



June 23, 2020

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

**Re: Docket No. FDA-2019-D-5392: Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations; Draft Guidance for Industry.**

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA or Agency) for the opportunity to submit comments on the Draft Guidance for Industry "Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations" (Draft Guidance or Guidance).

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 efforts to provide drug developers with guidance pertaining to what features FDA will consider when making determinations of "sameness" for gene therapies in the context of orphan drug designation, especially as the landscape for gene therapy products continues to evolve. BIO generally finds the Draft Guidance helpful and we believe that the framework is drafted in a way that supports development of innovative gene therapy products. BIO appreciates the three bulleted "cases" provided by FDA in the Draft Guidance and believes the "cases" are sufficiently exhaustive in demonstrating under what circumstances FDA would consider two gene therapy products either the same or different. However, we do request that FDA clarify that gene editing products are out-of-scope for the guidance and will be subject to case-by-case determinations.

The Draft Guidance notes that *"If two gene therapy products express the same transgene and have or use the same vector, determining whether the gene therapy products are the same drug for purposes of 21 CFR 316.3(b)(14)(ii) may also depend on additional features of the final product that can contribute to the therapeutic effect."* Similarly, FDA also indicates that *"In the scenarios described in the three bullets above, FDA generally does not intend to consider these principal molecular structural features to be different for purposes of 21 CFR 316.3(b)(14)(ii) if there are only minor differences in the transgenes and/or the vectors. In other words, FDA does not intend to consider two gene therapy products to be different drugs based solely on minor differences between their transgenes and/or vectors."*

BIO understands that regulatory discussions and certainly the science around gene therapy products are still evolving and there may not yet be sufficient information to understand all possible circumstance when gene therapies may be differentiated. Additionally, at present some factors that may ultimately result in substantially different clinical safety and efficacy



profiles cannot or have not been measured. We thus emphasize the importance of FDA updating and engaging stakeholders as additional experience is gained. To this end, BIO recommends that FDA conduct a public meeting and issue a discussion guide to collect additional input from stakeholders to be considered for incorporation prior to releasing the discussion guide as Q&A guidance in draft form, following Good Guidance Practices. The discussion guide and draft guidance should address FDA's thinking on, for example, the following questions:

1. What does FDA consider will constitute a "principal molecular structural feature" for the purpose of the gene therapy guidance?
2. What factors would FDA consider in "case-by-case" scenarios when two gene therapy products express the same transgene and use vectors in the same viral class?
3. What does FDA consider will constitute additional "regulatory elements" that may differentiate gene therapy products?
4. How will FDA consider other factors in their determination of sameness?

We think this would be a balanced approach to both update developers on FDA's thinking while also ensuring an opportunity for key stakeholders to contribute and share perspectives on FDA's approach for making determinations of sameness for gene therapy products.

BIO appreciates this opportunity to comment on FDA's Draft Guidance on Interpreting Sameness of Gene Therapy Products Under the Orphan Drug Regulations. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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Senior Director, Science and Regulatory Affairs  
Biotechnology Innovation Organization