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Biosimilars

FDA Releases Fifth Draft Guidance On Developing Biosimilar Products

The Food and Drug Administration May 13 released a draft guidance to assist sponsors in developing a clinical pharmacology program to support a decision that a proposed biosimilar isn't clinically meaningfully different from a branded or reference product.

The FDA said the draft guidance discusses some of the overarching concepts related to clinical pharmacology studies for biosimilar products; approaches for developing the appropriate clinical pharmacology database; and the utility of modeling and simulation for designing clinical trials.

A notice announcing the draft guidance, Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product, was published in the May 14 Federal Register (79 Fed. Reg. 27,622). The FDA is seeking comments on the draft guidance by Aug. 12, and comments must be identified by Docket No. FDA-2014-D-0234.

The 2010 health-care reform law established a pathway for the FDA to approve biosimilar drug products. The agency is in the process of implementing that law.

Demonstrating Biosimilarity. According to the draft guidance, biosimilarity means that ''the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components,'' and ''there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.''

''Clinical pharmacology studies are part of a stepwise approach to develop the data and information needed to support a demonstration of biosimilarity,'' the FDA said. ''Adequate and well-conducted clinical pharmacology studies can address the residual uncertainty in biosimilarity assessment from clinical perspectives and inform the design of subsequent studies to assess clinically meaningful differences between the biosimilar and the reference products.''

The draft guidance is meant to assist sponsors in designing clinical pharmacology studies in support of applications submitted under Section 351(k) of the Public Health Service Act, the notice said. Scientific principles described in the draft guidance also may be informative for developing biological products under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, the agency said.

Reaction. A spokeswoman for the Biotechnology Industry Organization (BIO) told Bloomberg BNA in an e-mail May 13 that BIO thinks it's promising that the FDA is moving forward, and the group will review the draft guidance to make sure it will meet the needs of stakeholders.

Michael Reilly, executive director of the Alliance for Safe Biologic Medicines (ASBM), told Bloomberg BNA May 14 that this draft guidance is similar to the FDA's other draft guidances on biosimilars in that it ''lacks specificity.''

Reilly said the draft guidance is ''generalized'' but is ''clearly an attempt to push the ball down the field'' and to get the conversation going. He added that while not overly specific, the document ''does attempt to provide helpful information for manufacturers to better understand the types and sources of data that are required for approval.'' Furthermore, he said, it reinforces ''what the FDA has been telling companies in meetings—and the feeling is that the feedback in the in-person meetings with the FDA has been very well received by the manufacturers.''

An attorney sees the guidance as being an important step in the process toward establishing interchangeability.

Reilly said companies are still waiting for guidance from the FDA on interchangeability and naming of biosimilars. These topics are expected to have a major impact on the actual use of biosimilars.

Members of the ASBM include the branded biologic companies Amgen and Genentech (part of Roche).

Attorney's Perspective. Stephen Paul Mahinka, an attorney with Morgan, Lewis & Bockius LLP in Washington, told Bloomberg BNA May 14 that the draft guidance is important because ''you won't get to interchangeability until you have a similar product.''

Mahinka, who is the chairman of Morgan Lewis's Life Sciences and Healthcare Interdisciplinary Group, said ''the basis for interchangeability is going to be the science'' and the draft guidance ''is an important issuance.''

In the draft guidance, the FDA ''has clearly set out a stepwise process'' for demonstrating biosimilarity, Mahinka said.

Mahinka said the draft guidance lists four assessment boxes for biosimilars, including a determination of not

similar, similar, highly similar and highly similar with fingerprint-like similarity.

''If you can show your product is highly similar with fingerprint-like similarity, you're very far along in establishing interchangeability,'' Mahinka said.

According to the draft guidance, highly similar with fingerprint-like similarity means ''the proposed biosimilar product meets the statutory standard for analytical similarity based on integrated, multi-parameter approaches that are extremely sensitive in identifying analytical differences. The results of these fingerprint-like analyses permit a very high level of confidence in the analytical similarity of the proposed biosimilar and the reference product, and it would be appropriate for the sponsor to use a more targeted and selective approach to conducting animal and/or clinical studies to resolve residual uncertainty and support a demonstration of biosimilarity.''

Other Draft Guidances. In February 2012 (10 PLIR 173, 2/10/12), the FDA issued three draft guidance documents on biosimilar product development, including:

■ Scientific Considerations in Demonstrating Biosimilarity to a Reference Product;

■ Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product; and

■ Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009.

In March 2013, the FDA released a draft guidance on formal meetings between the agency and biosimilar product sponsors (11 PLIR 437, 4/5/13). The draft guidance, Formal Meetings Between the FDA and Biosimilar Biological Product Sponsors or Applicants, is intended to assist sponsors and applicants in generating and submitting a meeting request and the associated meeting package to the FDA for biosimilar products.

On April 23, at the Food and Drug Law Institute's annual conference, FDA Center for Drug Evaluation and Research Director Janet Woodcock said the CDER is working on additional biosimilar guidances on interchangeability, labeling and exclusivity (12 PLIR 634, 5/2/14).

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The draft guidance is at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM397017.pdf.

The Federal Register notice is at http://www.gpo.gov/fdsys/pkg/FR-2014-05-14/html/2014-11053.htm.

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