BIO

BIOTECHNOLOGY
INDUSTRY
ORGANIZATION

2807 '03 JUN -3 A9:31

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, Maryland 20852

Re: Docket No. 02N-0528; Risk Management; 68 Federal Register: Pgs 11120-11121

Dear Sir/Madam:

The following comments supplement those presented by the Biotechnology Industry Organization (BIO) at FDA's public meeting to discuss the Risk Management Concept Papers on April 9-11, 2003. BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products. The Biotechnology Industry Organization (BIO) appreciates the opportunity to comment on the FDA concept paper #1: Premarketing Risk Assessments.

FDA considers Risk Management to be a continuous process of (1) learning about and interpreting a product's benefits and risks, (2) designing and implementing interventions to minimize a product's risks, (3) evaluating interventions in light of new knowledge that is acquired over time, and (4) revising interventions when appropriate.

General Comments

Section II (D) states that FDA defines a Risk Management Program (RMP) as a strategic safety program designed to decrease product risk by using one or more interventions or tools beyond the package insert.

In general, BIO agrees with these concepts, although there is confusion about whether a Risk Management Program is "beyond the package

1225 EYE STREET, N W, SUITE 400
WASHINGTON, D C 20005-5958

202-962-9200
FAX 202-962-9201
http //www bio org

02N-0528

EMC33-01

insert" (Section II D) or whether the package insert is a tool to be used as part of a Level I Risk Management Program (Section IV D). When labeling is submitted as part of an NDA/BLA, does this constitute a Level I Risk Management Program and if so, what additional information, if any, is required to support this decision? If it is intended to consider the package insert as a Level 1 Risk Management Program, BIO recommends this be considered the default level. We believe that a Risk Management Program submission containing a rationale and other elements described in Section VI should only be needed when additional risk management tools are considered necessary (e.g., levels 2, 3 or 4).

Section III states that the decision to develop, submit and implement a Risk Management Program will be made on a case-by-case basis. BIO recommends that criteria be developed to guide decision-making around when a Risk Management Program is indicated and at what level. We believe the four levels proposed by FDA seem simplistic and do not take into account other activities that support good risk management such as pharmacovigilance activities, post-marketing studies, etc. BIO recommends that Risk Management Plans be individualized to address the specific therapy, indication, and risk. We recommend the design of each Risk Management Plan be evidence-based and practical for implementation in the health care setting. In addition, since the decision to develop Risk Management plans will be made on a case-by-case basis, it would be useful to make FDA-approved Risk Management plans public and accessible so that all companies can learn and evaluate what has been acceptable to FDA in the past.

Also, it is not clear how FDA regards these four levels of Risk Management Plans and how they are to be regarded by the pharmaceutical industry, health care professionals and patients. Are these "official levels", and if so, how will these levels and their requirements be formally characterized and communicated to all stakeholders including health care professionals and patients? At this time, these levels are not defined in current regulation. BIO recommends that Risk Management Programs be customized to the risk, the drug, and the patients who will be exposed to the therapy; therefore, levels are unnecessary.

Section III states that "Since risk characterization... is an ongoing process throughout a product's lifecycle, a perceived need for a Risk Management Program may emerge pre-or post-approval. Ideally, a Risk Management Program would be developed, submitted and modified as risk reduction needs are identified in a product's lifecycle." We recommend this statement be clarified since it could be interpreted to suggest the possibility that a Risk Management Program could be submitted and implemented pre-approval. We believe that the types of controls routinely practiced in clinical research are generally sufficient for managing pre-approval risks, for example, the inclusion/exclusion criteria, frequent patient monitoring, laboratory tests, hospital or physicians office care, etc. We believe it would impose unnecessary burdens and likely introduce delays and added costs to drug development if Risk Management Programs were superimposed over the existing patient protections provided during the clinical research process. Therefore, BIO recommends that Risk Management Programs, as described in FDA's concept paper, be limited to the post-approval phase of the product life cycle.

It is not clear whether common Risk Management Programs will be required for all therapies in a class that share similar risks, and for generic versions of an innovator drug that has adopted a

Risk Management Program. It would be useful to hear FDA's views on how Risk Management Programs could be applied in a uniform manner to ensure consistency across common products.

BIO agrees that risk management plans should be evaluated to see if they have achieved their stated goals. However, we recommend the concept of "pre-testing" of risk management tools (Section V A) be clarified. In some situations, i.e. the need to deal with a significant safety issue, there may not be sufficient time to pretest risk management tools. On the other hand, pre-testing may delay the development and availability of a needed therapy.

Section VI. B. suggests the Risk Management Program should include conditions or outcomes that would lead to revising the Risk Management Program to a higher level. We suggest consideration also be given to criteria that would lead to revising the risk Management Program to a lower level, for example, if the data or outcomes acquired indicate the risks are not as great as initially perceived, or if other unintended consequences have resulted from implementation of the Risk Management Program (e.g., illicit access via the Internet, or increased utilization of less satisfactory therapy due to the burdens of adhering to the conditions of a Risk Management Program).

Finally, we recommend the benefits of implementing Risk Management Programs (maximizing patient safety) be balanced against the potential downside of added burden to the health care system with an additional layer of procedures that could potentially limit patients' access to life-saving therapies. To this end, we believe that Risk Management Programs should be evidence based, consistently applied and practical for implementation in the health care setting.

In conclusion, BIO looks forward to additional guidance from FDA to clarify outstanding questions regarding the creation and implementation of Risk Management Programs that will optimize benefit and minimize risk to patients while ensuring that safe and effective biologic products will continue to be developed and marketed to meet unmet medical needs.

Sincerely,

Gillian R. Woollett, MA, DPhil
Vice President Science and Regulatory Affairs