

Biosimilars in India: An Overview of Biological Challenges, Regulatory Evolution, Manufacturing Barriers and Future Perspectives

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ABSTRACT

Biosimilars have emerged as an important component of modern biopharmaceutical development, offering potentially more affordable alternatives to reference biological products while maintaining comparable quality, safety and efficacy. Unlike conventional small-molecule generics, biosimilars are produced using living cells and complex manufacturing processes, and therefore cannot be considered identical copies of their reference products. The demonstration of biosimilarity requires a comprehensive, stepwise and evidence-based comparison involving analytical characterization, functional assessment, pharmacokinetic/pharmacodynamic evaluation, immunogenicity assessment and, where scientifically justified, clinical studies. India has developed substantial expertise in the development and manufacture of biosimilars and has become an important contributor to the global biopharmaceutical landscape. However, developers continue to encounter scientific, technical, regulatory and clinical challenges. These include molecular heterogeneity, post-translational modifications, glycosylation variability, protein aggregation, process-related impurities, analytical comparability, immunogenicity, manufacturing consistency, extrapolation of indications, interchangeability and post-marketing pharmacovigilance. The Indian regulatory framework has evolved considerably since the introduction of the Similar Biologics Guidelines in 2012. The 2016 framework established a more structured stepwise approach, while the revised 2025 guidelines incorporate newer scientific and international developments. The revised framework places greater emphasis on advanced orthogonal analytical techniques, in-vitro functional characterization, reference standards and a scientifically justified approach to non-clinical studies. This review discusses the scientific basis of biosimilarity, major biological and manufacturing challenges, the evolution of India's regulatory framework, clinical and pharmacovigilance considerations, and the future opportunities for Indian biosimilar development. Particular attention is given to the transition toward a more analytical and evidence-driven regulatory paradigm and to areas requiring continued harmonization with international practices.

Keywords: Biosimilars, Similar Biologics, India, CDSCO, Biotechnology, Analytical Similarity, Immunogenicity, Glycosylation, Regulatory Science, Pharmacovigilance, Interchangeability, Biologics

INTRODUCTION

Biological medicines have transformed the management of numerous chronic, autoimmune, oncological, metabolic and inflammatory disorders. Therapeutic proteins, monoclonal antibodies, hormones, cytokines and other biologically derived products have provided treatment options for conditions that previously had limited therapeutic alternatives.[1]

However, biological medicines are generally more complex to manufacture than conventional small-molecule medicines. Their structural characteristics are strongly influenced by the expression system, cell

line, culture conditions, purification process, formulation and storage conditions. Consequently, even relatively small changes in manufacturing processes may influence product quality attributes.[2]

Biosimilars have been developed to provide highly similar alternatives to already approved reference biological products. The World Health Organization (WHO) describes biosimilar evaluation as a comparative exercise in which similarity to a licensed reference product is established through a comprehensive assessment.[3] The WHO's revised 2022 framework emphasizes scientific principles and allows regulatory

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pathways to be adapted according to the characteristics of the product and the residual uncertainty after analytical and functional assessment.[4]

India has been an early participant in biosimilar development. The country's regulatory pathway began with the 2012 Similar Biologics Guidelines, followed by the 2016 revision. The latest revision in 2025 reflects advances in analytical science and international regulatory approaches. [5]

The scientific challenge is therefore not simply to manufacture a biological product containing the same

active ingredient. Rather, the developer must establish that differences between the proposed biosimilar and reference product do not result in clinically meaningful differences in quality, safety or efficacy.[6]

2. Biosimilars versus Conventional Generics

A conventional generic drug normally contains the same active pharmaceutical ingredient as its reference small-molecule drug and can generally be characterized by chemical identity and bioequivalence.[7]

Biosimilars are fundamentally different.

Table 1: Biosimilar vs Innovator vs Generic

Feature	Conventional Generic	Biosimilar
Molecular complexity	Relatively low	High
Manufacturing	Chemical synthesis	Living cells/biological systems
Molecular structure	Usually well defined	Complex and heterogeneous
Manufacturing variability	Comparatively limited	Potentially substantial
Analytical characterization	Relatively straightforward	Extensive orthogonal characterization
Regulatory demonstration	Bioequivalence	Totality/evidence-based similarity
Immunogenicity	Usually limited	Important consideration
Manufacturing process	Generally independent of molecular structure	Closely linked to product attributes

Thus, the concept of biosimilarity is based on comparability rather than molecular identity.[8]

3. Scientific Basis of Biosimilarity

The development of a biosimilar generally follows a stepwise evidence-generation strategy.

Major stages

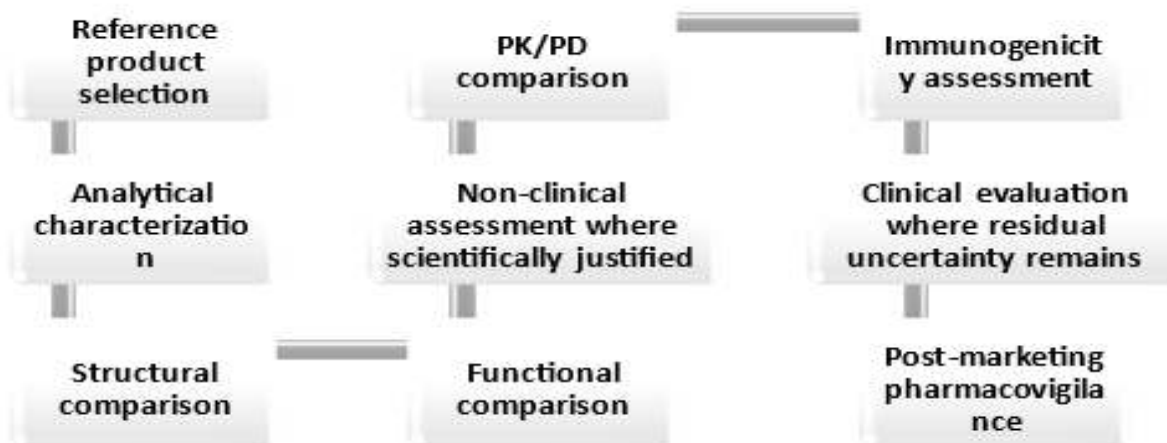


Figure 1: Biosimilar development pathway

This approach is consistent with the scientific principles described by WHO and reflected in India's revised regulatory framework. [9,10]

4. Major Biological Challenges

4.1 Molecular heterogeneity

Biological molecules are not necessarily single molecular entities. They may exist as populations of closely related molecular variants.

Examples include differences in:

- glycosylation
- oxidation
- deamidation
- charge variants
- aggregation
- clipping
- folding
- higher-order structure

The challenge is to determine whether observed differences are inherent variability or whether they could influence biological activity or clinical performance. [11]

4.2 Post-translational modifications

Post-translational modifications (PTMs) are particularly important for recombinant proteins and monoclonal antibodies. [12]

Common PTMs include:

- glycosylation
- phosphorylation
- oxidation

- deamidation
- acetylation
- methylation

Differences in PTMs may influence:

- receptor binding
- protein stability
- pharmacokinetics
- biological activity
- immunogenicity
- Fc-mediated functions.

Recent analytical literature continues to identify PTM characterization and higher-order structure as important challenges in biosimilarity assessment. [13]

5. Glycosylation: A Critical Challenge

Glycosylation represents one of the most important differences that can arise between biologics manufactured using different cell systems or processes.

Important characteristics include:

- glycan composition
- glycan distribution
- sialylation
- fucosylation
- high-mannose structures
- terminal galactose
- glycan branching

For monoclonal antibodies, glycosylation may influence Fc receptor interactions and effector functions

such as antibody-dependent cellular cytotoxicity. [14,15]

Therefore:

Different cell line → different processing environment → altered glycosylation → potentially altered biological properties

Advanced methods such as mass spectrometry, chromatography and electrophoretic techniques are increasingly important for characterization. [16]

6. Protein Aggregation

Protein aggregation is another important quality concern.

Aggregates may develop during:

- manufacturing
- purification
- formulation
- transportation
- storage
- repeated temperature excursions

Aggregation can potentially affect:

- biological activity
- stability • pharmacokinetics
- immunogenicity.

Consequently, aggregate characterization and control are important components of biosimilar development. [17,18]

7. Analytical Characterization

Analytical characterization forms the foundation of modern biosimilar development.[19]

Important analytical attributes include:

Primary structure

- amino acid sequence
- peptide mapping
- molecular mass

Higher-order structure

- secondary structure
- tertiary structure
- conformational characteristics

Purity

- product-related impurities
- process-related impurities
- aggregates
- degradation products

Charge characteristics

- acidic variants
- basic variants
- charge distribution

Glycosylation

- glycan composition
- glycan distribution

Biological activity

- receptor binding
- cell-based activity
- enzymatic activity
- functional assays.

Common analytical technologies include:

- LC-MS/MS
- peptide mapping
- SEC
- ion-exchange chromatography
- reverse-phase chromatography
- capillary electrophoresis
- cIEF
- circular dichroism
- FTIR
- bioassays.

Recent scientific reviews emphasize the importance of combining orthogonal analytical methods because no single analytical platform can fully characterize a complex biological molecule. [20,21,22]

8. Manufacturing Challenges in India

Biosimilar manufacturing requires highly controlled biological production systems.

Important manufacturing stages include:

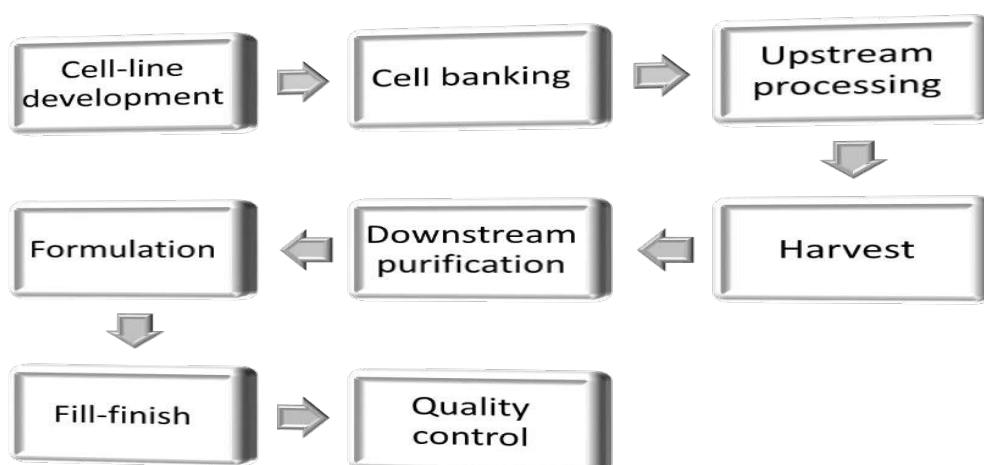


Figure 2: Major biological challenges

A major challenge is maintaining consistency between batches.

Small changes in:

- temperature
- pH
- dissolved oxygen
- culture medium
- feeding strategy

- purification conditions may affect critical quality attributes.

Therefore, “process consistency” is a central requirement for biosimilar quality.

Previous Indian literature has identified batch-to-batch consistency, skilled manpower, validated procedures and manufacturing controls as important practical challenges. [23]

9. Regulatory Evolution in India

India's biosimilar regulatory framework has undergone several stages.

Table 2: 2012 vs 2016 vs 2025 Indian regulatory framework

Year	Development
2012	Initial Similar Biologics regulatory framework
2016	Revised guidelines with stronger scientific/stepwise approach
2022	WHO revised global biosimilar principles
2025	Revised Indian Similar Biologics framework reflecting newer scientific developments

The 2025 CDSCO document explicitly states that it replaces the 2016 guideline and incorporates current scientific evidence and international developments, particularly WHO TRS 1043. [24]

10. Important Features of the 2025 Indian Framework

The revised framework introduces or strengthens several areas.

10.1 Advanced analytical methodologies

Greater emphasis is placed on modern analytical technologies and orthogonal approaches for demonstrating analytical similarity.

10.2 In-vitro studies

The revised framework provides a more elaborate consideration of in-vitro studies.

10.3 Reference standards

The guideline provides additional considerations regarding reference standards and the development/use of in-house reference standards.

10.4 Non-clinical studies

The need for animal studies is considered in a more scientifically justified manner.

The framework also refers to the 3Rs principle: Replace → Reduce → Refine with the objective of minimizing unnecessary animal testing. [25,26]

11. Clinical Development Challenges

Clinical development remains an important component of biosimilar evaluation.

Major considerations include:

Pharmacokinetics

Parameters may include:

- AUC
- C_{max}
- T_{max}
- clearance
- half-life

Pharmacodynamics

PD biomarkers can provide evidence of biological similarity where a sensitive and clinically relevant marker is available.

Immunogenicity

Anti-drug antibodies and neutralizing antibodies may be assessed.

Clinical efficacy and safety

The extent of clinical evaluation depends on the product, available analytical evidence and remaining uncertainty.

The modern regulatory philosophy increasingly emphasizes resolving uncertainty early through analytical and functional characterization rather than

automatically relying on large clinical efficacy trials. India's 2025 revision reflects this movement toward stronger analytical and in-vitro evidence. [27,28]

12. Immunogenicity

Immunogenicity refers to the ability of a biological product to stimulate an immune response.

Potential consequences include:

- anti-drug antibody development
- reduced therapeutic activity
- altered pharmacokinetics
- hypersensitivity reactions
- neutralization of endogenous proteins in certain situations.

Potential determinants include:

- protein sequence
- aggregates
- impurities
- formulation
- glycosylation
- manufacturing process
- route of administration
- patient-related factors.

Importantly, immunogenicity cannot be predicted solely from one analytical test. It requires an integrated assessment extending from product characterization to clinical and post-marketing monitoring. [29,30]

13. Interchangeability and Switching Interchangeability is distinct from biosimilarity.

Biosimilarity:

The product has been demonstrated to be highly similar to its reference product with no clinically meaningful differences in relevant characteristics.

Interchangeability:

Concerns the regulatory and clinical conditions under which one product can be substituted for another.

Different jurisdictions use different approaches.

The FDA maintains a separate regulatory concept for interchangeable biosimilars, whereas regulatory approaches in other jurisdictions may differ.

For India, interchangeability and substitution remain important areas for continued regulatory clarification and clinical-policy development. Earlier Indian analyses have specifically identified interchangeability, nomenclature and labelling as areas requiring attention. [31,32]

14. Extrapolation of Indications

One of the major advantages of biosimilar development is the possibility of using scientific justification to support multiple indications of the reference product.

However, extrapolation requires consideration of:

- mechanism of action
- receptor interaction
- PK/PD characteristics
- disease pathophysiology
- safety profile
- immunogenicity
- sensitivity of the studied population.

Therefore, extrapolation should be based on scientific evidence rather than simply assuming that similarity in one indication automatically proves equivalence in every disease.[33]

15. Pharmacovigilance

Post-marketing surveillance is particularly important for biological products.

A pharmacovigilance system should be capable of identifying:

- adverse drug reactions
- immunogenicity
- rare adverse events
- switching-related safety signals
- manufacturing-related quality problems.

Accurate product identification is essential for traceability.

A robust pharmacovigilance system should therefore integrate:

Product identification → adverse-event reporting → batch identification → signal detection → regulatory action. [34]

16. India-Specific Challenges India has several advantages:

- strong pharmaceutical manufacturing base
- large biotechnology workforce
- growing biopharmaceutical industry
- established experience with recombinant products
- increasing analytical capabilities
- potential for cost-efficient manufacturing.[35]

However, challenges remain.

Table 3: Major biological challenges and analytical solutions

Challenge	Potential consequence
Complex molecular characterization	Difficulty demonstrating similarity
Manufacturing variability	Batch-to-batch differences
High analytical cost	Increased development expenditure
Skilled manpower requirements	Development bottlenecks
Clinical development costs	Delayed commercialization

Immunogenicity uncertainty	Safety concerns
Pharmacovigilance limitations	Difficulty identifying rare signals
Physician awareness	Variable adoption
Interchangeability uncertainty	Switching concerns
International regulatory differences	Export barriers

Indian literature has previously identified industry-academia collaboration, regulatory complexity, physician awareness, manufacturing consistency and pharmacovigilance as relevant barriers. [36]

17. India versus International Regulatory Approaches

Table 4: India vs FDA vs EMA vs WHO

Parameter	India	WHO	United States	European Union
Regulatory authority/framework	CDSCO/Indian framework	WHO principles	FDA	EMA/EU framework
Basic concept	Similarity	Similarity	Biosimilarity	Biosimilarity
Analytical characterization	Central	Central	Central	Central
Functional studies	Important	Important	Important	Important
Clinical evidence	Risk-based/evolving	Stepwise	Risk-based	Stepwise
Interchangeability	Developing framework	Not a national substitution policy	Separate designation	National/EU policy considerations

Pharmacovigilance	Required	Recommended principle	Required	Required
Animal studies	Scientifically justified under revised framework	Flexible	Productdependent	Productdependent

WHO explicitly provides globally acceptable scientific principles that national regulatory authorities can adapt to their own regulatory systems.

The FDA also maintains specific guidance covering biosimilarity, interchangeability and comparative analytical assessment. In September 2025, FDA finalized updated guidance on comparative analytical assessment for therapeutic protein biosimilars.[37]

18. Recent Regulatory Direction

An important global trend is movement from clinical-heavy biosimilar development toward analytical and functional evidence-driven development.

The rationale is straightforward:

If a biosimilar can be demonstrated to be highly similar through sensitive analytical and functional methods, the residual uncertainty requiring additional clinical testing may be reduced.

This concept is reflected in the WHO's revised framework and India's 2025 regulatory revision.

Recent FDA guidance has similarly strengthened the focus on comparative analytical assessment and quality-related considerations. [38]

19. Future Perspectives

Future biosimilar development in India is likely to be influenced by several scientific and technological advances.

Artificial intelligence and machine learning

Potential applications include:

- process optimization
- prediction of critical quality attributes
- formulation optimization
- analytical data interpretation
- manufacturing process control.

Advanced analytical platforms

Future development will increasingly rely on:

- high-resolution mass spectrometry
- advanced chromatography • multi-attribute methods
- high-throughput bioassays
- advanced structural characterization.

Digital manufacturing

Process analytical technology and real-time monitoring may improve:

- process consistency
- quality control
- deviation detection
- manufacturing efficiency.

Reduced animal testing

The increasing adoption of the 3Rs principle and better in-vitro approaches may reduce unnecessary animal studies. India's revised 2025 guideline explicitly addresses this direction.

Global regulatory harmonization

Greater alignment between India, WHO, FDA and EMA principles could potentially reduce duplication and facilitate international development.[39,40]

20. Key Research Gaps

Despite considerable progress, several areas deserve further investigation:

- a) Standardization of analytical similarity criteria.
- b) Better prediction of immunogenicity.
- c) Development of sensitive in-vitro functional assays.

- d) Standardization of interchangeability approaches.
- e) Long-term pharmacovigilance.
- f) Real-world evidence following switching.
- g) Improved reference-standard strategies.
- h) Application of AI/ML in biosimilar characterization.
- i) Development of advanced cell-based assays.
- j) Harmonization of Indian and international regulatory requirements.

21. Proposed Conceptual Framework

“Biosimilar Development in India – From Cell to Patient”



Figure 3: Indian regulatory pathway

This framework can form the basis of Figure 1 in the final manuscript.

CONCLUSION

Biosimilars represent an important opportunity to expand access to biological therapies while maintaining rigorous standards of quality, safety and efficacy. However, the development of a biosimilar is considerably more complex than the development of a conventional generic drug because biological products are structurally complex and sensitive to manufacturing conditions.

For India, the evolution from the 2012 framework to the 2016 guideline and subsequently the revised 2025 framework represents an important progression toward a more scientifically integrated regulatory approach. The 2025 revision strengthens the role of advanced analytical characterization, in-vitro functional studies, reference standards and scientifically justified non-clinical testing.

The future success of India's biosimilar sector will depend not only on manufacturing capability but also on sophisticated analytical science, process control, skilled human resources, robust pharmacovigilance and greater regulatory harmonization. Continued

development of sensitive analytical and functional methods may reduce residual uncertainty and enable more efficient biosimilar development without compromising patient safety.

Ultimately, the advancement of biosimilars in India requires a balance between scientific rigor, regulatory efficiency, manufacturing quality, affordability and patient confidence.

REFERENCES

1. World Health Organization. Biologicals. Geneva: World Health Organization; [cited 2026 Sep 21].
2. International Council for Harmonisation (ICH). Q5E: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. Geneva: ICH; 2005. CPMP/ICH/5721/03.
3. World Health Organization. Guidelines on evaluation of biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022.
4. Kang H-N, Wadhwa M, Knezevic I, Ondari C, Simao M. WHO guidelines on biosimilars: Toward improved access to safe and effective

- products. *Annals of the New York Academy of Sciences*. 2023;1521 (1):96–103.
5. Central Drugs Standard Control Organization, Department of Biotechnology. Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India. New Delhi: CDSCO & DBT; 2025.
6. U.S. Food and Drug Administration. Review and Approval: Biosimilars. FDA; 2026.
7. Mora F, Bianchi G. Biosimilar: What it is not. *British Journal of Clinical Pharmacology*. 2015;80 (5):949–956.
8. Endrenyi L, Declerck P, van der Laan JW, editors. *Biosimilar Drug Product Development*. Boca Raton, FL: CRC Press; 2017.
9. World Health Organization. Guidelines on evaluation of biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022.
10. Stebbing J, Mainwaring PN, Curigliano G, Pegram M, Latymer M, Bair AH, et al. Understanding the role of comparative clinical studies in the development of oncology biosimilars. *J Clin Oncol*. 2020;38 (10):1070-1080.
11. Schachner LF, Mullen C, Phung W, et al. (2024). “Exposing the molecular heterogeneity of glycosylated biotherapeutics.” *Nature Communications*, 15, 3259.
12. Jenkins N, Murphy L, Tyther R. (2008). Post-translational modifications of recombinant proteins: significance for biopharmaceuticals. *Molecular Biotechnology*, 39 (2), 113– 118.
13. Liu L. (2015). Antibody glycosylation and its impact on the pharmacokinetics and pharmacodynamics of monoclonal antibodies and Fc-fusion proteins. *Journal of Pharmaceutical Sciences*, 104 (6), 1866–1884.
14. Kaur H. (2021). Characterization of glycosylation in monoclonal antibodies and its importance in therapeutic antibody development. *Critical Reviews in Biotechnology*, 41 (2), 300–315.
15. Cymer F, Beck H, Rohde A, Reusch D. (2018). Therapeutic monoclonal antibody Nglycosylation – Structure, function and therapeutic potential. *Biologicals*, 52, 1–12.
16. Yang Z, Halim A, Narimatsu Y, et al. (2016). Challenges of glycosylation analysis and control: an integrated approach to producing optimal and consistent therapeutic drugs. *Drug Discovery Today*, 21 (5), 740–765.
17. Pandey LM. (2022). Physicochemical factors of bioprocessing impact the stability of therapeutic proteins. *Biotechnology Advances*, 55, 107909.
18. Moussa EM, Panchal JP, Moorthy BS, et al. (2016). Immunogenicity of Therapeutic Protein Aggregates. *Journal of Pharmaceutical Sciences*, 105 (2), 417–430.
19. Analytical Similarity Assessment of Biosimilars: Global Regulatory Landscape, Recent Studies and Major Advancements in Orthogonal Platforms. *Frontiers in Bioengineering and Biotechnology*, 10, 832059.
20. ICH Q6B — Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
21. Tsuruta et al. (2022). Analytical Similarity Assessment of Biosimilars: Global Regulatory Landscape, Recent Studies and Major Advancements in Orthogonal Platforms.
22. Biopharmaceutical analysis — current analytical challenges, limitations, and perspectives (2025).
23. Jois R, Mukherjee S, Rajeswari S, Rath PD, Goyal V, and Gupta D. “Similar Biologics in India: A Story of Access or Potential for Compromise?” *The Indian Journal of Medical Research*, 2020, Volume 152, Issue 5, pp. 456–467.
24. Central Drugs Standard Control Organization (CDSCO) and Department of Biotechnology (DBT), Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India, Government of India, 2025, p. 6.
25. World Health Organization. Guidelines on evaluation of biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022. pp. 143, 146–157.
26. World Health Organization. WHO Expert Committee on Biological Standardization: Seventy-fifth report. WHO Technical Report Series No. 1043. Geneva: World Health Organization; 2022.
27. Kurki P, Kang HN, Ekman N, Knezevic I, Weise M, Wolff-Holz E, et al. Regulatory Evaluation of Biosimilars: Refinement of Principles Based on

- the Scientific Evidence and Clinical Experience. *BioDrugs*. 2022;36:359–371.
28. World Health Organization. Guidelines on Evaluation of Biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022.
 29. US Food and Drug Administration. Immunogenicity Assessment for Therapeutic Protein Products: Guidance for Industry. Silver Spring, MD: FDA; August 2014.
 30. US Food and Drug Administration. Immunogenicity Testing of Therapeutic Protein Products —Developing and Validating Assays for Anti-Drug Antibody Detection: Guidance for Industry. Silver Spring, MD: FDA; February 2019.
 31. Jois R, Mukherjee S, Rajeswari S, Rath PD, Goyal V, Gupta D. Similar biologics in India: A story of access or potential for compromise? *Indian Journal of Medical Research*. 2020;152 (5):456–467
 32. Barbier L, Declerck P, Simoens S, Neven P, Vulto AG, Huys I. Biosimilarity and Interchangeability: Principles and Evidence: A Systematic Review. *BioDrugs*. 2019
 33. World Health Organization. Guidelines on Evaluation of Biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022
 34. Central Drugs Standard Control Organization. Guidance Document for Industry on Pharmacovigilance Requirements for Biological Products. New Delhi: Ministry of Health and Family Welfare, Government of India; 2024.
 35. Gandhi S, Patankar D, Kashiramka S, Rathore AS. The economics of translating a biosimilar from lab to market in India. *Annals of the New York Academy of Sciences*. 2024;1541 (1):219–229.
 36. Ramesh Jois, Sukumar Mukherjee, S. Rajeswari, P. D. Rath, Vishal Goyal, Disha Gupta. *Indian Journal of Medical Research*. 2020;152 (5):456–467.
 37. US Food and Drug Administration. Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations. Guidance for Industry. Silver Spring, MD: FDA; September 2025.
 38. Guidelines on Evaluation of Biosimilars. WHO Technical Report Series No. 1043, Annex 3. Geneva: World Health Organization; 2022.
 39. Rathore AS, Nikita S, Thakur G, Mishra S. Artificial intelligence and machine learning applications in biopharmaceutical manufacturing. *Trends in Biotechnology*. 2023;41 (4):497–510.
 40. International Council for Harmonisation (ICH). Q5E: Comparability of Biotechnological/Biological Products Subject to Changes in Their Manufacturing Process. Step 5 guideline; 2004, implemented by regulators including the FDA and EMA.

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