VIA ELECTRONIC SUBMISSION

October 23, 2024

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

Re: Biosimilar Product Development Guidance; Establishment of a Public Docket; Request for Information and Comments (FDA Docket No. FDA-2024-N-3228)

Dear Sir/Madam:

The United States Pharmacopeia (USP) appreciates the opportunity to provide comments on the Food and Drug Administration's (FDA) Request for Information, "Biosimilar Product Development Guidance; Establishment of a Public Docket; Request for Information and Comments" (RFI). USP is an independent, scientific, global non-profit organization founded in 1820 and dedicated to building trust in medicines through rigorous science and public quality standards. We are guided by approximately 500 organizations, including scientific, healthcare practitioner, consumer, and industry communities, as well as dozens of government agencies, who together comprise the USP Convention. A core pillar of USP's mission is to help strengthen the global supply chain so that medicines are available when needed and meet quality standards as expected and required.

General Comments

USP recognizes the complex challenges inherent in developing biosimilar products and understands the critical need for clear, actionable guidance to accelerate their availability to patients. We applaud FDA's commitment to streamlining biologics product development through additional guidance and note the resource levels required to stand up this effort. The RFI itself seeks to identify useful elements from product-specific (PSG) and product-class-specific guidance (PCSG), each presenting unique advantages and challenges. Notwithstanding the advantages and challenges of either route, USP remains supportive of efforts to assist biosimilar development and is uniquely positioned to support these efforts regardless of how the FDA proceeds.

Biosimilar products play a crucial role in the healthcare system by increasing treatment alternatives and improving patient access to medications. USP is dedicated to supporting the development and testing of biosimilars through standards and solutions that streamline the process, aiming to increase the availability of cost-effective, quality biologic medicines for various conditions. Furthermore, USP strongly supports FDA's efforts to create efficient pathways for biologic drug development and promote a competitive biosimilar marketplace, sharing a common interest in ensuring the quality of biologics and providing support for developers.

USP is fostering innovation in the biosimilars space. Our extensive experience in developing quality standards and associated reference materials enables us to deploy the appropriate type of analytical tools that help address manufacturing challenges for biosimilar developers. USP provides best practices, reference materials, and documentary standards that manufacturers can use to develop, validate, and monitor the performance of their analytical methods. USP standards are also recognized internationally, which can help harmonize approaches to biosimilar development across different regulatory jurisdictions. Our scientific

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expertise and ability to convene stakeholders from industry, academia, and regulatory bodies allow us to adapt quickly to evolving regulatory approaches and emerging technologies in biosimilar development. As the biosimilar landscape continues to evolve, USP remains committed to leveraging its unique capabilities, global reach, and collaborative approach to support FDA's efforts, ultimately working towards increasing patient access to high-quality, affordable biosimilar therapies.

RFI Question 1: Which would be more useful for accelerating biosimilar development: guidance documents that focus on a particular product or guidance documents that are cross-cutting for a class of biosimilar products?

As a general matter, USP encourages FDA to focus on creating PCSGs. These documents provide a broader framework applicable to multiple products with similar CQAs, streamlining development processes across various biosimilars. This approach would benefit products with comparable structural and functional characteristics, such as erythropoiesis-stimulating agents. A class-specific guidance could, for example, outline common analytical approaches for assessing protein structure, glycosylation, and in vitro biological activity.[1] Additionally, these guidances may facilitate platform analytical methods and support ongoing development for ICH Q2 and Q14. PCSGs, however, may not capture product-specific nuances, potentially requiring sponsors to conduct additional studies to address unique aspects of their specific biosimilar candidate. In these cases, sponsors could leverage external resources, including pharmacopeial general chapters and reference materials, to facilitate development.

USP's broad portfolio of standards and reference materials can provide a solid foundation for assessing critical quality attributes (CQAs) across entire classes of biologics. Our comprehensive approach to quality standards can help ensure consistency and comparability within product classes, supporting FDA's broader guidance efforts. For instance, USP could develop additional documentary standards on analytical methods for assessing post-translational modifications in therapeutic proteins – a broadly applicable general chapter that aligns with FDA's class-specific guidance approach.

Conversely, PSGs can offer detailed, tailored recommendations that address the nuances within individual reference products. This approach may benefit biologics with unique structural characteristics or analytical challenges. For instance, a PSG for a complex monoclonal antibody like adalimumab could provide specific guidance on analytical methods to assess glycosylation patterns, a critical quality attribute. Developing PSGs for every biologic product, however, could be resource-intensive and time-consuming for the FDA, potentially slowing down the overall guidance development process.

For PSGs, USP can build on our existing portfolio of testing methods and related biological materials, and further develop targeted reference standards and documentary standards that align with FDA recommendations.[2] Our ability to create analytical tools that cut across platforms for testing technologies can help manufacturers demonstrate comparability to reference products with greater confidence.

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[1] *See, e.g.,* USP. <124> Erythropoietin Bioassays. In: USP-NF. Rockville, MD: United States Pharmacopeial Convention; 2024. DOI: https://doi.org/10.31003/USPNF_M3548_01_01; USP. <212> Oligosaccharide Analysis. In: USP–NF. Rockville, MD: United States Pharmacopeial Convention; 2024. DOI: https://doi.org/10.31003/USPNF_M5879_03_01; <210> Monosaccharide Analysis. In: USP–NF. Rockville,MD: United States Pharmacopeial Convention; 2024. DOI: https://doi.org/10.31003/USPNF_M5878_07_01. *See also*, Guo J, Tu H, Rao B, et al. More comprehensive standards for monitoring glycosylation. **Anal Biochem**. *2021*;612:113896. doi:10.1016/j.ab.2020.113896.

[2] USP develops standards through a transparent process which includes collaboration with industry, FDA, and other stakeholders, with public comment. The process is flexible and allows for frequent revisions to accommodate industry advances and new product approvals, including rapid revision processes known as the *Pending* and the *Accelerated Revision* processes.

RFI Question 2: Should FDA focus on development of guidance documents for biological products or classes of biological products for which there are no approved biosimilars?

USP believes developing guidance documents for biological products without approved biosimilars is the most effective use of Agency resources. These new guidance documents can be highly valuable in stimulating innovation and competition in underserved areas. By providing a clear roadmap for manufacturers considering entry into new biosimilar markets, such guidances can potentially accelerate the development of first biosimilars for important therapies. For example, guidance on analytical method development—including applicable reference materials—could significantly impact such programs.

There is merit, however, in developing guidance even after biosimilar approvals, particularly for products that address large patient populations. The biosimilar landscape is rapidly evolving, with new analytical technologies and manufacturing processes emerging regularly. Ongoing guidance development can help incorporate these advancements, ensuring biosimilar development programs remain state-of-the-art. Moreover, continued guidance development can address challenges that may only become apparent after initial biosimilar approvals. It can clarify issues such as post-approval manufacturing changes, which are critical for the long-term success of biosimilar products.

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We are ready to work closely with FDA to align our standards development efforts with the chosen guidance approach, ensuring that manufacturers have access to the most relevant and up-to-date tools for biosimilar development. We are eager to contribute our unique capabilities to support the agency's efforts in expanding patient access to biosimilar therapies.

Thank you for considering these comments. USP looks forward to continued collaboration with FDA on this critical initiative. Should you need additional information about USP's response, please contact Brett Howard, Senior Director, U.S. Regulatory Policy, at brett.howard@usp.org or (301) 692-3296.

Sincerely,

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