

Fact Sheet: Biosimilars

Overview

What is a biologic drug?

Biologic drugs come from living organisms or from their cells, and are often made using biotechnology. They are used to treat diseases and medical conditions including anemia, diabetes, inflammatory bowel disease, psoriasis, rheumatoid arthritis, hormone deficiency and some forms of cancer. Biologic drugs are generally larger and more complex than chemically produced pharmaceutical drugs. In Canada, biologic drugs are listed in Schedule D of the *Food and Drugs Act*.

What is a biosimilar?

A biosimilar biologic drug, or biosimilar, is a drug demonstrated to be highly similar to a biologic drug that was already authorized for sale (known as the *reference biologic drug*). Biosimilars were previously known in Canada as Subsequent Entry Biologics (SEBs). Biosimilars are approved based on a thorough comparison to a reference drug and may enter the market after the expiry of reference drug patents and data protection.

Are biosimilars different from generic drugs?

Biosimilars are not the same as generic drugs. Generic drugs are small molecules that are chemically synthesized and contain identical medicinal ingredients to their brand name reference products. Due to the size, complexity and natural variability of biologic drugs, and because biologic drugs are made in living cells rather than with chemicals, a biosimilar and its reference biologic drug can be shown to be similar, but not identical.

Regulatory Framework

How are biosimilars regulated by Health Canada?

Biosimilars are regulated as new drugs under the *Food and Drugs Act* and the *Food and Drug Regulations*. Health Canada's Biologics and Genetic Therapies Directorate (BGTD) regulates biosimilars in collaboration with the Regulatory Operations and Regions Branch (RORB) and the Marketed Health Products Directorate (MHPD). Health Canada has developed a robust, science-based regulatory framework for biosimilars that reflects many approaches adopted by other major drug regulatory agencies. Health Canada's [Guidance Document: Information and Submission Requirements for Biosimilar Biologic Drugs](#) communicates the regulatory framework for biosimilars and is intended to help manufacturers comply with the laws and regulations governing the authorization of biosimilars in Canada. Health Canada's rigorous standards for authorization mean that patients and health care providers can have the same confidence in the quality, safety and efficacy of a biosimilar as any other biologic drug.

How is similarity between a biosimilar and its reference biologic drug demonstrated?

Biosimilar manufacturers must provide information to Health Canada comparing the biosimilar with the reference biologic drug. Similarity is demonstrated using a step-wise approach beginning with structural and functional studies and continuing with human clinical studies. Because the purpose of these studies is to demonstrate similarity, the type of data required to support biosimilar authorization differs from that required for a stand-alone biologic drug. Health Canada evaluates all the information provided to confirm that the biosimilar and the reference biologic drug are similar and that there are no clinically meaningful differences in safety and efficacy between them. Once Health Canada authorizes a biosimilar for sale, a Notice of Compliance (NOC) and a unique Drug Identification Number (DIN) are issued.

Why can biosimilars be authorized for diseases or medical conditions for which no clinical studies have been done?

An indication is the use of a drug to treat a disease or medical condition. Many biologic drugs and biosimilars are authorized to treat more than one indication. The term extrapolation is often used to refer to the authorization of a biosimilar for indications where clinical studies were not done. Because a biosimilar is very similar in structure and function to a reference biologic drug with well-established safety and efficacy, clinical studies do not need to be repeated for each indication. Instead, Health Canada may authorize a biosimilar for use in more than one indication because of the rigorous demonstration of similarity between the biosimilar and the reference biologic drug. In order to authorize a biosimilar for use, Health Canada requires, in addition to the information noted above, detailed scientific evidence based on knowledge of the biosimilar, its reference biologic drug, and the specific diseases or medical conditions involved. Patients and physicians can have confidence in the use of a biosimilar in each indication authorized by Health Canada.

Why are some biosimilars authorized to treat fewer diseases or medical conditions than the reference biologic drug?

An indication is a use of a drug to treat a disease or medical condition. A biosimilar may be authorized for all or some of the indications of the reference biologic drug.

The indications authorized for a particular biosimilar depend on the following factors:

- Indications may be patented at different times and indications under patent and data protection cannot be authorized.
- The biosimilar manufacturer chooses which indications they wish to seek for the product. Health Canada does not force a manufacturer to apply for indications that the manufacturer does not wish to have.
- Health Canada may decide not to authorize a biosimilar for a certain indication based on scientific and benefit/risk-based considerations.

How will information on any differences in indications between a biosimilar and a reference biologic drug be communicated?

The [Summary Basis of Decision](#) (SBD) document communicates the basis for Health Canada's decision on authorization of a biosimilar. The SBD also provides detail on which indications were and were not sought by biosimilar sponsors and a scientific justification in the event an indication was not authorized.

Product monographs are available in the [Drug Product Database](#) for all biosimilars. Product monographs are intended to provide the necessary information for the safe and effective use of a new drug. Authorized indications for each drug are listed in the first section of Part I of the drug's product monograph. Information on indications that were not sought by the biosimilar sponsor or that were not granted by Health Canada will only be captured in the product monograph if deemed necessary to guide the safe and effective use of that drug. Otherwise this type of information will be captured in the SBD document.

What is immunogenicity and how is it addressed for biosimilars?

The immune system has evolved to recognize foreign proteins in the body. Biological drugs are usually injected into the body and the immune system often reacts to them. This reaction is referred to as the immunogenicity of the product. Sometimes immunogenicity can only be detected using sophisticated laboratory tests and has no impact on the patient. In other cases, immunogenicity can impact patient safety or how well the drug works. For these reasons, studies showing that there are no clinically meaningful differences in immunogenicity between the biosimilar and reference biologic drug are required for authorization of a biosimilar. In addition, a risk management plan is required by Health Canada for all biologic drugs, including biosimilars. This plan must explain how the manufacturer plans to monitor immunogenicity after the biosimilar is authorized.

How is the safety of biosimilars monitored after authorization?

Health Canada monitors the safety of all drugs on the market, including biosimilars.

Health Canada:

- Conducts market surveillance
- Monitors adverse reaction reports
- Investigates complaints and problem reports
- Takes action as appropriate

Each manufacturer must do its part for drug safety:

- Set up a system to monitor reported side effects
- Report any new information received about serious side effects to Health Canada
- Notify Health Canada about any studies with new safety information
- Request authorization for any major changes to
 - the manufacturing process,
 - dose regimen, or
 - recommended uses of the drug.

Does the biosimilar product monograph (label) need to be updated when a safety-related change is made to the product monograph of the reference biologic drug?

All drug manufacturers are required to ensure that the product monograph for each of their products is up to date and supports safe and effective conditions of use.

At the time of authorization, the safety information in the product monograph for a biosimilar is based on information in the reference biologic drug product monograph. However, once authorized, a biosimilar is considered a “stand-alone” product. Since a biosimilar and its reference biologic drug are not identical and are manufactured by independent processes, newly identified safety issues that affect the reference biologic drug may or may not also affect the biosimilar and vice-versa.

Biosimilar manufacturers are expected to monitor the post-market safety profile of their own product and the reference biologic drug product monograph and make safety updates to the biosimilar product monograph as appropriate. In addition, when a safety update is made to the product monograph of a biosimilar, a reference biologic drug, or any other drug with shared active ingredients, and the plausibility of a drug class effect is established, Health Canada will send an advisement letter requesting that all potentially affected manufacturers assess the need to update their product monographs in view of the new safety information. Manufacturers are expected to respond to the advisement letter within 30 days, and, if warranted, submit changes to their product monograph for review by Health Canada.

How do biosimilar regulatory frameworks compare between Canada and other countries?

The key principles that Health Canada uses to evaluate biosimilars align with those of other regulators and international organizations such as the European Medicines Agency (EMA), the United States Food and Drug Administration (FDA), and the World Health Organization (WHO). Health Canada engaged a broad spectrum of stakeholders when developing the regulatory framework for biosimilars. Health Canada reviews its approach to regulating biosimilars on an ongoing basis in response to scientific advances, best practices and experience gained.

Access

Does authorization by Health Canada mean that a biosimilar will be funded through drug benefit programs?

When Health Canada authorizes a biosimilar for sale, funding is not guaranteed through drug benefit programs. In Canada, federal, provincial, territorial and private plans reimburse drugs. It is up to each jurisdiction to make their final formulary listing and reimbursement decisions.

Can a biosimilar be used interchangeably with its reference biologic drug?

Health Canada's authorization of a biosimilar is not a declaration of equivalence to the reference biologic drug. There are varying definitions of interchangeability. In Canada, the term often refers to the ability for a patient to be changed from one drug to another equivalent drug by a pharmacist, without the intervention of the doctor who wrote the prescription. In Canada, the authority to declare two products interchangeable rests with each province and territory according to its own rules and regulations.

Can a patient already being treated with a reference biologic drug be switched to a biosimilar?

Switching generally refers to a one-time change from a reference biologic drug to a biosimilar. Health Canada recommends that a decision to switch a patient being treated with a reference biologic drug (innovator product) to a biosimilar should be made by the treating physician in consultation with the patient and taking into account available clinical evidence and any policies of the relevant jurisdiction. For questions related to changing from one biologic drug to another, patients should speak to their doctor.

What factors influence biosimilar availability in Canada?

The following factors affect the availability of biosimilars in Canada:

- Canada has a small population when compared to other world markets. Manufacturers may decide to submit first to larger markets such as the United States and the European Union.
- Reference biologic drug patent expiry dates may differ between Canada and other countries.

Additional Information

Where can I find out more information about biosimilars authorized in Canada?

1. Health Canada's [Drug Product Database](#) contains product specific information including product monographs for drugs authorized in Canada.
2. [Regulatory Decision Summaries](#) briefly explain Health Canada's decisions for drugs including biosimilars.
3. [Summary Basis of Decision](#) documents explain Health Canada's decision for drugs including biosimilars in detail.
4. The [Canada Vigilance Adverse Reaction Online Database](#) contains information about suspected adverse reactions (also known as side effects) to health products.
5. [Submissions Under Review](#) lists certain drug submissions currently under review by Health Canada.

For further information on biosimilars, please contact:

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