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FDA Issues Draft Guidance on How to Demonstrate Biosimilarity

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Advisory

New draft guidance released by the FDA on May 13, 2014 will assist drug companies in determining whether a proposed therapeutic biological product is “biosimilar” to its reference product. “Biosimilarity” under Section 351(k) of the Public Health Service Act is defined as “highly similar to the reference product notwithstanding minor differences in clinically inactive components” with ”no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.” A biosimilar’s applicant must demonstrate to the FDA that the biological product is biosimilar based on analytical studies, animal studies, and clinical studies, including the assessment of immunogenicity and pharmacokinetics (PK)/pharmacodynamics (PD).

The new guidance advises sponsors on how to develop clinical pharmacology data to demonstrate biosimilarity, including how to select study design, reference product, study population, dosage and route of administration, PK/PD measures and time profile, and statistical analyses.

Notably, the guidance promotes sponsor identification of four outcomes of biosimilarity assessment to help guide study design and implementation:

1. ***Not similar***

2. ***Similar***--Further information is needed to determine if the product is highly similar to the reference product. Additional analytical data or other studies are necessary to determine if observed differences are within an acceptable range to consider the proposed biosimilar product to be highly similar to the reference product.

3. ***Highly similar***--The proposed biosimilar product meets the statutory standard for analytical similarity. The results of the comparative analytical characterization permit high confidence in the analytical similarity of the proposed biosimilar and the reference product, and it would be appropriate for the sponsor to conduct targeted and selective animal and/or clinical studies to resolve residual uncertainty and support a demonstration of biosimilarity.

4. ***Highly similar with fingerprint-like similarity***--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.

The guidance emphasizes the importance of biosimilar applicants entering into discussion with the FDA in the early stages of the programs.

In March 2013, the FDA released a draft guidance on formal meetings between the agency and biosimilar product sponsors, which was intended to assist sponsors and applicants in generating a meeting request and submitting the associated meeting package to the FDA for biosimilar products. More recently, the FDA said that it is working on additional biosimilar guidance on interchangeability, labeling and exclusivity.

Comments and suggestions regarding this draft guidance should be submitted to the FDA within 90 days of publication, i.e., by **August 12, 2014**. Please contact any of the attorneys in Nutter's Life Science Group if you are interested in learning more about the FDA draft guidance or submission of comments.

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