December 18, 2018

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

Re: Docket No. FDA-2018-D-3103: Draft Guidance on Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications, Guidance for Industry and Review Staff.

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to submit comments regarding the FDA's Draft Guidance on Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications, Guidance for Industry and Review Staff.

BIO is the world's largest trade association representing 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.

BIO appreciates the Agency's efforts to update and release the Draft Guidance on Good Review Management Practices and Principles. BIO views this guidance as an important component for informing both Industry Sponsors and FDA staff and reviewers about the Agency's thinking around regulatory review practices and support for a more efficient and transparent review of new therapies. To both strengthen the document and ensure that all stakeholders have appropriate information and resources related to good review practices, BIO requests that the FDA cross reference other tools for Sponsors and reviewers in the finalized guidance. While we appreciate FDA's efforts to streamline the guidance, the current Draft Guidance removes a significant amount of information included in other FDA guidance documents including Manuals of Policies and Procedures (MAPPS), the FDA 21st Century Review Process Desk Reference Guide (DRG),[1] and the FDA guidance on Formal Meeting Between the FDA and Sponsors and Applicants or PDUFA Products[2] among others, however the Agency does not link to those resources in the Draft Guidance. Additionally, we also request that the FDA update the DRG (last updated in September 2014), CDER's Good Review Practices guidance, and CBER's review process to include information that was removed from the Good Review Management Practices and Principles guidance. Additionally, we note GRMPs are relevant for both original applications as well as efficacy supplements as noted in the Draft Guidance. The DRG should also be updated to add more specificity on the communication and review practices for efficacy supplements.

[1] https://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/UCM218757.pdf
[2] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM590547.pdf

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BIO also believes that review practices and principles should also allow for discussion of a potential Risk Evaluation and Mitigation Strategies (REMS), post-marketing requirements and post-marketing commitments, and labeling as early as possible in the review cycle to ensure the that these deliverables are well thought-out and feasible. To this end, BIO request that the FDA reference early discussions with Sponsors about these aspects as good review practices and principles in the Draft Guidance.

BIO would also like to emphasize the importance of both informal (non-binding) and formal (binding) meetings between Sponsors and the Agency as important mechanisms for Industry Sponsors to interact with the Agency and receive timely feedback during the review. To support communication and transparency, we encourage the Agency to continue to support development of communication plans and be open to providing such communications/advice for both original applications and efficacy supplements.

Finally, the PDUFA VI commitment letter contains a commitment that FDA will outline "*in the appropriate internal documents… the Agency's process for resolving internally any scientific or regulatory issues that arise, as well as a commitment for the medical product centers and OCP to coordinate and complete reviews and related activities when consults in timelines set forth by PDUFA and other published documents (e.g., the GRMP guidance and GRMP MAPP)"*. While the revised Draft GRMP Guidance contains an operating principle related to the importance of team collaboration, BIO suggests that the FDA more strongly add language in the Draft Guidance that reflects the PDUFA VI commitment that all medical product centers complete reviews and related activities (including resolving any scientific or regulatory issues) within a timeframe that allows for PDUFA goal dates to be met.

BIO appreciates this opportunity to submit comments regarding Draft Guidance on Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications, Guidance for Industry and Review Staff. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/
Danielle Friend, Ph.D.
Director, Science and Regulatory Affairs
Biotechnology Innovation Organization

SPECIFIC COMMENTS

SECTION	ISSUE	PROPOSED CHANGE
I. INTRODUCTION		
Lines 21-24	As described, the purpose of the guidance is to provide recommendations for GRMPs for review of NDAs, BLAs, and efficacy supplements/supplements with clinical data. Subsequently, the Draft Guidance specifically references (Lines 42-43) *the Program* (which is specific to NDAs and BLAs) and a section of the Draft Guidance dedicated just to the review of NMEs (Section V. New Product Review Process). It is not clear that the review concepts would be equally applied to the efficacy supplements and/or supplements with clinical data.	BIO requests that the FDA clarify in the Draft Guidance or in its related references that the Fundamental Values and review concepts should be consistently applied to efficacy supplements/supplements with clinical data.
Lines 38-48	This section indicates that the Draft Guidance was reissued to reflect updates in PDUFA, the implementation of BsUFA, the introduction of expedited pathways, changes to REMS, and other developments, however, aside from the bullets in lines 38-48, it is not clear what updates are in the good review management principles to reflect these new programs.	BIO requests that the FDA consider including in the introduction of the Draft Guidance how the Good Review Management Practices and Principles have changed or evolved as a result of these programs. The introduction of the Guidance could be more explicit about how the Guidance has changed since the previous version was issued.
II. BACKGROUND		
III. FUNDEMENTAL VALUES		
Lines 61-121	The 2005 Draft Guidance more distinctly captures Quality, Efficiency, Clarity, and Transparency as Fundamental Values, whereas the 2018 Draft Guidance captures these elements more loosely under the new categories of Accountability and	BIO requests that the FDA consider retaining the Quality, Efficiency, Clarity, and Transparency as Fundamental Values in the 2018 Guidance.

SECTION	ISSUE	PROPOSED CHANGE
	Communication and this new approach appears to diminish the importance of these elements.	
IV. OPERATIONAL PRINCIPLES		
Lines 145-146	In this section, the FDA indicates that "Open communication between FDA and applicants should occur at pivotal points during product development," however it is unclear what the "pivotal points" are.	BIO requests that the FDA clarify what is meant by "pivotal points" and more precisely and if possible, provide concrete examples.
Lines 169-170	The omission of important or relevant information may delay the formal review timeline, so FDA may want to make that point clear to Applicants.	For clarity, BIO requests the following edit: "Omission of important or relevant information can lead to a refusal to file action, or requests for additional information, or **a delay in the formal review timeline**".
Lines 204-210	The Draft Guidance discusses the need for flexibility in the review of an application, and that changes to the review plan are possible; however, while applicants may be told of the changes to the review timelines, sometimes they are not told why.	BIO suggests the following edit: "It also takes into account ongoing workload and other public health priorities. **The review team should inform the applicant of changes to any of the previously communicated dates within the timeline, with a brief description of the reason for the change, when feasible"** Similar language could also be incorporated the effective communication section (beginning on line 229).

SECTION	ISSUE	PROPOSED CHANGE
Lines 241-251	While we recognize the PDUFA VI agreement allows for the development of a formal communication plan for original applications, given that there can be significant new therapies that are developed and submitted as efficacy supplements, the Agency should also allow Sponsors the opportunity to enter into formal communication plans for efficacy supplements to help drive efficient development.	BIO requests that FDA consider adding language to allow for Sponsors of efficacy supplements to enter into formal communications plans.
Lines 271-276	Sponsor may decide for a wide variety of reasons not to pursue development after an initial submission. It should be at the Sponsor's discretion to make the decision to voluntarily withdraw a marketing application, taking into account a totality of factors. It may not be the best use of Sponsor or FDA resources to continue with a review of a submission that the Sponsor no longer supports.	BIO requests that the FDA consider the following edits: "~~**Although**~~ An applicant may voluntarily withdraw a marketing application at any time for various reasons, ~~**it is generally preferred that this not occur following the application's filing so that FDA can complete its review and issue a regulatory action.**~~ If an applicant voluntarily withdraws a marketing application in advance of an adverse regulatory action, the withdrawal acknowledgment letter generally includes any deficiencies identified by the review division at the time the application was withdrawn. The Sponsor should also be made aware of any user fee implications.[3]
V. NEW PRODUCT REVIEW PROCESS		
A. CDER's New Product Review Process		
Lines 30-306	Details about the specific processes mentioned in the Guidance (meetings, advisory committees) are not present on the FDA website as referenced.	BIO requests that the FDA consider including additional references, as appropriate, or ensure availability of information at the referenced website.
B. CBER's New Product Review Process		

[3] FDA Guidance for Industry: Assessing User Fees Under the Prescription Drug User Fee Amendments of 2017.