DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
[Docket No. FDA–2011–D–0602]

Guidance for Industry on Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product.” This guidance is intended to provide sponsors with an overview of analytical factors that are relevant to assessing whether a proposed product and the reference product are highly similar for the purpose of submitting a marketing application through an abbreviated licensure pathway. This guidance finalizes the draft guidance issued in February 2012.

DATES: Submit either electronic or written comments on Agency guidelines at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 2201, Silver Spring, MD 20993–0002 or the Office of Communication, Outreach and Development (HFM–40), Center for Biologics Evaluation and Research (CBER), Food and Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002.

FOR FURTHER INFORMATION CONTACT: Sandra Benton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 6340, Silver Spring, MD 20993–0002, 301–796–1042, or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993–0002, 240–402–7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product.” This guidance is intended to provide sponsors with an overview of analytical factors that are relevant to assessing whether a proposed product and the reference product are highly similar for the purpose of submitting a marketing application through the abbreviated licensure pathway under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)). Although the 351(k) pathway applies generally to biological products, this guidance focuses on therapeutic protein products.

The Biologics Price Competition and Innovation Act of 2009 was enacted as part of the Patient Protection and Affordable Care Act (Pub. L. 111–148) on March 23, 2010, created an abbreviated licensure pathway under section 351(k) of the PHS Act for biological products demonstrated to be biosimilar to or interchangeable with a reference product. Under this abbreviated licensure pathway, FDA will license a proposed biological product submitted under section 351(k) of the PHS Act if FDA “determines that the information submitted in the application . . . is sufficient to show that the biological product . . . is biosimilar to the reference product . . . .” and the 351(k) applicant (or other appropriate person) consents to an inspection of the facility that is the subject of the application (i.e., a facility in which the proposed biological product is manufactured, processed, packed, or held).

All product applications should contain a complete and thorough chemistry, manufacturing, and controls section that provides the necessary and appropriate information, including, but not limited to, characterization, adventitious agent safety, process controls, and specifications, for the product to be adequately reviewed.

This guidance describes important factors for consideration when assessing whether a proposed product and the reference product are highly similar, including:

- Expression System
- Manufacturing Process
- Assessment of Physiochemical Properties
- Functional Activities
- Receptor Binding and Immunological Properties
- Impurities
- Reference Product and Reference Standards
- Finished Drug Product
- Stability

In the Federal Register of February 15, 2012 (77 FR 8884), FDA announced the availability of the draft guidance entitled “Quality Considerations in Demonstrating Biosimilarity to a Reference Protein Product” dated February 2012. FDA received a number of comments on the draft guidance. In response to these comments, this guidance provides further clarification on general principles on topics including, but not limited to, the use of comparative analytical data to provide the foundation for a biosimilar development program, the timing of submission of analytical similarity data, the appropriate number of lots needed, and the type of bridging data needed when sponsors use a non-U.S.-licensed comparator product in certain studies.

The guidance provides additional clarification on the factors for consideration in assessing whether a proposed product is highly similar to the reference product. This guidance finalizes the draft guidance issued in February 2012.

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the Agency’s current thinking on quality considerations in demonstrating biosimilarity of a therapeutic protein product to a reference product. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES).

1 Section 7002(a)(2) of the Affordable Care Act, adding section 351(k)(3) of the PHS Act (citing section 351(a)(2)(C) of the PHS Act).
2 For CMC requirements for submission of a marketing application, applicants should consult current regulations, the guidance for industry for the “Submission of Chemistry, Manufacturing, and Controls Information for a Therapeutic Recombinant DNA-Derived Product or a Monoclonal Antibody Product for In-Vivo Use,” and other applicable FDA guidance documents.
DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2011–D–0605]

Scientific Considerations in Demonstrating Biosimilarity to a Reference Product; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Scientific Considerations in Demonstrating Biosimilarity to a Reference Product.” This guidance is intended to assist sponsors in demonstrating that a proposed therapeutic protein product is “biosimilar” to a reference product for the purpose of submitting a marketing application through the abbreviated licensure pathway under section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)).

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act), enacted as part of the Affordable Care Act (Pub. L. 111–148) on March 23, 2010, created an abbreviated licensure pathway under section 351(k) of the PHS Act for biological products demonstrated to be biosimilar to, or interchangeable with, a reference product. Under this abbreviated licensure pathway, FDA will license a proposed biological product submitted under section 351(k) of the PHS Act if FDA “determines that the information submitted in the application . . . is sufficient to show that the biological product is biosimilar to the reference product . . . ” and the 351(k) applicant (or other appropriate person) consents to an inspection of the facility that is the subject of the application (i.e., a facility in which the proposed biological product is manufactured, processed, packed, or held). The guidance gives an overview of FDA’s approach to determining biosimilarity.

IV. Electronic Access


Dated: April 24, 2015.

Peter Lurie,
Associate Commissioner for Public Health Strategy and Analysis.

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1 Section 7002(b)(3) of the Patient Protection and Affordable Care Act (Affordable Care Act), Pub. L. 111–148, “biosimilar” or “biosimilarity” means “that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components,” and that “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.”

2 Section 7002(a)(2) of the Affordable Care Act, adding section 351(k)(3) of the PHS Act (citing section 351(a)(2)(C) of the PHS Act).