FDA Issues Continued Guidance on Biosimilar Development and the BPCIA

The Biologics Price Competition and Innovation Act ("BPCIA") created an abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed biological reference product. The FDA periodically issues non-binding guidance documents to provide the public with FDA's current thinking on a topic, and has issued a number of BPCIA-related guidance documents in a question-and-answer (Q&A) format. In the agency's words, "The Q&A format is intended to inform prospective applicants and facilitate the development of proposed biosimilars and proposed interchangeable biosimilars, and also describe the FDA's interpretation of certain statutory requirements added by the BPCI Act." Guidance on a particular question is initially issued in draft form and is open for public comment. After reviewing comments, the FDA issues final guidance, which replaces the draft guidance provided in an earlier document on a question-by-question basis.

On September 20, 2021, the FDA issued its latest guidance documents on biosimilars and the BPCIA, providing final guidance on five of the Q&As that remained in draft form in the prior guidance. Specifically, the document *Questions and Answers on Biosimilar Development and the BPCI Act* provides answers in final form to the following questions.

Question	Summary of Final Guidance
How can an applicant fulfill the requirement for pediatric assessments or investigations under the Pediatric Research Equity Act (PREA)?	In a departure from the FDA's practice of granting waivers when PREA requirements were determined to be inapplicable to the reference product, the final guidance considers the waivers unnecessary. Instead, the guidance varies according to whether or not the reference product labeling contains adequate pediatric information, and it attempts to "[ensure] that biosimilar applicants are not subject to greater regulatory burdens than those faced by reference product sponsors with respect to the study of pediatric uses." (See I.16, pp. 13-16 & nn.11-13).
What is the nature and type of information that a sponsor should provide to support a post-approval manufacturing change for a licensed biosimilar product?	Generally, a sponsor intending to make such a manufacturing change should follow the principles outlined in the ICH guidance for industry regarding changes to the manufacturing process for traditional (PHS Act sec. 351(a)) biologics products, *i.e.*, they should provide sufficient data and information to demonstrate the comparability of the biosimilar product before and after the manufacturing change. (See I.20, pp. 19-20 & n.16).
May a sponsor seek approval of a route of administration, dosage form, or strength that is different from that of the reference product?	*No*. The application must include information demonstrating that the route of administration, the dosage form, and the strength of the proposed biosimilar or interchangeable product are the same as those of the reference product. (See I.21, p. 20).
May a sponsor seek approval for a condition of use that has not previously been approved for the reference product?	*No*. The application must include information demonstrating that the condition or conditions of use prescribed, recommended, or suggested in the labeling proposed for the proposed biosimilar or interchangeable product have been previously approved for the reference product. This is the case irrespective of whether the applicant seeks licensure for all or fewer than all of the conditions of use licensed for the reference product. (See I.22, p. 21 & n.10).
May an applicant submit data and information to support approval of a proposed biosimilar or interchangeable product for an indication for which the reference product has unexpired orphan exclusivity?	An applicant seeking licensure of such an indication should submit this information even though the FDA will not approve the proposed product for the protected indication(s). (See I.24, pp. 21-22 & nn.18,19).

**Questions are verbatim from the FDA, summaries are written by Choate, Hall & Stewart LLP*

Additionally, the FDA withdrew certain draft questions. One withdrawn question addressed a process for obtaining certain letters related to reference product access for testing for products with risk evaluation and mitigation strategy with elements to assure safe use. Following enactment of the Further Consolidated Appropriations Act, 2020 (FCA), which includes provisions related to this topic, the FDA intends to issue guidance describing how the existing process for obtaining these letters is being aligned with the framework set forth in the new law.

The FDA also withdrew a question that addressed the definition of "protein" as used in section 351(i)(1) of the PHS Act. The BPCIA amended the definition of "biological product" to include a "protein (except any chemically synthesized polypeptide)", and the question addressed the meaning of both "protein" and "chemically synthesized polypeptide". However, while the question was pending in draft form, the FCA eliminated the parenthetical phrase, rendering final guidance on its meaning unnecessary. Accordingly, applicants should look to the final rule entitled *Definition of the Term "Biological Product"*, *85 Fed. Reg*. 10057 (February 21, 2020), 21 C.F.R. § 600.3(h)(6)), for the definition of "protein" as used in the PHS Act.

If you have questions regarding these developments, please contact a member of the Biosimilar team.

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