

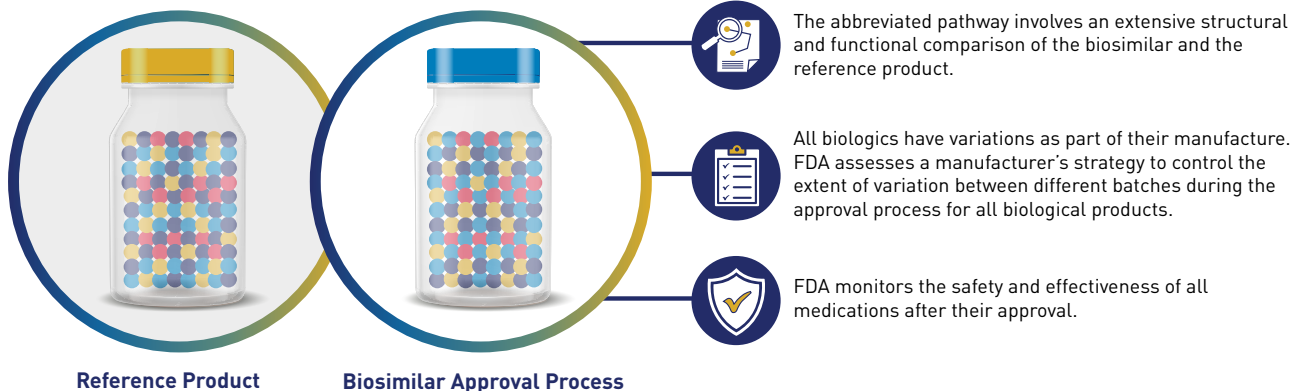


Biosimilar Regulatory Review and Approval

Biological products (biologics) are the fastest-growing class of medications in the United States and account for a substantial and growing portion of health care costs. The Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway to provide patients with greater access to safe and effective biological products. This pathway helps reduce the time and cost of development without compromising safety and effectiveness.

Overview of the Approval Process

- All FDA-approved biologics undergo a rigorous evaluation so that health care providers and patients can be confident of the safety, effectiveness, and quality of these products.
- A biosimilar is a biologic that is highly similar to and has no clinically meaningful differences from an existing FDA-approved biological medication, called a reference product.
- A reference product is approved in a standalone application that must contain all data and information necessary to demonstrate the product's safety and effectiveness.
- The goal of a biosimilar development program is to demonstrate biosimilarity between the proposed biosimilar and its reference product, not to independently establish the safety and effectiveness of the proposed biosimilar. This generally means that biosimilar manufacturers do not need to conduct as many expensive and lengthy clinical trials.
- The abbreviated pathway involves an extensive structural and functional comparison of the biosimilar and the reference product.
- Because biologics are usually made in cells, even with identical amino acid sequences, there will be inherent variations (for example, glycosylation) that result from the manufacturing process in any batch or dose.
- As part of the approval process for both reference products and biosimilars, FDA assesses a manufacturer's strategy to control for the pattern and degree of variations between different batches so that safety and effectiveness don't change.
- FDA monitors the safety and effectiveness of all medications after their approval. This involves inspecting manufacturing facilities and reviewing manufacturer, provider, and patient safety reports made to FDA.



Data Requirements for Biosimilarity

- FDA evaluates each biosimilar on a case-by-case basis and advises manufacturers on the scope and extent of testing needed to show biosimilarity.
- Determining what studies and data are needed to support biosimilarity starts with a comprehensive comparison of the analytical characteristics between the biosimilar and the reference product. **Analytical studies** are the foundation of biosimilar development. These studies provide data to support the structural and functional similarity of the proposed product to the reference product and evaluate the impact of any differences identified.
- FDA evaluates all the evidence, based on comparisons between the biosimilar and the reference product, in the context of the agency's previous finding that the reference product is safe and effective. In addition to analytical studies, other studies that may be needed include:
 - » **Animal studies** to provide toxicology or pharmacology information for the biosimilar as necessary.
 - » **Clinical pharmacology studies** to demonstrate that the proposed biosimilar moves through the body in the same way and provides the same effects as the reference product. This may include an immunogenicity assessment to evaluate a patient's immune response to the biosimilar.
 - » **Additional clinical studies**, sometimes conducted after the completion of other studies to address any remaining uncertainty about whether the proposed biosimilar has no clinically meaningful differences from the reference product.
- FDA may approve a biosimilar for an indication or population without direct studies in that indication or population when the manufacturer provides adequate scientific justification based on:
 - » All available information in the biosimilar application
 - » FDA's previous finding of safety and efficacy for other approved indications for the reference product
 - » Knowledge and consideration of various scientific factors for each indication

There is no one-size-fits-all approach to biosimilar product development. Biosimilars are evaluated for approval based on all the evidence presented by the manufacturer. The abbreviated approval process maintains the same high approval standards that are applied to all biologics, and FDA's rigorous standards help to ensure that all approved biosimilars are as safe and effective as their reference products.

Explore FDA's biosimilar resources for health care professionals at www.fda.gov/biosimilars.

Additional Data Requirements for Interchangeability

- Biosimilar products that meet additional requirements may be approved as interchangeable products, which means they may be substituted for the reference product at the pharmacy level, depending on state pharmacy laws. The specific laws vary from state to state.
- In addition to establishing biosimilarity, the manufacturer demonstrates that switching between the two products would not increase safety risks or decrease effectiveness. This may be done by a switching study in which a patient alternates between the reference product and the interchangeable product multiple times over a specific period of time.

