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

Docket Number: **FDA-2024-D-4609**

Dear FDA Dockets Management Staff,

I am submitting comments to Docket Number FDA-2024-D-4609, **Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products (Draft)** on behalf of the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). NIIMBL's mission is to accelerate biopharmaceutical manufacturing innovation and support the development of standards that enable more efficient and rapid manufacturing capabilities. As such, NIIMBL's comments on this Draft Guidance are limited in scope to the use of AI in manufacturing biopharmaceuticals. We have the following comments which we hope can improve the clarity and practical adoption of the draft guidance.

Definitions. We recommend adding a glossary section to define key terms. Whenever possible, it would also be beneficial to reference and/or build off existing definitions, such as those found in Computer Software Assurance for Production and Quality System Software (CDRH/CBER; September 2022) and Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence-Enabled Device Software Functions (CDRH/CBER/CDER/ OCS; December 2024). For example, existing standards and guidance documents typically refer to terms such as intended use, user/functional requirements, fitness for use, assurance and verification. In particular, the following terms would benefit from specific definitions: Question of Interest, Context of Use (COU), Credibility, Credibility Evidence, Model, Model Risk, and Decision Consequence.

Third Party Vendors. Third-party vendors of AI solutions may not wish to share proprietary information on AI model training, validation etc. and consequently sponsors cannot share this information with the agency. Explicit, unambiguous guidance that the sponsor is nonetheless responsible for risk assessments and assurance of control in the manufacture of pharmaceuticals, will aid in discussions within the industry.

Model Performance & Evaluation. The guidance states that all performance estimates should be provided with confidence intervals. We suggest this requirement be proportionate to the model's risk level and potential patient impact due to the resource requirements for data analysis and reporting. The guidance would benefit from additional clarity around the meaning of "agreement" when describing agreement between the model prediction and observed data. Lastly, we recommend suggesting that the same performance metrics should be used in model development and model evaluation when appropriate.

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NIIMBL, on behalf of our community, recognizes the individual efforts involved in developing this draft guidance and we appreciate the opportunity to comment. We appreciate that the Agency is supportive of the use of AI in manufacturing towards improving safety, effectiveness, and quality of life-saving medicines for patients.

Kind Regards,

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