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March 4, 2024

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

**Re: FDA-2023-N-5653; Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance**

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 **Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance**.

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/

Neil Ichiro Laruan  
Manager, Science & Regulatory Affairs  
Biotechnology Innovation Organization



## **General Comments**

BIO appreciates the FDA's commitment to assessing current practices in developing guidance documents and ensuring stakeholders are involved, specifically in their best practices for guidance development. BIO also commends the FDA's commitment to providing guidance documents to stakeholders to ensure transparency, predictability, and efficiency, considering the increasing number of guidance documents issued in the last 10-15 years.

BIO also appreciates the FDA's consideration of opportunities to streamline guidance document development processes and ensure that their regulatory thinking is communicated to stakeholders promptly. Clear and concise communication of FDA's policies and expectations through the development and timely publication of guidance documents are critical to fostering innovation and getting therapies to patients in need. Delays in issuing new guidance can undermine the industry's drug development efforts and ultimately impact patient access to needed medical products and therapies. Based on this draft report and plan, BIO finds the FDA is contemplating the broader use of an immediate implementation approach on Level 1 guidance. This practice was enacted under the COVID-19 public health emergency, which BIO found appropriate and effective in serving a critical public health need. However, we also note that public participation is essential for developing guidance that ensures public health needs are appropriately identified and addressed and that the guidance clearly outlines critical factors for consideration for those advancing important therapies for patients. Allowing stakeholders to provide feedback on draft guidance documents gives the Agency critical insights and helps identify gaps or issues. Additionally, public comments are essential to ensuring the Agency's recommendations meet stakeholders' needs. Because of this, we raise concerns regarding the shift to advance a greater number of guidance documents using an immediate implementation approach. Ideally, the guidelines for immediate implementation should remain limited to emergency situations.

Also, the report describes how different Centers and Offices have initiated best practices to guidance document development, however, it is not clarified if the Centers and Offices are collaborating on their efforts. We feel it is essential that the FDA look for efficiencies across Centers and Offices in implementing best practices for guidance. For example, regarding communicating withdrawn/obsolete guidance, the Centers do not share these updates consistently and efficiently. While all have a withdrawn/expired guidance list, only CDRH provides a link where viewers can easily access it.

Lastly, BIO would welcome the FDA in providing feedback on how comments may be more efficiently provided to the agency—for example, the use of general comments, specific-line item comments, and redlining edits. This can be useful to ensure that stakeholders provide input most preferred by the FDA and help the process be efficient.

## **Specific Comments based on Federal Register Prompts:**

### **1. FDA solicits input on whether there are additional or revised practices consistent with our statutory and regulatory framework for the Agency to consider.**

BIO appreciates the FDA in posting links to withdrawn guidance documents as they can be helpful to stakeholders in understanding the historical progression of a topic and what changes have been made based on public feedback. BIO recommends that the FDA continue providing links to withdrawn and obsolete guidance documents with clear



identification, such as to a certain date as a reference, for example, by including the link to the outdated version. Regarding changes within draft guidance documents, BIO requests that the FDA consider annotating any key differences from the original draft version to the newer/final version. We recommend the Agency provide a track-changes/redlined version of the final guidance as changes made to final documents can be challenging to identify. This ensures that the industry identifies and emphasizes the change more quickly. In addition, BIO recommends the FDA explain why specific changes were made. This helps ensure stakeholders' understanding regarding the updates to the guidance documents. In addition, while FDA provides and actively updates the list of guidance documents as they are released, BIO suggests FDA consider developing an enhanced and more robust guidance database. This can include summaries of current guidance, links to referenced, withdrawn, and obsolete guidance, better search functionality, and other enhancements.

- 2. In light of the above [referring to Federal Register (FR)], we seek input on whether there are any additional circumstances, categories of guidance documents, or topics for guidance for which it may be appropriate and consistent with the FD&C Act and FDA's GGP regulation for FDA to consider issuance as a Level 1 guidance document for immediate implementation without prior public comment. We also seek comment on whether there are additional categories or types of guidance documents that FDA should consider issuing as Level 2 guidance documents to streamline the guidance process and allow the Agency to better leverage its resources for the timely development of more guidance documents.**

No specific comments at this time.

- 3. FDA requests comment on any novel guidance document formats that would be of particular utility, such as the use of templates to accompany a guidance document, Q&A formats, flowcharts, etc., that are used in FDA guidance documents or that were used in guidance documents issued in response to the COVID-19 PHE**

BIO encourages FDA to consider additional methods and mechanisms to share their evolving thinking on specific topics. This can be particularly helpful in rapidly changing fields (e.g., cell and gene therapies) or areas where the FDA sees similar questions or issues from multiple sponsors. One example is the additional use of a brief, bulleted guidance format. BIO finds the format (similar to disease-specific guidance) appropriate and helpful in understanding FDA's current thinking. It also allows guidance documents to be revised to include additional detail as the FDA gains more knowledge and experience on the topic. Another method the FDA could consider is hosting "State of the Science" briefings whereby the Agency proactively identifies regulatory topics with known or potential impacts on multiple drug development programs and invites stakeholders to meet collectively with the Agency and to hear perspectives on the issue. Lastly, another example of ways the Agency can rapidly convey current thinking on topics is by conducting more Town Halls. For example, [CBER OTOT Town Hall: Clinical Development of Gene Therapy Products for Rare Diseases](#) offered registrants the opportunity to submit questions for the agency to address in real-time. The recordings



and transcripts of these events can serve as another resource for stakeholders looking for additional guidance.

BIO also notes the Q&A format for guidance documents can be very helpful in navigating a lengthy and complex document. Regardless of the format, BIO further recommends that FDA consider supplementing a published complex guidance document with a Q&A format on FDA's website. This allows the Agency to update direction to sponsors and other stakeholders in a timely manner. Two examples are [Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act: Frequently Asked Questions on Pediatric Exclusivity \(505A\)](#) and [FDA's Digital Health Policy Navigator](#). These provide and emphasize critical information, especially on complex topics touched on by multiple guidance documents. Lastly, BIO recommends that the FDA include guidance examples or hypotheticals within the guidance documents as much as possible, as these can augment a guidance's content by applying concepts to practical scenarios, providing greater clarity to stakeholders on the FDA's expectations for the industry. These practical scenarios could be gathered from stakeholders' experience on the topic received prior to the guidance's finalization (e.g., workshops.)

**4. FDA requests comments on the utility of guidance in streamlining regulatory submissions and whether there are additional categories or types of guidance that would be helpful to streamline processes for regulatory submissions to the Agency.**

No specific comments at this time.

**5. FDA requests comments on whether the currently available mechanisms for submitting suggested areas for guidance development and proposed guidance documents are useful and sufficient or whether additional mechanisms, for example, a Center-specific or Office-specific mailbox for such suggestions, would ease the process for such submissions.**

FDA has noted that requests for guidance documents come to FDA informally through various means such as advisory committees, industry meetings, roundtables, and listening sessions. BIO finds that all these avenues for providing such information are essential. BIO suggests FDA consider increasing its utilization of FR Request for Information (RFI) dockets to gather initial stakeholder input on topics in the early phases of development. When a topic is new or broad, an RFI could help the Agency understand what is important to stakeholders and where areas of focus and guidance may be most helpful or feasible in the short-, mid-, and long-term. For example, in 2023, the FDA [released](#) an FR Notice seeking comments on methodological challenges related to patient experience data. The broad request allowed stakeholders to provide robust feedback on various topics for FDA's consideration.

Given the various opportunities to provide information to FDA that can lead to developing new guidance documents, it would be helpful for FDA to share their preferred public mechanism for formally suggesting new or revised guidance documents. FDA's suggestion of Center-specific mailboxes is one option that would be less cumbersome



than a docket submission. FDA could then share proposed topics received at a determined frequency, prompting each Center to update its guidance agendas.

**6. FDA Centers publish guidance agendas on their web pages to give interested parties and the public notice of the areas in which FDA is considering upcoming guidance. We request comment on the utility of these guidance agendas and what, if any, modifications to these agendas would be helpful for the Agency to consider.**

BIO finds the FDA guidance agendas useful and valuable to inform and support policy-shaping activities. This often enables more detailed comments to be submitted once the guidance document is released as industry and other relevant stakeholders can be better prepared. BIO suggests that when guidance agendas are published, FDA allow comments or feedback from the industry and other stakeholders. This could help inform FDA topics that are important to stakeholders and provide another avenue of providing information to FDA regarding guidance topics, which can overall support FDA's prioritization. As the FDA notes that the guidance agenda lists "possible topics" for future guidance development or revision, it would be helpful if the FDA could provide a distinction of the guidance document's status (conceptualizing, drafting, clearance, not started) when possible, to support predictability. Currently, the guidance agendas only provide the categories and title of each guidance document. We recommend the Agency adopt a new template that would provide more details on the guidance documents, like development status. These changes will allow for greater transparency and remove uncertainty for stakeholders. Further, FDA should commit to reviewing these guidance agendas at a regular cadence and removing any items that are not anticipated to publish in the coming 1-3 years. Having an agency-wide guidance agenda as a list on FDA's website that can be filtered by topic area and center would help stakeholders navigate and search the agenda for topics of interest and increase visibility of cross-center topics, while retaining the center specific view, when preferred. This database should also retain obsolete guidance, mentioning their status as obsolete and providing a link to the version of the guidance replacing the obsolete document.