FDA ENACTS FASTER DRUG REVIEW

WASHINGTON, D.C.—This spring, top officials of the Bush Administration renewed a pledge from last year to expedite drug reviews at the U.S. Food and Drug Administration (FDA, Bethesda, MD), a move that could bring both direct and indirect benefits to biotechnology companies. Despite these and other recent changes at FDA, however, critics of the agency say that deeper reforms are needed.

The spring line-up was impressive. Vice President Dan Quayle, Secretary of Health and Human Services (HHS) Louis Sullivan, Assistant Secretary of Health James Mason, and FDA Commissioner David Kessler assembled to announce the four-part reform program, providing a display of unity for skeptics who have continued to question Kessler's endorsement of the changes. The regulatory reforms gained added political weight from being issued during President George Bush's "moratorium" period, in which new federal regulations considered to burden industry were to be blocked and changes considered beneficial were to be accelerated.

The reforms include accelerated approval of "breakthrough" drugs, parallel track use of drugs, international harmonizing of preclinical testing, and use of reviewers from outside FDA.

A reform quartet

The four-part reforms include accelerated approval of "breakthrough" drugs, acceptance of the parallel-track concept for authorizing therapeutic use of AIDS drugs before they are formally approved by the agency, harmonization of new product safety testing among major industrialized countries, and limited use of outside review panels to supplement work done by FDA reviewers.

In addition, although not touted as part of this package, FDA officials are implementing a reform intended to enable them to decide more effectively which centers within the agency should handle particular product reviews. These internal guidelines, which include criteria allowing separate centers in the agency to collaborate on product reviews, are part of a mechanism to expedite internal decision making.

The first reform—the accelerated-approval policy—is aimed at speeding review of drugs for treating AIDS, cancer, and similar life-threatening diseases, according to HHS Secretary Sullivan. One means for achieving this goal will be to put increased reliance on "surrogate endpoints" when evaluating new drugs, instead of relying exclusively on traditional measures of whether a drug prolongs life or decreases morbidity (as determined by more purely clinical determinants).

Initially, accelerated approval will be applied to drugs intended for treating AIDS patients, according to FDA's Kessler. Indeed, for several such drugs, the policy already has cut the time to approval to "months, not years, as would normally have been the case," he says.

The accelerated-approval process has shortcomings, however. It does not allow as much time to generate data as the traditional approval process. And since it's a highly touted procedure, there is pressure for it to succeed. An FDA advisory panel's recent evaluation of the AIDS drug dideoxycytidine serves as an example. Rather than not recommending the drug for approval because of skimpy, questionable data, panel members recommended restricted approval, insisting that the drug be used only in combination with AZT, an already approved AIDS drug.

Parallel track

The second reform being adopted by FDA—the parallel-track policy—also involves drugs for treating AIDS. Devised several years ago by Anthony Fauci, director of the National Institute for Allergy and Infectious Diseases at the National Institutes of Health (NIH), the parallel track grants AIDS patients who cannot participate in controlled clinical trials access to an experimental drug during its clinical testing and before it is formally approved. Officials say this policy may be extended to drugs aimed at treating other serious diseases.

The third program measure—the effort to harmonize international preclinical drug safety testing—is likely to benefit biotechnology companies directly. The new policy calls for data from animal tests performed in Japan, Europe, or the U.S. to be accepted in each of the participating countries, including by FDA reviewers. "Drug sponsors will no longer face the burden of performing multiple studies on new drugs to meet varying national requirements," Kessler says. "This will cut the time and resources required for such testing."

The fourth reform—the use of outside reviewers to reduce the backlog at FDA by evaluating some new drug applications—is still in the pilot stage, officials say. The current strategy is for outside reviews to be limited to "certain routine types of applications," including anti-allergy, anti-infective, and analgesic drugs, as well as some biologics. FDA officials say that the biotechnology industry may benefit because the approach will allow agency staff reviewers to spend more time on non-routine new products, including those from biotechnology companies.

Critics question changes

Although these reforms were announced with considerable fanfare, some critics are continuing to question whether they address deeper problems at FDA, namely staff morale, public credibility, and the overall effectiveness of the agency. For example, the blue-ribbon Edward's Commission last year framed a set of pointed recommendations for the agency. The panel urged that research programs be enhanced, financial resources be augmented, and that greater autonomy be provided for the agency, even suggesting that FDA be repositioned within (or even outside) HHS to strengthen its political independence and public visibility.

Frustrated with how little influence their report has had, members of the Edwards Commission are now planning to reconvene under private auspices to see whether the reform momentum they once had can be recovered. The commission officially disbanded when its report was delivered to HHS Secretary Sullivan in April 1991.

—Jeffrey L. Fox