Biotechnology Innovation Organization

January 4, 2020

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

Re: Docket No. FDA–2019-N-5157: 2019 Public Meeting on Center for Drug Evaluation and Research Standard Core Sets: Clinical Outcome Assessments and Endpoints Grant Program.

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks Food and Drug Administration (FDA or Agency) for the opportunity to submit comments following the 2019 Public Meeting on Standard Core Sets: Clinical Outcome Assessments (COAs) and Endpoints Grant Program.

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 commends FDA for its work to coordinate a pilot grant program with the goal of developing publicly available standard core set(s) of COAs and their related endpoints for specific disease indications. BIO appreciates that FDA held the public meeting on December 5, 2019 and sought feedback from various stakeholders through the docket following the public meeting. Below, BIO has provided additional comments for the FDA's consideration as the pilot grant program advances.

Consideration for Rigorously Developed, Fit-for-Purpose Core COAs and Active Engagement of Patients Throughout Core Set Development:
BIO urges the adoption of a strategic and systematic process, with primary focus on involving a representative group of patients in the planning and development of the core set. This will ensure that the patient perspective is systematically incorporated from the beginning and throughout development.

BIO recognizes that in the development of standard core set of COAs and related endpoints, the identified concepts, COAs, and endpoints should reflect what is most important and relevant to patients. To that end, input should be collected directly from patients. BIO strongly recommends that each grantee first understand the disease(s) by directly eliciting input from patients on disease and treatment burden and outcomes that matter most to them. The methods to measure the identified concepts for a given disease area should then be determined based on the collected patient input. This will ensure true incorporation of patient perspective into development and implementation of core set COAs and related endpoints.

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At the meeting, two programs—Clinical Outcome Assessments for Acute Pain Therapeutics in Infants and Young Children (COA-APTIC) and Migraine Clinical Outcome Assessment System (MICOAS)—clearly articulated the challenges in COA development in their disease area and recognized that successful core set development would require engaging with patients early and throughout development to obtain their perspectives on disease and treatment burden. The patient input on the given disease areas would then inform the approach for measurement development and related endpoints. However, it is unclear whether the physical function program would be applying a similar approach. This program plans to develop and validate COAs with applicability across a range of chronic conditions (e.g., rare disease and sarcopenia) that assess physical function using patient-reported and performance outcomes.

BIO requests that the grantees and FDA ensure that the core COAs that are developed do in fact represent COAs that are representative of the patient population at hand and are developed in a rigorous manner. It is important that the patient perspective be adequately represented in the standard COAs and that patients are part of the process from the very beginning. To this end, BIO requests that FDA work with the grantees to ensure that the COAs are developed in a manner that is consistent with FDA patient focused drug development guidance. We also recommend that FDA work with grantees to ensure that the tools developed are pragmatic and can be implemented in both research and clinical settings.

Considerations on development of COAs and endpoints to assess physical/functional status:
BIO recognizes the importance and complexity in the development of standard core set of COAs and related endpoints to assess physical/functional status. There are many aspects related to the patients and the patients' disease that can impact the development and implementation of core outcome sets. Some considerations include the disease the patient is living with, where the patient is in his/her life (e.g., young active parent vs. retired elderly individual), and what aspects matter most to the patient (e.g., continuing work, continuing physical activities and hobbies). In certain disease areas it can be appropriate to develop general, global COAs and related endpoints. However, in non-rare diseases, such as sarcopenia where there are multiple co-morbidities (e.g., heart failure, advanced cancer), a more targeted tool or set of tools will be necessary to capture the concepts that matter most to patients and to develop robust, fit-for-purpose, methodologically-sound COAs. BIO urges the grantee and FDA to consider these factors and potential reassessment of disease areas to include in this program before finalizing the plan for core set development to assess physical/functional status.

Consideration for Transparency and Communication Among Stakeholders:
BIO commends FDA for making the core set development process transparent. To continue to foster a transparent process, as noted in the Request for Applications, we urge grantees to develop a detailed protocol to describe how core set development will be conducted (study objective(s), design, methodology, operational considerations) and make it publicly available to ensure stakeholder awareness of relevant protocol content. BIO also suggests that the grantees make public their

detailed plan for multi-stakeholder engagement (e.g., how industry stakeholders were identified to sit on various expert panels) and identify opportunities for stakeholder engagement and input. To this end, we recommend that FDA develop a centralized mechanism for ongoing communication and interaction between all relevant stakeholders, including grantees, patients, drug developers, clinicians, regulators, and payers, to ensure that efforts are not duplicated and to develop an aligned view of the most important outcomes to measure within the priority areas. It would also be helpful for publications and presentations from the COAs programs to be made available on FDA's website.

Last, BIO requests that grantees and FDA ensure that relevant stakeholders (i.e., patients, patient organizations, industry sponsors) are represented on the scientific advisory panels. Additionally, based upon discussion at the public meeting, patient groups, drug developers and other stakeholders have already developed and use or are developing and using COAs in disease areas selected for COA development under the grant programs, such as for physical function. We appreciate FDA's intent to standardize the use of COAs in disease areas where there may be multiple overlapping efforts ongoing. However, we caution that current efforts should not be undermined. BIO requests that FDA and grantees partner with multiple stakeholders to ensure and promote consistency as well as leverage ongoing existing efforts to inform their COA development.

Consideration for Global Use of COAs:
While BIO recognizes that the pilot grant program's primary goal is the development of core COAs that can be used in patients within the United States, BIO member companies work on a global scale, developing therapies for patients world-wide and they include patients from several different geographic regions in their clinical trials. To this end, it would help maximize the impact and use of the developed COAs if the grantees consider and address possible differences in cultures that may impact the use of the COAs across geographic regions.

Consideration for Evaluating Existing Tools:
BIO would like the grantees and FDA to conduct a comprehensive evaluation of existing instruments and/or tools for potential inclusion in a minimum core set(s) of COAs and endpoints for each program. This would include performance of a gap analysis and literature review as well as application of other existing methodologies, and approaches.

Consideration for Maintenance of COAs:
During the public meeting, maintenance and updates to the core COAs was only briefly mentioned, and panelists acknowledged that maintenance will be important. BIO requests that FDA and grantees consider how the core COAs will be maintained and updated appropriately. We also request that FDA ensure that information on the maintenance and updating of the COAs is made public.

Consideration for Selection of Disease Areas to Develop COAs in Future:
Based upon discussion at the public meeting, there will be more disease areas selected for the COA on physical function. Also, FDA will consider future grants to

develop COAs in additional disease areas. It is important to exercise transparency and engage stakeholders in selection of diseases areas. BIO requests that the FDA consider seeking public input on selection of future disease areas. It would be helpful to explain the reasoning behind selection of diseases areas to focus on.

While BIO appreciates the effort that the FDA has undertaken with the pilot grant program, BIO would like to emphasize that there are many other types of patient experience data that can inform regulatory decision making and BIO encourages the Agency to continue to lead discussion and advance the science of all types of patient experience data, beyond COAs. Additionally, we appreciate the transparency that FDA is striving for related to the pilot program, however, BIO would like to emphasize the importance of alignment with PDUFA VI and FDA's PFDD efforts. BIO appreciates this opportunity to submit comments following FDA's public meeting on Standard Core Sets: Clinical Outcome Assessments and Endpoints Grant Program. 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