

Biosimilars Info Sheet

Level 1: Foundational Concepts

Generics and Biosimilars

Like generic drugs, biosimilar products (also called biosimilars) and interchangeable biosimilar products (also called interchangeable biosimilars), are versions of brand-name drugs that may offer more affordable treatment options to patients. Generics (typically small molecules) and biosimilars (typically larger, more complex molecules) are approved through different abbreviated pathways that avoid duplicating certain costly clinical trials. But biosimilars are not generics—and important differences exist between them.

For example, generic drugs are usually synthesized from chemicals, and the manufacturing process results in an active ingredient that is the same within each manufactured lot and between lots. However, biosimilars, like their reference biological products, are typically manufactured from living systems (e.g., microorganisms, like yeast, bacteria, and animal cells). Because biological products (also called biologics) are made from living systems, inherent variation (i.e., small changes to the protein molecule) is expected within each lot and between lots as a natural part of the manufacturing process. This is true for an original reference product, as well as for a biosimilar or interchangeable biosimilar.

For approval, the manufacturer of a generic drug must demonstrate, among other things, that the generic is bioequivalent to the brand-name drug. By contrast, biosimilar manufacturers must demonstrate that the biosimilar is highly similar to the reference product, except for minor differences in clinically inactive components. Biosimilar manufacturers must also demonstrate that there are no clinically meaningful differences between the biosimilar and the reference product in terms of the safety, purity, and potency of the product (i.e., safety and effectiveness).

Figure 1 compares the results of manufacturing a small molecule drug (e.g., generic aspirin) with a biologic (e.g., biosimilar monoclonal antibody). While the manufacturing process of chemically synthesized small molecule drugs typically results in a single version of an active ingredient that is the same within each lot and between lots, the manufacturing process of biologics, including both reference products and biosimilars, naturally results in small changes to the protein molecule (e.g., antibody).

For example, the different colored diamonds on the biologic (**Figure 1**, right panel) represent glycosylation sites with minor variations that occur during the manufacturing process. FDA assesses manufacturers' strategies to control for variability between lots of biologics to ensure consistency between lots so that the manufacturing process consistently produces a safe and effective product.

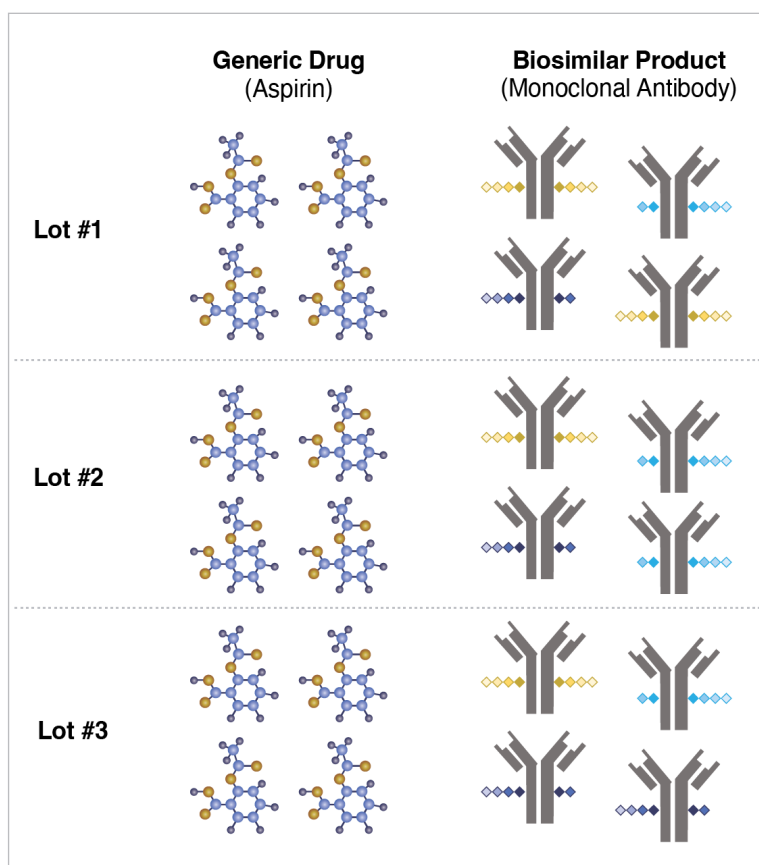


Figure 1: Lot-to-Lot Comparison of a Small Molecule Drug and a Biologic