



POLITICS

Crawford Named FDA Commissioner

In moving quickly to name a permanent commissioner for the US Food and Drug Administration (Rockville, MD, www.fda.gov), the Bush administration took a relatively easy path to filling the job by naming long-time Acting Commissioner Lester Crawford to the post. The nomination was viewed as a just reward for Crawford's four years of service as acting and deputy FDA commissioner. Crawford ran FDA for more than half of Bush's first term, a period filled with controversies over drug safety, importing, pricing, and vaccine shortages.

Pharmaceutical manufacturers expressed support for the nomination, pleased primarily at the prospect of filling the void created by years of uncon-

firmed FDA leadership. Crawford has been supportive of new drug development initiatives and efficient application approval processes, and is not likely to shake up the agency. He also has no ties to drug companies, a main requirement for Senate Democrats. A veterinarian with a doctorate in pharmacology, Crawford lacks the MD credential held by most of his predecessors and is regarded as having more expertise in food safety and animal medicine than in drugs and medical products for humans.

Although praised in general, Crawford's appointment raised protests. Public-interest consumer groups complained that he has been slow to respond to escalating concerns about safety issues related to painkillers, antidepressants, and dietary

supplements. FDA's delay in approving the "Plan B" (Barr Pharmaceuticals, Woodcliff Lake, NJ) emergency contraceptive pill, allegedly because of political pressure from the Bush administration, remains a bone of contention. Senate Republicans promised speedy confirmation hearings, which may be more interesting than usual; Crawford can't claim that he's new to Washington and thus unable to answer what are sure to be a host of tough questions about drug importing and safety.

The administration moved to defuse such criticisms by announcing new programs to enhance FDA's regulation of drug safety (see "FDA Retains Control over Drug Safety Monitoring").

—Jill Wechsler

NEWS & ANALYSIS

FDA Retains Control over Drug Safety Monitoring

The Bush administration has decided to leave drug safety oversight in the hands of the Food and Drug Administration instead of creating a totally independent panel similar to those that monitor highway and airline accidents. One significant change, however, is that a new panel and "Drug Watch" Web site will inform health professionals and the public of drug safety concerns as soon as they arise instead of waiting until the agency and manufacturer agree on needed labeling changes. FDA officials consider this a significant change, but members of Congress and patient advocates continue to complain that the new program lacks teeth and sufficient independence.

Health and Human Services (HHS) secretary Mike Leavitt rolled out the first elements in this overhaul of FDA's drug safety program in February with a cursory description of two new programs that aim

to create a "new culture of openness and enhanced independence" at the agency. FDA is establishing a Drug Safety Oversight Board of experts from FDA centers, HHS, and other government agencies that will examine and recommend disclosures about drug safety information. The panel will be appointed by the FDA commissioner, but housed within the Center for Drug Evaluation and Research, an arrangement that some critics consider tantamount to letting the fox keep track of the hen house. The board also will resolve internal disagreements on safety issues, assess the need for high-risk drugs to carry MedGuides (*i.e.*, printed prescription drug information distributed to patients with their prescriptions) and weigh the need for additional drug safety information sheets for healthcare professionals and patients.

One of the board's main tasks will be to identify information that should be posted on FDA's new "Drug Watch" Web site. Although it's not necessary for the deliberations of the drug safety board to be open to the public, the Web site is expected to ensure that important drug safety information reaches patients and doctors. FDA officials anticipate that any important safety information about new and marketed drugs that could be released under the Freedom of Information Act (FOIA) will be posted on the Web site. This information would allow the health-care community to learn about drug safety and prescribing issues long before the resolution of often lengthy negotiations between FDA and manufacturers over the need for labeling changes. FDA is developing guidance on procedures and criteria for identifying drugs and information



for the Drug Watch Web site and plans to explain how it will operate in more detail.

In unveiling these initiatives, FDA also indicated that it will be announcing further expansion of its Adverse Event Reporting System (AERS). FDA's 2006 budget request seeks resources to upgrade AERS to ease the electronic filing of adverse

event reports and to collect drug data from other federal agencies as well as healthcare organizations outside the government.

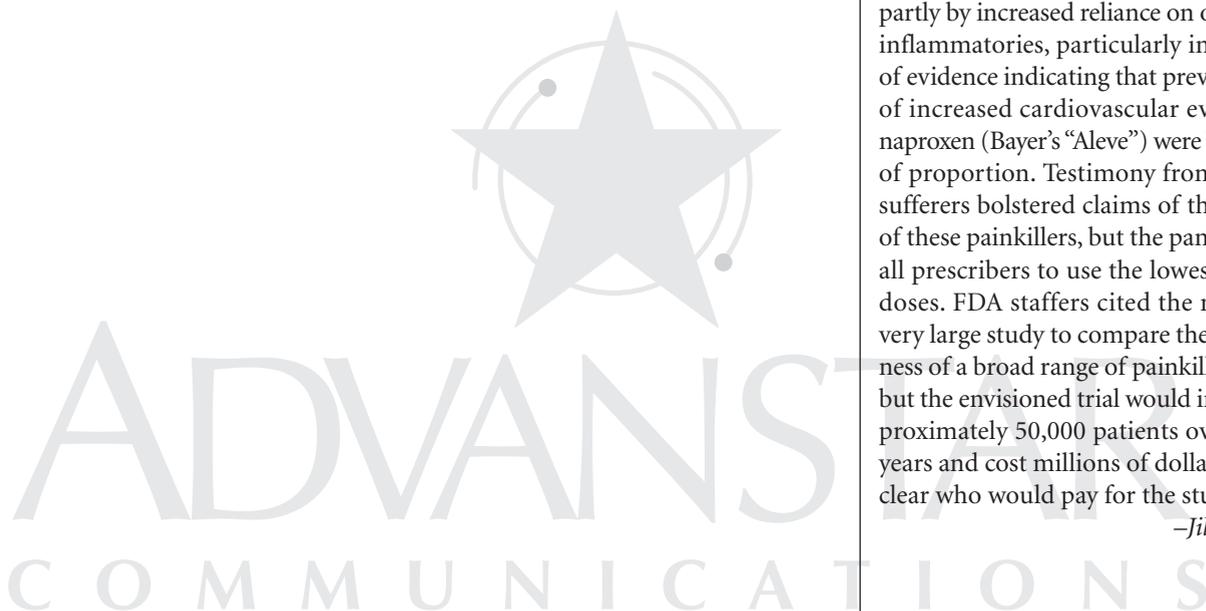
Cox-2s stay on the market

It was no surprise that these announcements came the day before the much-anticipated meeting of two FDA advisory

committees to discuss safety issues related to Cox-2 inhibitors and other anti-inflammatory drugs. The agency's advisory committees on arthritis and drug safety and risk management weighed the benefits of these painkillers for arthritis patients against the risks of cardiovascular events. In the end, the panel voted to keep the Cox-2s on the market, but recommended black box warnings and other limitations. Such labeling changes virtually rule out broadcast consumer advertising for these products, and prescribing of these therapies is likely to remain much lower than in the past.

The decline of Cox-2s may be offset partly by increased reliance on other anti-inflammatories, particularly in the wake of evidence indicating that previous hints of increased cardiovascular events with naproxen (Bayer's "Aleve") were blown out of proportion. Testimony from arthritis sufferers bolstered claims of the benefits of these painkillers, but the panel advised all prescribers to use the lowest possible doses. FDA staffers cited the need for a very large study to compare the effectiveness of a broad range of painkiller classes, but the envisioned trial would involve approximately 50,000 patients over several years and cost millions of dollars. It's not clear who would pay for the study.

—Jill Wechsler



FDA WARNING LETTER

On 4 February, the US Food and Drug Administration's Center for Biologic Evaluation Research (Rockville, MD, www.fda.gov/cber/) issued a Form 483 Warning Letter to Allergy Laboratories of Ohio, Inc. (Columbus, OH), a manufacturer of allergenic source material. The letter cited three deviations from current good manufacturing practices, including releasing multiple batches of "non-viable mold mat" which included living organisms and failure to do follow-up microbial testing on those batches.



POLITICS/FDA

FDA's \$1.9-Billion Budget Proposal Banks on User Fee Revenues

The administration's 2006 federal budget proposal released Monday includes \$1.90 billion for the US Food and Drug Administration (Rockville, MD, www.fda.gov): \$1.52 billion to be funded from tax revenues and \$0.38 billion from industry fees.

The budget request is \$86 million (4.7%) higher than this year's \$1.81 billion. The scheduled increase comes disproportionately from increases in user fee revenues, projected to increase \$32 million (11.3%) from 2005 levels. The fee revenues include \$20.9 million in Prescription Drug User Fee Act levies, \$6.4 million for medical device review, \$3.0 million for animal drug review, and smaller amounts for programs in mammography inspection, export certification, and color certification.

The proposal allocates most of the scheduled \$54-million increase (3.8%) in

taxpayer-funded budget to the food anti-terrorism program, a collaboration of FDA, the US Department of Agriculture's Food Safety and Inspection Service, and the White House Homeland Security Council. Food defense funding would increase by \$30.1 million (20%) to total \$180 million in 2006.

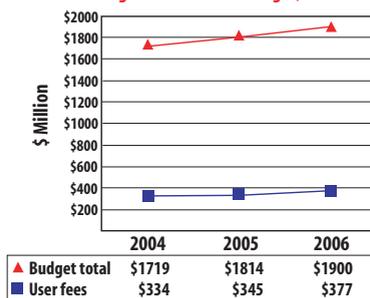
Of the remaining \$24 million in in-

creased tax support, \$6.0 million is earmarked for improving medical device review under the Medical Device User Fee and Modernization Act, \$5.0 million will go to the Center for Drug Evaluation's Office of Drug Safety for post-marketing monitoring, and \$15.2 million for facilities and relocation expenses. (The earmarks exceed the increase: the agency plans to offset these expenditures with savings, including \$1.6 million from administrative efficiencies and \$5.1 million by consolidating or postponing information technology projects.)

For further information, see the Federal 2006 Budget Proposal at the US Government Printing Office and FDA's 2006 Budget Summary press release on the agency's Web site.

—Douglas McCormick

US Food and Drug Administration budget, 2004–2006





REGULATION

CBER Draft Guidances for Spore Formers and Plasmid Vaccines

The US Food and Drug Administration Center for Biologics Evaluation and Research (CBER, Rockville, MD, www.fda.gov/cber) recently issued two draft guidance documents.

The 19-page “Manufacturing Biological Drug Substances, Intermediates, or Products Using Spore-Forming Microorganisms” document appeared on 23 February 2005. The draft updates CBER guidance to conform with the rule, “Revision of the Requirements for Spore-Forming Microorganisms,” which went into effect 1 June 2004. The proposed guidance covers containment, procedural controls, waste disposal, campaign changeovers,

sampling and testing, spill containment, maintenance, and decommissioning of dedicated and the newly authorized multi-product facilities.

The 10-page “Considerations for Plasmid DNA Vaccines for Infectious Disease Indications” document, issued 17 February 2005, updates the December 1996 “Points to Consider on Plasmid DNA Vaccines for Preventive Infectious Disease Indications.” In addition to R&D topics, the draft proposes guidelines for manufacturing this unfamiliar class of products. (The guidance defines plasmid DNA vaccines as “purified preparations of plasmid DNA designed to contain one or more genes

from a pathogen as well as regulatory genetic elements to enable production in a bacterial host system.” The pure plasmids are injected into the body, where they are taken up by the patient’s cells and produce antigens, which stimulates an immune response.) The draft guidance outlines which elements of the manufacturing process must be described in investigational new drug applications, and the release-testing components CBER will expect for bulk plasmid product release and final release.

—Douglas McCormick

ADVANSTAR
COMMUNICATIONS

PACKAGING AND LABELING

Lilly Implements Bar Coding on Individual Insulin Vials

Citing its commitment to patient safety, Eli Lilly and Company (Indianapolis, IN, www.lilly.com) will implement bar codes on individual vials of its insulin products, including “Humulin” and “Humalog.” Although bar codes have regularly appeared on the products’ outer packaging, this new process would be the first time the coding has been included on the vial labels.

Patient safety is of particular concern with frequently used life-saving products such as insulin, which is often removed from its outer packaging before administration to hospital patients. By matching the bar code on the vial to the bar code on a patient’s identification bracelet, the likelihood of a medication error incident decreases. Lilly’s medical advisor Scot J. Jacober observes that “with the new bar coded

vials, doctors can have greater confidence that the drug they are prescribing is given to the correct patient at the correct time.”

According to a Lilly press announcement released earlier this month, the US Food and Drug Administration estimates that bar code labeling on prescription drugs is projected to reduce error by 500,000 during the next 20 years and save an estimated \$93 billion in additional healthcare costs. In a Department of Health and Human Services regulation (*Federal Register*, 26 February 2004), the agency mandated that all new pharmaceuticals be bar coded within 60 days of approval and all existing medications be bar coded before April 2006 (two years after the Final Rule takes effect).

—Maribel Rios

PACKAGING AND LABELING

GlaxoSmithKline Rebrands AIDS Drugs

GlaxoSmithKline (GSK, Middlesex, UK, www.gsk.com) has differentiated key anti-retroviral drugs (ARVs) supplied through not-for-profit agreements from those supplied through other routes by changing the color coating on the tablets from white to red.

The medicines that will be available in the new color are “Combivir” and “Epivir-150 mg,” which are the medicines supplied in the largest volumes by GSK through not-for-profit programs.

Except for the color coating, the tablets are identical. According to the company, there will be no additional charge for the new tablet. This change will help ensure that medicines that are intended for the world’s poorest countries are not diverted and sold at premium prices in developed markets.

The red tablet coating is one of several antidiversion measures for medicines supplied under not-for-profit agreements such as unique packaging in a special, trilingual pack. GSK also has embossed Combivir and Epivir tablets and introduced unique batch

numbers for all heavily price-discounted orders so they will be more easily identified in the supply chain.

GSK has registered the red Epivir and Combivir tablets with the regulatory authorities in a number of countries in Sub-Saharan Africa. To date Ethiopia, Ivory Coast, Kenya, and Tanzania have approved their use. GSK has begun to supply these markets with the red tablets, starting with Ethiopia in January 2005.

As the red tablets are registered in more countries, GSK will begin to phase out its supply of white tablets in response to not-for profit orders. For the foreseeable future, however, both red and white tablets will be supplied to customers under not-for profit agreements.

—George Koroneos