December 23, 2020

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

Re: Docket No. FDA–2020-N-1550: New Drug Regulatory Program Modernization: Implementation of the Integrated Assessment of Marketing Applications and Integrated Review Documentation.

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments regarding the New Drug Regulatory Modernization: Improving Approval Package Documentation and Communication.

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 diseases, and to prevent diseases in the first place.

BIO appreciates FDA's goal of providing greater clarity on FDA's application review and decision-making process. We commend FDA's efforts to modernize the New Drug Regulatory Program and appreciate that the Agency is seeking feedback from stakeholders both through the public meeting that was held on October 30, 2020 and through this docket. BIO commends the Agency's efforts to improve transparency in the drug approval process and believes increased transparency will ultimately benefit patients.

BIO's Membership believes that FDA's new review documentation allows for the clear delineation of FDA's rationale for drug approval. FDA's new integrated review documentation constitutes, what BIO believes, to be an improvement over the older template, as it is easier to navigate and provides greater clarity and transparency on key information that was considered in the context of the review. This helps Sponsors better understand the Agency's thinking and, in turn, could lead to the submission of stronger marketing applications, more first cycle approvals, and ultimately benefit patients in need of new therapies. The information in the new integrated documentation can be used to understand how individual trials were designed, the outcome measures used, and results of the studies. In addition, it is possible to understand at a submission-level how the information from the individual trials was used by FDA for regulatory decision-making. Increased knowledge sharing can help to decrease development burdens across industry. Additionally, we envision that the integrated review should provide insights to other regulators who may refer to FDA's findings as they make their own regulatory decisions as long as FDA's decision making is clear and transparent.

1201 Maryland Avenue SW
Suite 900
Washington DC 20024

202.962.9200 P
202.488.6306 F
bio.org

We have outlined below several recommendations for FDA to consider throughout implementation of the integrated review assessment and documentation to ensure that the documentation is as useful as possible to all relevant stakeholders.

Information that is Difficult to Find or is not Located in the Integrated Review Documentation

BIO requests that the FDA ensure that any relevant information is not removed or omitted as the new documentation is implemented. There may be potential to inadvertently omit key information with the issue-focused approach to integrated review and template for topics which may not present an issue after appropriate review of data/information submitted by the Sponsor. Additionally, this information may be helpful to other regulators who are relying on FDA's findings. BIO requests that the FDA consider establishing mechanisms to ensure that all key information is captured in the template, even if it may not pose a question or raise an issue after review of the marketing application. Additionally, we request that if information is moved to the appendix of the document, that the information remain available to the public without the requirement of submitting a Freedom of Information Act (FOIA) request.

BIO's position is that FDA's full transparency in posting action packages for approved drugs and biologics is a critical part of FDA's relationship with the drug/biologic/combination product development ecosystem. However, in 2018, FDA changed its policy and no longer supports full transparency regarding its regulatory advice, decisions, and the administrative record. Specifically, there is significant content in the administrative correspondence section of action packages that is now omitted. BIO respectfully requests that FDA revisit its 2018 policy change and return to posting full and complete administrative correspondence packages as part of the FDA action package.

BIO also requests that the FDA provide in the appendices a summary of the regulatory exclusivity associated with the application (i.e., any FDA awarded exclusivity such as orphan drug, new chemical entity, pediatric exclusivity, etc.). Similarly, it would also be helpful if the FDA indicated the review designations (e.g., breakthrough therapy designation), as well as use or issuance of a priority review voucher. If the application under review is for a combination product, a summary of any human factors studies or other assessments required by the Agency for approval should also be included.

FDA publishes the redacted versions of the review package after product approval. For some sections (clinical, nonclinical) much of the review is unredacted. For chemistry, manufacturing, and controls (CMC), almost all of the information is redacted due to intellectual property reasons. This information is never shared with the Applicant and in some cases the FDA has told the Applicant that a FOIA request would be needed in order to obtain the information. BIO requests that FDA consider opportunities for sharing CMC information with applicants without the need for submission of a FOIA request.

BIO also requests that the FDA clearly reference information on the review of drug development tools and new technologies (e.g., clinical outcome assessments (COA), patient reported outcomes, digital tools, and real-world evidence). Specifically, we find that across reviews, different versions of the Patient Experience Data Table (PED Table) have been

used and different reviewers may populate the Table to varying degrees. We also recognize that in recent updates to the eCTD Technical Conformance Guide[1], FDA indicates that if submitting patient experience data as part of an application for marketing approval, the Sponsor should populate the PED Table. However, patient experience data other than those submitted by the Sponsor may also inform drug review. We thus encourage the Agency to consider mechanisms to ensure that patient experience data is provided in a complete and consistent format in dedicated sections of the integrated review for all patient experience data considered in the context of the review. FDA should also ensure the linkage between patient experience data provided or otherwise considered in the context of its review and regulatory decision-making is clearly reflected in both the benefit-risk assessment, as well as the PED Table, when applicable. To support consistency in how the PED Table is populated in the final review documentation, and to ensure the inclusion of the minimum amount of information that would make the PED Table informative and meaningful to a wide range of stakeholders, FDA may consider outlining a core set of information that reviewers should include in the populated PED Table and related sections of the review documents. BIO recommends the following three core areas of information regarding PED considered in the context of application review for inclusion in the multidisciplinary review documents:

1. Description: A brief description of the type(s) of patient experience data, study objective, design, and methods for collection (e.g., focus group, advisory boards, listening sessions, testimonials, survey, one-on-one interview, clinical outcome assessment, patient stakeholder meeting, FDA-led patient stakeholder meeting), including a description of who submitted or collected the data (e.g., sponsors, patient organization, FDA);
2. Assessment Considerations: Information on how FDA considered the patient experience data and to what extent.
    a. Information on what aspects of the review and regulatory decisions the patient experience data informed (e.g., benefit-risk assessment, review of the clinical study design, endpoint selection, other aspects of drug development, labeling or other patient communication), how the data was weighed in relation to other data considered, and where the discussion of the decision process can be found in the review document (e.g., benefit-risk framework, section of product label);
3. Exclusion Rationale: If patient experience data were not considered in the context of a regulatory decision, provide rationale as to why the patient experience data were not considered and what criteria were applied by reviewers to assess the utility of patient experience data (e.g., patient experience were not representative of the patient populations).

FDA's improvements in this regard, to better convey how patient experience data and information for other drug development tools (e.g., real-world data) influence its decision-making should be made available to stakeholders in a clear, plain-language format, to ensure broad and equal utility for those who study, develop, prescribe, and/or take therapies regulated by FDA.

[1] FDA eCTD Technical Conformance Guide: Technical Specifications Document.

Areas of the Integrated Review documentation of the Integrated Assessment that can be Improved to Meet the Needs of Stakeholders

Given current technology, we encourage FDA to consider providing the information included in the integrated review in an electronic format that can easily be searched across products. The ability to search across reviews increases shared learnings throughout the industry and has the potential to streamline drug development especially in therapeutic areas where there is no guidance. In addition, FDA should consider making the new review template available in downloadable formats other than PDF. We understand, for example, that, in connection with the Office of New Drug reorganization, and FDA's modernization efforts the FDA will be utilizing technology platforms that will facilitate review of similar issues across applications, improve accessibility to institutional knowledge based on existing reviews, and better support information sharing among review teams and across divisions (i.e., knowledge management). Other stakeholders looking at review information and decisions across review divisions likewise would benefit from being able to access this higher-level view through the use of updated technologies and media. It is unclear what tools, programs, or software FDA is using to facilitate its internal updates in this regard, so this request is not specific to what format (beyond PDF) should be used to publish the integrated reviews, but FDA might consider XML as this is recognized as a global standard.[2]

BIO also strongly takes the position that in order for FDA to support full transparency, in addition to publishing review documentation for original applications, the Agency should also make publicly available review documentation for supplemental applications. This is especially important as a greater number of supplemental applications are including patient experience data and/or using other drug development tools.

Industry feedback or Advice on Collaborative Writing

At the public meeting, FDA requested feedback from Industry on collaborative writing. Below are some Industry best practices on collaborative writing for FDA to consider:

- For interdisciplinary regulatory documents, separate disciplines own the content, but the document is owned overall by the Regulatory Affairs (RA) Lead on the project. The RA Lead is responsible for making sure all content owners' voices are heard and that the document as a whole is cohesive and "speaks with one voice."
- Regulatory asks each discipline to align with their management early and often in the process to promote efficient review cycles.
- The document is housed in a central online location where it can be edited and reviewed simultaneously in real time by all authors.
- Interdisciplinary comment resolution meetings are held after every review. The number of review cycles depends on the complexity of the document.
- Regulatory organizes and leads team and sub-team meetings as often as needed throughout the process in order to facilitate interdisciplinary conversations and resolve disagreements.

[2] Health Level Seven, Inc.

Thank you once again for allowing BIO to provide feedback on New Drug Regulatory Program Modernization: Implementation of the Integrated Assessment of Marketing Applications and Integrated Review Documentation. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

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