April 13, 2017

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

Re: Docket No. FDA–2017-D-0040: FDA Draft Guidance, How to Prepare a Pre-Request for Designation (Pre-RFD)

Dear Sir/Madam:

The Biotechnology Innovation Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments regarding FDA's Draft Guidance for Industry *How to Prepare a Pre-Request for Designation (Pre-RFD)* (Draft Guidance).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 members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products.

BIO appreciates this opportunity to submit comments regarding FDA's Draft Guidance for Industry *How to Prepare a Pre-Request for Designation (Pre-RFD)*. We support continued improvements to the review process of combination products. As such, we are supportive of the proposed Draft Guidance as it promotes early dialogue between Sponsors seeking approval of combination products and the FDA. While we find the Draft Guidance well organized and clearly written, we have included some comments for FDA's consideration:

- The stated goal of the FDA is to enhance transparency of the Pre-RFD process. However, it is not clear from the Draft Guidance how the proposed process will be transparent to industry. BIO requests that FDA add additional metrics in their reports to Congress to capture metrics, response times and number of extensions and make this information available on the website in a more real-time basis.

- Although this structured process should enhance tracking, documenting, and reviewing Pre-RFD requests, the formalization with timelines may result in delaying the pre-RFD process closer to the maximum timeframe provided of 60 days, which is equivalent to RFD-process statutory limit. Furthermore, the Pre-RFD process is iterative with extensions and possibly repeat submissions with subsequent 60 day clocks. As there is less information required for review in the pre-RFD than the RFD process we request that FDA consider shortening the timeframe for Pre-RFDs or establish tiered metrics to achieve a certain percentage within shorter timeframes.

- Section III.A. of the Draft Guidance makes the Sponsor recommendation of classification optional, which puts the FDA classification decision at the starting point. BIO believes that this may dissuade Sponsors from using the structured and documented Pre-RFD process. We request that FDA also consider clarifying how Sponsors may engage with FDA through informal dialogue in this process similar to what is allowed in the current RFD process.

- The 21st Century Cures Act provides an alternative to the regulatory appeal process noted in the Draft Guidance in Section III.G. We request that FDA consider revising the Draft Guidance to include the alternative regulatory appeal process when determining the Primary Mode of Action of a combination product.

- BIO also requests that FDA provide clarity on how confidentiality of the data and information provided under the Pre-RFD process will be protected by the Agency.

We look forward to additional insights on the Agency's current thinking and would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

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Vice President, Science & Regulatory Affairs
Biotechnology Innovation Organization