



Bush Budget Combats Bioterrorism, Promotes Drug Safety

Jill Wechsler

The White House wants to give FDA more resources to increase plant inspections and speed generics to market, but it seeks a big hike in user fees to pay for it.

Although the Bush administration's \$2 trillion federal budget proposal for fiscal year 2003 reduces spending on domestic programs, bioterrorism preparedness initiatives escaped the ax. The result is more funding for biomedical research by the National Institutes of Health (NIH) and increased efforts to spur development and approval of new drugs and vaccines by FDA.

The White House proposes to increase support for FDA by \$123 million for a total budget of \$1.7 billion next year. That plan includes \$450 million for the Center for Drug Evaluation and Research (CDER) and \$200 million for the Center for Biologics, Evaluation, and Research (CBER). However, those totals assume that Congress will approve a significant increase in manufacturer user fees.

An important feature of the budget for FDA is that it includes \$29 million to fund staff pay increases. Before 2002, the agency had to pay mandated cost-of-living adjustments and raises out of its general appropriation, which translated into an actual reduction in resources available for program operations. CDER will gain \$7 million and CBER, \$3 million to fund pay hikes so that neither office will have to cut staffers, as has been the case in the past.

Attack on terrorism

The FDA budget proposal includes \$160 million to support antibioterrorism activities, building on the \$150 million in extra funds provided to FDA last year as part of a Department of Defense counterterrorism 2002 budget supplemental. The budget request for next year would continue initiatives launched under this expanded counterterrorism program. Although most of this money would support a huge expansion in food import inspections, it also would provide \$54 million to encourage the development and production of

new vaccines, drugs, and diagnostic tests for public-health emergencies. Funds earmarked to overcome bioterrorism threats would support a significant expansion of CBER staffers involved in vaccine development and blood screening and processing.

To oversee all these initiatives, FDA is developing a more formal approach to address bioterrorism concerns. Andrea Meyerhoff leads this effort as director of counterterrorism in the office of the FDA commissioner and also is FDA's point of contact for other government agencies as well as for FDA centers. She seeks to identify medical products in the development pipeline that might address bioterrorism concerns. This information is necessary for early access to unapproved therapies that might be needed during emergencies. Meyerhoff also will help manufacturers who are unfamiliar with FDA policies but seek to develop new therapies or diagnostic technologies with public health benefits.

At a February program about bioterrorism sponsored by the Food and Drug Law Institute, Meyerhoff noted that one challenge for FDA is maintaining a balance between speeding new technologies to market while ensuring the safety and efficacy of drugs and medical products. FDA must encourage private industry to develop new products while remaining a strong regulator, commented FDA general counsel Dan Troy. He acknowledged a tension between FDA's efforts to ensure the safety and efficacy of new vaccines and therapies and to help the government purchase these products at low prices for the national pharmaceutical stockpile.

More inspections

Because of increased concern about the safety and quality of imports as well as a desire to achieve more timely inspections of regulated products, the FDA budget would support a noticeable expansion in the agency's field force. Although additional bioterrorism funding would increase inspections of domestic food processors and food imports, FDA also would gain about \$10 million to conduct additional inspections of US and for-

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eign manufacturers of drugs and medical products. This process would include significant increases in good manufacturing practices (GMP) inspections of drug manufacturers. Domestic GMP inspections for drugs are slated to jump from 949 in 2002 to 1450 in 2003. GMP inspections for biologics, including some devices, will increase from 77 to 90. GMP inspections of foreign drugs manufacturers will skyrocket from 111 to 240. The expansion in foreign GMP inspections reflects an effort to conduct significantly more reviews of overseas manufacturers of active pharmaceutical ingredients (APIs).

Other proposed increases in inspections include

- Domestic preapproval inspections for drugs (from 190 in 2002 to 360 in 2003)
- Domestic preapproval inspections for generics (165 to 170)
- Foreign preapproval inspections for drugs (199 to 280)
- Foreign preapproval inspections for generics (80 to 100)

FDA gets new deputy commissioner

After months of stalemate between the White House and Senate Democrats over the appointment of a new commissioner for FDA, Health and Human Services secretary Tommy Thompson took a shortcut and named a new deputy commissioner to head the agency temporarily. Thompson's appointment of Lester Crawford on 26 February allowed the new deputy to start immediately without having to undergo a lengthy Senate confirmation process.

Crawford had been considered a top candidate for the commissioner's job. As a food-safety expert and veterinarian, he reflected Thompson's interest in highlighting FDA's role in ensuring the quality and security of the nation's food supply. Crawford most recently headed Virginia Tech's Center for Food and Nutrition Policy. He also served in the Department of Agriculture and directed FDA's Center for Veterinary Medicine in the 1980s. However, consumer advocates objected to his appointment because of his strong ties to industry; Crawford also has held

positions at the National Food Processors Association and at an agricultural chemical firm. Moreover, Crawford is not an MD, the usual credential for the FDA commissioner.

With Crawford coming on board at FDA, Bern Schwetz can return to his job as the agency's senior advisor for science after being FDA's acting principal deputy commissioner for more than a year. Thompson and the White House insist that they are actively looking for a new permanent FDA commissioner; however, this appointment gives Crawford an opportunity to audition for the job. The Bush administration recently rejected Alastair Wood of Vanderbilt University, apparently because of strong objections from pharmaceutical manufacturers. Senate Democrats have nixed Crawford and other contenders as too pro-industry. If the impasse continues, Crawford could remain as the head of FDA for some time.

- Foreign inspections for biologics (91 to 95).
- In addition, added funding to prevent the spread of bovine spongiform encephalopathy (BSE) through US livestock would underwrite a major increase in inspections of animal feed and drug producers as well as food imports. BSE-

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related inspections will reach nearly 2700 this year, an increase from about 900 in 2001. FDA also has greatly expanded contracts with state agencies to inspect feed manufacturers and feed lots.

Support for generics

The boost in generic drug inspections would be funded partly by a \$4.6 million increase for improving the process for re-

viewing generic drug applications. This increase would bring total outlays for generic drug oversight to \$46 million. The budget would enable CDER's Office of Generic Drugs (OGD) to add nearly 30 reviewers and will support more timely preapproval inspections by FDA's field force. OGD's goal is to review 75% of abbreviated new drug applications (ANDAs) within six months (up from 55% in that time frame in 2001). The OGD budget also would underwrite more inspections of bulk drug substances and finished generic drug products imported from overseas.

Enhancing safe drug use

The budget plan also offers added resources for initiatives to ensure patient safety and reduce adverse events related to drugs and medical products. In one proposal, FDA will gain \$5 million to improve its adverse event monitoring system, develop a policy for bar coding pharmaceutical packages, and support FDA involvement in government-wide patient safety initiatives. These funds would support electronic data entry initiatives designed to enhance CDER's adverse event reporting system, thereby encouraging more reporting by drug manufacturers. Another proposal is to expand the number of hospitals reporting errors involving medical devices to FDA (the MeDSun program) as well as extend the program to include pharmaceuticals.

Related to these proposals are efforts to expand oversight of patients participating in clinical research. Instead of furthering last year's advancements in research-subject safety, the 2003 budget generally maintains current levels of bioresearch monitoring (BIMO) inspections of clinical-study sites. BIMO inspections for drugs would remain at 750 (up from 540 in 2001), at 100 for foreign drugs (up from 52 in 2001), and at 190 for biologics (up from 88 in 2001). Patient-safety initiatives also will cover some of the cost of FDA's participation in the International Conference on Harmonization and in global pharmacovigilance efforts.

User fees skyrocket

Proposed funding increases for FDA reflect plans to significantly increase user fees collected from manufacturers under

the Prescription Drug User Fee Act (PDUFA). The Bush budget called for a whopping jump to \$272 million in fees from industry next year. But last month, manufacturers and FDA officials finalized terms for PDUFA 3 following extensive negotiations. The agreement calls for boosting user fees next year to \$223 million, a \$91 million increase from the \$133 million collected in 2001. The total would

rise to \$260 million by 2007. The fee hike would apply to payments for filing applications as well as FDA oversight of products and facilities to distribute the burden between new and existing therapies.

FDA insists that it needs more money to balance the current mismatch of workload and revenues, according to Jeff Weber, FDA's acting senior associate commissioner for management and systems. The

agency has seen a big drop in fee revenues in recent years because sponsors have filed fewer New Drug Applications (NDAs) with the agency than anticipated. Moreover, Weber notes that 35% of applications have been qualifying for waivers from fee payments, compared with 18% originally projected. Some relief may come from recently approved legislation to renew the pediatric drug labeling program. That bill authorized application fees for pediatric supplements, which should reduce the number of waivers and generate nearly \$10 million in fee revenues this year.

FDA wants more user fee revenues to support risk management and postmarketing safety efforts, and manufacturers have agreed to this initiative. The PDUFA 3 plan calls for doubling the size of CDER's Office of Drug Safety (ODS) over five years, from about 80 to 160 staffers. This staff increase would enable the agency to boost oversight of safety and risk issues during the peri-approval period (between pre- and post-approval), which is defined as two years for a routine drug and three years for priority therapies. ODS also would be able to evaluate risk management plans that sponsors will have the option of submitting with NDAs for those therapies that raise specific safety concerns.

Other key provisions in the FDA-industry PDUFA 3 agreement include:

- continuation of current goals and procedures governing application reviews for new drugs and biologics as well as investment in new FDA information technology
- a new program allowing biotech manufacturers to request that CBER bring in a paid outside specialist to provide expertise on clinical trial design for innovative therapies
- allocation of some user fee revenues for the FDA commissioner to examine why application approval times vary between CDER and CBER and among review divisions of each center
- support for pilot testing a cumulative marketing application review concept that involves submission of NDA modules instead of delaying review until the entire application is complete
- early notification to manufacturers about deficiencies in applications following FDA's initial review of a new filing.

Now that FDA and industry have finalized the PDUFA 3 agreement, Congress is under pressure to reauthorize the user fee program before summer. PDUFA 2 expires 30 September, but FDA must warn staff of possible layoffs if the agreement is not reauthorized by 1 August. Unlike previous years, FDA has used all its user fee reserves and has no funding cushion. Continued uncertainty about the long-term fate of the program may prompt talented scientists to leave the agency for lucrative jobs in industry.

Budget winners and losers

With the Bush administration heavily promoting biomedical research to combat bioterrorism, it's no surprise that NIH is slated for another big funding boost. NIH funding could grow to \$27.3 billion, an increase of nearly \$4 billion, fulfilling promises by Congress and the White House to double the agency's budget in five years. Cancer research gets a big boost, as does R&D related to AIDS. The total includes \$1.75 billion to counter bioter-

rorism, an appropriation that would support a wide range of initiatives such as genomic sequencing of dangerous pathogens and construction of and improvements in laboratories to conduct bioterrorism-related research.

At the same time, Health and Human Services' (HHS) Agency for Healthcare Research and Quality (AHRQ) faces a \$50 million budget cut down to \$251 million. Although funding continues for several patient-safety initiatives, AHRQ will have much less money to fund outside researchers studying health quality and cost-effectiveness issues.

The Centers for Disease Control and Prevention (CDC) faces a squeeze on resources for a number of prevention and disease control programs. The White House said that it only looks like CDC funding is getting cut when it's compared with the agency's big increase last year for rebuilding the pharmaceutical stockpile and investing in antiterrorism facilities and infrastructure. CDC does not need quite so much money for those programs

this year, although it will receive nearly \$300 million to update and maintain the National Pharmaceutical Stockpile.

AIDS treatment funding also remains fairly flat as the Bush administration rules out a significant expansion in the Ryan White AIDS drug assistance program.

Congress now is taking its usual swipe at the administration's spending plan. AIDS activists are protesting cuts in HIV prevention programs, and AHRQ supporters are lobbying for a 30% increase in that agency's budget as opposed to a similar cut. Some policymakers are complaining that the continued boost in NIH funding deprives other agencies of a fair share of federal research spending. Double-digit increases in the NIH budget may be a thing of the past. **PT**