

Biosimilars Info Sheet

Level 1: Foundational Concepts

Biosimilar Regulatory Approval Pathway

All FDA-approved biological products (also called biologics) undergo a rigorous evaluation. Health care providers and patients can be confident in the safety, effectiveness, and quality of these products. FDA approves reference products, biosimilar products (also called biosimilars), and interchangeable biosimilar products (also called interchangeable biosimilars) through different statutory approval pathways (Figure 1).

A reference product is approved in a standalone 351(a) biologics license application (BLA), which must contain all data and information necessary to demonstrate the product's safety and effectiveness and generally includes data from clinical trials conducted in the relevant patient populations for each of the treatment indications being sought by the manufacturer.

A biosimilar, by definition, is highly similar to and has no clinically meaningful differences in terms of safety, purity, and potency (i.e., safety and effectiveness) from an FDA-approved reference product. The abbreviated approval pathway for biosimilars was created to help reduce the time and cost of development of biologics without compromising 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 biosimilar as with the 351(a) pathway. Therefore, all biosimilar and interchangeable biosimilar products are approved through the abbreviated 351(k) pathway based, in part, on a comparison of the biosimilar to the reference product.

Because biologics are generally made in cells, there are inherent variations that result from the manufacturing process. Biologics, such as therapeutic proteins like monoclonal antibodies, can contain millions of slightly different versions of the same protein (e.g., antibody) in a single lot. This inherent variation can be expected during the manufacturing process of both the reference product and biosimilar. The biosimilar manufacturer generates an array of data comparing the proposed biosimilar to the FDA-approved reference product to demonstrate biosimilarity. Manufacturers of biosimilars do not have to generate the same package of nonclinical and clinical data as required for the reference product. Rather, the biosimilar manufacturer provides comparative data beginning with a detailed analytical characterization and structural and functional comparison of the reference product and proposed biosimilar. Animal studies are conducted, if necessary. Finally, manufacturers conduct comparative clinical studies comparing the proposed biosimilar to the reference product, which typically include comparisons of pharmacokinetics, pharmacodynamics, and immunogenicity, when applicable.

The totality of these comparative analytical, nonclinical, and clinical data supports the determination that a biosimilar is highly similar to and has no clinically meaningful differences from an FDA-approved reference product. The biosimilar manufacturer may then rely on FDA's determination of safety and effectiveness for the reference product. Therefore, biosimilar manufacturers do not need to conduct as many costly and time-consuming clinical trials as a reference product manufacturer, which potentially leads to faster access to these products, additional therapeutic options for patients, and reduced costs.

The abbreviated approval process meets FDA's rigorous standards to help ensure that all approved biosimilars are as safe and effective as their reference products.

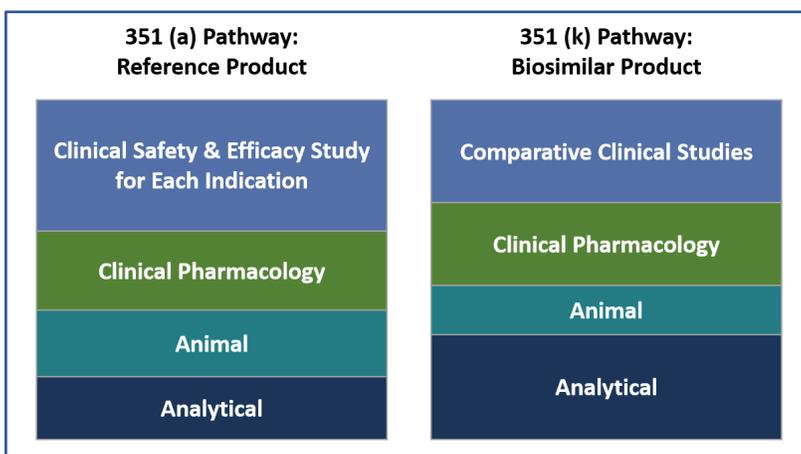


Figure 1: Reference products and biosimilar products are approved through different regulatory approval pathways