Discussion Questions

Level 1: Foundational Concepts

This document provides knowledge assessment questions to support Level 1 learning materials, which focus on foundational biosimilar concepts and the connection between reference products, biosimilar products (also called biosimilars), and interchangeable biosimilar products (also called interchangeable biosimilars). These questions are intended to aid in teaching biosimilar content by facilitating discussion and understanding of biosimilars among students enrolled in health care degree programs.

You may need to modify the questions or discussion responses to align with your specific health specialty or teaching needs. Refer to FDA's website for additional information and other teaching resources on biosimilars.

Knowledge Assessment Questions

What are biologics?

Biologics are generally large, complex molecules that are made from living sources such as bacteria, yeast, and animal or plant cells. This makes biologics different from other medications, which are typically made from chemicals.

Why can't a biologic be copied exactly?

Biologics, including reference products, biosimilars, and interchangeable biosimilars, are generally made from living organisms. The structures of biologics are generally more complex than those of conventional small molecule drugs and inherently contain many slight variations. Because they generally come from living organisms, and their structures are generally more complex than those of non-biologics, biologics are often more complicated to purify, process, and manufacture (**Figure 1**).

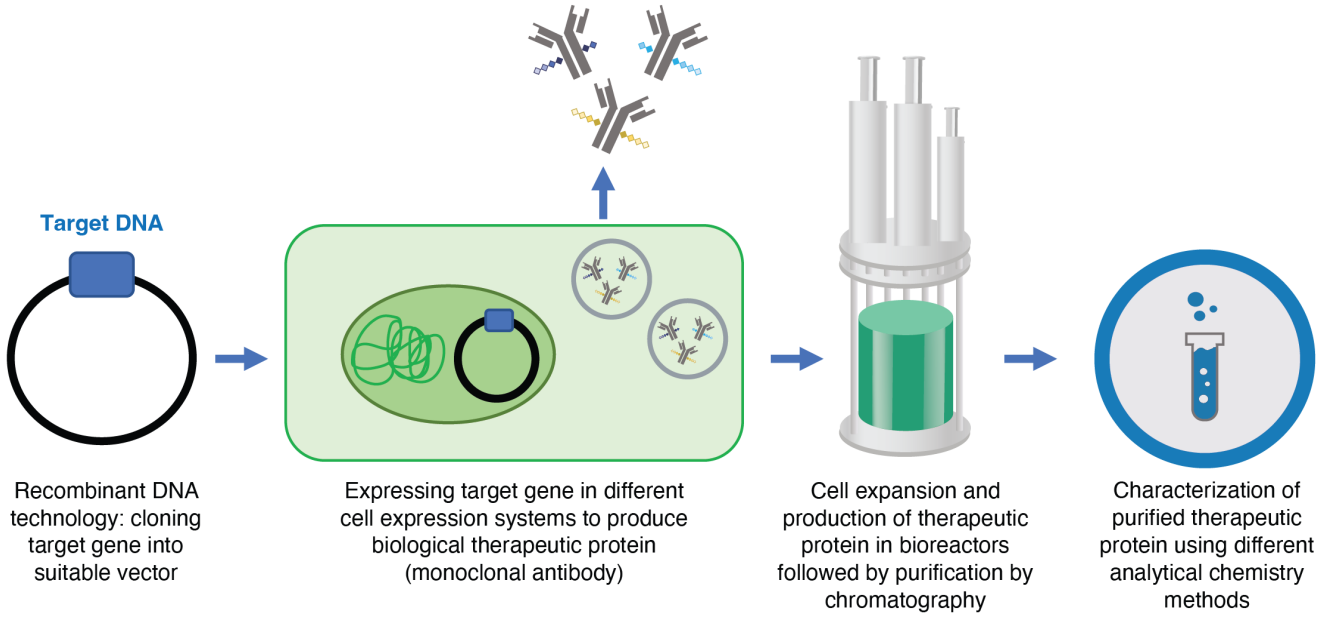

Figure 1: Summary of Manufacturing Process of Reference Products and Biosimilar Products

It is important for biosimilar manufacturers to understand and control sources of biological product variability. Biosimilar manufacturers design their manufacturing process so that the biosimilar is structurally and functionally similar to the reference productreference product.

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What is a reference product and how is it related to a biosimilar?

Biologics include reference products, biosimilars, and interchangeable biosimilars. A reference product is approved in a 351(a) application (i.e., a "standalone" application) that must contain all data and information necessary to demonstrate the safety, purity, and potency (i.e., safety and effectiveness) of the product.

A biosimilar is compared to and evaluated against a reference product to ensure that the biosimilar is highly similar to the reference product and that there are no clinically meaningful differences between the products. Biosimilar manufacturers then may rely on FDA's determination of safety and effectiveness for the reference product. The rigorous approval process ensures that biosimilars can be expected to provide the same potential treatment benefits and potential side effects as their respective reference products.

How is the relationship between generic and brand-name drugs different than the relationship between biosimilars and reference products?

Both biosimilars and generic drugs are versions of original medicines that may offer patients more affordable treatment options. A main difference between biosimilars and generic drugs is that the active ingredients of generic drugs are generally made up of smaller, simpler molecules that are the same within each manufactured lot and between lots. Biologics generally cannot be copied exactly, because the products contain a mix of many slight variations of the same protein. Minor variations to the protein structure can occur naturally during the manufacturing process of biologics, as shown in **Figure 2**. Different colored diamonds depict examples of glycosylation that may occur during the manufacture of therapeutic proteins such as monoclonal antibodies. This mix of individual protein molecules with slight variation is observed between different lots during the manufacturing process for both reference products and biosimilars (also called lot-lot variation). For this reason, biosimilar manufacturers must demonstrate that their products have similar types and levels of variation compared to the reference product.

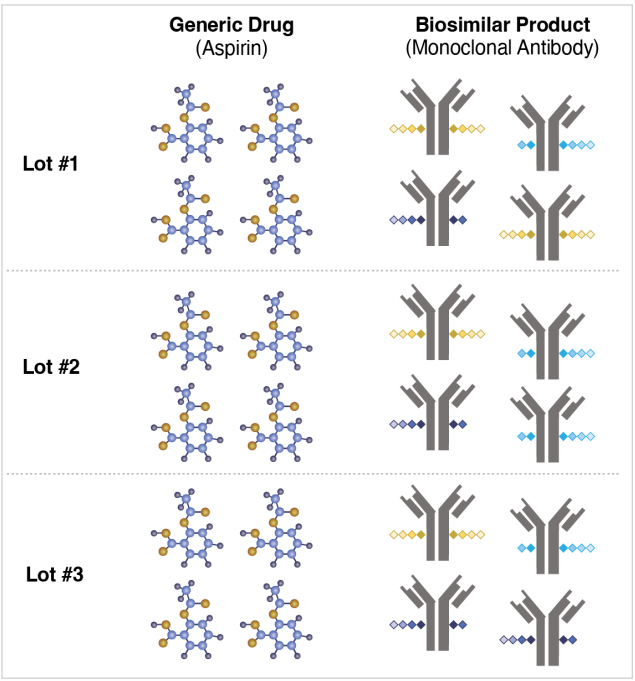

Figure 2: Lot-to-Lot variation is inherent during manufacture of biologics

What is the purpose of a biological product's core name and the 4-letter suffix?

Use of a shared core name indicates relationships among biological products, including biosimilars and interchangeable biosimilars. The unique, product-identifying 4-letter suffix is used to distinguish products that share a core name and facilitate safe use and pharmacovigilance. Health care professionals should include the suffix when ordering, prescribing, and dispensing biologics and when reporting adverse events to MedWatch, the FDA Safety Information and Adverse Event Reporting Program.

What benefits might biosimilars bring to patients and the health system?

Biosimilars may provide the following benefits to patients: (1) More treatment options; (2) Increased access to medicines; and (3) Potentially lower cost of the biosimilar medicine.

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Can biosimilars and interchangeable biosimilars be substituted for reference products by pharmacists?

Health care professionals can generally prescribe biosimilars and interchangeable biosimilars just as they would prescribe other medications. FDA-approved interchangeable biosimilars may be substituted for the reference product without the intervention of the prescribing health care provider, subject to state laws. State laws that address substitution of biologics at the pharmacy level vary; therefore, it is important for prescribers and pharmacists to understand the pharmacy practices in their state.

Do providers need to prescribe the biosimilar product? Or are pharmacy-level substitutions allowed like the process with brand name and generic drugs?

Providers generally need to prescribe a biosimilar specifically (i.e., using either the proprietary name or the nonproprietary name with the distinguishing suffix), whereas a pharmacist may, dependent on state law, substitute a reference product with its FDA-approved interchangeable biosimilar product without a specific action by the prescriber.

Where can medical providers find information on whether a biologic is an interchangeable biosimilar and other related information on FDA-approved biologics?

Medical providers and patients can find specific information related to biologics on the FDA Purple Book website. The Purple Book is an online database with information on FDA-approved biologics, including whether a specific biological product is a reference product, biosimilar, or interchangeable biosimilar. The Purple Book also provides links to the Prescribing Information (i.e., labeling), in addition to other information.

In March 2020, FDA began regulating insulins as biological products. Why is this change significant?

The transition of insulins to the biological product regulatory framework created the opportunity for manufacturers to submit applications for biosimilar and interchangeable biosimilar insulin products under section 351(k) of the Public Health Service Act.

Should a health care provider who is familiar with the reference product review the prescribing information for the biosimilar product?

Yes, FDA recommends that health care professionals review the prescribing information for biosimilar and interchangeable biosimilar products to determine the conditions of use and routes of administration for which the biosimilar or interchangeable biosimilar product is approved, and to review information specific to the biosimilar or interchangeable biosimilar product, such as preparation, administration, storage conditions, or safety information.

The labeling includes a biosimilarity statement, where can I find information about which biosimilars are interchangeable?

The biosimilarity statement clearly indicates that the drug is a biosimilar and identifies the reference product on which its approval was based. Information about interchangeability is relevant to substitution at the pharmacy. Therefore, information about which products are licensed as interchangeable is located in FDA's Purple Book: Database of Licensed Biological Products.

What are the benefits of biosimilar products to patients? Why should healthcare practitioners consider prescribing a biosimilar or interchangeable biosimilar product?

Biosimilar provides the same benefits and is as safe and as effective as its reference product. A healthcare provider may initiate treatment for a patient using a biosimilar or switch to a biosimilar because of a change in the patient's insurance coverage, product availability, or potentially meaningful cost savings for the patient. Patients may also ask their health care provider about biosimilars.