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Biotechnology
Industry
Organization
1625 K Street, N.W.
Suite 1100
Washington, D.C. 20006

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Response to Food and Drug Administration's Message to Stakeholders

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Alan Goldhammer, Ph.D.
Executive Director, Technical Affairs
Biotechnology Industry Organization

The Biotechnology Industry Organization welcomes the opportunity to address the questions that were recently posed by the Food and Drug Administration in its July 22 Message to stakeholders. In that message, FDA noted its obligations under section 406(b) of the Food and Drug Modernization Act (FDAMA) to meet with interested parties with the goal of receiving input as to how the agency can best meet its regulatory responsibilities. This document was frank in its mention that "innovations and efficiencies alone, however, may not be sufficient to deal with the enormous growth in FDA's obligations that has been fueled by rapid technological developments, increased complexity of regulated products, and mushrooming global trade."

The agency goes on to identify a series of areas that they believe are critical to its public health mission. FDA notes that "although we have shared areas where we have real concerns about our ability to meet our statutory obligations, our stakeholders can be assured that we are embarking on this consultation process with no preconceived conclusions." FDA set forth seven questions designed to assist it in developing its plan for complying with FDAMA. These are the issues that are before us today.

Before addressing the specific points, I would like to note the interconnecting thread that is implicit in FDA's message to stakeholders and the questions posed in the Federal Register. This theme in our minds is the need for adequate resources. Six years ago the Prescription Drug User Fee Act (PDUFA) was passed in response to the specific crisis that there were insufficient resources within FDA to review new drugs and biologics. FDA was not able to meet its obligation in reviewing drugs and biologics in a timely manner. The backlog of applications was growing out of control. A convincing case was made to augment the agency's resources in a targeted manner with performance goals so that new priority products could be reviewed and acted upon in six months, standard applications in twelve months. The success of the program is self evident. One of the critical sections of FDAMA is the reauthorization of PDUFA for an additional five years

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accompanied by program enhancements that should shorten drug development by 10-15 months.

The success of PDUFA should not be taken as a sign that the regulated industry only need give money to FDA and all the problems will be solved. Our industry is not the FDA's only constituent. Health care professionals, patients who rely on new medical technologies, and the general public all have a vested stake in an FDA that is fully funded so that it might carry out its responsibilities for all the publics that it serves. This means that FDA must have adequate appropriated Congressional funding. It has been our experience that user fees can best address certain narrow programmatic problems. However, the public constituencies' overall interest about FDA's ability to carry out its functions must continue to be addressed via the appropriations process. There is no question that recent efforts by both the Administration and Congress to seek a balanced budget have had an impact upon the FDA operating budget. The senior management at FDA must present its budgetary needs to both the Office of Management and Budget and the Congress in a realistic and forceful manner.

BIO offers specific responses to three of the posed seven questions.

Question 1 – What can FDA do to improve its explanation of the Agency's submission review processes, and make explanations more available to product sponsors and other interested parties?

1. Our industry has spent considerable resources trying to make the drug development process more predictable. FDAMA clarifies many FDA responsibilities regarding its role in improving the predictability of drug development. However, FDA's increasing reliance on advisory committees both to answer general questions about products during the development process and to review information as the penultimate step prior to licensure is often times unpredictable. Outcomes of Advisory committee decisions often surprise both sponsors and the FDA. There appear to be different internal practices between different Centers use of advisory committees. BIO believes that it is useful for the agency to have a mechanism by which it can receive sound advice on scientific questions. It may be appropriate to convene a working group from the regulated industries to review present agency use of advisory panels and make recommendations as to how the process might be improved to maximize their utility to the FDA.
2. Often times agency actions highlight an outdated or vague regulation or guidance is in need of revision. In such cases, these should be identified as early as possible and FDA should reach out to the stakeholders for discussion of the issues. An example of this are the definitions of same versus different for orphan drugs. This has a particular implication for the biotechnology industry because of the chemical structures of monoclonal antibodies and recombinant proteins. If a biological product is not the "same" it can receive a separate orphan drug designation. If not, then clinical superiority or a reduction in adverse reactions must be demonstrated. Would demonstration of a major improvement in patient care (combination of factors such as

higher effective dose and ease of administration) qualify? It would be useful to consider developing a guidance document addressing these issues.

Question 3 – Assuring Product Quality/Safety

The issue of product quality and safety is one that is never compromised within our industry. Our products are mostly large molecular weight proteins. The manufacturing process and purification procedures are complex. Much time and effort is spent during the development process to design the manufacturing process controls and a quality assurance process that leads to a final product of the highest possible quality and consistency.

FDA has in place regulations that require the reporting of adverse reactions. One of the key agreements reached during the renegotiation of PDUFA is to provide FDA with the funding to move towards a fully electronic filing environment over the next five years. Adverse event reporting is to be part of this. This should streamline reporting and data analysis.

Question 4 – Science Infrastructure

BIO believes that there needs to be a strong commitment within FDA towards maintaining an appropriate science base. Regulatory decisions including development of guidance and regulations should be made on the best available science. The experience of BIO member companies points to numerous examples relating to both clinical development and complex manufacturing issues were speedily resolved because of the scientific expertise within CBER. The recent FDA Science Board review of CBER activities was positive in outcome. There needs to be a closer tie with industry in identifying research areas and reviewing ongoing programs. Our Board of Directors has been carefully examining this issue and we expect to file specific comments with the docket.