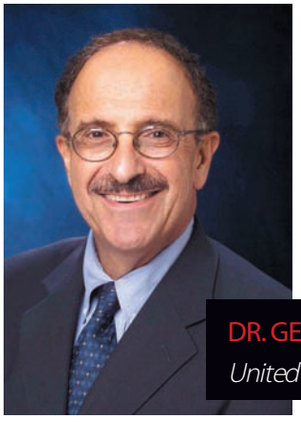

DR. GERALD FAICH
United BioSource

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DR. BARTON COBERT
Medidata Solutions

COMPANIES WILL NEED TO MAKE SIGNIFICANT INTERNAL PREPARATIONS to supply needed data to the FDA and perform more work before and after marketing.

gent on the safety data that arise in the first few months or years after marketing begins," he says. "There will be more accountability and scrutiny on safety."

In 2008, Dr. Cobert says, much of the FDA's resources will be diverted from current tasks to get this law's requirements in place.

"The FDA also has a mandate dating from 2006 that it will begin tighter regulation of OTC products, which is due to start in December 2007," he says. "This will probably impact those companies involved to a significant degree. The FDA will start setting up additional public-private partnerships and hiring new people in 2008."

Nagaraja Srivatsan, VP, head of life sciences, North America, at Cognizant Technology Solutions Corp., says this effort to augment FDA teams could result in significant reduction in evaluation cycle times, which will directly aid the pharmaceutical and biotech industry.

"Revenue generated from the act, specifically PDUFA, will be used to increase regulatory supervision, and hopefully the approval process will be shortened," he says.

Additionally, with further advantage now attached to pediatric research, some companies might undertake research in this field and may come up with more products catering to the needs of this population, Mr. Srivatsan says.

"There is greater effort by pharmaceutical companies to gain pediatric and/or data exclusivity to secure revenue from drugs going off-patent in the near future," he says.

IMPLICATIONS FOR PHARMA

Dr. Stoddard says careful observation and tracking in the coming year of approvals, including time to approval and rate of approvals, will be telling.

"It is very likely that in the coming year new product approvals may well be relatively few and far between as the new regulatory environment takes hold," he says. "New approvals probably will not only occur at lower rates than they have in the past, but when they do transpire, they are likely to be substantially more encumbered. In essence, we predict increased difficulty bringing products to market, slower and more cautious regulatory reviews, more restrictive labeling, tighter oversight once approved, and less fanfare and flash for newly launched products once approval occurs."

In short, he says, there will be more stringent and more continuous regulatory reviews, making product life-cycle management substantially more complex.

Gerald A. Faich, M.D., senior VP, epidemiology and risk management, at United BioSource Corp., agrees that under the new law there will be an expansion of the FDA's scrutiny of safety at time of approval and afterward.

"This means that sponsors will have to be ready to provide risk management plans, risk minimization programs, and postmarketing safety studies to avoid approval delays," he says. "These plans should be accounted for and pilot tested a year or two before submission. No doubt there will be some delayed approvals while safety data are re-analyzed and risk management programs are requested."

To avoid potential stumbling blocks, Dr. Faich says manufacturers must try to get early communication from the FDA about what postapproval requirements may be imposed.

Patricia A. Steigerwald, VP, global late phase, at Kendle, says many companies will be re-evaluating their portfolios to determine what additional studies should be included in their development programs.

"The immediate impact of this legislation will be an increase in the volume of post-approval studies," she says. "Companies with near-term approvals may expect additional requests for Phase IV programs, including studies with specific safety endpoints, registries, or expanded risk minimization programs.

"Long term, the regulation is likely to lead to more registries designed to collect drug class data that will facilitate collaboration between biopharmaceutical companies, spread the burden of continued study, and provide a vehicle to use Medicare and Medicaid data, ultimately demonstrating the effectiveness and safety among and between a large demography of patients," Ms. Steigerwald says.

Dr. Cobert says companies will need to make significant internal preparations to supply needed data to the FDA and should be prepared to perform more work before and after marketing. He outlined several areas that most companies will need to review in light of the new regulation.

First, he says, device companies now need to be able to track their individual products to the lot and serial number level and there will be more self inspections and postmarketing surveillance.

Next, more clinical studies will be posted on a Website registry, and more adverse event and side-effect information will be made available in these registries. A database for generic drug adverse events will be set up as well.