Biotechnology Industry Organization

February 4, 2013

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

Re: Docket No. FDA–2012–N–1248: Creating an Alternative Approval Pathway for Certain Drugs Intended to Address Unmet Medical Need; Public Hearing; Request for Comments

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to provide comments on the proposal to create an alternative approval pathway for certain drugs intended to address unmet medical need, also referred to as a Special Medical Use (SMU) designation. BIO appreciates the Agency's ongoing efforts to identify creative approaches to speed the development and availability of innovative new therapies to address our nation's public health priorities, particularly for serious and life-threatening conditions. BIO also thanks the President's Council of Advisors for Science and Technology (PCAST) for its work on promoting biomedical innovation.

BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

BIO is currently evaluating the SMU designation concept and assessing several key issues to inform the discussion. We are committed to working together with FDA and other stakeholders to articulate a potential new regulatory pathway that can successfully advance the development of new therapies for serious manifestations of disease. BIO anticipates submitting more detailed written comments to the docket specifically to address the six questions posed in the January 15th Federal Register notice. The following questions represent considerations BIO hopes FDA and other stakeholders take into account in further dialogue regarding the proposed process.

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1. Will FDA Continue to Prioritize Implementation of the FDASIA Expedited Approval Pathways?

In the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA, P.L. 112-144), Congress directed FDA to modernize and expand the existing Accelerated Approval pathway and implement a new Breakthrough Therapies process. In light of the resource commitment of these activities, we encourage FDA to continue to prioritize the implementation of the FDASIA expedited approval pathways.

2. Does FDA require Additional Authority to Implement the Pathway?

As noted in the PCAST report, it is unclear as to what extent FDA's existing statutory authorities are sufficient to implement the SMU pathway. BIO would like to have a clear understanding of what new authorities may be necessary or how current authorities, including those related to labeling, restrictions on use, and Risk Evaluation and Mitigation Strategies (REMS) could be applied. We note, for example, that FDA commonly approves therapies intended for specific sub-populations if the product is appropriately labeled for that sub-population. Additionally, FDA has considerable regulatory flexibility embodied under existing authorities and expedited approval programs to address serious or life-threatening conditions and unmet medical needs, while ensuring safety[1].

To advance the discussion, we encourage FDA to discuss publicly whether this pathway can be established administratively via revised regulation and guidance, or whether Congress must pass legislation, and the relative merits of each approach if both are feasible.

3. How can the Pathway be Designed to Balance Expedited Development and Post-Market Restrictions?

It is important that any pathway equally balance the dual priorities of expediting clinical development through smaller and more targeted studies and use of authorities that promote responsible prescribing for specific sub-populations through appropriate labeling and restrictions of use. BIO believes that any potential SMU proposal should provide clarity about mechanisms or processes to expedite the clinical development of these products if it is to include post-market restrictions of use.

4. Will only the Sponsor be able to Request SMU Designation? When in Drug Development will Designation be Available?

The PCAST report states that "the FDA should implement a drug approval pathway under which *Sponsors could propose, early in the development process,* to study a

[1] 21 CFR 312 Subpart E, 21 CFR 314 Subpart H, and Section 505-1 of the Federal Food, Drug, and Cosmetic Act

drug for initial approval under a designation of Special Medical Use (SMU)" (emphasis added, p. 64). However, it is unclear from the FDA Federal Register Notice if the SMU designation would be "voluntary," *i.e.,* available solely upon the Sponsor's request, similar to the existing Fast Track, Breakthrough Therapies, and other processes. It is our view that this pathway should be at the request of the Sponsor.

Additionally, it is unclear whether designation for the pathway would be granted early during the drug development process, like Fast Track or Breakthrough Therapies, or upon the time of FDA review and approval, like Priority Review. We suggest that designation should be available early in drug development so that the Sponsor can design appropriate clinical studies for use under the pathway, for example by conducting clinical studies based upon only the most severe manifestation of the disease without having to progress through more moderate disease populations first.

5. How will the Sub-populations and Eligibility Criteria be Defined?

The new pathway may lend itself to certain indications characterized by specific sub-populations with a severe form of a more common condition, such as drug resistant pathogens or morbid obesity, with a notably different benefit-risk profile. With more restrictive labeling, this may facilitate the approval of treatments for the sub-population that would not be justified for use in the broader population. However, it is important to develop greater clarity on how these sub-populations will be characterized. What exactly is meant by accepting a different benefit-risk profile and how would FDA and Sponsors achieve a common understanding of this criterion?

We also request clarification as to whether the terms "serious", and "life-threatening" condition, and "unmet medical need" would be interpreted in the same manner as in the Fast-Track statute[2], or as the terms will be applied under the new FDASIA pathways.

Additionally, it is important to ensure that efforts to make more medicines available to patients suffering from the most severe forms of a condition do not hinder the development and approval of medicines for broader populations of patients. FDA must always strive for a balanced benefit-risk approach when reviewing medicines for any disease, including Alzheimer's, diabetes, and other chronic diseases that affect millions of patients. It is imperative that while recognizing patients suffering from the most severe forms of a condition may have a different benefit-risk profile than those suffering from less severe forms of condition, any new pathway should not translate into prohibitive standards and requirements to obtain approval for a broader set of patients.

[2] FFDCA Sec. 506

6. How will the Pathway be aligned with Existing Incentives for Innovation?

BIO also believes that consideration should be given as to how this program would align with existing incentives for innovation, including market or data exclusivities. Given the intertwined complexities of these various incentive structures, many of which begin upon the date of initial FDA approval, we believe FDA and other engaged stakeholders should seek as much clarity as possible about these issues, so that Sponsors may make SMU designation decisions that permit appropriate development and commercialization of products.

We are also evaluating how this pathway may relate to rare disease drug development. Orphan drugs are already used in small patient populations, and there already are concerns about the ability to enroll studies and the economic viability of rare disease drug development. It is unclear how the SMU designation will interact with orphan drug designation and, in particular, the interaction between the SMU proposal and the proposal published last year by FDA, regarding orphan disease population subsets.

7. What will be the Impact on the Practice of Medicine?

BIO supports efforts to help healthcare providers appropriately understand and utilize the information in product labels and better evaluate the benefit-risk profile of different therapeutic alternatives for unmet medical needs. An SMU logo may be another tool to help inform providers and others of unique prescribing considerations, but we would like to understand what impact this proposal may have on the practice of medicine.

Sponsor and FDA involvement in the practice of medicine should be kept to a minimum. Whatever limits any institution places on SMU products should not prohibit judicious prescribing by trained physicians based upon their informed judgment of what they deem to be the best treatment for an individual patient based on their unique needs and circumstances. Limits found, for example, in formularies and health system guidelines should not foreclose physician exercise of such sound medical judgment.

FDA's current initiatives related to education, outreach, and training, and improved professional and patient labeling are positive ways to ensure that healthcare providers appropriately understand and utilize the label and better understand benefit-risk for unmet medical needs. These initiatives should continue to be an element of this broader conversation.

Conclusion:

In conclusion, thank you for the opportunity to provide BIO's initial perspectives on the Special Medical Use designation proposal. We look forward to engaging constructively with the FDA and other stakeholders as these discussions progress,

with the shared goal of advancing the development of new therapies for serious and life-threatening diseases. I would be happy to answer any questions.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science and Regulatory Affairs
Biotechnology Industry Organization (BIO)