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Review Article

An overview of scientific principles, regulatory progress, and clinical integration of biosimilars in modern healthcare

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Abstract

Biosimilars are therapeutic alternative options to originator biologics and can help address challenges to healthcare accessibility and sustainability. However, several scientific, regulatory, and practical issues stand in the way of their implementation, which need a thorough review. This review comprises an analysis of evidence available to date on the development, regulation, and clinical implementation of biosimilars, based on analyzing regulatory databases, peer-reviewed papers, and official guidance from the main regulatory agencies. The process of developing biosimilars requires a systematic and rigorous demonstration of similarity by analytical, non-clinical, and clinical studies. Regulatory systems have undergone dramatic change, and 144 biosimilars had been authorized in the European Union and 75 licensed in the United States by January 2025. Economic analyses suggest that biosimilar competition can reduce healthcare expenditure in Europe and the United States. However, there are implementation challenges arising from knowledge gaps between healthcare providers, patient concerns, and the need for regulatory harmonization. The immunogenicity profiles of biosimilars remain comparable to those of the reference products, supporting the principle of extrapolating indications based on the totality of the evidence. Biosimilars have proven to be safe and effective alternatives to reference products, but they must be implemented successfully, which requires continued education for stakeholders, regulatory harmonization, and evidence-based approaches. Advancements in analytical technologies and the science of regulation will further strengthen biosimilar development and help maintain high-quality standards, as established to be important to patient safety and therapeutic effectiveness.

Keywords: *Biological products, Biosimilar pharmaceuticals, Drug approval, Pharmacovigilance, Therapeutic equivalency*

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INTRODUCTION

In the 1980s, the pharmaceutical industry was transformed by the introduction of biological medicines [1]. The formation of these complex molecules involves advanced biotechnological processes involving living organisms, which have greatly influenced the treatment of some life-threatening and chronic diseases [2]. Biological medicines include various therapeutic proteins, particularly monoclonal antibodies and fusion proteins, rather than small-molecule drugs made via chemical synthesis [3,4]. The evolution of these drugs has offered many new therapeutic possibilities to patients with cancer, metabolic disease, and rheumatoid arthritis. It has led to improved clinical outcomes and quality of life for millions of patients worldwide [5–7].

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While biological medicines have a significant therapeutic benefit, they have a high economic cost as well [8]. Their complex development and manufacturing technologies, together with significant clinical trial requirements and the relative absence of competition during the period of patentability, result in very high treatment expenditures. Such access costs are a challenging issue for global healthcare systems and are limiting patient access to potentially lifesaving care and impacting the sustainability of healthcare budgets. In many countries, the expense of biological therapies is high, priced at hundreds of thousands of dollars per year and often excluding costs to the private sector. Hence, these therapies are inaccessible to large parts of the population and are a heavy burden to public healthcare [9].

With the expiry of patents and regulatory exclusivity periods for biological drugs, biosimilars have become an important answer to the challenges of accessibility and sustainability. The European Medicines Agency (EMA) defines a biosimilar as a biological medicinal product in the European Economic Area (EEA) that contains a version of the active substance of an already authorized biological medicinal product [10,11]. To be considered comparable to reference products, biosimilars must undergo extensive testing, including in-depth analytical, non-clinical, and clinical activities. The emergence of biosimilars is unique both scientifically and in terms of regulation, and differs notably from that of novel biologics and generic small molecules [12].

To understand the development and regulation of biosimilars, it is important to recognize the differences between generic and biosimilar drugs. Generic drugs are exact copies of their reference products, with the same chemical structure, which analytical methods can fully characterize. However, due to natural fluctuations in living cells and complex manufacturing processes, biosimilars are not identical to the reference biologic but are typically very similar. The slightest differences in the processing methods may have a profound effect on the resulting product. Therefore, a more advanced approach to biosimilar development is needed, as simply comparing the two will not be sufficient; determining comparable safety and efficacy will require functional characterization and clinical confirmation [13].

Much progress has been made since the EMA approved the first biosimilar, somatropin, in 2006 [14]. This pivotal decision marked a turning point in drug development and regulatory practices. A significant boom has occurred in the biosimilar market since the first biosimilars were approved; approved products have come to include complex monoclonal antibodies once considered difficult to replicate [13]. A major contributor to this shift has been the European Union (EU), which has provided comprehensive regulatory frameworks that other jurisdictions around the world have emulated [15]. Later, the United States (US) introduced its biosimilar pathway through the Biologics Price Competition and Innovation Act of 2009, with its first biosimilar approval in 2015 [12].

The scientific principles for the development of a biosimilar are based on the totality-of-evidence approach, which means gathering all data at each stage of development to establish biosimilarity. This includes comprehensive analytical characterization of the molecule to define the structural and functional similarity of the molecule, targeted non-clinical studies to resolve any remaining uncertainties, and focused clinical trials to establish similarity in pharmacokinetics, efficacy, safety, and immunogenicity. This focus on analytical characterization is due to the advances in analytical technologies that are available, allowing detailed molecular characterization, thereby enabling more efficient clinical development programs than those for novel biologics [16,17].

Biosimilars have brought opportunities and challenges to clinical practice. While biosimilars promise significant cost savings and an improved patient journey, several factors determine whether they will be adopted, including physician awareness, patient uptake, and regulatory implications regarding interchangeability and substitution [18]. All of these will require difficult choices among healthcare providers regarding the use of biosimilars, weighing economic considerations against clinical evidence, and making adjustments to address patient concerns about switching from proven therapies. Various countries and regions have different regulatory approaches, resulting in a varied landscape of development and use worldwide and posing implementation challenges.

This mini-review comprehensively explores biosimilars, biosimilar regulation, and clinical implementation. The development pathway leading to approval of a biosimilar will be discussed, including analytical, non-clinical, and clinical studies that comprise the totality of evidence. Some salient regulatory aspects in selected jurisdictions, such as interchangeability

and indication extrapolation, are discussed in the review. Discussed in detail are critical scientific topics in immunogenicity assessment, namely, post-translational modifications and manufacturing consistency. In addition, the review focuses on the practical challenges of biosimilar use, including economic considerations, provider training, patient engagement, and post-marketing surveillance regulations. The main purpose of this review is to provide information to help healthcare providers, regulators, and researchers make decisions about biosimilar development and use. It also identifies future avenues for optimizing clinical implementation by summarizing available evidence and emerging trends.

Evolution of biological medicines and emergence of biosimilars

Biological medicines represent an important step in modern therapeutics. These complex molecules have revolutionized the way treatment is thought about when treating disease states that were once thought to be unresponsive or hard to treat [19]. Biological medicines are made using cutting-edge biotechnology methods, and genetically modified living cells are used as biological production platforms for therapeutic proteins to be made during production [20]. This intrinsic variability and complexity are key differences from chemical synthesis and are characteristic of biologics when compared to traditional small-molecule drugs [21,22].

The first step in the manufacture of biological medicines is the selection of host cells, which can be from bacteria, yeast, or mammalian cell lines, and their modification by gene transfer. Manufacturers create proprietary cell banks and manufacturing protocols that have a significant effect on the characteristics of the resulting product [22]. When proteins are expressed by cells, they can undergo a variety of post-translational modifications such as glycosylation, phosphorylation, and other processes that can significantly affect the resulting protein's biological activity, stability, and immunogenicity [23]. The profile of the final product is dependent on the environmental conditions during cell culture, purification technique, and formulation strategy, which makes each biological medicine unique to its method of manufacture [22]. The end-to-end design and manufacturing continuum for a biosimilar is depicted in Figure 1.

With the patents and regulatory exclusivity for the first biological drugs nearing their end, the chance for creating similar versions of the product arose [24]. But because of the complexity of biological medicines, it is not possible to make copies that are the same [22,25]. These are called biosimilars and are highly similar products that may deliver the same clinical outcomes and have economic benefits as a result of competition [26,27]. When biosimilars were introduced, new scientific and regulatory frameworks needed to be developed that take into account both the similarity and the potential differences between the biosimilar drug and its reference medicine [26].

Scientific foundations of the development of biosimilars

The process of developing biosimilars depends on advanced scientific principles, using the latest developed analytical techniques and focused biological and clinical evaluations [28]. At the heart of biosimilar development is thorough analytical characterization, which serves as the basis for the similarity assessment. This process starts with an exhaustive study of several lots of the reference product. It includes an assessment of its physical, chemical, and biological characteristics, as well as the natural variation that is intrinsic to the biological manufacturing process. The characterization of complex biological molecules has been greatly improved by modern analytical technologies, as demonstrated in Figure 2. High-resolution mass spectrometry enables detailed analysis of primary structure and post-translational modifications, and allows the identification of sequence variants and chemical modifications that may affect function. Furthermore, multidimensional chromatography can separate product variants and quantify them, while biophysical techniques such as circular dichroism, nuclear magnetic resonance, and analytical ultracentrifugation can reveal higher-order structural features [29]. These analytical methods represent an orthogonal approach to assessing molecular similarity, encompassing several aspects of molecular structure and behavior. A summary of the five-step totality-of-evidence pathway is included in Table 1.

Functional characterization of biosimilars goes beyond biological activity evaluation and structural analysis. This includes target binding affinity and kinetics using a variety of biophysical assays, including surface plasmon resonance, as well as cell-based assays that assess downstream biological consequences [30]. These include binding to target antigens, binding to F_c receptors, and various effector functions, including antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity [31].

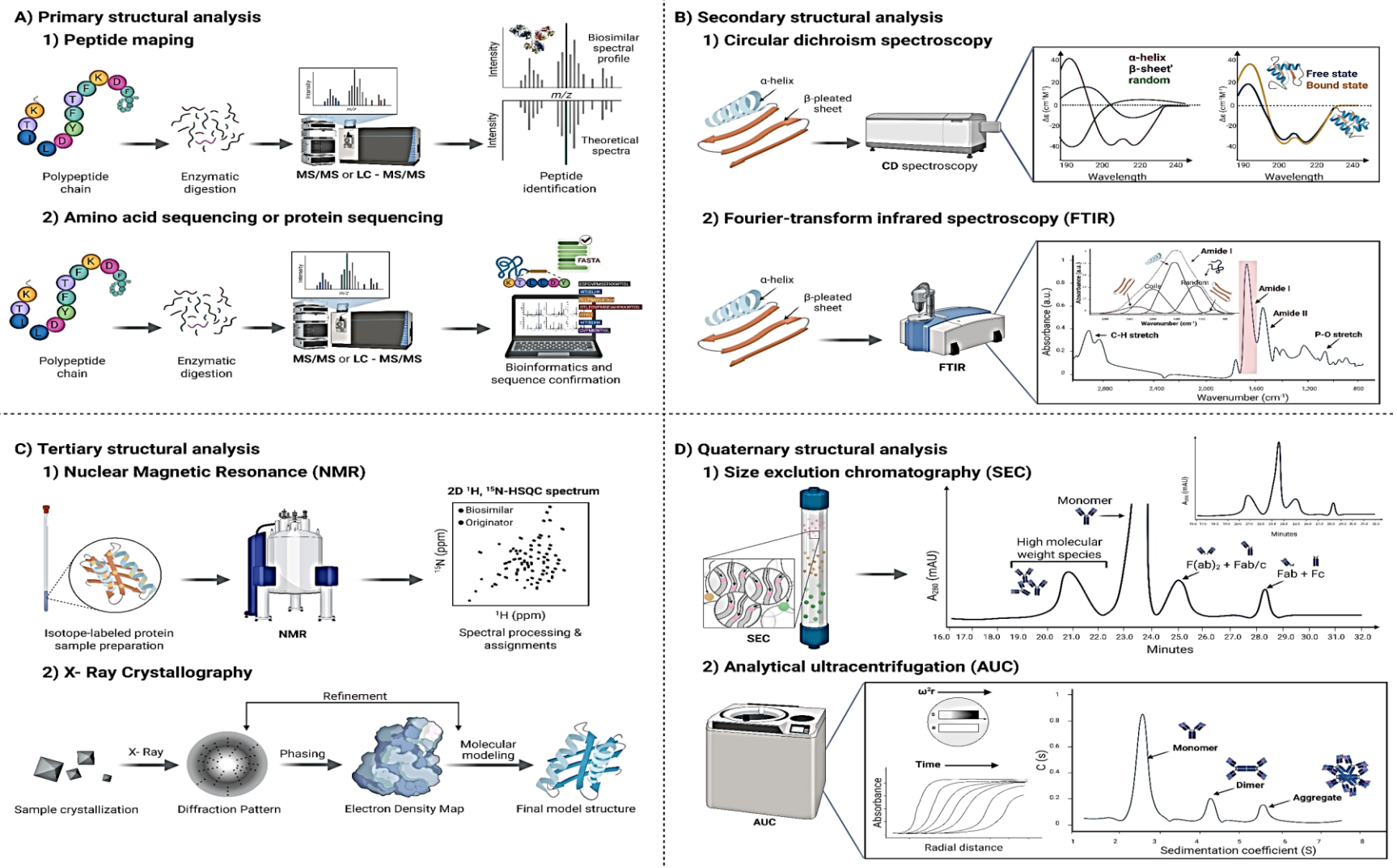


Figure 1: Design innovations, manufacturing workflow, and comparability strategy for biosimilar therapeutics

Table 1: A step-wise "totality of evidence" framework for biosimilar development

Stage	Core objective	Typical assays/endpoints	Decision criterion
Analytical characterization	Confirm structural and physicochemical similarity	High-resolution LC-MS, peptide mapping, glycan profiling, circular dichroism	All critical quality attributes fall within the reference product's variability window
Functional/non-clinical	Demonstrate comparable bioactivity and mechanism of action	Cell-based potency, F_c-effector panels, SPR/BLI binding kinetics	No statistically or biologically meaningful differences in functional read-outs
PK/PD bridging	Exclude clinically relevant PK/PD divergence	Crossover PK trials; AUC_{0-t}, C_{max} ± sensitive PD biomarkers	90% CI of the geometric-mean ratio contained in the 80-125 % equivalence margin
Comparative efficacy & safety	Confirm no residual efficacy or safety gap	Randomized (equivalence-design) patient trials, disease-specific primary endpoints, and immunogenicity incidence	The point estimate lies inside the prespecified equivalence margin; immunogenicity is comparable
Post-marketing pharmacovigilance	Detect rare or long-term safety signals	Brand- and batch-level AE reporting; EU & US real-world registries (> 1 million patient-treatment-years)	Safety profile remains aligned with reference; risk-management plan adapted as needed

Notes: AE: Adverse event; AUC_{0-t}: Area under the concentration-time curve from time 0 to t; BLI: Biolayer interferometry; CI: Confidence interval; C_{max}: Maximum observed concentration; EMA: European Medicines Agency; EU: European Union; FDA: U.S. Food and Drug Administration; F_c: Fragment crystallizable (antibody region); ICH: International Council for Harmonisation; LC-MS: Liquid chromatography mass spectrometry; PD: Pharmacodynamics; PK: Pharmacokinetics; SPR: Surface plasmon resonance; US: United States of America

Evaluating the mechanism of action of the reference product and the clinical relevance of its various biological activities is an important factor in selecting appropriate functional assays.

Designing a process to produce a biosimilar product is a complicated process, and the developers need to design a process that can produce a highly similar product without access to the specific details of the reference product processes and data [32]. This requires an iterative optimization of the cell line, culture conditions, purification strategies, and formulation development [33]. An analytical comparison of the product is done continuously to achieve process optimization, obtaining the target similarity profile along the process [28]. Because of the inherent variability of biological systems, there are inevitably differences between the biosimilar and the reference product that must be evaluated scientifically to identify which differences are clinically relevant [11].

Regulatory evolution and global frameworks

The regulatory landscape for biosimilars has changed significantly since the early 2000s, and several jurisdictions have established regulatory regimes tailored to their regulatory systems, yet fostering scientific integrity [34]. In the arena of biosimilar regulation, the EMA was first to release guidelines in 2003 and to approve a biosimilar in 2006 [35]. This first leadership was effective in the accumulation of rich experience in biosimilar assessment and post-marketing monitoring, which has since fed global regulatory developments [36].

The European regulatory strategy for biosimilars is based on a sequential approach: first, complete quality characterization; then, the non-clinical study phase to address any remaining uncertainties; and finally, the targeted clinical trial phase [36]. EMA guidelines have changed, with growing experience and recent guidance that show greater confidence in analytical methods and a reduced reliance on wide-ranging clinical trials when robust analytical and functional similarity is demonstrated. Extrapolation is a vital part of the European regulatory strategy that allows the approval of all indications of the reference product based on a full set of similarity data and scientific reasoning [37].

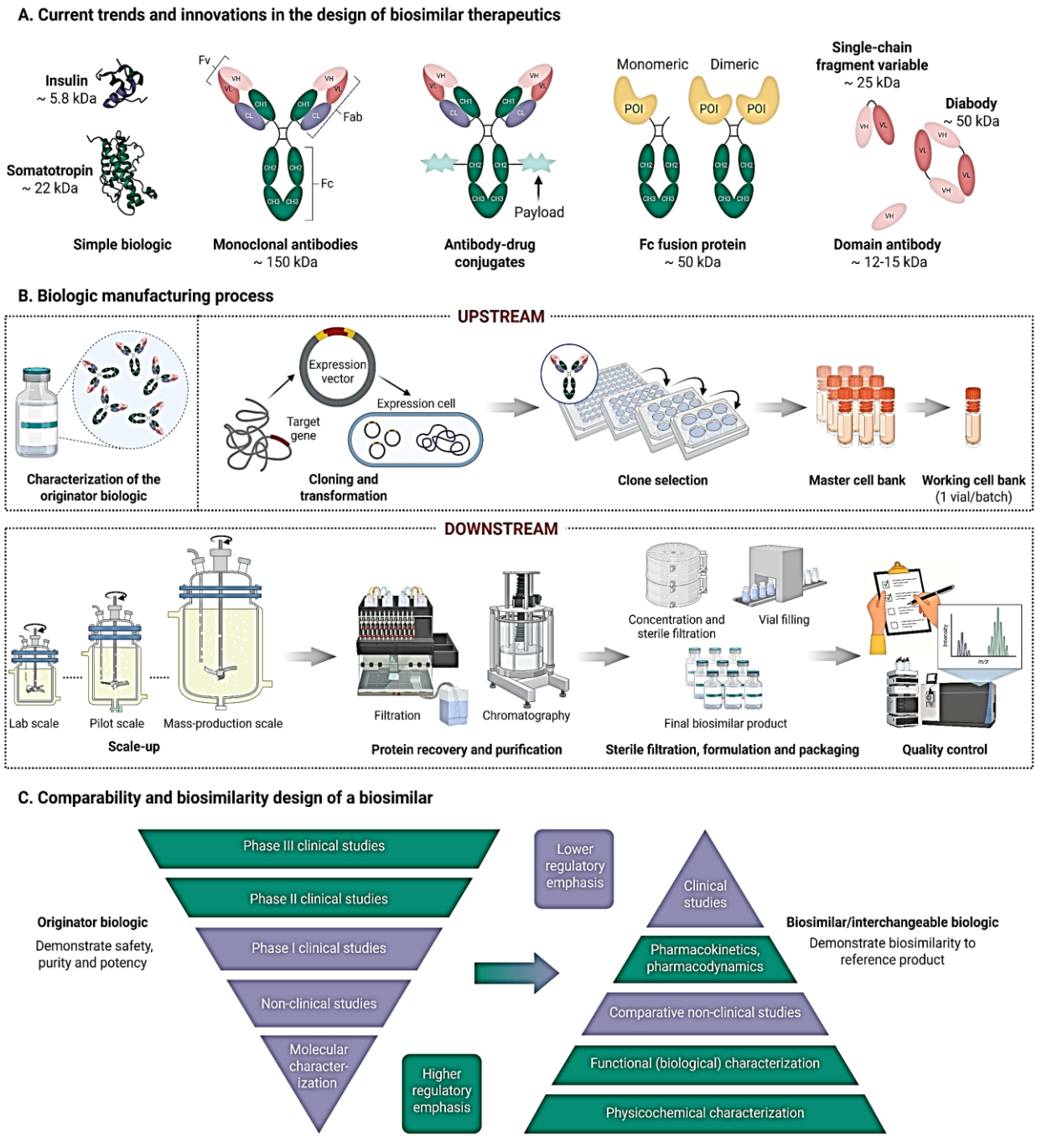


Figure 2: Orthogonal structural characterization of biosimilars from primary to quaternary analyses

The United States Food and Drug Administration (FDA) created its biosimilar pathway through the Biologics Price Competition and Innovation Act of 2009, and the first biosimilar was approved in 2015 [38,39]. The FDA's policies on biosimilars have been consistent with several scientific principles of the European model, with some additional features, such as the designation for interchangeability. To achieve this designation, the biosimilars must be able to show they produce the same clinical results as the reference product in any patient, and that there are no increased safety risks or loss of effectiveness when switching between products [40]. Interchangeability also allows for the substitution of interchangeable drugs at the pharmacy level if allowed by state law, and is not implemented evenly across the US [41]. Table 2 provides an overview of EMA, FDA, and World Health Organization (WHO) requirements, side by side.

Table 2: Key features of leading biosimilar regulatory frameworks

Attribute	European Union (EMA)	United States (FDA)	WHO guidelines
Year of first biosimilar approval	2006 (somatropin)	2015 (filgrastim-sndz)	N/A - WHO issues guidance, not approvals
Latest major update (as of 2025)	2022 EU-wide statement confirming interchangeability	The 2024 draft guidance proposes the removal of mandatory switching studies for interchangeability	2022 full revision of the WHO evaluation guideline (TRS 1030)
Explicit interchangeability pathway	No separate designation; substitution decided at the Member-State level	Distinct “interchangeable biosimilar” label (evidence threshold under review)	Not addressed (left to national law)
Extrapolation of indications	Permitted when the mechanism of action and PK/PD are shared	Same principle; case-by-case scientific justification	Endorsed when the totality of evidence is adequate
Trend in clinical data requirements	Shift from large phase III trials to targeted PK/PD + immunogenicity packages	Similar shift, though interchangeability data are often still requested	Encourages risk-based, minimal-redundancy dossiers
Number of approved biosimilars (Jan 2025)	144 authorized (over 30 molecules)	75 licensed; 13 designated interchangeable	-

Notes: EMA: European Medicines Agency; EU: European Union; FDA: U.S. Food and Drug Administration; PK: Pharmacokinetics; PD: Pharmacodynamics; TRS: Technical Report Series; US: United States of America; WHO: World Health Organization

Key regulatory agencies across the globe have implemented biosimilar frameworks that take regional considerations into account and often cite European and American examples [34,42]. Harmonization of global regulations has been greatly facilitated by the WHO biosimilar evaluation guidelines, which provide a scientific framework that can be tailored to different regulatory settings. These harmonization initiatives have not eliminated significant discrepancies in regulatory requirements, clinical trial standards, and post-approval surveillance regulations, with implications for global biosimilar development programs.

Clinical development strategies and considerations

The clinical development of biosimilars differs in essence from that of novel therapeutics. But instead of demonstrating efficacy and safety de novo, biosimilar clinical programs are designed to ensure that any differences identified through analytical and functional characterization are not reflected in clinically meaningful differences in performance [43]. Such a paradigm change requires well-designed studies that can identify a difference if one exists, and do not repeat the comprehensive clinical trial programs already completed for the reference product [37].

The first phase of clinical evaluation is usually composed of pharmacokinetic (PK) and pharmacodynamic (PD) studies, which yield sensitive measures of *in vivo* similarity [44]. These studies aim to identify possible differences in absorption, distribution, metabolism, and elimination, and to assess possible pharmacological effects if measurable biomarkers are present. The selection of the subjects, healthy volunteers or actual patients, depends on safety concerns and the possibility of reducing the variability that may obscure any real differences between products. While single-dose studies tend to be the most sensitive comparisons, multiple-dose studies may be needed for products that exhibit nonlinear PK or for which immunogenicity may affect drug exposure over time.

Comparative efficacy and safety trials conducted in patients are the final stage in establishing biosimilarity, and the trials are specifically tailored to the product and therapeutic area. Patient population and endpoints must be sensitive enough to detect any differences, and there is a preference for indications and outcomes in which the reference product is known to have a consistent and measurable effect [45]. Mostly equivalence or non-inferiority designs are used, with margins designed to exclude clinically meaningful differences whilst allowing for the normal fluctuation found in biological systems and clinical measurements. The length of these trials should be sufficient to evaluate efficacy and safety, including the emergence of immunogenicity and its clinical consequences.

Because biological therapeutics have the potential to trigger immune responses that may impact safety and efficacy, immunogenicity assessment is a key part of the clinical development of biosimilars [46]. Validated,

sensitive assays are required for comparative immunogenicity evaluation of both binding and neutralizing antibodies. Immunogenicity needs to be correlated with PK, efficacy, and safety to determine clinical relevance. While most biosimilars have immunogenicity profiles comparable to those of their reference products, product- and patient-specific factors must be carefully assessed during development and post-marketing surveillance [47].

Post-marketing surveillance and risk management

Approval of a biosimilar requires the maintenance of a long-term safety monitoring program via pharmacovigilance systems that have been put in place to identify rare adverse events and confirm the acceptable safety profile of the clinical development programs [48]. However, because of the complex nature of biological medicines and the possibility of changes in drug manufacturing, there is a need for robust post-marketing surveillance strategies to distinguish between different products and manufacturers and to obtain complete safety data from drugs in real-world use [48].

Clear product identification in medical records and adverse event reports is essential to effective pharmacovigilance for biosimilars, including the use of the brand name and a batch number, in addition to the international nonproprietary name. This traceability is essential for correctly identifying safety signals for specific products and for enabling regulatory authorities and manufacturers to take appropriate risk-management action as needed. To ensure accurate product identification, healthcare systems employ various strategies, including electronic prescribing systems to capture specific product information and education programs to highlight the importance of detailed adverse event reporting [49].

The product-specific considerations and the broader safety context of biological medicines should be taken into account in risk management plans. Typically, these comprise standard pharmacovigilance activities and other activities if there is a specific safety concern to be monitored more closely. Real-world evidence from registries, observational studies, and analyses of healthcare databases provides valuable information on the long-term safety and efficacy across various patient groups and clinical contexts [48,50]. These evidence-based findings have continually been validated for both biosimilars and their reference products.

Impact and healthcare system considerations

Biosimilars have a great impact on the economic sustainability of global healthcare systems. Biological medicines are costly, and the availability of biosimilars is key to ensuring current and future access to these important medicines for patients and maintaining sustainable health sector budgets worldwide [51]. Potential savings from biosimilar use have been highlighted by economic analyses in the United States [52] and Europe [53]. However, these savings are not only due to the lower prices of biosimilars but also to the competition they introduce, which lowers prices for reference products as well.

The benefits of biosimilars go beyond cost savings to include the potential to improve the healthcare system. The money saved on the use of the biosimilar can be reinvested into developing new drugs, expanding the availability of drugs in regions where they do not exist, or other healthcare services [51]. Various healthcare systems have developed gain-sharing programs that encourage the use of biosimilars and ensure that savings are shared among multiple stakeholders, including patients, clinicians, and hospitals. The key design of such programs is to strike a balance between the incentive to use biosimilars and the need to retain clinical autonomy and patient choice.

The market dynamics for biosimilars are distinct from those of traditional generic products, with implications for market sustainability and manufacturer investment [54]. Because of the complexity and cost of biosimilar development, ranging from 5 to 9 years of development and hundreds of millions of dollars in investment, fewer competitors than small-molecule generics find a path to the market [54]. These facts, coupled with post-marketing commitments and continual investment in manufacturing, mean that policies should be carefully designed to encourage a competitive and sustainable biosimilar market while providing rational incentives for continued investment in biosimilar design and manufacturing [54,55].

Healthcare provider and patient perspectives

To successfully integrate biosimilars into clinical practice, one must consider healthcare providers' knowledge, attitudes, and concerns when prescribing decisions are made. Although there is a vast body of data confirming the safety and effectiveness of biosimilars, a systematic review has identified knowledge gaps among healthcare professionals concerning biosimilar development,

regulation, and clinical practice [18]. These knowledge gaps can lead to reluctance to prescribe biosimilars or to move patients from reference products, thereby limiting the potential benefits of biosimilars.

Developing confidence in the use of biosimilars is essential, and education of healthcare providers is an important enabler. However, education programs are not limited to the definition and regulatory requirements and can also include specific clinical challenges, practical guidance on communicating with patients, and experience from early adopters. Professional societies have also played several key roles in developing position statements and clinical guidance that promote the evidence-based use of biosimilars while affirming that, in some cases, clinical judgment remains necessary [56]. Opinion leaders and peer education have proved particularly successful in disseminating information, boosting confidence in biosimilars, and changing prescribing habits.

Patients' attitudes are influenced by their trust in their healthcare providers, their understanding of the science, and their concerns about cost and efficacy of the biosimilars. Similarly, the negative expectations that lead to reduced efficacy or adverse events, known as the nocebo effect, have also been seen in biosimilar switching literature and are a significant challenge for clinical implementation [57]. This means that clear and understandable communication is vital, patients' perspectives and views must be taken into account, and relevant information on biosimilar development and evidence of use must be provided. Shared decision-making models that engage patients in decision-making regarding their care are successful regarding acceptance and adherence.

Future directions and challenges

Biosimilars are a growing industry, and developments in science and regulations are shaping future opportunities and challenges. Marked advances in analytical technology have now enabled the detailed characterization of complex biological molecules, potentially shortening the time required to complete clinical trials and accelerating biosimilar development. Similarity assessment is complemented by novel analytical approaches, such as hydrogen-deuterium exchange mass spectrometry, ion mobility spectrometry, and advanced bioinformatics, which can provide new insights into protein structure and dynamics [58,59].

Biosimilars are now more sophisticated molecules, and with their introduction come benefits and challenges to the field. The targets of the first-generation biosimilars were relatively simple proteins, and the current pipeline includes complex monoclonal antibodies, fusion proteins, and antibody-drug conjugates [60]. The molecules pose additional technical and analytical challenges that a maturing regulatory scientific-technical capability must address. The adoption of cell and gene therapy products as biosimilars introduces new challenges regarding the extrapolability of the existing biosimilar principles to new products [61].

Experiences and regulatory science on biosimilars continue to mature worldwide. An understanding of regional differences and regulatory convergence will improve the effectiveness of development programs worldwide. Key milestones in regulatory evolution include European guidance on biosimilar interchangeability [62] and the FDA approval of interchangeable biosimilars [63]. Ongoing discussions between regulators, developers, and healthcare stakeholders will be critical to ensure optimal regulatory frameworks that balance patient safety with the need to avoid unnecessary hurdles to biosimilar development and adoption [42].

Limitations

This study has several limitations. Because it is a mini-review, it only uses a selected set of peer-reviewed articles, regulatory documents, and available guidance. This study does not follow a formal systematic review protocol, which would include predefined search criteria, a structured quality assessment, or a meta-analysis. Some relevant studies, regional regulatory updates, or jurisdiction-specific implementation experiences may have been omitted. Evidence is also uneven across biosimilar product classes and healthcare settings. While there is substantial clinical and post-marketing data for many established biosimilars, evidence for newer complex molecules, emerging markets, long-term outcomes after repeated switching, and real-world implementation in resource-limited settings is comparatively limited. Economic projections and uptake data should be interpreted with caution, as local pricing policies, reimbursement systems, prescribing practices, and pharmacovigilance capacity strongly influence them. These limitations do not weaken the overall evidence supporting biosimilar approval; however, they highlight the need for ongoing surveillance, transparent reporting, and

context-specific studies to guide their safe and effective integration into clinical practice.

CONCLUSIONS

The approval and maturity of biosimilars in the biopharmaceutical therapeutics market demonstrate the complexity of the process, as these products must achieve two goals: patient access and healthcare sustainability, while complying with strict quality, safety, and efficacy standards. The current scientific and regulatory paradigm is sound, and significant real-world evidence over the last two decades shows that the clinical outcomes of approved biosimilars are similar to those of the reference products. The biosimilarity concept and the strategies used to evaluate biosimilars have been validated by millions of patients worldwide who have been treated with the same products. However, the potential of biosimilars can be fully realized only through the continued cooperation of all stakeholders in the healthcare system. Manufacturers face the challenge of consistently maintaining the quality and innovation required to serve the demanding global markets in which they operate, as well as regulatory requirements. The regulators should continue to work on a science-based approach without creating unnecessary hurdles to development and/or adoption, or compromising patient safety. Ongoing education and orientation of healthcare professionals are essential to ensure they are up to date on the scientific best-practice prescribing options, rather than being driven by misconceptions or economic incentives. Treatment needs to be communicated to patients clearly, and they should be informed correctly, as they should be involved in decisions about the therapy and know how safe and effective biosimilars are. Overall, the future of biosimilars is complex, with the potential for significant expansion and intersectoral integration in the healthcare sector, but also potential conflicts of interest and competition. This is due to the growing number of increasingly complex molecules, new manufacturing and testing techniques, and greater real-world evidence. However, if biosimilars are to fully deliver on their promise to healthcare systems and individual care, the issues of regulatory harmonization across countries, market viability, and stakeholder awareness will need to be addressed. Three pieces will remain central to the biosimilars' future promise: interconnectedness, commitment to scientific rigor, and patient safety. All these combine to help deliver sustainable, quality healthcare services.

DECLARATIONS

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Ethical approval

Not applicable.

Use of Artificial intelligence/Large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tools were used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript are the original work of the authors.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Conceptualization, A-D.H.N., T-T.T.H., and M.T.Q.; Writing original draft, A-D.H.N.; writing - review & editing, M.T.Q. and T-T.T.H.; Visualization, A-D.H.N. and M.T.Q. All authors have read and agreed to the published version of the manuscript.

Use of research reporting tool

Not applicable.

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