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October 6, 2008

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2008-D-0417: Draft Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings; Availability

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the *Draft Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings.* This draft guidance, as part of FDA's recently released series of Advisory Committee guidances, helps to establish a reasonable framework for Advisory Committee procedures that promotes transparency and high ethical standards, while preserving the Agency's flexibility to obtain needed expert advice on critical scientific and technical matters. However, BIO suggests that FDA ensure that this draft guidance not compromise the Agency's long-standing approach of convening Advisory Committees based on the need to solicit expert external advice relating to scientific, medical, and public health questions, rather than factors relating to non-scientific public discourse or any type of sensationalism.

BIO represents more than 1,200 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.

GENERAL COMMENTS:

BIO member companies, which are working on the forefront of science, recognize that it is often of paramount importance for FDA to obtain external expertise. FDA Advisory Committees provide such specialized expertise across a wide array of scientific, medical, and technical disciplines. BIO generally supports the development of transparent factors to help determine when an Advisory Committee should be convened. Such established factors can bring additional predictability to the Advisory Committee process and ensure that the valuable time and resources of Agency staff and external experts are utilized most efficiently.

However, BIO believes that, as currently described in the Draft Guidance, the factors listed in Section III will contribute to an environment where science and medical opinion may become secondary to non-expert interpretations that then may be mis-communicated to the public. For example, the Draft Guidance employs phrases such as "significant public interest" and "so controversial," which are open to such broad interpretation that the process of determining the need to convene Advisory Committees could become bogged down and the committee meetings could be devoted far less to scientific discussions than is in the interest of efficiency and the public health or that has been the traditional intention of these committees.

We encourage the Agency to modify the factors discussed in Section III, to ensure that FDA discussions with its Advisory Committees are centered on sound science as it relates to appropriate regulatory decisions. We believe the Guidance should state directly that Advisory Committee expertise will be sought to resolve differing scientific and medical opinions, address regulatory decisions with no previous precedent, or resolve questions that require additional specialized scientific or medical expertise.

Specifically, BIO recommends that FDA consider revising the draft guidance to reflect the following factors when determining whether to convene an advisory committee:

(a) Is the matter at issue open to differing scientific and medical interpretation such that it may be highly beneficial to obtain the advice of an Advisory Committee as part of the Agency's regulatory decision-making process?

(b) Does the matter include issues that have yet to be addressed in any previous Agency regulatory decision or has the state of science changed since a regulatory decision was made, such that the expertise of an Advisory Committee is necessary for the Agency to protect the public health?

(c) Is there a special type of expertise that an Advisory Committee could provide that is needed for the Agency to consider this matter fully?

The biotechnology industry shares FDA's commitment to ensuring that sound scientific and medical judgment is utilized to make regulatory decisions; we believe that the factors above reflect that ideal.

Additionally, the Federal Register Notice and the Background section of the Draft Guidance (page 3) state that, "An advisory committee meeting also provides a forum for a public hearing on important matters." However, we note that the Federal Advisory Committee Act does not provide for the use of Advisory Committee meetings to obtain general public input on issues. The federal government should solicit general public information by holding public hearings under 21 CFR Part 15, rather than through the advisory committee process.

SPECIFIC COMMENTS

Section, Page, Line Number	Comments and Rationale	Recommendations, Clarifications, and Proposed Changes (if applicable)
Section III.2 Examples of Scenarios in which One or More of the Factors are Often Met	We note that the FDA included examples of how/when the factors will be applied in specific circumstances. We believe the final guidance would be enhanced if it related the examples to the determining factors. For instance, it would seem that bullet 7 (safety concerns about a class) is related to factor "a." We believe the references will make the document easier to read and more comprehensible.	We believe the final guidance should include a reference in each example to the factor to which it is related.
Section III.2; Bullet 1	The phrase "first of a kind, first-in-class" is used in the draft guidance. This phrase is undefined and open to widely different interpretations. It would be preferable to use terminology that is well-understood and well-accepted, such as “new molecular entity.”	We believe this unless this phrase is defined so that it is more clear, or replaced by terminology that is well-known and accepted, it should be deleted. (Section III C and a cross reference to the point in Section III A.2.). We recommend further that, if the concept of new molecular entity is used in this context, the final Guidance make clear not only that the medicinal product involves a molecular entity not yet approved by the Agency, but also that the Agency requires additional expertise – namely, that of an advisory committee, to assist its regulatory decision process.

Section III.2; Bullets 3-4	The phrases "significant new indication," "novel product" and "new technology" are used in the draft guidance. These phrases are unclear and open to widely different interpretations, and their use could lead not only to inappropriate or unnecessary use of advisory committees, but also to inconsistencies in decision-making across FDA review divisions. Specifically, it is unclear how the vague terminology from the draft guidance can be uniformly applied across all products. We recommend in particular that the modifier "significant," to describe a new indication, be deleted or at a minimum carefully defined. Further, many of the examples in the bulleted list seem to refer to instances where the expertise of the FDA will often suffice to make regulatory decisions. We believe the convening of an advisory committee for this purpose should be confined to instances where the newness or novelty of the product, technology, or indication exceeds the expertise of the Agency, thereby necessitating the specialized expertise of an Advisory Committee.	If these terms are included in the final guidance, not only should they be clarified so that they may be more helpful with respect to triggering the decision to convene an advisory committee, but the guidance also should clarify how these terms will be applied consistently across FDA review divisions. In either case, we strongly suggest that the term "significant" be deleted. In addition, the guidance should make explicit that an Advisory Committee meeting will be convened only if and when internal FDA expertise is insufficient to resolve the scientific or medical questions.
Section III.2; Bullet 5	The bullet correctly identifies risk/benefit ratio for a product or class as a key part of the drug development and regulatory decision-making process. However, the bullet includes the phrase "…is likely to be controversial..." As noted above, we believe the guidance should be based on the FDA's commitment to utilizing sound science and medical judgment as part of its public health mission. The incorporation of "controversy" appears to suggest a willingness to allow other, non-scientific, factors to influence regulatory decision-making.	To ensure that the final guidance reinforces that FDA's public health mission should be grounded in sound scientific and medical interpretation of regulatory issues, we suggest that the final guidance read as follows: "The scientific and/or medical assessment of risk/benefit ratio of a product or class of products may differ among experts, or it appears the risks and benefits are of similar…"

Section III.2; Bullet 9	The draft guidance states that an Advisory Committee may be sought if the Agency "has significant questions or concerns about a study, including a clinical trial, post-market assessment, or product development protocol (PDP)." It is unclear from the draft guidance when the FDA would send this type of issue to an Advisory Committee. For example, does FDA envision that such a meeting would be called at the time of end-of-Phase II meetings? Or, if such a meeting were scheduled late in development, would sponsors be forced to halt ongoing clinical trials, thereby causing significant delays in development programs? And, would the data then need to be unblinded? It is also not clear whether such meetings would be closed to the public. If the FDA referred a clinical trial protocol issue to an Advisory Committee, it is of great proprietary consequence to the sponsor whether the information contained in briefing materials to Advisory Committee members would be considered confidential. Finally, it is unclear what the term "PDP" is referencing in the context of drugs and biologics. For instance, was the term generated to refer to all protocols within a product development program?	If an Advisory Committee must be consulted to provide input on a protocol or study design issue, such matters should be referred well in advance of the initiation of the trial in support of the development program. This will allow sponsors to plan development milestones and allocate resources accurately. FDA also should notify sponsors as early as possible following submission of an IND or a BBIND that a particular indication may require Advisory Committee input on key clinical trials, so any development delays incurred can be planned for. If an Advisory Committee is requested to review a program while a drug product is still in development, all briefing materials should be classified and all related meetings should be closed to the public to protect proprietary and business confidential development information. Finally, a definition of "PDP" should be included in the final guidance. If a definition is not provided, then we request the omission of the PDP acronym in the guidance.
Section III.2; Bullet 11	This bullet appears to reference joint Advisory Committee meetings. We believe further clarification should be provided to ensure that the intention of this bullet is clear.	We recommend that the bullet read as follows: "FDA has questions or concerns involving the intersection of two or more Advisory Committees (e.g., several scientific disciplines are

		required for review)."
Section III.2; Bullet 12	The draft guidance states: "FDA is seeking outside expertise on scientific techniques or research." It is unclear from the draft guidance what exactly the FDA is discussing in this bullet. For instance, this could refer to drug development paradigms for a specific product or for a class of products. We note that, if the FDA is referring to a specific product, there is the prospect of significant delays for sponsors if an Advisory Committee is convened during development.	If an Advisory Committee is consulted to provide input on a protocol or study design issue, then such matters should be referred well in advance of the initiation of the trial in support of the development program. This will allow sponsors to plan development milestones and allocate resources accurately. FDA also should notify sponsors as early as possible following submission of an IND or BBIND that a particular indication may require Advisory Committee input on key clinical trials such that the development delays incurred can be planned for.
Section III.C First of a Kind, First in Class Medical Products	The title of this section should be Section III, B, not C. As discussed above, the phrase "first of a kind, first in class" is undefined and should be replaced by well-understood, defined terminology.	We suggest that, rather than using the term "first of a kind, first in class," the guidance use a term such as "new molecular entity," which is well-known.

CONCLUSION:

BIO appreciates this opportunity to comment on *Draft Guidance for the Public and FDA Staff on Convening Advisory Committee Meetings.* We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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