



July 20, 2023

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

Re: Docket No. FDA-2022-N-2480 Rare Disease Endpoint Advancement Pilot Program Workshop: Novel Endpoints for Rare Disease Drug Development

Dear Recipient:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to submit comments regarding the recent Rare Disease Endpoint Advancement (RDEA) Pilot Program Workshop, held June 7-8, 2023.

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.

BIO appreciates FDA's initiation of this pilot program under PDUFA VII, which we believe will:

- Provide greater clarity for sponsors on how to develop novel endpoints,
- Identify current limitations to regulatory flexibility regarding acceptance of novel endpoints for rare disease drug approval and,
- Improve or establish more efficient, effective, and sustainable regulatory pathways for endpoint development.

BIO was encouraged at the workshop to hear the collective emphasis placed on making tangible progress on the regulatory acceptance of patient experience data via clinical outcomes assessments (COAs), patient preference information, and other similar tools. We also strongly endorse regulatory advancements in digital health and decentralized clinical trials, as it is through these means that the industry can best serve the needs of patients, including the diverse patient populations with rare diseases who are often disenfranchised or underrepresented. BIO has created tools for industry and patients



on these topics, including our [COA Development Framework for Industry, Digital Health Framework for Industry, and Decentralized Clinical Trials Facts Sheet for Patients](#). It welcomes an opportunity to share our tools with the FDA.

Furthermore, BIO appreciates the additional information that FDA has posted on its RDEA pilot website in advance of the workshop, as well as the deep-dive discussions on Day 2. During “Session 8: RDEA Pilot Program Q&A,” FDA answered many questions that provided helpful insight, including that products utilizing the accelerated approval pathway with a surrogate endpoint or a supplemental application could be eligible for the pilot, information regarding the disclosure agreement (more details below), and that FDA will have a cross-functional and multidisciplinary group to review applications, along with providing information regarding FDA’s review and selection process.

BIO offers the following general comments and recommendations:

We kindly request FDA incorporate key workshop discussions into the RDEA pilot website or other material resources to ensure all stakeholders have a full understanding of the pilot, how it will be operated, and provide potential applicants with all the relevant information for submission.

Application content: BIO agrees with FDA that pilot applications should include a detailed plan for patient engagement. BIO further recommends that FDA considers selecting applications for the pilot which feature the following characteristics:

- Programs addressing areas that have not benefited from high engagement
- Rare diseases with some notable failures due to endpoint issues
- Situations where the ability to employ regulatory flexibility is high and where biomarker data may be supportive of a clinical outcome trending in the right direction
- Programs which offer equal opportunity to advance both CDER and CBER-regulated product development

Disclosure Agreements: BIO appreciates that FDA has added information regarding the [RDEA pilot program disclosure agreement](#) to its website including a robust list of topics/information FDA intends to include. We also appreciate the breakdown of what would be disclosed for different types of applications (e.g., all novel endpoints, endpoints with a COA, a biomarker, or a DHT). It was helpful that during the webinar



FDA clarified that while sponsors and FDA will negotiate the specifics regarding disclosure, this will not be an opportunity to eliminate categories of information from the agreement, but rather to assess whether there is something specific to the development program that needs to be described in a certain way to ensure the integrity of the trial. We recommend that FDA include this statement on the pilot website to ensure all sponsors that are interested in the pilot program understand this.

Operational challenges: BIO recommends that FDA should identify operational or process challenges and that these are publicly disclosed in a timely manner to ensure that they can be mitigated at an early stage, rather than in the post-pilot analysis. Providing this high-level information early on in the pilot could help sponsors adjust their applications to better meet FDA application expectations. This is corroborated by discussions at the Brookings 2015 meeting, "[Breakthrough therapy designation: Exploring the qualifying criteria](#)," where it was noted that providing stakeholders with key information and insight into what FDA may designate as an approval application or illustrate any hurdles FDA or sponsors are experiencing.

Knowledge sharing beyond the pilot: BIO acknowledges that there is a limited number of programs that can be accepted into the RDEA Pilot Program according to the PDUFA VII agreement. As a result, there may be proposals for novel endpoints for rare diseases that are addressed through existing mechanisms for FDA-sponsor interactions (e.g., PDUFA meetings) should those proposals not be accepted into the pilot. Because a key feature of the program is transparency for the purpose of enhancing understanding among all stakeholders, we encourage FDA to capture the best practices and lessons learned from these proposals that are discussed outside of the RDEA pilot program. We further encourage FDA to determine on a case-by-case basis whether general knowledge sharing is possible for these proposals without the need to have a formal disclosure agreement. This would enable stakeholders to benefit from a potentially larger population of novel endpoint proposals than only those accepted into the pilot.

BIO thanks the FDA for the opportunity to publicly comment on the Rare Disease Endpoint Advancement Pilot Program. We look forward to continuing to engage with patients, the FDA, and other relevant stakeholders to drive rare disease endpoint advancement.

Sincerely,

E'Lissa Flores, Ph.D.
Director, Science and Regulatory Affairs
Biotechnology Innovation Organization