

1987-2002  
**15** years  
**Revolutionizing Biologics Regulation**

by **Jill Wechsler**

**F**DA's September announcement (see Info+, p. 14) that it plans to transfer therapeutic biologic review functions from the Center for Biologics Evaluation and Research (CBER, [www.fda.gov/cber](http://www.fda.gov/cber)) to the Center for Drug Evaluation and Research (CDER, [www.cder.gov](http://www.cder.gov)) caught most agency officials and Washington observers by surprise. The move, however, is not radical; FDA has often changed oversight for drugs and biologics. The current CBER-CDER structure was established in 1987, but FDA has since moved toward harmonizing application and manufacturing data requirements as well as other regulatory procedures. Several streamlining initiatives were codified in the FDA Modernization Act of 1997, and the Prescription Drug User Fee Act (PDUFA) established common standards and time frames for application review procedures. Manufacturers recently succeeded in adding provisions to May's PDUFA 3 agreement that promote early consultation on research protocols and prevent later disputes over the adequacy of study data.

In his memo to FDA staff, deputy commissioner Lester Crawford emphasized that during the past year, agency management had examined proposals for improving review processes of drugs and biologics. Crawford said that shifting therapeutics to CDER made more sense than completely combining the two centers because other CBER functions, such as regulating vaccines and ensuring the safety of the U.S. blood supply, are distinguishable from therapeutic biologic review.

### Why Now?

The decision to consolidate in CDER the oversight of biotech therapeutics partly reflects the maturation of biotech manufacturing and quality control processes. Manufacturers and regulators recognize that adherence to good manufacturing practices (GMPs) and validation methods can ensure the reliable production of therapies that meet standards for potency, purity, and quality.

The move also arises from industry's desire for greater consistency in how FDA regulates drugs and biotech therapies. Manufacturers point out that CBER takes much longer than CDER to approve licenses and applications for standard new therapies. A main complaint is that CBER has more difficulty approving

applications in the first review cycle, indicating problems in negotiating drug development plans with sponsors. The issue gained the spotlight during the congressional investigation into ImClone's development of the colorectal cancer therapy Erbitux. At a hearing in June before the House Committee on Energy and Commerce, CBER officials were criticized for failing to convince the company to delay filing a license application on what appeared to be an inadequate drug development program. The investigation by the House committee into the resulting insider trading scandal highlighted the need for more consistent review procedures by CBER and CDER.

### Industry Concerns

Biopharmaceutical manufacturers, however, are worried that they may have to meet stricter data standards at CDER, that drug reviewers don't fully understand the science, and that CDER systems for electronic submissions and for toxicology studies are very different from CBER's.

Probably biotech's biggest fear is that the shift to CDER will open the door to generic biologics. Manufacturers welcomed assurances from Crawford that there would be no legislative change in the statutory governance of biologics, which sets a high barrier to generics. However, these products will now be regulated by CDER officials who are familiar with generic drug policies and who are interested in exploring options for the development of "therapeutically equivalent" biotech therapies.

### Breaking Up Is Hard to Do

CBER retains authority over vaccines, blood and blood products, and over its newly created Office of Cells, Tissues, and Gene Therapy, which includes somatic cell products and other "cutting edge" technologies. But the rest of CBER's Office of Therapeutics Research and Review, which regulates monoclonal antibodies and proteins, will move to CDER. CBER funding will be a critical topic, as it stands to lose about three-quarters of its user fee revenue. Crawford noted that there will be no staff reductions, but there is considerable uncertainty about how the change will affect CBER's strong emphasis on its "research-review" model. Biotech companies planning to file new license applications in the next few months are concerned about how the change will affect the approval process. In addition to reviewers, some CBER compliance and advisory functions also may shift to CDER. The change could affect programs to inspect biotech manufacturing facilities and to monitor product quality. The long-term expectation is that streamlined regulatory and review processes will spur biotech research and development of new therapies, but change is always disruptive and will present new challenges to manufacturers. **BP**



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