

Case Study

Level 1: Foundational Concepts

Introduction

Biological products (also called biologics) represent a growing field of therapies in the U.S. health care market. Biologics treat a number of chronic illnesses like cancer, rheumatoid arthritis, ulcerative colitis, Crohn's disease, and diabetes. In this case study, you will learn about biosimilar products (also called biosimilars), their relationship to reference products, inherent variation in biologics, and how the entry of biosimilars into the U.S. health system may provide multiple benefits to patients.

Topics

- Terms related to biologics
- Potential benefits of biosimilars in U.S. health care
- Biosimilars and generic drugs
- Variation in biologics
- Naming of biologics and biosimilars
- Biosimilar resources

As You Read...

- What is biologic?
- What is biosimilar?
- Is biosimilar a generic drug?
- Can a biological product have slight variations but still be safe?
- What is the benefit of biosimilars in U.S. health care?

What Is Biosimilar?

A registered nurse explores the term “biosimilar” and its connection to biologics

What Is a Biologic? What Is a Biosimilar?

Martin, a registered nurse working in primary care, walked down the hall and saw his colleague Patricia, a nurse practitioner who works in rheumatology. Patricia noted that she was heading to check the formulary system to see whether a new biosimilar, replicamab-cznm, was included. Martin hadn't heard the term “biosimilar” before, so he asked for more information. “Have you heard about biologics?” asked Patricia. “Yes, but we don't prescribe a lot of biologics in our practice,” answered Martin. “Biologics include therapeutic proteins that treat a number of chronic conditions,” Patricia explained. “They are a very important therapy in rheumatology, so we prescribe them frequently.”

“Examples of ‘biologics,’ or ‘biological products,’ include growth factors, such as filgrastim; hormones, such as insulin; monoclonal antibodies, such as adalimumab; and vaccines, such as those for influenza and tetanus. Biosimilars are biologics that have been demonstrated to be highly similar to and have no clinically meaningful differences from a reference product. You might also see the term ‘interchangeable biosimilar product’ or ‘interchangeable biosimilar,’ which is a biosimilar that meets additional requirements and may be substituted for the reference product without consulting the prescriber, depending on state pharmacy law, similar to how generic drugs are substituted” (Figure 1).

Potential Benefits of Biosimilars in U.S. Health Care

“What's the benefit of having reference products and biosimilars?” asked Martin. Patricia responded, “Biosimilars can increase the number of available treatment options in the marketplace, potentially helping to reduce costs and increase access for patients.”

Differences Between Biosimilars and Generic Drugs

“Are biosimilars and reference products just like generics and brand-name drugs?” asked Martin.

Patricia explained that generic drugs and biosimilars have some similarities, but important differences exist between biosimilars and generic drugs. “Typically, generic drugs are made from small molecules like chemicals and are easier to make than biologics. Because biologics, including biosimilars, are generally more complex than small molecules and generally are manufactured from living systems, manufacturers can't make exact copies due to inherent variations that naturally occur. However, biosimilars have been shown not to have any clinically meaningful differences from the reference product.”

Variation in Biological Products

Martin asked if variations are normal and whether they only occur in biosimilars or are common to all biologics.




 REFERENCE PRODUCT	 BIOSIMILAR	 INTERCHANGEABLE PRODUCT
Original FDA-approved biological product.	Highly similar and with no clinically meaningful differences when compared to the reference product.	Highly similar and with no clinically meaningful differences when compared to the reference product.
Prescribed by a provider.	Prescribed by a provider.	The application includes additional data and information about the impact of switching or alternating between the product and reference product. Prescribed by a provider or may be substituted at the pharmacy without the intervention of the prescribing provider.

Figure 1: Descriptions of Reference Product, Biosimilar Product, and Interchangeable Product



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Nodding, Patricia added, “Biologics are generally made from living cells, and as part of the natural process, sugar molecules may be added or removed from each molecule produced. These small variations in the molecule’s structure are observed in both the reference product as well as the biosimilar. There’s even variation within each lot of the reference product and biosimilar (**Figure 2**). Even though they can’t make exact copies, manufacturers can control the range and size of the variations.” Patricia continued,

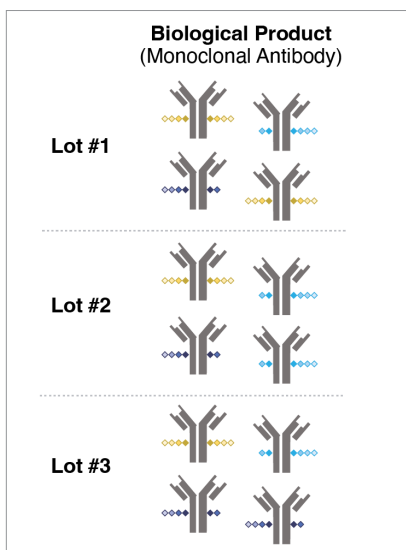


Figure 2: Monoclonal Antibody Products Are a Mix of Different Variations in Each Lot (the Colored Diamonds Depict Varying Levels and Types of Glycosylation)

“FDA requires extensive and rigorous testing and assesses a manufacturer’s strategy to control for the pattern and degree of variations between different lots so that any variations that exist don’t impact the safety or effectiveness of the product. Biosimilars also must have the same dosing and route of administration as the reference product. The side effects are expected to be the same, too. If a reference product works for a patient, a biosimilar approved for that use would be expected to work, as well.

Naming of Biologics and Biosimilars

Martin asked about the name “replicamab-cznm” and whether it had some specific meaning.

“Actually, replicamab-cznm is a nonproprietary name. The reference product and biosimilar also have proprietary names, or brand names, that you’ll see on packaging or in advertisements. Many biologics have a nonproprietary name consisting of a core name plus a unique, product-identifying 4-letter suffix (**Figure 3**). The core name is shared between reference products and their approved biosimilars or interchangeable biosimilars while the 4-letter suffix helps to distinguish the products from each other. The one I’m checking on today is called replicamab-cznm.”

As they reached the pharmacy, Martin thanked Patricia for the introduction to biosimilars. “I’m going to look into this more when I get home. See you tomorrow!”

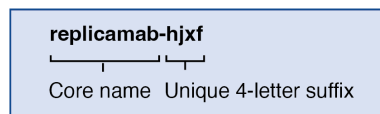


Figure 3: FDA's Naming Convention for Reference Products and Biosimilar Products Includes a Shared Core Name Followed by a Unique, Product-Identifying 4-Letter Suffix

Biosimilar Resources

Familiar with other resources on FDA’s website, Martin did an internet search for “FDA provider materials and biosimilars” and landed on the [FDA Biosimilar page](#). He was pleased to find that FDA already has educational materials available on the topic of biosimilars.

In addition to information on the approval process, Martin noted the website has multiple resources available for health care providers, including prescribers, and for patients.

Martin clicked a link for a database of FDA-licensed biologics called the [Purple Book](#). As he began typing the name “replicamab-cznm” in the search bar, the screen populated with all the approved biologics, including biosimilar and interchangeable biosimilars, which shared the core name. It also included information about dosage forms, strengths, product labeling, and more. “This ought to keep me busy for a while!”

Biosimilar Resources

FDA Pages

- [Biosimilar Materials](#)
- [Provider Materials](#)
- [Patient Materials](#)
- [Purple Book](#)
- [Drugs@FDA](#) (Drug Information)
- [Search Page for FDA Guidances](#)
- [Advisory Committee Materials for Biosimilars](#)
- [Biosimilar Approval Process Information](#)

Additional Resources

Slide Decks

- Foundational Concepts
- Regulatory and Scientific Concepts

Case Study

- What Is a Biosimilar?
- Biosimilars in Patient Care
- Interchangeable Biosimilars
- Insulins/Interchangeable
- Comparative Analytical Assessment

Info Sheets

- Biological Products, Biosimilar Products, and Interchangeable Biosimilar Products
- Generics and Biosimilars
- Manufacturing and Variation
- Biosimilar Regulatory Approval Pathway
- Variation in Biological Products
- Comparative Clinical Studies
- Prescribing Biosimilar and Interchangeable Biosimilar Products
- Purple Book
- Comparative Analytical Assessment
- Quality Attributes
- Labeling/Package Insert
- Insulins/Interchangeable

Explanatory Videos

- Biosimilars: Manufacturing and Inherent Variation
- Biosimilars: Approval Process
- Biosimilars: Critical Quality Attributes
- Biosimilars: Interchangeability
- Purple Book
- Procedural Purple Book
- Totality of the Evidence
- Comparative Analytical Assessment

Discussion Questions

- Foundational Concepts
- Regulatory and Scientific Concepts
- Exercises (Provided in the Resource Guide for Teaching Faculty)

