



REGULATORY CHALLENGES IN THE APPROVAL OF BIOLOGICS AND BIOSIMILARS: A COMPARATIVE ANALYSIS OF GLOBAL REGULATORY PATHWAYS

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ABSTRACT

Biologics and biosimilars are crucial to modern health care, but their complex structure and manufacturing methods necessitate specialised regulatory assessment of quality, safety, efficacy, and consistency. This is a comparative evaluation of the global regulatory trajectories for biologics and biosimilars for the FDA, EMA, MHRA, CDSCO/DBT, PMDA and Health Canada. A comparative qualitative research design is adopted and is based on second hand regulatory information of the major regulatory frameworks and the relevant WHO and ICH guidelines. Analytical comparability, clinical evidence, immunogenicity, selection of the reference product, interchangeability, manufacturing variability, and pharmacovigilance are analyzed. The comparative assessment reveals that all major regulatory authorities are founded on the same scientific approach, which involves a step-wise evaluation and analytical comparison, whereas discrepancies exist in clinical evidence requirements, interchangeability, reference-product requirements and national implementation. The study identifies and outlines key regulatory issues and the need for advanced analytical technologies, risk-based assessment, regulatory reliance, international harmonisation, and enhanced post-marketing surveillance. In general, increased regulatory harmonization may help to streamline biosimilar development and to ensure quality, safety, and effectiveness.

Keywords: *Biologics; Biosimilars; Regulatory Pathways; Analytical Comparability; Regulatory Harmonisation; Pharmacovigilance.*

1. INTRODUCTION

The effectiveness of these biological medicines in managing complex and chronic diseases such as cancer, autoimmune diseases, hormonal diseases and inflammatory conditions make them an important part of modern healthcare. Unlike small molecule medicines, biologics are large and complex molecules that are made by living things and present greater challenges to the assessment of their quality, safety, effectiveness and consistency of manufacture. Biosimilars have since become highly similar versions of approved biological reference products, providing an opportunity to increase access to biological therapies while decreasing costs of treatment. They cannot be, however, reproduced as a perfect molecule and therefore have to be evaluated and approved by special regulatory assessments.



Figure 1: Biological Medicines

The regulators around the world have thus established specific procedures for the assessment of biologics and biosimilars. The U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), Medicines and Healthcare products Regulatory Agency (MHRA), Central Drugs Standard Control Organization (CDSCO), Pharmaceuticals and Medical Devices Agency (PMDA), and Health Canada use generally similar scientific principles, but with some variation in requirements for analytical comparability, clinical evidence, immunogenicity, interchangeability, reference-product selection and pharmacovigilance.

Biosimilars are being used more and more around the world, which has put regulatory harmonisation as a key challenge for pharmaceutical innovation and access to patients on the agenda. Regulatory variations between countries can add to the complexity, cost and uncertainty of development for manufacturers. Hence, the current study compares key regulatory initiatives with regard to biologics and biosimilars in the

major regulatory markets worldwide, highlights the key regulatory issues, and considers how the regulatory arena can be enhanced in terms of scientific convergence and regulatory efficiency whilst maintaining the proper level of quality, safety, and efficacy.

2. LITERATURE REVIEW

Kang et al. (2021) analyzed regulatory issues of biosimilars in 20 countries. A comparison of national regulatory approaches was made, and differences were observed in the regulatory requirements for approval, interchangeability, reference-product selection, and post-approval monitoring. The study emphasized the need for international cooperation and harmonization of regulation for consistent and efficient development of biosimilars.

Kang et al. (2020) conducted a global regulatory landscape of biosimilars and explored the advancement of biosimilars along the WHO initiatives between 2009 and 2019. The authors discussed how WHO guidelines have provided a scientific foundation for assessment of biosimilars and for countries to create regulatory frameworks. The authors highlighted the significance of harmonisation, regulatory capacity development and ongoing international cooperation in building up biosimilar regulation.

Joshi et al. (2022) summarized the latest developments and regulatory landscape of biosimilars in oncology. The study touched on the increase in the use of biosimilars for cancer treatment and reviewed key regulatory issues such as extrapolation of indications, immunogenicity, safety, clinical evaluation and analytical characterisation. The researchers also found that the proper regulatory assessment of biosimilars was critical to guarantee quality, safety and effectiveness of biosimilars, apart from achieve greater entry to biological therapies.

3. RESEARCH METHODOLOGY

The study used a comparative qualitative research design that was based on secondary regulatory information. Information was gathered from regulatory guidance and regulations of key regulatory bodies such as FDA, EMA, MHRA, CDSCO/DBT, PMDA and Health Canada as well as relevant WHO and ICH guidelines. The analysis was limited to regulatory pathways, analytical comparability, clinical evidence, immunogenicity, selection of reference product, interchangeability, manufacturing variability, and pharmacovigilance.

4. GLOBAL REGULATORY FRAMEWORK FOR BIOLOGICS AND BIOSIMILARS

The international regulatory landscape of biologics and biosimilars aims to guarantee the quality, safety, effectiveness and consistency of biological medicines before and after market approval. Biologics are complex products made by biological processes, and the process, molecular properties, biological activity, impurities, stability, and possible immunogenicity are all heavily emphasized when evaluating products for regulatory approval. The regulatory agencies hence use its special requirements as compared with those used for traditional chemically synthesized medicines.

4.1 Regulatory Principles for Biologics

The regulation of biologics relies mainly on the ability to demonstrate consistent manufacturing to established quality standards and that the product's expected clinical advantages exceed any potential hazards. The entire manufacturing process, such as cell substrates, raw materials, production systems, purification, formulation, storage and quality-control procedures are assessed by regulatory authorities. Special emphasis is placed on key quality parameters including identity, purity, potency, structural features, biological activity, stability and immunogenicity. The ICH guidelines, in particular those in the Q5 and Q6B series, are an important scientific basis for the evaluation of the quality of biotechnology derived products.

4.2 Scientific Basis of Biosimilarity

Comparative assessment of the proposed biosimilar with an authorised reference biological product is the basis for biosimilarity. Since biological products are naturally variable in structure, it is not expected that a biosimilar would be an exact molecular copy of a reference product. Rather, the goal will be to achieve a high level of similarity and to show that any differences that are found do not lead to clinically meaningful differences in safety or effectiveness. Modern analytical and functional technologies are thus crucial to biosimilar development as they can offer detailed information regarding molecular structure and biological activity.



Figure 2: Biosimilar

4.3 Stepwise Regulatory Assessment

The development of biosimilar products is typically a step-by-step process, with evidence building from one step to the next dictating the amount of development at each step. Typically, the process starts with a thorough analytical and/or structural comparison, a functional evaluation, and (if scientifically warranted) a non-clinical evaluation. Residual uncertainty may then be addressed through clinical pharmacokinetic / pharmacodynamic studies, and/or through comparative clinical studies. Immunogenicity is assessed during the development process. The goal of this approach is to prevent unnecessary duplication, and to provide adequate information to prove that they are biosimilar.

4.4 Quality, Safety and Efficacy Requirements

The regulation of biologic and biosimilar products are built on the premise of quality assessment. It contains intrinsic molecular characterization, purity, potency, biological activity, impurities, aggregation, glycosylation, stability and batch-to-batch consistency determination. The focus of safety assessment is on adverse effects, immunogenicity, toxicity (if applicable), and other potential risks. Efficacy is based upon the proper clinical and pharmacological evidence needed for the product.

4.5 Role of WHO and ICH

The World Health Organization (WHO) has contributed to important scientific principles for biosimilar evaluation that are shared internationally. It gives general guidance for the evaluation of quality, safety and efficacy and also allows for country-specific requirements to be modified as per national legal frameworks and healthcare systems. International Council for Harmonisation (ICH) facilitates the harmonisation of

regulatory regulations with documents on the quality, safety and effectiveness, and development of pharmaceuticals. It has biotechnology-related quality guidelines that are important for biological products, such as ICH Q5A–Q5E and Q6B. These are both important building blocks for creating evidence-based and science-based regulatory policies in various jurisdictions, working together, WHO and ICH.



Figure 3: World Health Organization (WHO)

5. COMPARATIVE ANALYSIS OF GLOBAL REGULATORY PATHWAYS

This section provides an overview of the regulatory processes of key regulatory agencies used to approve biologics and biosimilars. The United States and the European Union (EU), United Kingdom (UK), India, Japan and Canada in general rely on the scientific principle of similarity to an approved reference biological product, but there are some differences in clinical evidence, interchangeability, the requirement for a reference product and post-marketing monitoring.

This is significant because the regulatory frameworks differ across countries and may affect the time to develop the product, cost, criteria for obtaining approval and the pathway for entry into the market for biosimilar manufacturers. The key regulatory strategies taken by the jurisdictions selected are summarised below.

5.1 United States – FDA

The U.S. Food and Drug Administration (FDA) regulates biosimilars mostly via the 351(k) pathway in the United States Public Health Service Act (PHS Act). The regulatory assessment process starts with a detailed

analysis and functional comparison of the proposed biosimilar with the reference product. The continued scientific uncertainty calls for the additional pharmacological, clinical and immunogenicity studies. The overall goal would be to demonstrate that the product is very similar to the reference product, and that there are no clinically significant differences in safety, purity and potency.

United States also has a separation between biosimilar and interchangeable biosimilar. The interchangeability is a regulatory distinction based on other requirements related to anticipated clinical performance and, if applicable, interchangeability. The FDA maintains the Purple Book, which contains information about licensed biological products and biosimilarity/biosimilars determinations, and interchangeability determinations.

5.2 European Union – EMA

The European Medicines Agency (EMA) has a well-established biosimilar regulatory system. The EU pathway is founded on a multi-layered, step-by-step comparability exercise that starts with a detailed assessment of quality and analysis. Non-clinical, pharmacokinetic/pharmacodynamic, clinical, and immunogenicity studies may be required based on the product and any remaining uncertainties. All the evidence is considered together to assess if a biosimilar is sufficiently similar to the reference medicine.

In addition, the EU has adopted a special strategy for interchangeability. EMA and the Heads of Medicines Agencies said that approved biosimilars are scientifically interchangeable with the reference medicines and other biosimilars of the same reference medicine, as appropriate. But whether to allow automatic substitution at the pharmacy level is subject to individual EU Member States' decision.

5.3 United Kingdom – MHRA

The Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom has an established licensing pathway for biosimilars. The assessment deals with establishing biosimilarity based on quality, analytical, pharmacological and appropriate clinical evidence. The new guidance from MHRA focuses on the stepwise and scientifically appropriate comparison of the biosimilar to be developed with the reference product, not on simply replicating the entire development program of the originator.

Safety, immunogenicity, extrapolation of indications and post-authorisation monitoring are also taken into account in the UK framework. The extent of clinical evidence will be based on the attributes of the product

and the amount of uncertainty remaining. This way can regulate needs be adjusted according to the scientific evidence without sacrificing proper quality, safety and efficacy requirements.

5.4 India – CDSCO/DBT

The biosimilars are governed by the Similar Biologics framework laid down by the Central Drugs Standard Control Organization (CDSCO) and the Department of Biotechnology (DBT) in India. The Framework for 2016 outlined criteria for quality comparability, non-clinical evaluation, clinical trials, immunogenicity and post-marketing monitoring. The Indian framework thus adheres to the principle shared by most nations around the world, which is that biosimilarity needs to be established by conducting a structure comparison with a reference biologic.

India is also in the process of updating this framework to match the development of international regulatory science. The 2025 revised Similar Biologics framework focuses more on advanced analytical methods and in-vitro evaluation, and offers a more scientifically-based approach to assessing the need for additional non-clinical and clinical studies.

5.5 Japan – PMDA

The Japanese Pharmaceuticals and Medical Devices Agency (PMDA) analyzes the quality, safety and efficacy of biosimilars compared to an approved biotechnology-derived product. An important component of the evaluation is analytical characterisation and functional comparison, with pharmacokinetic/pharmacodynamic and other clinical evidence taken into account based on the scientific nature of the product.

The evidence proportionality principle is becoming a more salient theme in recent Japanese regulatory developments. According to PMDA's recent documents, comparative efficacy studies are not always required if the uncertainty addressed by the study is sufficiently answered via analytical, non-clinical, and/or PK/PD data.

5.6 Canada – Health Canada

In Canada, the Food and Drugs Act and the Food and Drug Regulations are the regulations which Health Canada oversees for biosimilars. The applicant should be able to submit evidence that proves substantial similarity of the biosimilar to the reference biologic. The submission can contain quality information, non-clinical pharmacology information, clinical pharmacology information, clinical information,

immunogenicity information and post market information as per the product and the scientific uncertainties remaining.

Health Canada's regulatory approach also provides for authorisation of a biosimilar, rather than the usual notion of generic equivalence. The regulatory decision is not based on the evidence that the biosimilar is an exact molecular copy of the reference product, but rather on the entirety of the evidence that shows the similarity. The new Canadian guidelines also demonstrate progress towards incorporating updates in the scientific literature in the assessment of biosimilars.

5.7 Comparative Regulatory Overview

The main regulatory systems discussed above are summarized in the following table. It identifies the regulatory powers, main road, scientific focus and distinguishing features of each jurisdiction.

Table 1: Comparative Regulatory Pathways for Biologics and Biosimilars

Region	Regulatory Authority	Principal Pathway	Major Scientific Focus	Distinguishing Feature
United States	FDA	351(k) pathway	Analytical similarity, functional assessment, clinical pharmacology and appropriate clinical evidence	Separate interchangeability designation
European Union	EMA/EU Regulatory Network	Biosimilar marketing authorisation	Comprehensive stepwise comparability	EU-level scientific interchangeability
United Kingdom	MHRA	Biosimilar licensing pathway	Quality, comparability, clinical pharmacology and safety	Case-specific scientific assessment
India	CDSCO/DBT	Similar Biologics pathway	Analytical, in-vitro, non-clinical and clinical assessment	Revised framework emphasises modern analytical approaches

Japan	PMDA/MHL W	Biosimilar regulatory pathway	Quality, PK/PD and appropriate clinical evidence	Increasing emphasis on evidence proportionality
Canada	Health Canada	New-drug biosimilar pathway	Comparative quality, safety and efficacy assessment	Biosimilar approval based on totality of evidence

In general, the comparison suggests that the major regulatory agencies share a similar scientific basis, represented by a comprehensive analytical comparison, a biological function assessment, a residual uncertainty assessment and suitable clinical and post-marketing evidence. But the different jurisdictions have different legal frameworks for their approval processes, as well as for addressing interchangeability, clinical evidence, and national implementation.

6. MAJOR REGULATORY CHALLENGES IN BIOLOGICS AND BIOSIMILAR APPROVAL

There are several scientific and regulatory challenges associated with approval of biologics and biosimilars, since biological products are structurally complex and are very sensitive to manufacturing processes. While the principles are similar, the amount of evidence required and the differences in regulatory process may pose other challenges for the biosimilar developer.

- **Analytical Similarity:** The basis of biosimilar development is analytical similarity. The manufacturers need to compare the proposed biosimilar with the reference product based on its structure, purity, potency, stability and biological activity. The challenge is to ascertain if any observed difference falls within acceptable biological variation, and whether such differences are clinically significant.
- **Clinical Evidence Requirements:** Regulators require the sufficient evidence to demonstrate that there is no clinically meaningful difference between the biosimilar and the reference product. However, the amount of clinical evidence needed is different across the different regulatory authorities.
- **Immunogenicity:** Biological medicines may trigger unwanted immune responses in patients. These reactions can make treatment less effective, or lead to side effects. Thus, immunogenicity

assessment is an important part of biosimilar development, and should be sustained throughout the post-marketing period.

- **Reference-Product Selection:** Selection of an appropriate reference biologic is crucial for the determination of biosimilarity. There can be variations in what is acceptable on a country-by-country basis as to what can be used as a reference product. These differences may necessitate further bridging studies or comparative evidence when the manufacturer has to launch a biosimilar in different countries.
- **Extrapolation of Indications:** A biosimilar may want to be approved for multiple indications for which its reference product is approved. The decision to extrapolate should be based on the available evidence and the product's mechanism of action, and be made by the regulatory authorities.
- **Interchangeability:** Interchangeability is the ability to interchange a biosimilar with the reference product without an expected difference in clinical outcome. There are many differences in regulatory methods among countries. There are some systems where the interchangeability is specifically designated, and others where the system deems approved biosimilars to be scientifically interchangeable, but the substitution is left to national authorities.

Table 2. Major Regulatory Challenges in Biologics and Biosimilar Approval

Regulatory Challenge	Key Issue	Regulatory Importance
Analytical Similarity	Differences in structure, purity, potency, and biological activity must be carefully evaluated.	Establishes the scientific foundation of biosimilarity.
Clinical Evidence	Determining the appropriate extent of clinical and pharmacological studies.	Ensures that no clinically meaningful differences remain.
Immunogenicity	Potential immune responses may affect safety and treatment effectiveness.	Requires pre-approval assessment and post-marketing monitoring.
Reference-Product Selection	Different jurisdictions may have different requirements for acceptable reference products.	Can affect global development and require additional bridging evidence.

Extrapolation of Indications	Evidence from one indication may be used to support other approved indications when scientifically justified.	Requires a strong scientific rationale.
Interchangeability	Regulatory definitions and substitution policies differ between countries.	Affects switching practices and market implementation.

Overall, these challenges indicate that a balance is to be maintained between science and regulation in the process of biosimilar regulation. Advanced analytical technologies, risk-based clinical needs, international harmonisation, and more robust post marketing surveillance can help overcome these challenges while ensuring quality, safety and efficacy of biological medicines.

7. DISCUSSION AND FUTURE REGULATORY PERSPECTIVES

The comparative analysis demonstrates similarities in the scientific considerations for biosimilar approval, including those of analytical comparability, quality assessment, clinical evaluation, immunogenicity, and pharmacovigilance, across key regulatory authorities, including FDA, EMA, MHRA, CDSCO/DBT, PMDA and Health Canada. But there are still variations in clinical evidence needed, interchangeability, choice of reference product, and the national regulatory process.

- **Major Similarities and differences between jurisdictions:** Most jurisdictions take a step-by-step comparison approach starting with analytical and functional assessment. Requirements for clinical studies and interchangeability vary across countries, however. These differences can add to the complexity of manufacturers aiming to gain regulatory approval in multiple markets.
- **Regulatory Convergence:** WHO and ICH have contributed to greater international alignment of regulatory principles. Further alignment of analytical, clinical, and safety requirements may minimise the duplication of efforts and optimise global biosimilar development.
- **Risk Based Regulatory Approaches:** Risk based approaches are a growing trend, with regulators deciding on extra studies based on the amount of scientific uncertainty that remains. This can help to minimize unnecessary clinical studies without compromising safety and efficacy.
- **Advanced Analytical Technologies:** Analytical technologies of the modern world enable the detailed characterization of molecular structure and purity, potency, and biological activity. Incorporation of these methods can help build the scientific foundation of biosimilarity and minimise uncertainty in development.

- **Regulatory Reliance and Harmonisation:** Regressive reliance and information sharing between trusted regulators can minimize re-assessment and more streamline approvals. Harmonisation of the requirements for reference products, analytical studies and pharmacovigilance would further support international development.
- **Future Directions for Biosimilar Regulation:** Advanced analytical methods, proportionate clinical requirements, regulatory reliance, international harmonisation, and enhanced pharmacovigilance are likely to be key areas of the future of biosimilar regulation. The overall goal will be to reduce the inefficiencies of regulatory pathways, while maintaining the quality, safety and efficacy of biological medicines.

8. CONCLUSION

The present study concludes that the regulation of biologics and biosimilars should adopt a scientifically grounded and well-structured approach to ensure quality, safety, efficacy, and consistency. Although there are differences in clinical evidence requirements, reference-product selection, interchangeability, and national regulatory procedures, the major principles of FDA, EMA, MHRA, CDSCO/DBT, PMDA, and Health Canada regulatory systems are similar, including analytical comparability, stepwise assessment, clinical evaluation, immunogenicity assessment, and post-marketing surveillance. The main challenges that have been identified are: analytical similarity, clinical evidence, immunogenicity, manufacturing variability, extrapolation of indications, and pharmacovigilance. The study also shows that advanced technologies for analysis, risk-based assessment, a reliance on regulatory standards, international harmonisation, and enhanced post-marketing monitoring can enhance the regulatory effectiveness without compromising quality, safety or efficacy standards.

REFERENCES

1. Kang, H. N., Thorpe, R., Knezevic, I., Casas Levano, M., Chilufya, M. B., Chirachanakul, P., ... & Yamaguchi, T. (2021). *Regulatory challenges with biosimilars: an update from 20 countries. Annals of the New York Academy of Sciences*, 1491(1), 42-59.
2. Kang, H. N., Thorpe, R., Knezevic, I., Blades, C. D. R. Z., Levano, M. C., Chew, J. Y., ... & Yamaguchi, T. (2020). *The regulatory landscape of biosimilars: WHO efforts and progress made from 2009 to 2019. Biologicals*, 65, 1-9.

3. Joshi, D., Khursheed, R., Gupta, S., Wadhwa, D., Singh, T. G., Sharma, S., ... & Singh, S. K. (2022). *Biosimilars in oncology: latest trends and regulatory status. Pharmaceutics, 14(12), 2721.*
4. Iqbal, Z., & Sadaf, S. (2022). *Biosimilars: A comparative study of regulatory, safety and pharmacovigilance monograph in the developed and developing economies. Journal of Pharmacy & Pharmaceutical Sciences, 25, 149-182.*
5. Nupur, N., Joshi, S., Gulliarne, D., & Rathore, A. S. (2022). *Analytical similarity assessment of biosimilars: global regulatory landscape, recent studies and major advancements in orthogonal platforms. Frontiers in bioengineering and biotechnology, 10, 832059.*
6. Ratih, R., Asmari, M., Abdel-Megied, A. M., Elbarbry, F., & El Deeb, S. (2021). *Biosimilars: Review of regulatory, manufacturing, analytical aspects and beyond. Microchemical Journal, 165, 106143.*
7. Bennett, C. L., Schoen, M. W., Hoque, S., Witherspoon, B. J., Aboulafia, D. M., Hwang, C. S., ... & Yang, Y. T. (2020). *Improving oncology biosimilar launches in the EU, the USA, and Japan: an updated policy review from the southern network on adverse reactions. The Lancet Oncology, 21(12), e575-e588.*
8. Sharma, A., Kumar, N., Kuppermann, B. D., Bandello, F., & Loewenstein, A. (2020). *Understanding biosimilars and its regulatory aspects across the globe: an ophthalmology perspective. British Journal of Ophthalmology, 104(1), 2-7.*
9. Punia, A., & Malhotra, H. (2020). *International regulatory processes and policies for innovator biologics, biosimilars, and biobetters. Biologics, Biosimilars, and biobetters: An introduction for pharmacists, physicians, and other health practitioners, 159-176.*
10. Rahalkar, H., Sheppard, A., Santos, G. M. L., Dasgupta, C., Perez-Tapia, S. M., Lopez-Morales, C. A., & Salek, S. (2021). *Current regulatory requirements for biosimilars in six member countries of BRICS-TM: challenges and opportunities. Frontiers in medicine, 8, 726660.*
11. Wilsdon, T., Pistollato, M., Ross-Stewart, K., Saada, R., Barquin, P., Alnaqbi, K. A., ... & Werutsky, G. (2022). *Biosimilars: a global roadmap for policy sustainability. Charles River Associates.*
12. Rathore, A. S., & Bhargava, A. (2020). *Biosimilars in developed economies: overview, status, and regulatory considerations. Regulatory Toxicology and Pharmacology, 110, 104525.*
13. Gherghescu, I., & Delgado-Charro, M. B. (2020). *The biosimilar landscape: an overview of regulatory approvals by the EMA and FDA. Pharmaceutics, 13(1), 48.*

14. Rahalkar, H., Sheppard, A., & Salek, S. (2021). *Comparison of BRICS-TM countries' biosimilar regulatory frameworks with Australia, Canada and Switzerland: benchmarking best practices. Frontiers in pharmacology, 12, 711361.*
15. Singh, M., & Solanki, P. R. (2022). *An overview of legal and regulatory challenges of biological products. Biomedical Product and Materials Evaluation, 275-286.*
16. Rathore, A. S., & Bhargava, A. (2021). *Regulatory considerations in biosimilars: Latin America region. Preparative biochemistry & biotechnology, 51(2), 201-206.*
17. Rahalkar, H. (2021). *Evaluation of the Regulatory Requirements for Development and Approval of Biosimilar Medicines in the BRICS-TM Countries: Improving Patients' Access (Doctoral dissertation, University of Hertfordshire).*
18. Rahalkar, H., Sheppard, A., Lopez-Morales, C. A., Lobo, L., & Salek, S. (2021). *Challenges faced by the biopharmaceutical industry in the development and marketing authorization of biosimilar medicines in BRICS-TM countries: An exploratory study. Pharmaceutical Medicine, 35(4), 235-251.*
19. Rahalkar, H., Sheppard, A., & Salek, S. (2022). *Biosimilar development and review process in the BRICS-TM countries: Proposal for a standardized model to improve regulatory performance. Expert Review of Clinical Pharmacology, 15(2), 215-236.*
20. Halimi, V., Daci, A., Ancevska Netkovska, K., Suturkova, L., Babar, Z. U. D., & Grozdanova, A. (2020). *Clinical and regulatory concerns of biosimilars: a review of literature. International journal of environmental research and public health, 17(16), 5800.*