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FDA Issues Draft Guidance with Updated Recommendations for Assessing the Need for Comparative Efficacy Studies in Biosimilar Development

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Last week, FDA released draft guidance titled "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies." This draft guidance reflects an evolution in FDA's approach to determining whether a comparative clinical study with efficacy endpoints (a comparative efficacy study or CES) is necessary to support a demonstration of biosimilarity. Specifically, the agency notes that a comparative analytical assessment (CAA) is generally more sensitive when it comes to detecting differences between products than a CES.

In the draft guidance, FDA specifies that a CES may not always be necessary for sponsors to demonstrate whether there are clinically meaningful differences between products. Instead, a CAA indicating that the proposed biosimilar is highly similar to the reference product, along with a human pharmacokinetic similarity study and an assessment of the immunogenicity, may be sufficient to make this demonstration. FDA notes that a streamlined approach, i.e., an application that does not include a CES, should be considered when:

- "The reference product and proposed biosimilar product are manufactured from clonal cell lines, are highly purified, and can be well-characterized analytically;"
- "The relationship between quality attributes and clinical efficacy is generally understood for the reference product, and these attributes can be evaluated by assays included in the CAA; and"
- "A human pharmacokinetic similarity study is feasible and clinically relevant."

However, FDA urges sponsors to engage with the agency early in their development processes to determine which studies may be most appropriate, as there are circumstances in which a CES may inform a demonstration of biosimiliarity.

In making this draft guidance available on the FDA's website, the agency notes that it is posting it to provide advance notice to the public and, after the lapse in appropriations ends, a notice of availability for the guidance will be published in the *Federal Register*, which will detail how to submit comments on the guidance.

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