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

Docket Number: **FDA-2023-D-4974**

Dear FDA Dockets Management Staff,

I am submitting comments to Docket Number FDA-2023-D-4974, **Advanced Manufacturing Technologies Designation Program: Guidance for Industry (Draft)** on behalf of the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). NIIMBL's mission is to accelerate biopharmaceutical manufacturing innovation and we aim to reduce barriers to adoption of advanced manufacturing technologies. We thank the Agency for continuing to support the need for modernization of manufacturing technologies, especially for biologics and emerging modalities. It is very progressive and appropriate to link the AMT designation to how technology is used rather than developing lists of equipment or processes. We have the following suggestions to improve the clarity and practical adoption of the draft guidance:

- **AMT designation impact.** The guidance document could benefit from additional clarity on the benefits of receiving AMT designation for the industry. The document states that FDA will expedite development and assessment of an application for drugs manufactured using an AMT, however accelerated review programs already exist and review cycles are defined by in-place user fee agreements. It has been made clear the license holder or sponsor is responsible and accountable for ensuring fit-for-purpose quality, not third-party vendors or equipment services, so an AMT designation by FDA for a technology developed by a vendor to the industry may raise unwarranted expectations. The Quality by Design (Qbd) guidance document, which articulated excellent and responsible design principles, generated confusion in the industry as some anticipated a transactional pathway to toward regulatory relief. A more explicit description of the benefits of AMT designation, perhaps with reference to CTD modules, difference in the Establishment section of the BLA, or PAS designation for BLA amendments would be helpful and could mitigate the risk of a missed opportunity and confusion.

- **A spectrum of advanced manufacturing technologies.** The regulated industry might choose to adopt the definitions and designations to be applied in contractual, transactional, or compliance actions, however the definition of AMT as written lacks the criteria of a so-called "bright line" definition needed for contract law or litigation. Instead, we encourage the agency to not look upon AMT as a binary designation, but to consider technology maturity as a spectrum, as implied in Technology Readiness Levels (TRL; NASA, ISO), Manufacturing Readiness Levels (MRL; Department of Defense) and our own Biomanufacturing Readiness Levels (BRL[1]).

- **Biologics-specific guidance.** The Agency's understandable desire to assure flexibility and consistency, especially when applying technical standards across such diverse sectors as small molecule generics, biologics and biosimilars, and emerging modalities, may have

[1] Kedia et al., Biomanufacturing readiness levels [BRL]—A shared vocabulary for biopharmaceutical technology development and commercialization. *Biotechnology and Bioenginering,* 119, 3526-3536. https://doi.org/10.1002/bit.28227

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unintentionally compromised the crispness of the AMT definition, making it challenging to anticipate the Agency's intent with respect to what is and is not AMT. Specifically for biologics, as defined in section 351(i)(1) of the PHS Act, it is difficult to reconcile many of the elements of AMT designation with the requirements for establishment licensure. The AMT designation and associated implication that "family" approaches to qualification may be applied to biologics is a significant change from current practice, and if intended, should be explicitly discussed. Similarly, there are suggestions that AMT designation could be used in management of Drug Master Files associated with API and NDP manufacture of biologics. This too would be a significant change in practice and might shift the role of FDA in curating confidential and proprietary information in DMFs for biologics, perhaps adding complexity to review, inspection, and life-cycle quality management. Given these divergences as well as other biologic-specific practices within the FDA, we suggest that separate AMT guidance be developed for biologics manufactured under Section 351 of the USPHS Act and drugs manufactured per Section 505 of the FD&C Act. This would allow FDA to offer more detail with respect to requirement and benefit and allow the Agency to build upon the concept of context so carefully advanced in the Guidance.

- **AMT lifecycle.** A central element of the AMT designation as described in the draft guidance is that the technology is, in fact, new or is being used in a new way. Because of the proprietary nature of many manufacturing processes, applications, and supplements it is difficult for an applicant to know what is and is not new. As a result, the industry tends to see business risk with the adoption of innovative manufacturing technologies and the AMT designation program is an opportunity to establish a better understanding of the landscape of technology innovation. This should help the entire ecosystem more rapidly implement novel technologies that can lead to a more resilient drug supply and better patient access to high quality medicines. It would be helpful if the Agency could share current thinking around if/how the FDA will communicate to industry and academia what technologies have been granted AMT designation. It would also be helpful to include the current thinking around when an AMT ceases to be an AMT (perhaps then becoming a platform technology). If, indeed, the Agency anticipates public sharing of transformative technology by posting details of AMT designations, this should be made clear so appropriate decisions regarding intellectual property may be made.

NIIMBL, on behalf of our community, recognizes the individual efforts involved in developing this draft guidance and we appreciate the opportunity to comment. We agree that supporting modernization of manufacturing technologies, especially for biologics and emerging modalities, is critical to improving quality and supply of life saving medicines and look forward to continued conversations about advanced manufacturing technologies for biopharmaceuticals.

Kind Regards,

Gene Schaefer
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On behalf of the NIIMBL Dockets Response Committee