July 30th, 2020

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

Re: Docket No. FDA–2019-D-5799: FDA's Public Meeting, Modernizing the Food and Drug Administration's Data Strategy.

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to submit comments regarding FDA's Public Meeting, Modernizing the Food and Drug Administration's Data Strategy.

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.

When discussing "data" throughout this letter, BIO takes a broad definition as laid out in FDA's Technology Modernization Action Plan (TMAP), "…the data that is collected during the routine care of patients, coupled with traditional clinical trial evidence, will be used to generate steady improvements in future patient care. Other data types, such as genomic or toxicology data, and output from medical devices, are a part of the data ecosystem. Data-informed technologies, such as distributed ledger solutions like blockchain, will be critical to support FDA's track-and-trace priorities."

We support FDA's efforts to modernize its data strategy to ultimately transform the way data is shared, analyzed, and utilized for regulatory purposes. It will be important to keep in mind, however, as FDA considers these advancements that just as it will take FDA time to implement appropriate IT infrastructure and capabilities to enable these modernizations, industry will need time to implement compatible technologies and processes as well. FDA's engagement with stakeholders, including industry, in these cases is critical and should, most importantly, allow for flexibility, optional adoption by industry, and/or a phased approach with ample time for implementation as appropriate.

BIO requests the following key features be considered as FDA continues discussions regarding its modernization efforts:

I. Transparency on FDA's Data Strategy and Inclusion of Sponsors in Discussions

BIO appreciates that FDA is involving stakeholders in its planning and discussions regarding modernizing its data strategy, engagement with stakeholders on all these aspects is

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important to ensure broad understanding and to provide a clear, consistent, and predictable approach to these modernized initiatives. By ensuring common understanding across stakeholders early on in development and by allowing routine input and engagement, it will be more likely that these modernization efforts will meet the needs of all involved and will have the greatest chance of success to drive true transformation and innovation.

We are encouraged by FDA's repeated comments during the Public Meeting of the importance of stakeholder input and the many other meetings to come. This inclusion of broad stakeholder input and expertise can help FDA understand what can or cannot be feasibly accomplished and should be done in concert with Sponsors as one of the key stakeholders.

As these discussions continue, and as FDA begins to make further plans towards implementation, BIO encourages additional transparency on key topics such as data ownership, funding, privacy, data protections, Third Party Agreement (TPAS) with Sponsor data partners, and data automation. It will also be important to understand FDA's use and functionality of algorithms and artificial intelligence (AI) for things such as signal detection and adverse event reporting. This should include routine assessment of the inherent limitations of AI as the understanding of the field develops, particularly as it relates to biases or errors as the machine learning evaluates associations. Further, understanding of FDA's specific goals and targets for data use across the Agency, including understanding ongoing evaluation of progress and how success will be measured, will build confidence among stakeholders in the overarching modernization effort.

We suggest that FDA develop a methodology for periodic review of its data strategy to ensure it is current, fit for purpose, and transparent. This will allow FDA and other stakeholders to make adjustments as new technologies are developed and data use evolves. Further, we greatly support FDA's use-case approach of matching the right technology to the right public health problem, rather than creating a strategy that is tied to a particular technology. This ensures that the right approach is taken for the specific instance and helps to manage rapidly changing options in technologies.

We request more clarity in the Agency's long-term data strategy, particularly for regulatory submission and review (e.g., 5 and 10 year outlook), and the relationship of that strategy with Center-level technical roadmaps, pilots with industry, and global considerations such as harmonization through the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and Council for International Organizations of Medical Sciences (CIOMS) Working Group.

It will be important to understand the holistic view of the various ongoing initiatives within FDA and how they fit together with the data modernization efforts. Examples of these ongoing initiatives include the Pharmaceutical Quality/Chemistry Manufacturing & Controls (PQ/CMC) data standardization effort and Knowledge-aided Assessment & Structured Application (KASA) in the quality space, as well as the initiatives listed in FDA's Data Standards Program Action Plan v4.0, among others. It will be important to understand how PQ/CMC and KASA are envisioned in relationship with overall e-submissions and internal assessments initiatives at FDA, and with global agreements (ICH eCTD) as well as their relationship to cloud-based submissions in the future. Further, as IT tools and data modernization will help other ongoing regulatory programs such as Project Orbis and real-

time oncology review (RTOR), we request that FDA keep such initiatives in mind as the modernization work and data strategy frameworks are developed.

To minimize any misalignments, we urge the fullest engagement with Sponsors on Agency assessment and adoption of data management and analysis tools used by FDA to view datasets. This includes participation in FDA initiatives to establish standards and algorithms for risk assessment, control, and communication, and definition of the future model submissions. FDA has discussed opportunities to move towards a "continuous" real-time build into a live eCTD/submission, and moving from static "point-in-time data sets" to updating digital data streams for analyses, so collaboration on standards, processes, and validation is critical.

Further, FDA should ensure that Sponsors and other stakeholders are involved in discussions regarding the development of algorithms and analysis. Discussions should include the topics of governance of data, the ownership of the master data, ability of the Agency to use the data for other things than review of applications, as well the logging, audit and traceability of algorithm performance related to supervised and unsupervised learning models and/or robotic process automation (RPA).

II. Expertise to Support FDA's Data Strategy

As with other new initiatives, particularly those that include technical aspects, it is critical to ensure that FDA has the ability to access and utilize appropriate experts in various fields in order to establish and carry out the data strategy. Expertise in establishing and interpreting algorithms, privacy, data security, among others will be essential to the success of FDA's new data strategy.

As such, BIO supports FDA's discussion of engaging broader technology and healthcare industry data expertise in the development and adoption of a new data strategy and urge continued engagement with Sponsors. Leveraging common regulatory data standards and transparency in analytical tools to assess data will enable efficiency in use of healthcare data, submission and review processes, and minimize the need for text-based summations in dossiers. Broader industry expertise can also ensure the strongest cybersecurity strategies and access controls to allow for safe access to Sponsor/vendor-managed datasets and maintaining patient-privacy considerations.

III. Cross-Center, Cross-Government Alignment and Interoperability

Paramount to a new data strategy is close coordination across and between Centers, Divisions, and reviewers to align implementation, adoption, and consistent application across FDA. This will promote seamless access to information across Centers. Some of these aspects will include use of common data elements, connecting and ensuring interoperability of all systems including eCTD, and the ability to easily link to other Federal repositories (e.g., CT.gov).

BIO notes that there has historically been disconnect between each Center's IT system that is the repository for review documentation and submission content. For instance, the Center for Devices and Radiological Health (CDRH) has not utilized the eCTD and there are different platforms and technologies used throughout the Agency. This has historically resulted in

difficulties sharing information across the Agency and may cause delays in the review process because of the lack of access to review data. We understand that this is currently being addressed within the Agency, but additional details and transparency would be appreciated.

There is also now a significant need to align within the Agency as there is greater overlap of product areas (e.g., digital health, combination product, combined use applications, digital therapeutics), to ensure clear and consistent understanding of the regulatory requirements, and to enable consistent application of guidances and regulations across the Agency. To the extent the Agency's TMAP intends to address this issue, it would be helpful to have transparency around these efforts, so industry can lend its support.

We also believe that discussion and alignment within the FDA on the interpretation and enforcement of guidances and policies is critical for success. Increased collaboration and communication within the Agency and across Centers and Divisions, including technical teams downstream to review divisions such as the Office of Business Informatics is important as they give advice or guidance on specific questions, to ensure the review divisions are consulted with, and that decisions are communicated across the Agency. This will help ensure consistent application of guidances and policies and reduce confusion among Sponsors.

IV. International Harmonization and Interoperability

To reflect a globally regulated marketplace, we encourage active harmonization and convergence with other health authorities, particularly within international forums such as ICH, the International Organization for Standardization (ISO), and the Identification of Medicinal Products (IDMP). This international engagement will help to drive international harmonization and convergence of regulatory requirements alongside global data modernization initiatives and to promote the design of systems that optimize secure confidential exchanges between regulators to support cooperation, reliance, and regulator work-sharing internationally.

Important topics for consideration within an international context will include the use of international standards and terminology, an effort to increase the reliability and speed of the gateway, harmonizing globally on the eCTD, and understanding how these data efforts will ensure consistent implementation of ICH guidelines.

We also urge FDA to consider how this initiative can support, make use of, and broaden various ongoing convergence work, including work-sharing and mutual reliance efforts. BIO also notes that "data-based" submissions efforts for various parts of the eCTD are currently underway (e.g., PQ/CMC and KASA are focused on the Quality Section of the eCTD), and that there are additional discussions and initiatives that will impact other parts of the submissions and review. However, there is currently no long-term roadmap that lays out how FDA sees all of this coming together for both the FDA and for ICH standardized submission. We recommend FDA use this modernization effort as well as the TMAP as a collaboration opportunity to clearly develop these ideas further and develop approaches for cloud-based submission. Included in this conversation should be discussion of what will be needed on both the FDA and Sponsor end to support any efforts and build in appropriate flexibility and potential phase-in approaches to implementation.

Finally, we encourage FDA and other regulators to leverage the ICH M2 working group on electronic standards to drive the use of modern electronic data standards across the entire eCTD. It is our understanding that during a recent ICH conference held by FDA and Health Canada, there was a discussion regarding a potential project opportunity for developing electronic standards for products quality, chemistry, and manufacturing controls data. Harmonization efforts such as these are important to keep in mind as FDA continues work on its own data modernization.

V. Collection of Data through Clinical Trials

At the Public Meeting, there was discussion regarding the use of digital technologies in clinical trials and the use of data from digital technologies to support regulatory submissions and regulatory decision-making. BIO encourages FDA to continue to consider these types of data and how they may fit into the FDA's larger data modernization efforts. BIO supports the effort to advance the use digital endpoints and acceptance of decentralized trials, and BIO looks forward to working with the Agency to modernize clinical trial data collection and use of new sources of data for regulatory decision making.

VI. Conclusion

BIO appreciates this opportunity to submit comments regarding FDA's Public Meeting, Modernizing the Food and Drug Administration's Data Strategy. In addition, BIO would like to understand how FDA's TMAP, cloud-based submissions, and plans to adopt IDMP will address the requested key features for FDA's Data Strategy listed above. We appreciate that at the end of the Public Meeting, Dr. Abernethy noted that this Public Meeting is just the beginning and that FDA will be holding additional large and small meetings on various related topics. We remain committed to engaging with the Agency on these important topics. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/
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