FDA User Fee Law Poised for Passage in Congress but Not Without Stirring Up Controversy

By Joel Finkelstein

T he fourth iteration of the 1992 law that allows the U.S. Food and Drug Administration to levy user fees on drug companies contains several reforms that could create a major change in how the agency monitors the safety of new drugs after they enter the market.

Lawmakers are using reauthorization of the Prescription Drug User Fee Act (PDUFA) to overhaul the agency’s authorities and responsibilities for ensuring drug safety. The legislation would allow the FDA to collect $393 million in fees annually from the industry starting in 2008. That is up from $305 million this year and includes another $30 million to fund the agency’s postmarketing drug safety programs. The bill passed the Senate on May 9. A companion bill has been introduced in the House.

“The resources and additional staffing made possible by the fees charged by the FDA have enabled the agency to review new medicines more efficiently, while maintaining its stringent safety and efficacy standards,” said Billy Tauzin, president of Pharmaceutical Research and Manufacturers of America, the drug industry trade group. “The significant increases in user fees will provide the FDA the resources necessary to improve and modernize its already strong drug safety monitoring system.”

According to FDA recommendations to Congress, higher user fees will enable the agency to hire 82 new employees devoted to postapproval safety efforts. However, the bill passed by the Senate, in a 93–1 vote, actually contains an even bigger increase in user fees than the FDA requested.

In addition to increasing user fees, the Senate’s measure would require the FDA to modernize its postmarketing surveillance procedures and allow the agency to levy fines against drug companies for misleading direct-to-consumer advertising.

“This is going to be the biggest set of changes in postmarket drug regulation since at least 1962,” Mark McClellan, M.D., former director of the FDA and now a fellow at the American Enterprise Institute, said at a recent forum on drug safety. “FDA will be doing no less than entering a new era of postmarket drug regulation.”

Many of these reforms have come about in light of high profile safety problems, such as the heart risks associated with cyclooxygenase 2 (COX2) inhibitors that were not identified until after the drugs had been widely prescribed. The current system relies on physicians or patients to voluntarily report potential adverse events to drug companies, which in turn report them to the FDA.

“This goes into a database that collects several hundred thousand—and growing—adverse event reports per year. … It’s very important for helping the FDA identify problems but it is not population based. It is not systematic. It doesn’t capture anywhere near all of the adverse events out there,” McClellan said.

The Senate legislation would give the FDA the resources to modernize its electronic systems and software. It would also give the agency access to both public and private databases to build a more complete picture of possible safety problems. According to one analysis, if the FDA had had such an active surveillance system in place when Vioxx (rofecoxib) went on the market, it would have taken months instead of years to pick up a safety signal, McClellan said.

On the Senate floor, lawmakers added an amendment that would give the FDA some new authority over drug ads. It would create a voluntary user fee program for drug companies to submit their ads for staff review before airing them, thereby avoiding FDA sanctions later. If an ad is not approved by the FDA, the agency can fine drug companies for running false or misleading claims. The bill would allow the agency to charge companies $150,000 for the first offense and $300,000 for a second offense. The amendment negated a provision that would have allowed the FDA to place a moratorium on advertising for some new drugs.

“While it’s important FDA has the power to hold a drug company’s feet to the fire when it comes to misleading ads, we’d urge the House to support restrictions on massive ad campaigns for those new drugs with early danger indications,” said Bill Vaughan, a senior policy advisor for the Consumers Union. “When a company can make more than a million dollars a day in drug sales, a $150,000 fine for running a misleading advertisement won’t have much impact.”

The bill as passed by the Senate contained several other provisions: allowing
the FDA to impose new fines on companies that don’t comply with postmarketing study commitments, requiring companies to submit many of their ongoing trials to a public registry, promoting the status of the Office of Drug Safety, creating a foundation for the study of drug safety, and requiring public disclosure of conflicts of interest within FDA advisory committees. The Senate also passed an amendment that would allow drug importation from other countries; however, a later amendment effectively neutralized it by requiring that the Secretary of Health and Human Services certify the safety of those imported drugs.

A companion House bill was introduced in March but as of press time had yet to be brought before the committee of jurisdiction. While similar to the Senate measure, that bill would require drug companies to list all, not just some, of their studies in the clinical trial registry and would allow the FDA to impose a 3-year moratorium on advertising for drugs with potential safety issues.

“We need only look to recent high-profile postmarket safety problems, like Vioxx, to know that our drug safety system is in desperate need of some serious improvements,” Rep. Henry Waxman, D-Calif., one of the sponsors of the bill, said in a statement.

“We also cannot continue to allow drug companies to cherry-pick and distort the clinical trial information on which physicians rely about which drugs work and the risk those drugs pose. The Enzi–Kennedy bill is a significant step forward addressing these concerns. Our legislation goes even further in giving FDA the full complement of tools it needs to protect our citizens from unsafe products.”

If and when that bill passes the House, it will have to be consolidated with the Senate’s version before it can be sent on to the president for signing.

The Means, But Not the Will?

Many of the new authorities that the legislation proposes giving the FDA are welcome, but that is no guarantee that the agency will use them effectively, said Curt Furberg, M.D., a professor at Wake Forest University School of Medicine and a member of the FDA Drug Safety and Risk Management Advisory Committee.

“The FDA does not have a good track record. I’m not optimistic,” he said. He cited a recent report from the Institute of Medicine finding that drug companies have failed to complete more than 1,200 postapproval studies, often required as part of approval, without the FDA imposing any consequences.

“The FDA loses interest in a drug after it is approved. They just don’t pay much attention to it,” he said.

The FDA must be willing to take drug companies to task for their failure to comply with advisory committee requests, and that won’t happen until the agency is no longer beholden to drug companies, he said. “You don’t bite the hand that feeds you,” he said.

That sentiment has gained some support among a few Democrats in the House, who have urged their fellow lawmakers to do away with the user fee or at least scale it back. Such a move has been advocated by four former FDA commissioners and, in an open letter to Congress, by a long list of prominent researchers, including Furberg.

First Speed, Now Safety

When PDUFA was originally enacted in 1992, it required the FDA to negotiate with drug companies to decide how the new funding would be spent. The industry wanted it spent exclusively on speeding approvals, he said. “For 10 years, not a penny [of the user fees] was spent on safety,” Furberg said. Nowhere else in government do user fees come with strings attached, he added.

Although he admits that the user fees have been instrumental in enabling the FDA to hire more staff and more efficiently process drug approvals, the money should come without conditions, such as allowing drug companies to negotiate how the money is distributed and setting prescribed response times.

Establishing the safety of drugs must be as important as establishing their effectiveness. By making risk evaluation and mitigation strategies mandatory, this legislation takes an important step in that direction but doesn’t go far enough, Furberg said.

However, some experts think the legislation goes too far by allowing the FDA to invade upon the practice of medicine.

“Ultimately, we need a more robust system for the more rapid accumulation of postmarket information that encourages collaboration among providers, payers, and product developers around issues of drug safety. The expansion of risk management tools is an imprecise solution to the wrong problem,” Scott Gottlieb, M.D., a fellow with the American Enterprise Institute and a former deputy commissioner with the FDA wrote in the May–June issue of Health Affairs. “When it comes to improving on drug safety, our challenge is not to directly manage the way drugs are used but to seek out better tools for how they are evaluated.”

In the same issue, the bill’s authors, Sens. Michael Enzi (R-Wyo.) and Edward Kennedy (D-Mass.), argue that managing the use of drugs may not be ideal, but it is still necessary.

“If restrictions on distribution or use allow a drug to remain on the market, the limits on patients’ access and the practice of medicine (which we acknowledge can be burdensome and undermine the ability of doctors and patients to make completely individualized risk–benefit decisions) are acceptable.”

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