



## Frequently Asked Questions

**Biosimilars**  
FORUM

## BIOSIMILARS FAQs

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## ABOUT THE BIOSIMILARS FORUM

In 2015, the first biosimilar was approved in the U.S., and there are more than 50 biosimilars on the way. Their introduction may help expand access to high-quality treatment options for clinicians and patients as well as reduce costs to the health care system. Everyone involved—health care providers, payers, regulators, policymakers, patient advocates, and patients—needs a source of clear, unbiased, evidence-based information to better understand biosimilars and make wise decisions on policy and use.

The Biosimilars Forum was incorporated in Washington, DC, as a nonprofit organization to raise awareness on biosimilars and provide evidence-based biosimilars education and advocacy in the U.S. The founding members of the Biosimilars Forum represent the majority of companies with the most significant U.S. biosimilars development portfolios, including: Allergan, Amgen, Boehringer Ingelheim, Coherus BioSciences, EMD Serono, EPIRUS Biopharmaceuticals, Merck, Pfizer, Samsung Bioepis, Sandoz, and Teva.

The Biosimilars Forum launched the *Partnership for Biosimilars Education and Access* to provide an opportunity for stakeholders, health care professionals, patients, and companies developing biosimilars for the U.S. to work together to help shape the development of biosimilars, improve education, and expand treatment options and access to biological medicines.

These FAQs answer the most common questions people have about biosimilars, including how they may be developed and manufactured, the regulatory procedures around approval and use, and how they will be used to expand treatment options for U.S. patients.

To learn more about biosimilars, the Forum, and how to get involved, visit [BiosimilarsForum.org](http://BiosimilarsForum.org) or go to [@USBiosimilars](https://twitter.com/USBiosimilars) to follow related conversations and join the dialogue.

# Biosimilars FAQs

Here are answers to some of the most common questions people have about biosimilars and how they'll be used and regulated in the U.S. If you don't find the information you need, [contact us](#).

## What is a biologic medicine?

Biological medicines, also known as biological therapies or “biologics,” are medicines that are produced by living organisms, including human, animal, or microorganism cells. Today, they are commonly produced through biotechnology. Biologics can include proteins, sugars, and nucleic acids, as well as living entities such as gene therapies.

Most medicines available today are known as “small molecule medicines,” which are chemically synthesized drugs. Biologics make up a smaller subset of medicines and generally operate within a patient’s body by supplementing or interrupting natural processes and signals in order to treat a specific disease or disorder.

## What is a biosimilar medicine?

A biosimilar medicine is a biologic that is approved based on a demonstration that it is highly similar to an FDA-approved biological medicine, known as a reference product. A biosimilar must be determined by the FDA (1) to be highly similar to the reference product notwithstanding minor differences in clinically inactive components and (2) to have no clinically meaningful differences compared to the reference product in terms of safety, purity, and potency.

Some biosimilars may be nearly indistinguishable at a particular time from their reference biologics, while others may justifiably exhibit some differences in structure or biologic function. Biosimilars are neither required nor expected to be identical to the reference biologic, which itself has inherent variability, as long as the biosimilars are highly similar and without clinically meaningful differences.

## What does interchangeable mean?


An interchangeable biologic is a biosimilar that produces the same clinical result as its reference product in any given patient. It must be demonstrated that for a product that is

administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the interchangeable biologic and its reference product is not greater than the risk of using the reference product without alternating and switching. In essence, an individual experiences the same level of safety and effectiveness using the interchangeable product or its reference product.

The term "interchangeable" or "interchangeability," in reference to a biological product that is shown to meet the additional standards described in the Public Health Service Act, means that the biosimilar may be substituted by a pharmacist for the reference product or vice-versa without the intervention of the health care provider who wrote the prescription.

While the FDA will designate biologic interchangeability, U.S. states regulate the practice of pharmacy, including laws describing how and when a pharmacist can substitute one drug for another. Initial state substitution laws were written based on generic drugs. The laws in each state must be updated to permit pharmacy substitution of an interchangeable biologic for a reference product and vice-versa. Many states have either passed or are considering the needed legislation.

## What are the benefits of biosimilars?

Some of the most difficult-to-treat diseases, such as cancer, anemia, and autoimmune disorders (e.g., multiple sclerosis, rheumatoid arthritis, psoriasis, and inflammatory bowel disease) are best treated with biologics. Many biologic treatments are delivered in a health care setting in the form of an injectable or in a solution to be administered intravenously. While biologics make up a small percentage of the total number of drugs on the market, they still pose a significant health care cost, representing 23 percent of global pharmaceutical expenditures in 2014 (which are in turn 9.3 percent of total U.S. health care spending). Since their origins in the 1980s, biologics have grown to be a \$179 billion market in 2014 ([EvaluatePharma](#) ). World Preview 2015, Outlook to 2020. 8th Edition – June 2015). This impact is predicted to grow because many new drugs under development are biologics.

The introduction of biosimilars is anticipated to help drive lower cost burdens for the U.S. health care system, and help expand earlier, more consistent access to biological medicines. The [RAND Corporation](#) has projected that the introduction of biosimilar medicines in the U.S. will reduce direct spending on biologics by \$44.2 billion from 2014

to 2024. Several biological medicines will lose patent protection by 2020, creating an opportunity to develop biosimilars to these reference products.

## **What are the benefits to providers?**

The growth of the biosimilars market may provide greater and earlier patient access to these important treatment options. These therapies have the potential to improve patient access due to reduced financial and administrative barriers, although this has not yet been demonstrated given that only one biosimilar is currently available in the U.S.

## **What are the benefits to patients?**

Biosimilars may offer a number of benefits for patients, including greater insurance plan access within a class of treatments ([FTC Report](#), June 2009) if both the reference product and biosimilar are available in a given formulary or if used in first-line therapy when medically appropriate.

Increased access then can lead to patients being able to take prescribed biologics as directed, as well as an increased likelihood that these biologics will be prescribed earlier to patients, leading to better patient outcomes that will in turn provide significant savings to the U.S. health care system.

## **What is the benefit to payers and health care systems?**

The introduction of biosimilars on the market means more treatment options and increased competition by providing comparatively effective therapies. This competition may lead to high-value therapies at reduced prices. Industry experts have suggested the savings obtained with biosimilars could enable funding of new medicines.

## **Do biosimilars work in the same way as their biological reference products?**

Yes. There are no clinically meaningful differences in terms of safety, purity, and effectiveness between a biosimilar and its reference product. A biosimilar must have the

same mechanism(s) of action as its reference product to the extent they are known, which means it will work in the same way. The FDA will only approve a biosimilar if:

- It is found to be biosimilar
- It utilizes the same mechanism(s) of action for the condition or conditions of use prescribed (to the extent they are known for the reference product)
- Condition(s) of use have been previously approved for the reference product
- Route of administration, dosage form, and the strength of the biological product are the same as those of the reference product
- The facility in which the biosimilar is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent.

Biosimilars work in the same way as the biological reference product they were compared to; biosimilars have no clinically meaningful differences in terms of safety and effectiveness from the reference product.

## **How are biosimilars prescribed?**

A biosimilar is prescribed by a physician in place of its reference product. Unless and until the FDA determines it to be interchangeable and appropriate to allow pharmacy substitution, a provider must write the specific name of the biosimilar on the prescription or order. Once a biosimilar is approved by the FDA as an interchangeable biologic it may be substituted by a pharmacist without prior notification of the prescribing physician, subject to the appropriate state laws governing the practice of pharmacy.

## **Are biosimilars generic versions of their reference biological products?**

No. Biosimilars are not like generic drugs because most generic drugs are chemically synthesized while biosimilars are manufactured using living systems. Generics are copies of brand-name drugs and are considered equivalent. This means they have the same active ingredient, and are identical in terms of dose form, safety, strength, administration, quality, performance characteristics, and intended use. In contrast, biosimilars are derived from living systems. Biosimilars are highly similar to their respective reference product, notwithstanding minor differences in clinically inactive

components. There are no clinically meaningful differences between a biosimilar and reference product in terms of safety, purity, and potency.

## How are biosimilars approved?

The “totality of evidence” regarding a biosimilar is assembled through analysis of public information, testing of the reference product, and the “stepwise” development of the biosimilar compared to the reference product. Once satisfied that the totality of evidence is both substantial and sensitive to detect any potential differences, the FDA will approve the biosimilar for use in one or more indications of use on the basis of the biosimilar being highly similar to the reference product notwithstanding minor differences in clinically inactive components, and that there are no clinically meaningful differences between the biosimilar and the reference product in terms of safety, purity, and potency.

## What is “extrapolation”?

A biosimilar may be approved for one or more conditions of use (known as “indications and usage”) for which its reference biological product is licensed but for which there was no head-to-head clinical comparison. This approval is based on the extrapolation of the totality of data obtained with the biosimilar in direct comparison to the reference product.

The FDA examines requests for extrapolation on a case-by-case and indication-by-indication basis. Every indication for which extrapolation is sought must be scientifically justified. Approval of an additional indication through scientifically valid extrapolation expedites the development of biosimilars and eliminates unnecessary clinical studies, thereby increasing patient access to important therapies.