ALL PARTIES DELIGHTED

CONGRESS OKAYS FDA USER FEES

WASHINGTON, D.C.—In the waning days of the fall session, the 102nd Congress passed legislation authorizing user fees for the Food and Drug Administration (FDA, Bethesda, MD). When implemented, the measure is expected to bring new revenues and new staff to the agency, thereby speeding the review and approval of new products (Table 1).

Amazingly enough, all parties are delighted, including FDA, the biotechnology and pharmaceutical industries, and even Congress, some of whose members were blocking the legislation until the eleventh hour, hoping to win approval for their own favorite FDA-related issues, including orphan drugs and vitamins.

FDA officials are relieved at the imminent prospect of increased resources for the agency. "It's like hitting the lottery," says one insider. And Henry Miller, director of FDA's Office of Biotechnology, adds that "it's the most important development" during Commissioner David Kessler's stewardship.

The new revenues, which are intended to augment rather than replace annual budget appropriations, will allow officials to expand the agency's staff considerably, with 600 new reviewers slated for hire. This change is particularly welcome following a period of budget shortfalls that have been cramping efforts to implement broad reforms and other management changes.

According to one reading of the legislation, the biotechnology side of the drug industry could benefit almost disproportionately because the Center for Biologics Evaluation and Research (CBER) is being asked to add as many new people as is the center for drugs. Because CBER starts out smaller than its sister center, the changes will lead to a near doubling of its current review staff, a "windfall" for biotech, according to some observers.

However, those anticipated changes will not be immediate, agency officials are cautioning. The user fee legislation carries certain start-up costs that need to be dealt with before the proposed new program gets off the ground. FDA officials say that because of current tight budgets, they will need a preliminary infusion of money from Congress just to implement the user fees. For instance, they need to set up a collection and tracking system and other elements of the requisite bureaucracy to manage the program. These steps could even require a special supplemental appropriation from Congress, a measure that may delay the user fee reforms until sometime next spring.

Regardless of these remaining technical hurdles, however, representatives of the biotechnology industry are delighted with the legislation. The new-product review staff at FDA will "clear up the enormous backlog of biotechnology and other drug products awaiting approval," says Richard Godown, president of the Industrial Biotechnology Association (IBA, Washington, DC). "This will provide a powerful forward thrust for the industry."

Moreover, the legislation contains an IBA-promoted provision reducing by 50 percent the new-product application fee for small companies. The reduced fee applies to the first product from those companies with fewer than 500 employees. The final version of the bill also includes another boost for new companies, allowing them to defer such fees for one year.

—Jeffrey L. Fox

TABLE 1. FDA user fee schedule

Fiscal Year	NDA/PLA Application Fees*	Supplemental Application Fees	Annual Establishment Fees	Annual Product Fees	Total Fee Revenues
1993	$100,000	$50,000	$60,000	$6,000	$36,000,000
1994	150,000	75,000	88,000	9,000	54,000,000
1995	208,000	104,000	126,000	12,500	75,000,000
1996	217,000	108,000	131,000	13,000	78,000,000
1997	233,000	116,000	138,000	14,000	84,000,000

*Small companies eligible for reduced rate and deferred payment.
The program will expire on October 1, 1998 unless reauthorized by Congress.
Source: Industrial Biotechnology Association (Washington, DC)

total, 11 are part of direct therapeutic manipulations, whereas 21 are for gene marking purposes.

Gathering data

With so many clinical trials under way, some NIHRAC committee members are becoming increasingly insistent that the committee be informed systematically about results, particularly as they pertain to overall safety. "Our charter says we'll get reports every 12 months," says committee member Brigid Leventhal of Johns Hopkins Hospital (Baltimore, MD). But, so far, little information has been forthcoming, since researchers find such reporting burdensome and since the information reported, if made public, could ruin their chances of publishing in peer reviewed journals.

Leventhal argues that the committee has not been "hard nosed" in insisting that clinical researchers furnish reports. However, she says, "We're at a point where many protocols are ongoing, and this issue is becoming more urgent. It's sort of like toilet training. We've already been through the good boy routine."

In that spirit, the committee agreed to issue a friendly-but-firm letter to all investigators with continuing clinical gene transfer procedures. In it, investigators are being notified that previous approvals will be "reconsidered" if they fail to provide status reports and other information from clinical trials that the committee says is vital to future deliberations over human gene transfer proposals.

Safety standards

NIHRAC members also are seeking a more even-handed means to review slightly differing protocols with regard to overlapping issues of safety. Meeting this goal is proving challenging, because views about safety standards and how to set or measure them are rapidly changing.

The nature of tests used to judge the safety of viral vectors is at the center of this debate, which includes NIHRAC members, FDA officials, and researchers active in the field. No one is sure what the best assays are for judging questions of vector safety in the context of human gene therapy protocols. For example, although FDA officials acknowledge that "more stringent" safety tests soon will be instituted, they insist that retroviral vectors considered for previously approved protocols have undergone adequately rigorous safety testing, so there is no need to revisit those evaluations. Nonetheless, this "transitional phase" creates a degree of uncertainty for those protocols now being reviewed by NIHRAC and FDA. It also remains unsettled whether members of RAC or FDA will take the lead in resolving these issues.

—Jeffrey L. Fox