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## FDA Releases Final Guidance Documents on Biosimilars

The US FDA issued three final guidance documents on biosimilars for pharmaceutical manufacturers in late April. These three documents have been in draft form since 2012 include "Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009," "Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product," and "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product."

The Quality Considerations document offers an in-depth view on the analytical studies relevant to assessing whether the proposed biosimilar and reference product are highly similar. The document also considers the manufacturing of biosimilars and the way that sponsors should consider manufacturing changes after completing the initial analytical similarty assessment or after completing clinical studies intended to support a 351(k) application. The guidance provides that analytical similarity studies should include a sufficient number of lots of the proposed biosimilar used in clinical trials, as well as from the proposed commercial process if the process is different from that used to make trial products.

Specifically, the guidance notes "FDA anticipates that more data and information will be needed to establish biosimilarity than would be needed to establish that a manufacturer's post-manufacturing change product is comparable to the pre-manufacturing change product."

The Scientific Considerations document remains largely unchanged from the 2012 draft document in terms of substantive information; however, some changes were made for clarity and information was reorganized. The document details the approach that sponsors should take when developing the evidence needed to demonstrate biosimilarity to a reference product, as well as FDA's "totality-of-the-evidence" approach for reviewing biosimilar applications. The agency continues to stress that sponsors should consult with FDA early and often during the development process because "the type and amount of analyses and testing that will be sufficient to demonstrate biosimilarity will be determined on a product-specific basis."

The Questions and Answers document presents many of the questions first presented in the draft guidance, while omitting several other questions and also indicating that a few of the questions are in the process of being revised and will be released again for public comment. Significant issues that have been omitted from the Q & A document include those related to interchangeability, biosimilar naming, and standards for indication extrapolation and labeling requirements.

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