

Government Strategies Alert: FDA Releases Long-Awaited Draft Guidances on Biosimilar Product Development

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written by [Paul T. Kim](#), [James M. Flaherty, Jr.](#), [Barbara A. Fiacco](#), [Donald R. Ware](#)

Today, the U.S. Food and Drug Administration (FDA) released three draft guidance documents designed to assist industry in developing biosimilars. Biosimilar products are biological products shown to be highly similar (biosimilar) to biological products previously approved by FDA (known as reference products). Section 351(k) of the Biologics Price Competition and Innovation Act of 2009 (BPCI Act), signed into law in March 2010 as part of the Patient Protection and Affordable Care Act, established an abbreviated approval pathway for biosimilar products. Applications to FDA seeking approval of biosimilar products are known as 351(k) applications.

The draft guidances, which have been eagerly anticipated by biosimilars stakeholders for some time, address both scientific and quality considerations for demonstrating biosimilarity to reference products and also provide information about implementation of the BPCI Act in a Q&A format. Each guidance is briefly summarized below.

Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (Scientific Guidance)

According to the [Scientific Guidance](#), “FDA intends to consider the totality of the evidence provided by a sponsor to support a demonstration of biosimilarity, and recommends that sponsors use a stepwise approach in their development of biosimilar products.” (Scientific Guidance at 2.) The Guidance first acknowledges the unique complexities of protein products, and addresses the resulting scientific and manufacturing process considerations. The Guidance then outlines the stepwise approach to demonstrating biosimilarity and explains how FDA will use the totality of the evidence approach to assess that demonstration.

The Guidance also includes a detailed discussion of the data and information needed to support a demonstration of biosimilarity, including guidance relating to (i) structural analysis, (ii) functional assays, (iii) animal data, and (iv) clinical studies. The guidance concludes by briefly discussing postmarketing safety monitoring considerations and consultation with FDA.

Guidance for Industry: Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product (Quality Guidance)

The [Quality Guidance](#) “focuses on therapeutic protein products and provides an overview of analytical factors to consider in demonstrating biosimilarity between a proposed protein product and the reference product.” (Quality Guidance at 1.) After first setting forth general principles regarding the importance of performing a robust characterization of the proposed biosimilar product as part of an analytical comparison of the proposed product and the reference product, the Guidance identifies and explains nine factors for consideration in assessing whether the products are highly similar: (1) expression system, (2) manufacturing process, (3) assessment of physiochemical properties, (4) functional activities, (5) receptor binding and immunochemical properties, (6) impurities, (7) reference product and reference standards, (8) finished drug product, and (9) stability. The Guidance also lists twenty-one “relevant guidances” for potential consideration during biosimilar product development.

Guidance for Industry: Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009 (Q&A Guidance)

The [Q&A Guidance](#) “provides answers to common questions from sponsors interested in developing proposed biosimilar products, biologics license application (BLA) holders, and other interested parties” regarding FDA’s interpretation of the BPCI Act. (Q&A Guidance at 1.) The Q&A Guidance is organized into three sections: (1) Biosimilarity or Interchangeability; (2) Provisions Related to Requirements to Submit a BLA for a “Biological Product”; and (3) Exclusivity.

First, the Biosimilarity or Interchangeability section addresses fundamental questions such as whom to contact at FDA with questions about biosimilars development, when to request an initial meeting to discuss a proposed biosimilar development program, and what types of information are needed to support a 351(k) application, including issues relating to differences between proposed products and reference products. Second, the Provisions Related to Requirements to Submit a BLA for a “Biological Product” section provides information on FDA’s interpretation of the term “protein (except any chemically synthesized polypeptide)” as used in the definition of “biological product” under the BPCI Act, and also explains when a proposed biological product will be considered to be in the same “product class” as a protein previously approved under section 505 of the Food, Drug, and Cosmetic Act. Third, the Exclusivity section includes information about reference product exclusivity and orphan exclusivity. Finally, the Q&A Guidance states that “FDA intends to update this guidance to include additional Q&A’s as appropriate.” (Q&A Guidance at 2.)

Conclusion

The issuance of these three draft guidance documents is an important step in establishing a regulatory process for bringing biosimilar products to market under the framework established by the BPCI Act. To further this effort, FDA is seeking public comment on the draft guidances. Instructions and timing for submitting comments will be announced in a forthcoming Federal Register notice. Stakeholders should carefully review the draft guidances and provide comments to the Agency to make their views and concerns about the biosimilar product development process known and begin a productive dialogue. Further, the Q&A Guidance specifically notes that proposed questions for inclusion in future updates to the guidance are encouraged. The process for raising such questions will be described in the upcoming Federal Register notice.