World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

Regulatory requirements for biosimilars as per CDSCO in India in comparison with Yemen

Ashok Kumar P *, Nayana G U, Nithin N, Sharath Kumar N, Sharvari B and Yashaswini P R

Department of Regulatory Affairs, Sree Siddaganga College of Pharmacy, 1st Left Cross, 3rd Block, Mahalakshmi Nagar, Near Railway Gate, 80 feet Road, Batwadi, Tumkur – 572103. Karnataka, India.

World Journal of Advanced Research and Reviews, 2024, 23(03), 2292–2303

Publication history: Received on 05 August 2024; revised on 18 September 2024; accepted on 20 September 2024

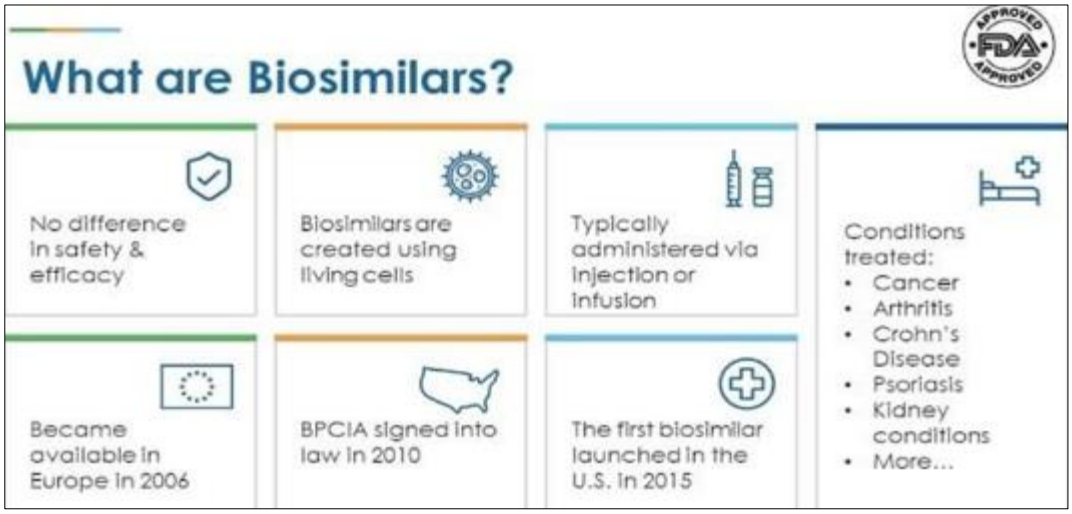
Article DOI: https://doi.org/10.30574/wjarr.2024.23.3.2830

Abstract

This study examines the regulatory requirements for biosimilars in India and Yemen, highlighting similarities and differences between the Central Drugs Standard Control Organization (CDSCO) and the Ministry of Public Health and Population (MOPHP). The regulatory landscape for biosimilars is evolving globally, with varying requirements across countries. This comparative analysis examines the regulatory requirements for biosimilars in India, governed by the Central Drugs Standard Control Organization (CDSCO), and Yemen. A comprehensive review of guidelines, regulations, and approval processes reveals both similarities and differences between the two countries. While both CDSCO and Yemen require a comparability exercise to demonstrate bio similarity, differences exist in the regulatory framework, clinical trial requirements, and approval processes. CDSCO has a separate regulatory framework and abbreviated pathway for biosimilars, whereas Yemen adopts the MOPHP guidelines and has a registration process. This analysis highlights the need for manufacturers to understand the nuances of each market's regulatory requirements to ensure successful approval and commercialization of biosimilars. The findings of this study can inform regulatory agencies, industry stakeholders, and researchers working in the field of biosimilars.

Keywords: Biosimilars; Regulatory requirements; Yemen; CDSCO; Clinical trials; Approval process[1].

Graphical abstract



* Corresponding author: Ashok Kumar P

Copyright © 2024 Author(s) retain the copyright of this article. This article is published under the terms of the Creative Commons Attribution Liscense 4.0.

1. Introduction

The creation of biosimilars has become necessary due to the rising cost of biological medications on a global scale. These remarkably similar off-patent biological product variants were approved for use in the EU in 2006 and the US in 2015. Biosimilar goods cannot be chemically identical to their originator medicines due to the nature of biological molecules, in contrast to small molecule generic pharmaceuticals. But as over ten years of experience in Europe has shown, the minor variations between a biosimilar and its original product do not translate into clinically significant variations in the drug's safety and effectiveness. The main regulatory bodies have created distinct biosimilar regulatory methods because of the complexity of biosimilars. Biosimilar developers need to provide comprehensive analytical characterization packages, pharmacokinetic and pharmacodynamic profiles, and comparative clinical trial data to remove any remaining question before these drugs may be approved. Biosimilars are comparable biological drug formulations that are no longer protected by patents, providing a more affordable option than pricy biologic therapies. Because of their unique biological makeup, biosimilars cannot be exact copies of generic small molecule medications. Regulatory agencies have set up specific approval procedures for biosimilars that include continuing monitoring to guarantee safety and efficacy, comparative clinical trials, and complete data packages. Biosimilars were authorized in the European Union in 2006, and the US did the same in 2015. The experience of more than ten years in Europe has demonstrated that small differences between biosimilars and originators have little bearing on clinical outcomes. For approval, biosimilar developers need to submit comparative clinical trial data, pharmacokinetic and pharmacodynamic profiles, and comprehensive analytical data. Biosimilars are safe and efficient treatments for a wide range of disorders, including cancer, irritable bowel syndrome, psoriasis, Crohn's disease, and colitis, as well as arthritis and kidney problems. Biosimilars might result in cheaper costs while increasing access to lifesaving drugs[2].

Background

A variety of case studies in the developing biosimilar market are the result of global healthcare regulations. The goals of biosimilars are to increase access to biologic therapies while lowering healthcare costs. Clinical studies, nonclinical in vivo research, physicochemical and biological characterization, and a step-by-step comparison with the reference biologic are all part of the approval procedure. The extent and type of necessary studies are determined by the quality of the data collected.

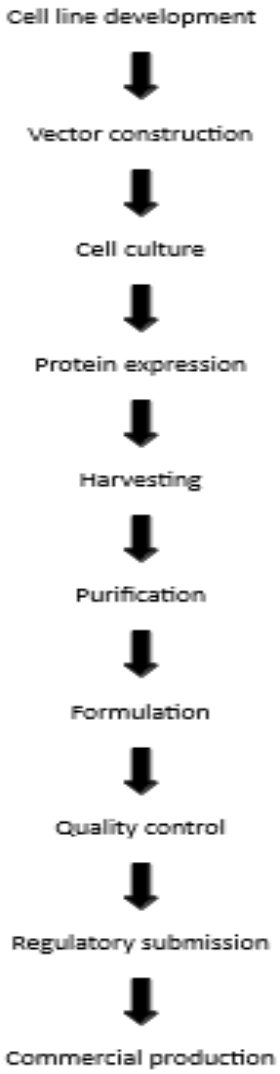
Objectives:

This article's goal is to examine the background of biosimilars, legal requirements, and obstacles to biosimilar approval. Along with describing the obstacles that patients and physicians face when using biosimilars, this article also intends to highlight the advancements made since the first biosimilars were approved in Europe in 2006 and the US in 2015.

2. Manufacturing of biosimilars

Biologics that are very close to previously approved biologics but not exactly the same are known as biosimilars. Biosimilars must be administered in the same manner, have the same strength and dosage, and have the same possible adverse effects as the original biologic in order to the FDA to approve them. They also need to demonstrate that they are just as safe and effective. Although biosimilars are frequently produced from the same kinds of sources as biologics, they cannot be precise replicas due to biologics' unpredictability. Rather, genetic instructions are inserted into a cell to generate a particular candidate biologic, and a series of variants are screened to see which is most similar to the original. This is how biosimilars are generated[3].

Here is a detailed flow chart:



3. Approval process of biosimilars

Biosimilars are approved by the FDA and the European Medicines Agency (EMA) according to the same standards of safety, efficacy, and pharmaceutical quality that apply to all biological medicines. The biosimilars approval process involves a comprehensive evaluation by regulatory agencies to ensure safety, efficacy, and quality.

Here's a step-by-step overview:

Step 1: Development Phase:

i. Preclinical Trials:
- In vitro studies (cell-based assays)
- In vivo studies (animal modules)
- Pharmacokinetic (PK) and pharmacodynamic (PD) studies
- Toxicology studies
- Immunogenicity assessment

ii. Clinical Trials:
   a. Phase I:
      - Safety and tolerability
      - PK and PD profiles
      - Dose-finding studies

b. Phase II:
   - Efficacy and Safety
   - Dose-response relationships
   - Immunogenicity assessment

c. Phase III:
   - Confirmatory efficacy and safety
   - Comparative studies with reference biologic
   - Immunogenicity and PK/PD assessment

Step 2: Regulatory Submission:

i. Biologics License Application (BLA) or Marketing Authorization Application (MAA)
ii. Includes data on:
   - Quality module (manufacturing, characterization)
   - Safety module (toxicology, pharmacokinetics, immunogenicity)
   - Efficacy module (clinical trials)

Step 3: Regulatory Review:

i. Regulatory agency review (FDA, EMA, etc.)
ii. Assessment of:
   - Bio similarity (comparability to reference product)
   - Safety and efficacy
   - Quality and manufacturing
   - Immunogenicity

Step 4: Approval:

i. Granting of marketing authorization
ii. Labeling and packaging approval

Step 5: Post-Approval:

i. Pharmacovigilance
   - Safety monitoring
   - Adverse event reporting
ii. Periodic safety update reports (PSURs)
iii. Post-marketing surveillance
   - Long term safety and efficacy
   - Immunogenicity monitoring
iv. Continuous quality monitoring
v. Comparative effectiveness research
   - Real world data analysis
   - Outcomes research

Timeline
1. Development phase: 2-5 years

2. Regulatory submission: 1-2 years

3. Regulatory review: 1-2 years

4. Approval: 1-2 years

5. Post-approval: Ongoing

Note: The timeline may vary depending on the specific biosimilar product and regulatory agency requirements[4].

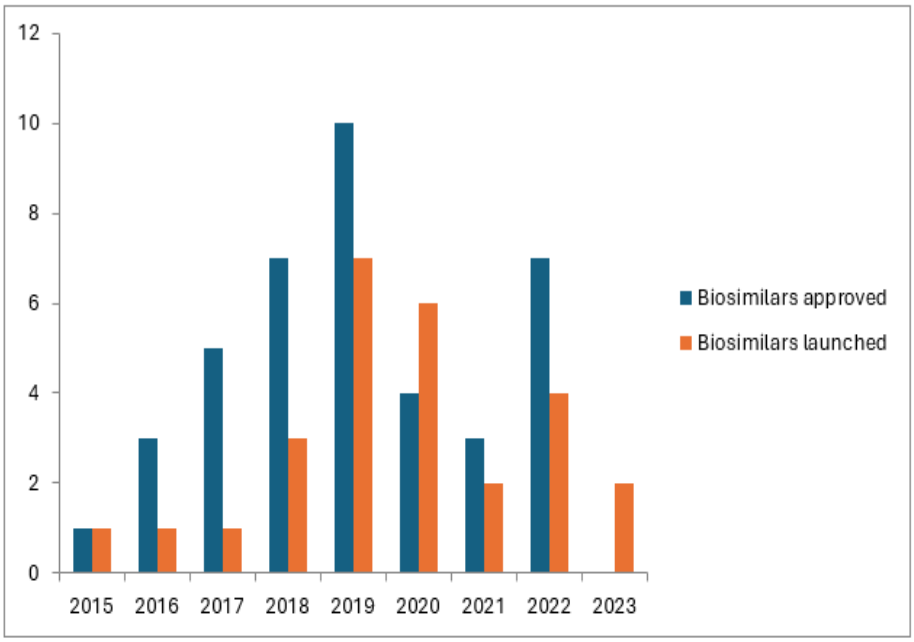


Figure 1 The state of Biosimilars from 2015 to 2023

4. Comparison of the regulatory requirements for biosimilars between Yemen and CDSCO (central drugs standard control organization) in India

The regulations may have evolved since then, and it's essential to refer to the most recent guidelines and consult with regulatory experts when dealing with biosimilars in these regions.

Table 1 Comparison of the regulatory requirements for biosimilars between Yemen and CDSCO (central drugs standard control organization) in India

Sl.no	FEATURES	INDIA	YEMEN
01	REGULATORY AUTHORITY	The CDSCO, which operates under the ministry of Health and Family welfare, governs the regulation of biosimilars.	The Ministry of Public Health and Population (MOPHP) is the primary regulatory authority responsible for overseeing biosimilars and their approval.
02	GUIDELINES	• Detailed guidelines for biosimilars as per CDSCO • Has specific guidelines for biosimilars (2012, 2016)	• Limited guidelines for biosimilars as per MOPHP guidelines • Lacks in specific guidelines
03	CLINICAL TRIALS	Mandatory	No Requirement
04	BIOEQUIVALENCE STUDIES	Mandatory	No Requirement
05	LOCAL CLINICAL TRIALS	Requirement	No requirement
06	PHARMACOVIGILANCE REQUIREMENTS	Stringent	Less Stringent
07	QUALITY CONTROL	Requires more rigorous quality control measures	Requires less rigorous quality control measures

08	GMP CERTIFICATION	GMP certification for manufacturing facilities	No GMP certification requirement for manufacturing facilities
09	GMP COMPLIANCE	Stricter GMP compliance	Less stringent GMP compliance
10	SCHEDULE M COMPLIANCE	Requires compliance with schedule M guidelines	No such requirement
11	REGISTRATION PROCESS	Online registration portal	Offline registration process
12	REGISTRATION FEES	Higher (₹50,000 - ₹1,00,000)	Lower (YER 500,000 – 1,000,000)
13	BIOSIMILAR CHARACTERIZATION AND ANALYTICAL STUDIES	Requires	No such requirement
14	BIOSIMILAR APPROVAL PATHWAY	Biosimilar approval through separate pathway (similar to innovator drugs)	Biosimilar approval through abridged pathway (relying on reference product's data)
15	APPROVAL TIMELINE	Longer approval (12 - 24 months)	Faster approval (6 - 12 months)
16	IMPORTANCE	Emphasis on demonstrating bio similarity and interchangeability	Less Emphasis on demonstrating bio similarity and interchangeability
17	SAFETY MONITORING	Requires more extensive safety monitoring	Requires less extensive safety monitoring
18	IMMUNOGENICITY STUDIES	Requires	No such requirement
19	POST MARKETING SURVEILLANCE	Stringent	Less Stringent
20	ADVERSE EVENT REPORTING	Stringent	Less Stringent
21	REFERENCE PRODUCT	Requires comparison with Indian – licensed reference product	Allows comparison with international reference product
22	INSPECTIONS	Regular inspections by CDSCO	Less frequent inspections

These differences reflect varying regulatory approaches to ensuring biosimilar quality, safety, and efficacy in India and Yemen.

India has more stringent regulatory requirements for biosimilars compared to Yemen, including mandatory clinical trials and bioequivalence studies[5].

Yemen's regulations are less stringent, relying on international guidelines and reference products[6].

This difference impacts the approval timeline, registration fees, and overall biosimilar development process.

5. Comparative market analysis of biosimilars in INDIA AND YEMEN:

5.1. Indian biosimilar market

The Indian biosimilars market size was valued at approximately INR 2.20 billion in 2023[7]. Alternatively, it was valued at USD 6,734.9 Million in 2022 and is anticipated to grow at a CAGR of 27.6% over 2023-2029[8]. The market is expected to reach INR 16.6 billion by 2032, growing at a CAGR of 25.20% during the forecast period of 2024-2032.

5.1.1. MARKET SIZE

• India:

USD 6,734.9 million (2022), growing at 27.6% CAGR (2023-2029).

• Yemen:

USD 10 million (2022), growing at 15% CAGR (2023-2029).

5.1.2. GROWTH DRIVERS

• India:

Initiatives, and rising research and development activities. Increasing prevalence of chronic diseases, growing healthcare demand government.

• Yemen:

Growing healthcare demand, increasing prevalence of chronic diseases, government initiatives, and international aid and support for healthcare development.

5.1.3. CHALLENGES

• India:

Regulatory hurdles, high cost of development and clinical trials.

• Yemen:

War-torn economy and infrastructure limited regulatory framework, and limited access to healthcare services.

5.1.4. KEY PLAYERS:

• India:

Amgen, Biogen, Cipla limited, Glenmark pharmaceuticals, Novartis, Pfizer.

• Yemen:

Local pharmaceuticals companies (Yemen company for pharmaceuticals industry, Al-Nasr pharmaceuticals), international companies (Pfizer, Novartis, Sanofi) through partnerships and imports.

5.1.5. REGULATORY FRAMEWORK

• India

Well – established regulatory framework, with guidelines for biosimilars approval and marketing.

• Yemen:

Limited regulatory framework, with reliance on international guidelines and approvals.

5.1.6. MARKET MATURITY

• India:

Mature market with established players and growing competition.

• Yemen:

Emerging market with limited players and high growth potential.

5.1.7. OPPORTUNITIES:

• India:

Partnerships, government support, and increasing demand for affordable treatments.

• Yemen:

Partnerships, government support, international aid, and growing demand for affordable treatments.

In summary, India's biosimilars market is larger, more established, and growing faster than Yemen's.

India's market is driven by a strong regulatory framework, growing healthcare demand, and increasing research and development activities.

Yemen's market faces significant challenges due to its political and economic situation, but has opportunities for growth through partnerships, government support, and international aid.

5.2. Estimated global market size of biosimilars

The global biosimilars market size is estimated at USD 35.47 billion in 2024 and is expected to reach USD 82.27 billion by 2029, growing at a CAGR of 18.32% during the forecast period (2024-2029).

Here are the detailed notes on the global biosimilars market size estimated:

Global Biosimilars Market Size Estimated:

2025: USD 44.7 billion (Source: Grand View Research)

2027: USD 63.8 billion (Source: Markets)

2030: USD 102.4 billion (Source: IQVIA)

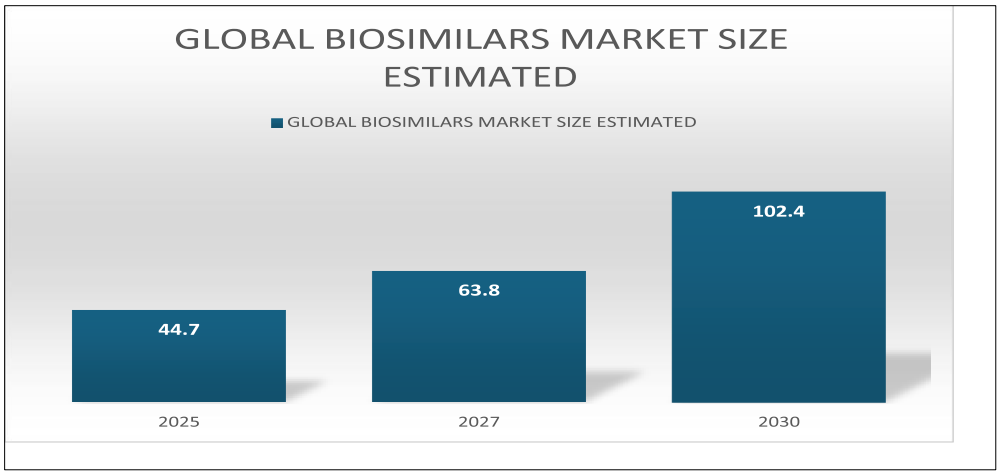


Figure 2 Global biosimilars marked size estimated

Growth Rate Estimated:

2022-2025: 21.5% CAGR (Source: Grand View Research)

2022-2027: 24.1% CAGR (Source: Markets)

2022-2030: 26.4% CAGR (Source: IQVIA)

Segmentation Estimated:

By Product:

Monoclonal Antibodies (mAbs): 50.2% market share by 2025 (Source: Grand View Research)

Recombinant Proteins: 26.1% market share by 2027 (Source: Markets)

Peptides: 12.5% market share by 2030 (Source: IQVIA)

By Application:

Oncology: 51.3% market share by 2025 (Source: Grand View Research)

Autoimmune Diseases: 23.2% market share by 2027 (Source: Markets)

Diabetes: 10.5% market share by 2030 (Source: IQVIA)

By Region:

North America: 45.1% market share by 2025 (Source: Grand View Research)

Europe: 28.3% market share by 2027 (Source: Markets)

Asia-Pacific: 20.6% market share by 2030 (Source: IQVIA)

Key Players Estimated Market Share:

Pfizer: 14.2% market share by 2025 (Source: Grand View Research)

Novartis: 11.5% market share by 2027 (Source: Markets)

Merck & Co.: 9.8% market share by 2030 (Source: IQVIA)

Figure 3 Biosimilars market share, by region, 2023 (%)

Note

The estimated market size and growth rate may vary depending on the source and methodology used. These numbers are based on a combination of reports from reputable market research firms, such as Grand View Research, Markets and IQVIA[9].

6. Applications

Biosimilars have a wide range of applications across various medical fields. Some applications include:

- Cancer Treatment: Biosimilars are used as supportive care or in conjunction with other medicines to treat a variety of illnesses, including leukaemia, colorectal cancer, and breast cancer.
- Autoimmune Diseases: They are used in the treatment of autoimmune conditions such as inflammatory bowel illnesses, psoriasis, and rheumatoid arthritis. For the treatment of diseases like psoriasis, Crohn's disease, and rheumatoid arthritis, biosimilars to the drugs infliximab (Remicade) and adalimumab (Humira) offer more affordable alternatives.
- Blood Disorders: Patients with blood problems can utilize biosimilars to treat symptoms like anemia and neutropenia.
- Infectious Diseases: Certain viral infections and hepatitis B are among the infectious disorders that some biosimilars are used to treat.
- Growth Hormone Deficiencies: Children and adults with growth hormone insufficiency have inexpensive treatment options with biosimilars for somatropin (Genotropin).
- Diabetes: Insulin biosimilars are used to treat diabetes. Patients now have easier access to vital medications because of biosimilars for insulin and other diabetic therapies like glargine (Lantus) and lispro (Humalog).
- Neurological Disorders: They could be used to treat neurological diseases like multiple sclerosis.
- Chronic Kidney Disease: These are used to treat anaemia brought on by long-term renal dysfunction.
- Oncology Supportive Care: Neutropenia and anaemia are two side effects of cancer treatment that can be managed with biosimilars. Patients now have more affordable options due to biosimilars for cancer medicines including trastuzumab (Herceptin) and rituximab (Rituxan).
- Fertility Treatment: In order to promote follicle development in women undergoing assisted reproductive procedures, biosimilars are utilized in fertility treatments.
- Transplant Medicine: Patients undergoing transplants can avoid organ rejection by using biosimilars.
- Dermatology: Biosimilars can be used in dermatological conditions such as psoriasis.
- Ophthalmology: Certain biosimilars are used to treat conditions affecting the eyes, such as macular degeneration. Treatment options for age-related macular degeneration and other retinal disorders are made more economical by the availability of biosimilars for bevacizumab (Avastin) and ranibizumab (Lucentis).
- Anaemia and neutropenia: Patients with cancer can now treat their anaemia and neutropenia at a lower cost due to biosimilars of filgrastim and epoetin alfa (Epogen).
- Inflammatory conditions: Psoriasis, rheumatoid arthritis, and Crohn's disease can be treated alternatively using biosimilars for etanercept (Enbrel) and certolizumab pegol (Cimzia).
- Similar medications that are equally safe and effective hit the market.
- Wide selection of therapy options.
- For biosimilars, development expenses and times are significantly lower.

These applications show how biosimilars are a useful part of modern healthcare since they may be used to treat a range of medical conditions at a fair price and with ease. By increasing access to biological medications that can change lives, these applications advance healthcare fairness and lower costs for both individuals and healthcare systems[10].

7. Conclusion

The regulatory frameworks for biosimilars in India and Yemen exhibit significant differences, reflecting varying levels of stringency and comprehensiveness.

India's framework is more rigorous, with detailed guidelines, mandatory clinical trials, and bioequivalence studies, ensuring high standards of quality, safety, and efficacy. The country's regulatory authority, CDSCO, has a well-established online registration portal and emphasizes post-marketing surveillance and adverse event reporting.

In contrast, Yemen's framework is less comprehensive, relying on WHO guidelines, with no mandatory clinical trials or bioequivalence studies. The regulatory authority, SBDMA, has a more basic offline registration process, and pharmacovigilance requirements are less stringent.

These differences have implications for:

1. Quality and safety of biosimilars: India's framework ensures higher standards, while Yemen's may pose quality and safety risks.

2. Accessibility and affordability: Yemen's less stringent regulations might facilitate faster market entry, potentially increasing accessibility and affordability.

3. Innovation and investment: India's rigorous framework may attract more investment and innovation in biosimilars development.

In conclusion, while both countries aim to regulate biosimilars, India's comprehensive framework prioritizes quality, safety, and efficacy, whereas Yemen's basic framework may compromise on these aspects. Harmonization of regulations could balance accessibility, affordability, and quality, ensuring better healthcare outcomes in both countries.

Compliance with ethical standards

Acknowledgments

We owedee the person our deepest gratitude for providing us with the guidance and assistance we needed to complete our assignment. We are quite happy that this task has been completed. We are grateful to Sir Dr. P Ashok Kumar, a professor in the pharmaceutical regulatory science department at Sree Siddaganga College of Pharmacy in Tumkur, for assigning us this task, which aimed to broaden our knowledge and involve some practical work.

The administrators and staff of Sree Siddaganga College of Pharmacy in Tumkur, Karnataka, are appreciated by the authors for providing the space needed to conduct this study.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Key words for Regulatory requirements. Available from: URL: https://images.app.goo.gl/UgooNqDFe6Q375ra9

[2] Ashok Kumar P*, Bhavana S, Jayashree A, Kavya N, Mahalakshmi K S, Manasa T G. Regulatory Requirements for Biosimilars as per CDSCO and UAE. American Journal of Pharmtech Research. 2023; 13(05):91-102.

[3] Anshul Bansal*, Vikesh Kumar Shukla, Shikha Chauhan. A Comparative Study of Regulatory Compliance for Biosimilars in US, EU and India. International Journal for Drug Regulatory affairs. 2019; 7(2):17-34.

[4] Ashok Kumar P*, Bhavana S, Jayashree A, Kavya N, Mahalakshmi K S, Manasa T G. Regulatory Requirements for Biosimilars as per CDSCO and UAE. American Journal of Pharmtech Research. 2023; 13(05):91-102.

[5] Regulatory requirements for biosimilars in India as per CDSCO. Retrieved from CDSCO Official Website: https://cdsco.gov.in

[6] Regulatory requirements for biosimilars in Yemen as per MOPHP. Retrieved from MOPHP Official Website: https://mohfw.gov.in

[7] Indian biosimilar market analysis in 2023. Available from: URL: https://www.expertmarketresearch.com/articles/top-india-biosimilar-companies

[8] Indian biosimilar market analysis estimated. Available from: URL: https://www.precisionbusinessinsights.com/market-reports/india-biosimilars-market

[9] Global biosimilar market analysis. Available from: URL: https://www.precisionbusinessinsights.com/market-reports/india-biosimilars-market

[10] Ashok Kumar P*, Bhavana S, Jayashree A, Kavya N, Mahalakshmi K S, Manasa T G. Regulatory Requirements for Biosimilars as per CDSCO and UAE. American Journal of Pharmtech Research. 2023; 13(05):91-102.

[11] Graphical abstract image. Available from: URL: https://www.google.com/imgres?h=720&w=1280&tbnh=168&tbnw=300&osm=1&lns_uv=1&source=lensnative&usg=AI4_-kRu8cihOp-WHEfEsqx93VjsLo-Mag&imgurl=https://biosimilarsforum.org/wp-content/uploads/What-is-a-biosimilar.png&imgrefurl=https://biosimilarsforum.org/biosimilars-101/foundations/&tbnid=WjmH9yrP_YILgM&docid=diKTCEZzgQYjXM

[12] The state of Biosimilars from 2015 to 2023 image. Available from: URL: https://images.app.goo.gl/iv9dk3tumrhxWjzy5

[13] Biosimilars market share by region 2023 (in %) image. Available from: URL: https://images.app.goo.gl/sXo1GuhHK4igytCBA