590 Avenue 1743
Newark, DE 19713
P 302.831.0663

Dockets Management
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Docket Number: **FDA-2023-D-4299**

Dear FDA Dockets Management Staff,

I am submitting comments to Docket Number FDA-2023-D-4299, **Potency Assurance for Cellular and Gene Therapy Products – Draft Guidance for Industry** on behalf of the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). NIIMBL, a part of the ManufacturingUSA network, is a public private partnership of approximately 200 members in academia, government service, and across the biopharmaceutical supply chain. NIIMBL collected feedback on this Draft Guidance from its membership and aggregated the responses.

NIIMBL, on behalf of our community, recognizes the individual efforts involved in generating the Draft Guidance and appreciate the Agency's efforts to clarify expectations and expand the scope from Potency Tests (2011) to Potency Assurance Strategy in a new and continuously evolving product area. The feedback provided in this response to the docket focuses on assuring the utility of the document for advancing risk-based, patient-centered biopharmaceutical manufacturing through clarity of expectations, consistency with existing guidance and regulation, and technical excellence.

We recommend providing additional clarification around the following points:

1. **Purpose.** Lines 19-21 state "the goal of a potency assurance strategy is to ensure that every lot of a product released will have the specific ability or capacity to achieve the intended therapeutic effect" however potency assays are one piece of an overarching control strategy and reflect one (albeit very important) product quality attribute, as stated in the 2011 Guidance that this Draft Guidance will supersede. Requiring potency assays to provide assurance for a therapeutic effect may be beyond the current intended scope of potency assays and could limit and slow down the development of medicines for patients.

2. **Assay Qualification and Validation.** In Section IV, it would be helpful to have additional explicit clarity around expectations for when characterization assays must be qualified and subsequently validated or a clear reference to later sections of the document that discuss validation (e.g. Section V. C. 3.). It would improve clarity if the guidance document explicitly stated that this approach is or is not consistent with existing ICH guidelines.

3. **Characterization Assays.** The discussion around characterization assays (Lines 263-272) is unclear and would benefit from additional explanation. For example, line 268 suggests that characterization methods be "sufficiently precise to detect meaningful

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differences." It would be helpful to understand the recommendations for minimum performance characterizations like precision and accuracy. Additional clarity about how characterization assays differ from release tests and how their use can inform product understanding in an orthogonal way would improve the consistency of the document internally and with existing Guidance.

4. **Selection of Assays.** The document discusses developing multiple potency assays in parallel and seeking further understanding of mechanisms of action during development. The document would benefit from a discussion around an approach to selecting the primary potency assay or determining relative ranges for multiple assays when the MOA is complex, there are challenges with establishing correlation to clinical outcome, or there is significant variability in patient responses.

We appreciate this opportunity to provide feedback to this request and would be happy to follow up.

Kind Regards,

Gene Schaefer
NIIMBL Senior Fellow
On behalf of the NIIMBL Dockets Response Committee