March 14, 2016

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

Re: Docket No. FDA-2015-N-5106: Clinical Outcome Assessment Compendium

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) applauds the Food and Drug Administration's (FDA's) efforts to compile and provide information to the public regarding Clinical Outcome Assessments (COAs) that can be incorporated into clinical trials to better serve patients.

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 strongly supports efforts by the Agency, such as the Pilot COA Compendium and recent updates to the FDA's drug development tool (DDT) qualification website, to promote the efficient development and use of COAs and other DDTs for drug development and regulatory decision-making. We believe that the COA Compendium is a good step in providing information to the public about COAs in development and use, providing a level of transparency and increasing awareness of efforts towards patient-focused drug development and COA information.

We encourage FDA to continue to explore ways to provide additional information regarding COAs in development and use in a manner that promotes innovation and protects confidential commercial information.

BIO offers the following comments on the three points of discussion raise in the Federal Register Notice and Request for Comments:

1. *Utility of the COA Compendium*

BIO views the COA Compendium as a good resource and starting point for Sponsors, researchers, consortia, and other stakeholders in determining available COAs, and for considering how specific COAs have and may be utilized in clinical trials. The information

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included in the COA Compendium may be especially helpful to stakeholders who do not have access to proprietary databases, such as PROLabels (offered and maintained by MAPI).

While we recognize that the COA Compendium is a pilot document, at present, the utility of the document may be limited for many industry stakeholders, as, for most COAs, it provides neither sufficient information nor guidance to aid in the selection of appropriate endpoints for clinical trials. Furthermore, COAs, even if listed in the COA Compendium, will still need to be validated for a specific context of use, a process which will involve consultation with and advice from the relevant Office of New Drug review division early in drug development. The industry needs guidance for routine, consistent, and early interactions with the Agency to ensure that endpoint measures are appropriately developed or adapted for a new context of use and that endpoint measures are well-defined by the time Phase 3 protocols are defined. Therefore, for the purposes of communicating with FDA and coordinating with both FDA review division and COA staff, the timing and scope of communications to facilitate timely and predictable review should be part of the compendium's instructions for use.

Again, BIO recognizes the importance of collecting and providing information on outcomes that are important to patients to the broader stakeholder community and is supportive of the effort.

2. *Best Approach for Developing Future Iterations of the COA Compendium*

The COA Compendium will provide increased visibility, transparency, and awareness about clinical outcome measures that have been developed and used in the context of drug approvals. In future iterations, BIO recommends that the Agency expand the COA Compendium to include COAs developed or used prior to 2003, as many COA claims predate this cutoff.

In order to increase the utility of the COA Compendium, BIO recommends that the FDA include additional elements and information in the document, including:

- The text of the actual "claim" or language associated with the instrument (independent of the drug);
- Information on the data used to support the claim (*e.g.*, mean change, percent responders);
- In addition to listing the instrument, a reference to the product approval(s) based on initial evidence supporting validation of the instrument, the year it was approved, and the indication(s) for which it was approved should be included;
- For COAs that have been qualified through the public pathway, a hyperlink to their approval package;
- Whether the COA instruments have been translated;
- For instruments currently listed as being in some stage of COA Qualification, it would be helpful to note if the COAs are "qualified," "partially qualified," or "in the process of qualification," and if the latter, the stage in the qualification process at time of publication;
- Whether the tools were qualified in paper or ePRO form; and
- References to the COA instrument and any available publications.

Additionally, we encourage FDA to explore ways to include information about COAs that were not included in the compendium, particularly those that the FDA believes to no longer be fit-for-purpose, or otherwise inappropriate for ongoing or planned drug development programs.

Similarly, in future iterations of the COA Compendium, BIO encourages FDA to provide more insight into the regulatory perspectives on existing COAs that may be amenable to modification to expand the context of use, or make the COA fit-for-purpose in another therapeutic area (*e.g.*, the potential applicability of Duchenne muscular dystrophy (DMD) COAs to other dystrophic diseases).

Lastly, the COA Compendium is a lengthy document in its present form, and is likely to become more complicated and unwieldy in future iterations. BIO recommends converting the Compendium into a searchable database so as to improve the utility of the Compendium. This database could include hyperlinks to relevant labeling and correspondence in Drugs@FDA where COAs were used successfully in order to allow stakeholders to understand the context in which the Agency allowed the use of these instruments in the development of a drug.

3. *COA Compendium-Related Questions FDA Should Address in Future Communications*

BIO respectfully requests that FDA address the following COA Compendium-related questions in future communications:

- How frequently will the COA Compendium be updated? Will there be a mechanism to update the COA Compendium if there are updates to therapeutic guidance documents? BIO recommends that the COA Compendium be updated as often as feasible (*e.g.*, quarterly) to ensure that the information it contains reflects FDA's current thinking, and the state of the science of developing and using COAs.
- When the COA Compendium was announced at the April 2015 Prescription Drug User Fee Act (PDUFA) V Stakeholders Meeting, it was noted that a guidance document would accompany the COA Compendium. What is the status of this guidance?
- What criteria are being used to select COAs for inclusion in the COA Compendium? BIO recommends greater transparency regarding the exclusion of well-established COA measures from the COA Compendium in assessed disease states. For example, the inclusion of the Montgomery-Asberg Depression Rating Scale (MADRS) and Hamilton Depression Rating Scale (HAM-D) in major depressive disorder, but exclusion of Beck Depression Inventory (BDI) and the Quick Inventory of Depressive Symptomology – Self Report (QIDS-SR) that have similar content validity and psychometric properties. Is there a preference over the measures included in the COA Compendium from a regulatory standpoint?
- Is it possible, without disclosing confidential commercial information, for FDA to provide additional information regarding COAs that are in use in registrational trials, including those COAs that have been developed by consortia? In particular, analysis methods and psychometric properties submitted as evidence.

- Will the Agency include COAs that are added to supplemental labels (supplemental New Drug Applications (sNDA) or supplemental Biologics Licensing Applications (sBLA)) or line extensions in future iterations of the COA Compendium?
- Does the Agency intend to focus on COA endpoints that target efficacy only, or will COAs that are used to better understand tolerability be included as well (*e.g.*, Arizona Sexual Experiences Scale (ASEX) in assessment of sexual function)?
- Does the Agency intend to include COAs for devices in subsequent iterations of the COA Compendium?
- How many submissions include COAs, and of that total, how many submissions were ultimately approved to include COAs in the label?

BIO appreciates this opportunity to provide comments on the Clinical Outcome Assessment Compendium. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely

/S/

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