IFPMA

Policy considerations for the development, regulation and adoption of biosimilars

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Introduction

IFPMA is committed to supporting capacity building, technical guidance, and regulatory cooperation globally to ensure biosimilars contribute fully to equitable and sustainable healthcare.

What are biological products?

Biological products encompass a large range of medicinal products, obtained from biological source (e.g., recombinant proteins produced by rDNA technology). Biological products are generally larger and more complex (from the structural perspective) than small molecule products. Biological products range from short single chain, non-glycosylated peptide to more complex proteins composed of several subunits that may be glycosylated.

The production of biological products involves a complex manufacturing process that is generally based on the culture of recombinant living cells that express the protein of interest that will be refined through several purification steps.

The quality profile of biological products corresponds to a mixture of several variants that has been demonstrated to be consistently produced using a validated process. Changes in the manufacturing process can lead to changes of the quality profile, which could potentially have an impact on the safety and efficacy profile of the product.

Vaccines, plasma-derived products[1] , and advanced therapy products are out of scope for this document.

What is a biosimilar product?

A biosimilar is a biological product that is shown to be highly similar in terms of its quality, safety and efficacy to an already licensed reference product.

Unlike biosimilars, generics are chemically synthesized, typically have simpler chemical structures, and are considered identical to their reference product. Biosimilars are produced in living organisms through a process of complex manufacturing and are not exact copies of their reference products.

The biosimilar manufacturer must re-create the entire manufacturing process from a new master cell bank. A small change in this process may lead to changes in product characteristics, which can affect product safety and efficacy.

It is essential that the manufacturer of a biosimilar thoroughly understands which characteristics of the reference product are critical to ensuring its safety and efficacy. These are known as critical quality attributes. For now, most biosimilars have been in the range from small peptides to monoclonal antibodies (mAbs) and fusion proteins.

[1] https://www.who.int/publications/m/item/guidelines-on-evaluation-of-biosimilars (last accessed May 27, 2025)

What are the steps for rigorous development and regulatory evaluation of a biosimilar?

A biosimilar is submitted using a specific regulatory pathway and dossier content that differs from the biological stand-alone dossier for the reference product.

Approval is based on the "totality of evidence" approach to mitigate residual uncertainties related to clinical/safety impact of potential structural or functional differences.

Quality attributes are measured through physicochemical and functional (biological) studies and compared in a head-to-head similarity assessment between the biosimilar and the reference product.

Characterization of both the reference product and the biosimilar should be carried out using state of-the-art, fit for purpose chemical, biochemical, biophysical and biological analytical techniques. The most frequently used approach for similarity assessment relies on demonstrating that the quality attributes of the biosimilar batches lie within predetermined similarity ranges.

Comparative clinical studies are also generally needed to confirm the absence of any clinically relevant differences between the biosimilar and the reference product. This would typically be a PK or PK/PD study, with the need for comparative efficacy/immunogenicity studies determined on a case-by-case basis (i.e., based on risk-based criteria).

Regulatory frameworks and requirements for biosimilars vary significantly across regions and countries. To ensure consistency and safeguard patient safety, biosimilar approval guidelines should be globally harmonized — at a minimum, aligned with the latest WHO recommendations[2]. In particular, the use of non-comparable biotherapeutic products [2] — those developed without a thorough comparability exercise — should be avoided.

Why is immunogenicity assessment important?

Biologicals, including both reference products and biosimilars, have a risk of immunogenic response. Differences in product characteristics can profoundly impact its immunogenicity.

Upon a risk assessment, a comparative assessment of immunogenicity using the most sensitive population, will typically be a core part of the clinical comparability assessment.

The formation of anti-drug antibodies (ADAs) can have significant implications for patient safety, yet pharmacokinetics studies often lack the necessary power to adequately assess this risk, especially when the incidence is low. The challenge lies in determining the appropriate duration of monitoring and the number of administrations needed to capture potential immunogenic responses.

[2] IFPMA policy statement on Non Comparable Biotherapeutic Products

What are considerations for healthcare systems for biosimilars?

Biosimilars are important in promoting the availability of biological medicines worldwide and introducing competition to optimize healthcare investment for patients and society. IFPMA supports an ecosystem that preserves incentives for innovation and ensures a level playing field for novel biologics and biosimilars.

Tendering and other procurement practises involving biological medicines (including biosimilars) should encompass a variety of selection criteria and not only price. To ensure stable supply and create markets that are both sustainable and competitive, procurement practices should provide for a sufficiently broad choice of products to patients.

Other considerations include pharmacy-mediated substitution, which is a framework permitting substitution of medicines at the retail pharmacy without the consent or oversight from the prescribing physician [3]. Generally, it should be allowed if available evidence provides reassurance that repeated switching between biosimilar(s) and the reference product will not pose an increased risk to patients. In addition, the patients' ability to use the medical device associated with the biosimilar without supervision from the prescribing physician or nurse should be evaluated. Furthermore, the prescribing physician should have the right to refuse substitution[4,5].

Finally, any biosimilar should as a minimum be subject to the same pharmacovigilance activities and risk minimisation measures in place for the reference product. For effective pharmacovigilance, traceability must be ensured by applying a unique name to the biosimilar that is distinguishable from the reference product. In adverse event reporting, this unique name as well as batch information must be provided as the International Non-proprietary Name (INN) alone will be insufficient.

What measures can empower patients and physicians to make informed decisions when prescribing treatments?

Data relating to product information, public assessment reports, and rationale for regulatory approval must be transparent and publicly available. The prescribing information for a biosimilar should closely match that of the reference product. Differences are allowed for product-specific aspects such as different excipients, device, presentation, omitted indications. Highlighting the source of evidence would ensure that prescribers and patients have the necessary information to make informed treatment decisions.

[3] IFPMA position paper on pharmacy mediated substitution

[4] Biosimilars Toolkit | International Alliance of Patients' Organizations

[5] Use of Biosimilars: A Systematic Review of Published Position Statements and Recommendations from Health Organisations and Societies | BioDrugs

Recommendations

Biosimilars can play a role in expanding patient access to biological medicines and in supporting the sustainability of healthcare systems. To fully realize this potential, the following policy actions are recommended.

→ **Strengthen regulatory alignment and capacity building**

- Promote international cooperation and global convergence to uphold science-based quality, efficacy and safety standards (such as WHO guideline on biosimilars), and facilitate reliance
- Support training and technical resources for National Regulatory Authorities (NRAs)
- Foster reliance and mutual recognition agreements where feasible

→ **Promote clear and science-based substitution policies**

- Encourage clear and case-by-case switching and substitution determinations
- Safeguard informed physician and patient decision-making in pharmacy substitution frameworks

→ **Ensure robust pharmacovigilance and traceability systems**

- Implement globally distinguishable naming and batch tracking
- Strengthen adverse event reporting infrastructure
- Engage all stakeholders in real-time signal detection and risk mitigation

→ **Ensure transparency for healthcare providers and patients**

- Develop training activities for healthcare providers
- Support clear, consistent communication tools for patients

About IFPMA

IFPMA represents the innovative pharmaceutical industry at the international level, engaging in official relations with the United Nations and multilateral organizations. Our vision is to ensure that scientific progress translates into the next generation of medicines and vaccines that deliver a healthier future for people everywhere.
To achieve this, we act as a trusted partner, bringing our members' expertise to champion pharmaceutical innovation, drive policy that supports the research, development, and delivery of health technologies, and create sustainable solutions that advance global health.

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