Biotechnology Innovation Organization
1201 New York Ave, NW
Suite 130
Washington, DC, 20005

December 18, 2023

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

Re: FDA-2017-D-6530; Formal Meetings Between the Food and Drug Administration and Sponsors or Applicants of Prescription Drug User Fee Act Products

Dear Recipient:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments regarding the request for information and comments on the **Formal Meetings Between the Food and Drug Administration and Sponsors or Applicants of Prescription Drug User Fee Act Products.**

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's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place.

Sincerely,

/s/
Steve Berman
Sr. Director, Science & Regulatory Affairs
Biotechnology Innovation Organization

General Comments

Consistent policies and procedures for timely, productive interactions between industry product teams and FDA reviewers are essential to efficiently advance drug and biological products through the development process. This is especially important as the complexity of drug development continues to increase. Opportunities for collaborative dialogue on innovative approaches and for rapid clarification of FDA responses were priorities for the industry as part of PDUFA VII. To this end, we applaud the Agency for timely implementation of new formal meetings (Type D and INTERACT) as well as a new follow-up opportunity for clarifying questions. We believe this is an important step to bring much needed efficiency to the drug development process. However, Sponsors continue to experience considerable variation across review divisions and centers with respect to meeting formats, ability to engage with reviewers on complex topics in the context of a specific product, and ability to obtain timely clarifications.

The guidance speaks of the different meeting formats in Section IV (In-person F2F, Virtual F2F, Teleconference, and Written Response Only (WRO)) but it doesn't indicate which meeting types are more acceptable for in-person versus virtual. While we appreciate that this may depend on the specifics of the topics being discussed, it would be helpful for the guidance to include some general parameters regarding when FDA is more likely to grant an in-person meeting.

- **WRO:**
  - Industry Sponsors have experienced an increasing shift towards use of WRO in lieu of teleconference or face-to-face meetings, even for meetings intended to address complex topics such as INTERACT meetings. While we recognize that the FDA applies the same level of consideration to WRO responses as it does to live meetings, we note that WRO limits the ability for dynamic exchange which is particularly important when Sponsors are employing novel approaches. We encourage FDA to outline the criteria applied in determining the appropriateness of WRO. [See CBER SOPP noted in comment] BIO acknowledges the "Request for Clarification" process, but considering the scope (clarification), the timeline of those (20 days for each part to respond), it should complement rather than replace the opportunity for a sponsor to respond or clarify its position. Alternatively, we ask FDA to consider other opportunities to interact with the Agency after a WRO beyond the limited clarification process.
- **Type D meeting:**
  - Per the guidance, innovative topics are listed as those that could be discussed at the Type D meeting. However, innovative topics usually involve complex issues which require more extensive advice than currently considered appropriate for this meeting Type. Therefore, we encourage the Agency to provide more examples of when requesting a Type D meeting would be most appropriate, or not appropriate, and to include such examples in public workshops as appropriate.
- **INTERACT:**
  - BIO requests the Agency consider clarifying the difference between the INTERACT and pre-IND meetings to minimize the risk of INTERACT meeting requests being rejected or re-classified by the FDA.

- **Number of Meetings Granted:**
    - The draft guidance encourages Sponsors to address product development issues in the fewest possible meetings while also avoiding meetings with too many questions. While the guidance notes that novel programs with many complex issues can discuss the need for additional meetings with the division, we find that experience in obtaining meetings to address such complex issues varies across review divisions and by topic (i.e., some divisions are more willing than others to discuss innovative topics than others). We encourage the Agency to describe how Sponsors can work with FDA regulatory program managers to develop a communication plan to ensure timely discussions when necessary.

LINE-BY-LINE RECOMMENDED EDITS

SECTION/LINE	ISSUE	PROPOSED CHANGE
I. Introduction		
II. Background		
III. Meeting Types		
A. Type A Meeting		
B. Type B Meeting		
	Historically, Type B Meetings have been used to discuss efficacy supplements (sNDAs/sBLAs) based on new clinical data, but the guidance is silent about applicability to efficacy supplements.	BIO recommends FDA that the final guidance states that Type B meetings can also be used to discuss efficacy supplements based on new clinical data. BIO also recommends that this be clarified for Type B (EOP) meetings such that sponsors can request end-of-phase 2 (i.e., pre-phase 3 meetings) for new indications.
C. Type B Meeting (EOP)		
D. Type C Meeting		
E. Type D Meeting		
132-133	Original text: "A Type D meeting is focused on a narrow set of issues that are used to discuss issues at key decision points to provide timely feedback critical to move the program forward (e.g., often one, but typically not more than two issues and associated questions)." This sentence is confusing. We recommended changes to clarify FDA's intent.	BIO recommends FDA consider the following language: "A Type D meeting is focused on a narrow set of issues. These meetings ~~that~~ are used to discuss issues at key decision points to provide timely feedback critical to move the program forward (e.g., often one, but typically not more than two issues and associated questions)."
154	The Draft Guidance states, "FDA will inform Sponsor that the Agency will be converting the meeting to the appropriate meeting type…"	BIO asks FDA to clarify whether this will be done within the 14-day timeline and if so, suggest referencing the table(s) later in the document for conversion to other Meeting type.

	It is unclear what the timeline for FDA to inform the sponsor regarding its decision to convert the request to another meeting type (e.g., is it the same 14-day timeline for Agency to respond to meeting request for Type D meeting).	
F. INTERACT Meeting		
197	It is unclear what CMC issues and testing strategies are appropriate for discussion.	BIO recommends FDA provide examples what CMC issues and testing strategies to demonstrate adequate safety to support a FIH study should be discussed in an INTERACT meeting versus a pre-IND meeting.
200	It is unclear what falls into "overall advice related to the design" in the text below: "Overall advice related to the design of proof-of-concept or other pilot safety/biodistribution studies necessary to support administration of an investigational product in a first-in-human clinical trial"	BIO recommends FDA provide examples and/or clarify the specific parameters that are appropriate to discuss relative to the design of POC/safety/BD studies and if they are necessary to support FIH clinical trials. It would be helpful to specifically clarify what parameters should be discussed in an INTERACT meeting versus a pre-IND meeting.
IV. Meeting Formats		
V. Meeting Requests		
330-336	The Sponsor may not be in a position to determine which individual FDA attendees would be considered as nonessential FDA attendees, particularly for products early in development (e.g., for PIND meetings). FDA themselves may determine whom from a particular discipline at FDA would be determined as a core or nonessential attendee.	BIO recommends FDA provide clarification regarding "nonessential FDA staff or disciplines"
346/323	In the previous guidance (2017) numbering point 4 stated "A list of the specific objectives or outcomes the requester expects from the meeting". Per	BIO recommends FDA clarifies if a separate 'list of objectives' section is still the expectation.

	line 346 (new guidance), the expectation is for objectives to be included. However, there is no clarity if this should be a separate section or should be a part of the agenda or as part of the statement of purpose of the meeting. We further note that the purpose and objectives for a meeting are closely related and can be difficult to distinguish. The current draft proposes a single section and BIO agrees that a single section is sufficient. However, we would propose that the term objectives be used as the term is more specific and less ambiguous.	If yes, BIO recommends that FDA clarify the difference between purpose and objectives, and reinstate the text for requiring list of objectives. If separate objectives are not expected then, our recommendation is to remove the text from line 346.
355-356	In some cases, in order to avoid duplication, a sub-question may be the most appropriate and clearest way to format a question. For example, if the response to a question is dependent upon the response to a prior question.	BIO recommends FDA acknowledge that in some circumstances a sub question may be the most appropriate/clearest format – even if the sub question counts toward the total number of questions
361 - 363	Original text: “The numbering of each question in the meeting request (see section VI, Assessing and Responding to Meeting Requests) should be identical to the numbering of each question in the meeting package.” We note that a rigid specification of identical numbering questions between the meeting request and meeting package	We recommend that FDA consider a more flexible approach that would allow for minor changes, as new evidence is often generated during drug development, and suggest the following revision: “The topics/disciplines covered in the meeting request (see section VI, Assessing and Responding to Meeting Requests) should be consistent with the topics/disciplines covered in the meeting package.”

	may result in sub-optimal discussion or written feedback. It is possible that Sponsors may revise the list of questions on the same topic/disciplines in a pre-meeting package to help ensure clarity is received in the resulting discussion or written feedback. For example, if a new analysis or publication becomes available between the time of meeting request submission and the time of pre-meeting package submission, it may be beneficial to revise the question list accordingly.	
VI. Assessing and Responding to Meeting Requests		
369-371	Original text: "The FDA will review the request and make a determination on whether a WRO is appropriate or whether an in-person face-to-face, virtual face-to-face, teleconference, or WRO (see section IV., Meeting Formats) meeting is necessary." The structure of this sentence suggests that alternatives that are not WRO would be contemplated if a WRO is deemed inappropriate. We recommend changes for clarity.	BIO recommends FDA consider the following edit: "The FDA will review the request and make a determination on whether a WRO is appropriate or whether an in person face-to-face, virtual face-to-face, <u>or</u> teleconference~~, or WRO~~ (see section IV., Meeting Formats) meeting is necessary." Furthermore, as noted earlier, we request that the FDA outline the criteria applied in determining the appropriateness of WRO.
375	"For pre-IND, Type C, Type D, and INTERACT meetings, although the sponsor may request an in-person, virtual, or teleconference meeting, the Agency may determine that a written response to the sponsor's questions would be the most	Understanding that the list would not be definitive or exhaustive, it would be helpful to sponsors preparing meeting requests if the Agency could provide examples of the factors it uses when determining the most appropriate meeting/response format.

	appropriate means for providing feedback and advice to the sponsor. “	
A. Meeting Denied		
B. Meeting Granted		
VII. Meeting Package		
A. Timing of Meeting Package Submission		
B. Where and How Many Copies of Meeting Packages to Send		
C. Meeting Package Content		
500-504	Original text: “Meeting packages generally should include the following information, preferably in the order listed below: Meeting packages should include the same first nine items provided for the meeting request (see above section V.), and in addition, should include:” We recommend rewriting this text for clarity.	BIO recommends FDA consider the following edit: “~~Meeting packages generally should include the following information, preferably in the order listed below:~~ Meeting packages should include the same first nine items provided for the meeting request (see above section V.)~~., and in addition, should include:~~ In addition to the first nine items described in section V., the following information should be included, preferably in the order listed below:”
VIII. Preliminary Responses		
IX. Rescheduling and Canceling Meetings		
X. Meeting Conduct		
639-641	Original text: “Presentations by requesters are usually unnecessary because the information necessary for review and discussion should be part of the meeting package. If a requester plans to make a presentation, the presentation materials should be provided ahead of the meeting.”	We encourage FDA to outline considerations for when use of slides may be helpful and or appropriate.

	We agree that any information shared or discussed in a meeting should be provided ahead of the meeting. However, we believe that in some cases, the use of slides may be helpful to present complex information during meetings, and we note that in such cases proposed slides can potentially be included as part of the meeting package (i.e., as a figure). We also note that in some cases after receipt of preliminary comments, FDA program managers have requested slides be shared in meetings.	
XI. Meeting Minutes		
732-733	Original text: "…to include if the preliminary comments serve as the final minutes for a canceled meeting." BIO suggests that FDA clarify this line as it can be interpreted several ways e.g., 1) that a Sponsor needs to send a "Request for Clarification" to confirm the preliminary comments serve as the final minutes for a canceled meeting, or 2) that a Sponsor is eligible to submit a request for clarification in instances where the preliminary comments serve as the final minutes for a canceled meeting.	BIO requests that FDA clarify the intent of this sentence.
References		
Appendix: Summary of Meeting Management Procedural Goals		