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ALERT

FDA Seeks to Accelerate Biosimilar Development by Easing Data Requirements

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The U.S. Food and Drug Administration (FDA) significantly revised its approach to biosimilar drug development on October 29. Specifically, FDA issued a draft guidance recommending when comparative analytical assessments (CAA) may be used instead of comparative efficacy studies (CES) to demonstrate biosimilarity to a reference product in a Biologics License Application (BLA). The guidance reflects FDA's evolving perspective on using analytical technologies to reduce regulatory burdens and accelerate development timelines for biosimilar products licensed under Section 351(k) of the Public Health Service Act. Despite this data moderation, obstacles to biosimilar market access will remain, as discussed below in "**Implications for Sponsors and Industry**."

Overview of Draft Guidance

In its latest guidance, *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies*, FDA suggests that the typical, expensive CES may not be necessary in biosimilar development programs for "therapeutic protein products" (TPPs) to demonstrate that they are "highly similar" to the reference product. This is a significant change from FDA's final guidance issued in 2015, *Scientific Considerations in Demonstrating Biosimilarity to a Reference Product*, which recommended CES if there was residual uncertainty regarding biosimilarity after analytical, toxicity, pharmacokinetic (PK), and immunogenicity assessments. FDA's shift in approach reflects its "significant experience in evaluating data from comparative analytical and clinical studies" over the past 10 years.

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Under the draft guidance's "streamlined approach," FDA states that CES may not be necessary for TPPs under the following conditions:

- *Analytical Similarity:* The proposed biosimilar and reference product are derived from clonal cell lines, are highly purified, and can be well characterized using modern analytical techniques.
- *Quality-Efficacy Link*: The relationship between product quality attributes and clinical efficacy is well understood and can be evaluated through validated assays.
- *PK Study Feasibility*: A human PK similarity study is feasible and clinically relevant for the drug.

In such cases, FDA may accept a totality-of-evidence approach that includes comparative analytical assessments (CAA), PK data, and immunogenicity results to support biosimilarity, without requiring CES.

The guidance acknowledges that CES may still be necessary in certain cases, such as for locally acting products (e.g., intravitreal drugs) where PK studies are not feasible, or when a clinically relevant endpoint other than efficacy is needed. In those cases, sponsors should consult with the agency to determine what studies may be required.

Implications for Sponsors and Industry

1. FDA is signaling its confidence in analytical technologies for biosimilar approvals.

This guidance reflects the FDA's evolving willingness to rely on analytical technologies. For example, the draft guidance emphasizes that "currently available analytical technologies can structurally characterize highly purified therapeutic proteins and model in vivo functional effects with a high degree of specificity and sensitivity." FDA concludes that CAA are often "more sensitive" than CES for detecting differences between a biosimilar and its reference product. While reliance on analytical technologies may be limited to biosimilar approvals for now, we anticipate FDA may integrate these technologies in other product areas as the agency continues to streamline regulatory burdens during market authorization processes.

2. Biosimilars remain a key component of the Trump Administration's approach to drug pricing reform.

The U.S. Department of Health and Human Services (HHS) continues to emphasize biosimilars as a cornerstone of its drug pricing reform efforts. In a related Fact Sheet, HHS addressed what it deems a "patient affordability crisis" for biologic products and identified broad "solutions" to combat the limited access to affordable biologics:

- *Eliminating unnecessary clinical trials* by relying on improved analytical testing methods instead of requiring expensive human studies.
- *Facilitating pharmacy-level substitution* by advancing interchangeability so pharmacists can substitute lower-cost biosimilars.
- *Reducing red tape to lower the barriers to market entry* by providing clearer guidance and more efficient processes to speed approvals and licensures and reduce development uncertainty.

3. Obstacles to the FDA approval of and market access for biosimilars will remain for the near future.

While we expect to see more movement in this area in the coming months as HHS and FDA act to advance their proposed solutions for bringing lower-cost biosimilar products to market, biologics companies should expect that obstacles will continue for some time. For example:

- The individual members of FDA's BLA review teams may be slow to accept this policy adjustment. FDA's reviewers will likely continue to expect CES when evaluating 351(k) BLAs, and biosimilar sponsors should be prepared to establish the scientific value of CAA on a product-by-product basis.
- Original biologics (reference product) sponsors may disagree with the new policy and submit comments to FDA in opposition to it. Biosimilar companies should watch Docket FDA-2011-D-0605 and plan to address any opposing comments that may apply to their specific biosimilar products.
- Even for licensed biosimilars, it will take more time for insurers and pharmacy benefit managers to expand formularies to include biosimilars, and for state legislatures to update state pharmacy laws to permit the substitution of biosimilars in place of brand-name biologics.

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Wiley will continue to provide ongoing analysis of regulatory requirements for the development of drug, biologic, and biosimilar products. We have a team of experienced attorneys who are prepared to address client issues arising from this FDA guidance. Please reach out to the authors of this alert for additional information.