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New FDA Guidance Could Speed Biosimilar Approvals and Cut Costs

Key Takeaways:

- The FDA released draft guidance indicating it may approve certain biosimilars without requiring a comparative efficacy study (CES), traditionally a costly and time-intensive step.
- Instead, advances in analytical technologies may allow comparative analytical assessments (CAA) and pharmacokinetic data to demonstrate biosimilarity — potentially saving years and millions in development.
- Biosimilar developers should expect case-by-case evaluations, as the draft offers no hard rules on when CES will be waived. Developers are encouraged to consult the FDA early to understand evidentiary expectations and to monitor potential legal challenges from both originators and competitors.

On Oct. 29, 2025, the FDA announced[1] draft guidance on how it will assess biosimilar medicines. The 2025 Draft Guidance[2] is intended to reduce the time and expense necessary to bring a biosimilar product to market by proposing changes to the way the FDA assesses a biosimilar product compared to the originator's biologic medicine.

A biosimilar is a "generic" version of a large molecule, biologic medicine. Like the Hatch-Waxman Act for generic small molecule medicines, the Biologics Price Competition and Innovation Act (BPCIA) established a regulatory pathway by which companies can create a biologic medicine that is highly similar to the originator's FDA-approved biologic medicine, or reference product.

To assess biosimilarity, the FDA requires a comparative analytical assessment (CAA), comprising physicochemical and functional studies of the biosimilar (e.g., biological assays, binding assays, and enzyme kinetics assays). To date, the FDA has also generally insisted on a CES through a clinical trial to establish biosimilarity. As HHS's announcement of the 2025 Draft Guidance indicates, a CES typically adds one to three years of time and $24 million to the cost of developing a biosimilar.

Relying on the experience FDA has gained over a decade of reviewing biosimilars, the 2025 Draft Guidance proposes that the FDA will be open to approving a biosimilar without

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a CES. The 2025 Draft Guidance explains that "currently available analytical technologies can structurally characterize highly purified therapeutic proteins and model in vivo functional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 using in vitro biological and biochemical assays." Instead of an expensive and time-consuming clinical trial-based CES, the FDA may accept CAA analytic studies of the molecules in combination with a pharmacokinetic study to demonstrate biosimilarity.

The 2025 Draft Guidance outlines three factors that indicate when relying on a CAA approach may be appropriate:

- 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.

The 2025 Draft Guidance cautions that the CAA framework may not be appropriate for all biosimilars. For instance, the 2025 Draft Guidance provides the example of locally acting products such as intravitreally administered drugs (*i.e.*, eye injections), where comparative pharmacokinetics may not be feasible or clinically relevant. Likewise, the FDA cautions that there may be circumstances where a comparative clinical study with a clinically relevant endpoint other than an efficacy endpoint may be useful to demonstrate biosimilarity.

In short, the FDA offers no "bright lines" in the new draft guidance by which a company could determine when a biosimilar under development will need a full CES or whether a less burdensome CAA approach will suffice. The 2025 Draft Guidance suggests that biosimilar applicants should work with FDA to determine the types of analytical or clinical studies necessary for demonstrating biosimilarity for a given biosimilar. Given the potential ambiguity, one issue to watch is whether there will be future litigation from originators disappointed that a biosimilar entrant will be able to skip a CES or, for that matter, from a biosimilar developer disappointed to be forced to go through the lengthy and time consuming CES.

Part of a Trend Domestically and Abroad

The FDA's announcement follows its first-of-its-kind action in September 2025 to waive the requirement for a clinical efficacy study in an application for a biosimilar referencing STELARA® (ustekinumab).[3]

Further, the 2025 Draft Guidance parallels a similar policy under consideration from the European Medicines Agency (EMA). In April 2025, the EMA announced a reflection paper, stating that "...at least for some less complex biologicals with a straightforward mechanism of action, the importance of dedicated clinical efficacy and safety data should be re-evaluated" in favor of analytical studies.[4]

The 2025 Draft Guidance follows other draft guidance and policy changes proposed by the FDA to ease the regulatory burdens for biosimilar adoption. For instance, FDA draft guidance issued in June 2024 (2024 Draft Guidance) lowers the barrier to designating a biosimilar "interchangeable" with the reference product biologic.[5] (Interchangeability makes it easier for pharmacists to substitute a biosimilar for a reference product biologic.) Prior to the 2024 Draft Guidance, the FDA's guidance indicated that a switching study would be required to show interchangeability with the reference product.[6] The 2024 Draft Guidance stated that the FDA could instead accept "an assessment of why the

comparative analytical and clinical data provided in the application or supplement support a showing that the switching standard… has been met."[7] The FDA also proposed in a legislative priority document that the interchangeability distinction be eliminated altogether, a proposal that Congress has not acted on to date.[8]

Implications for Biosimilars and Originators

While the Hatch-Waxman Act has been successful in driving down drug costs by rapidly bringing generic versions of small molecule medicines to market, the BPCIA has not met with the same success, and biologics costs have remained high. By their nature, biologics and biosimilars are significantly more difficult and expensive to make than small molecule drugs, requiring materials and processes like genetically modified cell lines, bioreactors, careful purification and formulation.

On top of the increased expenses to manufacture the actual biologics or biosimilars, biosimilars have historically had to go through extensive clinical testing involving a Phase III clinical trial as part of the CES process. The revised guidance could reduce the cost, time and complexity — typically years and millions of dollars — to bring biosimilar medicines to market.

According to the Association for Accessible Medicines, many biologic medicines that have exited the period of regulatory exclusivity and thus are eligible for biosimilar competition have only one or two biosimilar competitors, effectively limiting price competition.[9] Likewise, the Association for Accessible Medicines estimates that only 10% of the 118 originator products that are currently slated to face biosimilar competition over the next decade actually have biosimilar competitors under development.[10] By attracting more biosimilars to enter the market, the 2025 Draft Guidance presents the opportunity to both increase the number of biologic medicines subject to biosimilar competition as well as increase the number of biosimilars competing with a given originator biologic.

For originators, the draft guidance presents the possibility of increased price competition with biosimilars. Originators may also place increased emphasis on their patent portfolios to slow market entry of biosimilar medicines. While the 2025 Draft Guidance portends an easier path through the FDA for at least some biosimilars, recent guidance from the Patent Office on inter partes reviews (IPRs) creates a tougher path for companies — including biosimilar developers — looking to invalidate patents as part of a freedom-to-operate strategy.

[1] FDA Moves to Accelerate Biosimilar Development and Lower Drug Costs, https://www.hhs.gov/press-room/fda-accelerates-biosimilar-development-and-lowers-drug-costs.html

[2] Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies, https://www.fda.gov/media/189366/download.

[3] Briana Contreras, "FDA Allows First Biosimilar Without Clinical Efficacy Trials," Managed Healthcare Executive, Sept. 10, 2025, https://www.managedhealthcareexecutive.com/view/fda-allows-first-biosimilar-without-clinical-efficacy-trials.

[4] Reflection paper on a tailored clinical approach in biosimilar development, https://www.ema.europa.eu/en/reflection-paper-tailored-clinical-approach-biosimilar-

development

[5] Considerations in Demonstrating Interchangeability With a Reference Product: Update, June 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update

[6] Considerations in Demonstrating Interchangeability With a Reference Product Guidance for Industry, May 2019, https://www.fda.gov/media/124907/download.

[7] Considerations in Demonstrating Interchangeability With a Reference Product: Update, June 2024, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-demonstrating-interchangeability-reference-product-update

[8] *See* FDA FY 2025 Legislative Proposals, https://www.fda.gov/media/176924/download#page=2

[9] *See* Association for Accessible Medicines, *The U.S. Generic & Biosimilar Medicines Savings Report SEPTEMBER 2025*, at 32-33, available at https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf.

[10] *See* Association for Accessible Medicines, *The U.S. Generic & Biosimilar Medicines Savings Report SEPTEMBER 2025*, at 36, available at https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf.