



## **Statement of the Biotechnology Industry Organization**

### **Before the Food and Drug Administration Public Meeting on the Prescription Drug User Fee Act (PDUFA)**

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The Biotechnology Industry Organization welcomes this opportunity to comment on the effectiveness of the Prescription Drug User Fee Program and to support its continuation.

BIO membership includes many small, start-up companies in earlier stages of product development, which have not yet applied for FDA approval; biotechnology companies, whose exclusive focus is on the development of biological products; and large, well-established pharmaceutical companies that simultaneously pursue the research and development of small-molecule, conventional drug products and complex biological products. Our member companies, regardless of their size or situation, all recognize the crucial importance of three general PDUFA goals: expediting the review and approval of new therapies; reducing the length of time it takes to bring an innovative concept through the development process to completion as an approved, safe and effective therapy; and making FDA processes and outcomes transparent and predictable to industry and the public. BIO believes that the overarching aim of the PDUFA program should continue to be measurable improvement in access for patients to new, life-saving and life-altering medicines.

In large measure, the goals of PDUFA are being achieved. The statistics are clear: post-PDUFA, U.S. patients are the first in the world to have access to new products as a percent of total drug launches by country. Prescription drug user fees, added to a sound base of appropriations for FDA, have provided the additional resources needed by the agency to reduce the backlog of applications that led to the so-called “drug lag” in existence before enactment of PDUFA. PDUFA fees are intended to provide FDA with the ability to increase its review capacity, including medical and scientific expertise, so the agency can become more efficient without reducing its commitment to the highest standards of review. The intention of Congress in enacting PDUFA initially and in renewing it twice was – and we believe remains – that this program significantly contributes to and supports the safety and efficacy of prescription drug and biological products. PDUFA does this by providing FDA the resources it needs to continue to make sound scientific, medical, and regulatory decisions.

The PDUFA program both supports new medical innovation and is itself an innovation. Since its inception, PDUFA has helped to speed more than 220 new, cutting-edge drugs and biologics sponsored by BIO members to the patients our industry serves. Indeed, the PDUFA program is considered

highly innovative and in 1997 received the prestigious Innovations in American Government Award, sponsored by the Ford Foundation and Harvard University's John F. Kennedy School of Government. PDUFA has earned this high praise as a mechanism for consistent multi-year FDA funding needed to conduct more predictable, empirically-based product reviews.

We strongly support the renewal of PDUFA in 2007 when the current program expires, and believe that maintaining level funding will allow the successful continuation of the program. As we examine the data being collected during the course of the present program, we hope to achieve a better understanding of causes and possible solutions that will show what modest programmatic changes may contribute to even greater success. We have some specific comments in three areas: safety, information technology, and performance goals.

### **Safety**

BIO believes it is important to recognize that safety is an integral and paramount part of companies' considerations during research and development and of FDA's deliberations during its application review. Indeed, FDA has stated that it spends half of its effort and resources during the course of a review in considering the product's safety profile and determining whether limitations on use or specific content in the labeling are needed to assure consumer safety. Because PDUFA funds were specifically designed to be allocated for activities related to application review, they clearly should be used by FDA for pre-market safety-related activities.

During the most recent congressional renewal of PDUFA, Congress, FDA, and companies agreed that user fee resources should also be allocated to safety-related activities that occur in the early post-market period, when a great deal of safety information may be obtained as products transition from use in a relatively small number of patients enrolled in clinical studies to use by many more people. This new PDUFA allocation, \$63 million, provides for additional personnel, data base enhancements, funding of outside reviews, etc., focused particularly on the so-called peri-approval period -- that is, the first several years the product is on the market.

BIO does not agree with suggestions that PDUFA has contributed to a lowering of FDA's safety review standards or reduction in product safety, or that safety has taken a back seat to speed. PDUFA fees are, in fact, applied directly to safety evaluations, both in the pre- and post-market stages. Indeed, a recent study from the Tufts Center for the Study of Drug Development has demonstrated that there is no evidence of a correlation between the length of the application review and product withdrawal.

As PDUFA moves towards renewal, we want to focus on safety-related areas to determine if and how improvements can be made, and we look forward to discussing these in more detail as the process evolves. BIO would like to see some emphasis placed on greater efficiency, consistency, and predictability in the process of evaluating trade names. Trade-name evaluation is an important aspect of safety in that it helps minimize medication errors. Currently, we believe trade name review is not conducted in a timely manner and consistent procedures do not seem to be in place for this aspect of application review. This is a significant issue for BIO member companies and we believe that statutory changes are not necessary to make these improvements. BIO looks forward to working with FDA to expeditiously improve the evaluation of trade names.

### **Information Technology**

Implementation of data and document standards is generally embraced by the biotechnology industry. During the course of PDUFA III, there have been promising steps toward establishing the base architecture for paperless submissions. This goal is critically important and we look forward to its achievement. However, FDA appears to continue to struggle with the existence of multiple external standards groups and numerous IT groups within FDA. We encourage the agency better consolidate and coordinate IT activities related to electronic submissions. We also encourage – and will continue to work with FDA to achieve this – better communication of IT initiatives and implementation. In addition, it is crucial for companies to have sufficient advance notice of changes and of implementation of new requirements, to be able to comply with the agency's IT changes; that is not happening uniformly now.

### **Performance Goals**

In general, we believe appropriate goals for review performance are in place and should be retained, but we want to highlight several matters.

Statistics currently available, including FDA's annual performance reports, indicate that median approval times are not changing, notwithstanding the fact that overall PDUFA spending on application review has continued to increase annually. Moreover, the current median time to approval is longer than the comparable 1999 time. It will be helpful for FDA to provide additional details regarding this issue and develop a clearer understanding of whether and how use of PDUFA funds are contributing to this apparent slippage.

One of BIO's key priorities in the most recent PDUFA renewal was to achieve an understanding of differences in product approval times between biological products and drug products, among review divisions, and between the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research. In particular, FDA used PDUFA resources to fund several studies designed to shed light on this, including studies of first-cycle review, the results of which will be helpful in understanding the time-to-approval issue. We look forward to more data from these ongoing studies.

A critical issue identified in PDUFA renewal discussion was that of inconsistencies between and among reviewers and divisions. One goal of PDUFA III was the development and implementation of Good Review Management Principles (GRMPs). FDA has developed and disseminated GRMPs guidance and has begun training of reviewers in both CDER and CBER regarding these best practices. This was an important achievement. However, sustained and continued commitment to observing the principles articulated in the guidance is critical to success. This includes continued dedication to performance and communication goals, training, and implementation of the GRMPs. While progress is being made, two areas represent opportunities for further examination and possible enhancements – labeling and post-market commitment negotiations. Again, we feel that changes in the law are not necessary to achieve these efficiencies and we look forward to continuing our productive dialogue on this issue.

Another PDUFA III activity, predicted to be a potential route to enhanced communication and reduced review time, was the establishment of two Continuous Market Application (CMA) pilot programs. These programs have been implemented and are being evaluated by FDA. We look forward to learning from FDA how the CMA programs were implemented and used and FDA's views of the programs. We also will do our own assessment of

the programs, although our preliminary assessments appear to indicate that the programs were not used as often as might have been anticipated. In addition, it appears that, while these programs were worth evaluating on a pilot basis, without compelling data regarding their success, they may not be worth continuing, especially if they have a significant impact on FDA resources.

Overall, BIO believes that good progress is being made in meeting PDUFA III performance goals. As FDA itself has acknowledged, however, there has been lower success with respect to meeting goals for management of meetings and other communications with applicants. Because this is an area of great importance to BIO member companies – who view good communication with FDA as their lifeline to predictability and success – we hope to continue to work with FDA to realize the meetings management goals established in PDUFA II.

We are aware that, over the last several years, FDA appropriations for drug and biologics review have remained flat when adjusted for inflation. Consequently, the agency has struggled to keep up with its review activities and with the multiple other tasks with which it is charged. We will continue to urge Congress to ensure adequate FDA appropriations.

### **Conclusion**

In conclusion, BIO believes that reductions in overall product development time and in FDA review time both are critical factors in improving access to medicines. PDUFA is key to these goals. The program should be reauthorized in a timely manner and not redesigned with reforms unrelated to PDUFA's goals. User fees at current levels should continue to provide reliable, additive resources for human drug and biologic review while FDA works towards realizing the goals established in PDUFA III, with minor programmatic improvements. I want to emphasize again BIO's view that the program has been highly successful and is a direct contributor to increased patient access to life-saving, breakthrough therapies.

We look forward to working with you in the coming months. Thank you for the opportunity to be part of the process and part of this meeting.